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Template Synthesis of Macrocyclic Complexes of Co(II), Ni(II) and Cu(II) Metal Ions: Spectroscopic and Biological Evaluation

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ABSTRACT

Macrocyclic complexes with bivalent metal ions Co(II), Ni(II), Cu(II) have been synthesized by [2+2] condensation of 2,6 pyridine di carboxylic acid and thiourea by template method in ethanolic medium. The synthesized complexes have been characterized with the help of various physico-chemical techniques viz. elemental analyses, magnetic susceptibility, conductivity measurements and spectral (IR, UV and EPR) techniques. The low value of molar conductivity indicates the non-electrolyte nature of the complexes. All the complexes are of high-spin type. On the basis of above studies an octahedral geometry has been assigned for Co(II) and Ni(II) complexes whereas tetragonal geometry around the Cu(II) ion. The biological activities of the metal complexes have been tested *in vitro* against a number of bacterial species to assess their inhibiting potential. Cu(II) complexes were found to more active as compared to Co(II) and Ni(II) complexes.

KEYWORDS: Co(II), Ni(II), Cu(II), spectral, antibacterial

INTRODUCTION

Synthetic macrocyclic are a growing class of compounds with varying chemistry with a wide range of different molecular topologies and sets of donor atoms [1]. The chemical properties of macrocyclic complexes can be tuned to force metal ions to adopt unusual coordination geometry [2]. Macrocyclic complexes are thermodynamically more stable and selective toward metal ion chelate complexes as compared to open chain analogs [3,4]. Tetraaza macrocyclic ligands and their metal complexes have attracted growing interest as models for intricate biological systems such as metalloporphyrins (hemoglobin, myoglobin, cytochromes, chlorophylls), corrins (vitamin B_{12}), and antibiotics (valinomycin, nonactin) [5].Such chelating molecules are capable of furnishing an environment of controlled geometry and ligand field strength. In situ one pot template condensation reactions lie at the heart of the macrocyclic chemistry [6,7]. Therefore, the template reactions have been widely used for synthesis of macrocyclic complexes [8], where generally the transition metal ions are used as templating agent [9]. Transition metal macrocyclic complexes have received a great attention because of their biological activities, including antiviral, anticarcinogenic, antifertile, antibacterial and antifungal [10-15]. Prompted by these, in the present paper, synthesis and characterization of Co(II), Ni(II) and Cu(II) macrocyclic complexes derived from 2,6 pyridine di carboxylic acid and thiourea have been discussed. The complexes are characterized by various technique like, elemental analyses,

magnetic susceptibility, molar conductance measurements, IR, electronic and EPR spectral studies. *In vitro* antibacterial screening was evaluated against the bacterial species.

EXPERIMENTAL

Materials

All the chemicals used were of Anala R grade and received from Sigma-Aldrich and Fluka. Metal salts were purchased from E. Merck and were used as received.

Instrumentation

The stoichiometric analyses were carried out on a Carlo-Erba 1106 analyzer. Metal contents were estimated on an AA-640-13 Shimadzu flame atomic absorption spectrophotometer in solution prepared by decomposition of the complex in hot concentrated HNO_3. IR spectra were recorded as KBr pellets in the region 4000–200 cm^{-1} on a FT-IR spectrum BX-II spectrophotometer. The electronic spectra were recorded on Shimadzu UV mini-1240 spectrophotometer using DMSO as a solvent. The molar conductance of complexes was measured in DMSO at room temperature on an ELICO (CM 82T) conductivity bridge. The magnetic susceptibility was measured at room temperature on a Gouy balance using $CuSO_4 \cdot 5H_2O$ as callibrant. ESR spectra of the complexes were recorded as polycrystalline sample at liquid nitrogen temperature (**LNT**) for the Co(II) complexes and at room temperature (**RT**) for the Cu(II) complexes on an E4-EPR spectrometer using DPPH as the *g*-marker.

Isolation of complexes

All the complexes were synthesized by template method since any attempt to isolate the free macrocyclic ligand was unsuccessful. A hot ethanolic solution (15 mL) of thiourea (10 mmol) was added in the ethanolic solution of metal salts (5 mmol) of cobalt (II), nickel (II) and Cu II).

The resulting solution was refluxed for one hour. After that ethanolic solution (20 mL) of 2,6 pyridine di carboxylic acid (10 mmol) was added in the refluxing mixture. The reaction mixture was refluxed at 76-80 ^{0}C for 36-48 h. The completion of reaction was confirmed by Thin Layer Chromatography. The reaction mixture was degassed over a Rotary Evaporator. On cooling of degassed reaction mass a colored complex was separated out, which was filtered washed with cold ethanol and dried under vacuum over P_4O_{10} (Yield 60–64%).The template synthesis of macrocyclic complexes of Co(II), Ni(II) and Cu(II) metals ions with thiourea and 2,6 pyridine di carboxylic acid is shown in Fig.1.

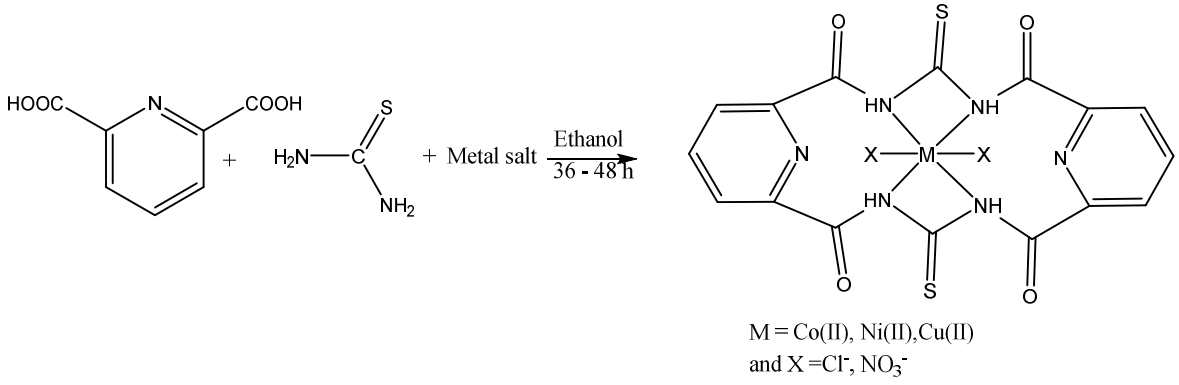


Figure 1: Synthesis of metal complexes

Antibacterial screening

In vitro antibacterial action of ligand and its Co(II), Ni(II) and Cu(II) complexes was checked by Disc Diffusion Method [16] against the bacterial species i.e. *Escherichia coli* and *Pseudomonas striata*. The test compounds in measured quantities were dissolved in DMSO to get concentrations of 500 and 1000 ppm of compounds. The disc of Whatmann no 1 filter paper having the diameter 5.00 mm each

containing (1.5 mg cm^{-1}) of compounds were placed at 4 equidistant places at a distance of 2 cm from the center in the inoculated petriplates. Filter paper disc treated with DMSO served as control and Gentamycin used as a standard drug. All determinations were made in triplicate for each of the compounds. Average of three independent readings for each compound was recorded. These petriplates were kept in refrigerator for 24 hrs for Pre-diffusion. Finally petriplates were incubated for 28-30 hours 28±2^0C. The zone of inhibition was calculated in mm carefully.

RESULTS AND DISCUSSION

The analytical data of the complexes is summarized in Table 1 and corresponds to the formula that may be represented as $[M(C_{16}H_{10}N_6O_4S_2)X_2]$ where M= Co(II), Ni(II) and Cu(II) and X = Cl^- and NO_3^-. are in good agreement with those required by the general composition. The obtained complexes are insoluble in water, methanol and ethanol but soluble in DMF and DMSO [17]. Molar conductance values (9.6–13.6 $\Omega^{-1}cm^2mol^{-1}$) of complexes in DMSO indicate the non-electrolyte nature.

Table 1: Physical measurements and analytical data of metal complexes (1–6).

S. no.	Molecular mass/ molecular formula	Yield (%)	Melting Point (^oC)	Elemental Analysis (%) found (calc.)				Molar Conductance ($\Omega^{-1}cm^2mol^{-1}$)
				C	H	N	M^a	
1	$[Co(C_{16}H_{10}N_6O_4S_2)Cl_2]$ $C_{16}H_{10}Cl_2CoN_6O_4S_2$	60	>260	35.28 (35.31)	1.83 (1.85)	15.40 (15.44)	10.78 (10.83)	10.8
2	$[Co(C_{16}H_{10}N_6O_4S_2)(NO_3)_2]$ $C_{16}H_{10}CoN_8O_{10}S_2$	60	>260	32.11 (32.17)	1.67 (1.69)	18.72 (18.76)	9.83 (9.87)	13.6
3	$[Ni(C_{16}H_{10}N_6O_4S_2)Cl_2]$ $C_{16}H_{10}Cl_2N_6NiO_4S_2$	61	>260	35.31 (35.33)	1.80 (1.85)	15.39 (15.45)	10.71 (10.79)	9.6
4	$[Ni(C_{16}H_{10}N_6O_4S_2)(NO_3)_2]$ $C_{16}H_{10}N_8NiO_{10}S_2$	62	>260	32.15 (32.18)	1.65 (1.69)	18.75 (18.77)	9.77 (9.83)	10.5
5	$[Cu(C_{16}H_{10}N_6O_4S_2)Cl_2]$ $C_{16}H_{10}Cl_2CuN_6O_4S_2$	64	>260	34.79 (35.01)	1.83 (1.84)	15.25 (15.31)	11.55 (11.58)	11.2
6	$[Cu(C_{16}H_{10}N_6O_4S_2)(NO_3)_2]$ $C_{16}H_{10}CuN_8O_{10}S_2$	64	>260	31.85 (31.92)	1.61 (1.67)	18.55 (18.61)	10.55 (10.55)	11.8

M^a =Co(II), Ni(II) and Cu(II)

Infrared-Spectra

In the IR spectra of the metal complexes the bands corresponding to –NH shifts to a lower value and appeared in the range of 3140–3198 cm^{-1}, which indicates the coordination of –NH to metal centre. Formations of new bands take place at 416 – 456 cm^{-1}. These bands corresponds to υ(M–N) bond. Similarly, bands in far IR at 342 – 388 cm^{-1} are due to υ(M–Cl) bond. Nitrato complexes show bands at 1448–1454 cm^{-1} (υ_5), 1022–1042 cm^{-1} (υ_2) and 1301–1310 cm^{-1} (υ_1) for Cu(II) and Ni(II) complexes [18–20]. The value of $\Delta(\upsilon_5 - \upsilon_1)$, i.e. 144 and 147 cm^{-1} suggests the unidentate coordination of NO_3^- ions.

Magnetic moments and electronic spectra

At room temperature the magnetic moment of Co(II) complexes at room temperature lie in the range 4.85–4.90 BM corresponding to three unpaired electrons (Table 2).The electronic spectra of the complexes were recorded in DMSO solution. The electronic spectra of cobalt (II) complexes display the d–d transition bands in the region 11,212-11,918, 14705-14794 and 18657-18692 cm^{-1}. These transitions may be assigned to the $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ (F) υ_1, $^4T_{1g}$ (F)$\rightarrow {}^4A_{2g}$ (F) υ_2 and $^4T_{1g}$ (F)$\rightarrow {}^4T_{1g}$ (P) υ_3 respectively. The transitions correspond to the octahedral geometry of the complexes [21].

At room temperature the magnetic moment of nickel (II) complexes at room temperature lie in the range 2.86-2.92 BM corresponding to two unpaired electrons. The absorption spectra of Ni(II)

complexes display three d-d transition bands in the range 11,182 -11,252, 18,650-18,686 and 21,468-25,411 cm^{-1}. These transitions correspond to the $^3A_{2g}$ (F) $\rightarrow ^3T_{2g}$ (F) ν_1, $^3A_{2g}$ (F) $\rightarrow$ $^3T_{1g}$ (F) ν_2 and $^3A_{2g}$ (F) $\rightarrow$ $^3T_{1g}$ (P) ν_3, respectively [22]. These transitions reveal that the nickel complexes possess an octahedral geometry and D_{4h} symmetry.

The magnetic moment of the Cu (II) complexes at room temperature lie in the range 1.95–1.98 BM corresponding to one unpaired electron. Electronic spectra of Cu(II) complexes show the d-d transition bands in the range 11,330−11898, 18,530 −18,622 and 27,380- 27,425 cm^{-1}. These bands correspond to $^2B_{1g} \rightarrow {}^2A1g$ ($d_{x2-y2} \rightarrow d_{z2}$) ν_1, $^2B1g \rightarrow {}^2B_{2g}$ ($d_{x2-y2} \rightarrow d_{xy}$) ν_2 and $^2B_{1g} \rightarrow {}^2E_g$ ($d_{x2-y2} \rightarrow d_{xz}$, d_{yz}) ν_3 and transitions, respectively. A tetragonal geometry has been assigned for Cu(II) complexes [23]. The spectra of all the complexes have been vibronically assigned to D_{4h} symmetry with a d_{x2-y2} ground state.

Table 2: Magnetic moment, electronic spectral and ligand field parameter of the macrocyclic complexes

Complexes	μ_{eff} (BM)	λ_{max} (cm^{-1})	Dq (cm^{-1})	B (cm^{-1})	B	LFSE (kJ mol^{-1})
$C_{16}H_{10}Cl_2CoN_6O_4S_2$	4.85	11,212, 14,705,18,692	1401	688	0.61	134
$C_{16}H_{10}CoN_8O_{10}S_2$	4.90	11,918, 14,794, 18,657	1400	729	0.65	134
$C_{16}H_{10}Cl_2N_6NiO_4S_2$	2.86	11,252, 18,650, 21,468	1125	427	0.41	161
$C_{16}H_{10}N_8NiO_{10}S_2$	2.92	11,182, 18,686, 25,411	1118	702	0.65	160
$C_{16}H_{10}Cl_2CuN_6O_4S_2$	1.98	11,330, 18,530, 27,425	-	-	-	-
$C_{16}H_{10}CuN_8O_{10}S_2$	1.95	11,898, 18,622, 27,380	-	-	-	-

Electronic paramagnetic resonance spectra

The X-band EPR spectra of Co(II) complexes were recorded at liquid nitrogen temperature in polycrystalline form. The line shaped EPR spectra of Co(II) complexes with g_{iso} = 2.0927-2.1992 correspond to the octahedral symmetry around the Co(II) ion [24].

EPR spectra of the Cu(II) complexes were recorded , at room temperature as polycrystalline samples, on the X-band at 9.1 GHz under the magnetic field range 3000 G. The analysis of spectra of Cu(II) complexes give $g_{||}$ 2.1722-2.2086 and $g_{|}$ 2.0776-2.0882. The trend $g_{||} > g_{|} > 2.0023$, observed for the complexes, under study, indicate that the unpaired electron is localized in the d_{x2-y2} orbital of the Cu(II) ion and the spectral figures are characteristic for the axial symmetry [25].Tetragonally elongated geometry is thus confirmed for the afore-said complexes. $G=(g_{||} -2)/(g_{|} -2)$, which measure the exchange interaction between the metal centres in a polycrystalline solid has been calculated. According to Hathaway and Billing [26] if G>4 the exchange interaction is negligible, but G indicates considerable exchange interaction in the solid complexes. The complexes reported in this paper gives the 'G' value (Table 3) in the range 2.2190-2.3650 which is <4, indicating exchange interaction in the solid complexes.

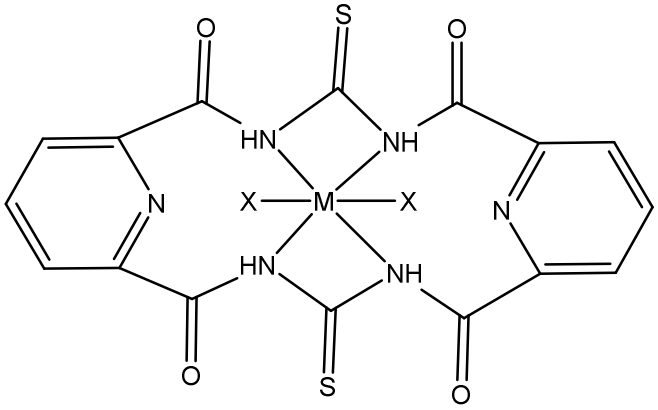
Table 3: EPR spectral data of the Co(II) and Cu(II) complexes

Complexes	$g_{|}$ (RT /LNT)	$g_{||}$ (RT /LNT)	g_{iso}(RT /LNT)	G
$C_{16}H_{10}Cl_2CoN_6O_4S_2$	1.9903	2.4081	2.1992	-
$C_{16}H_{10}CoN_8O_{10}S_2$	1.9318	2.2536	2.0927	-
$C_{16}H_{10}Cl_2CuN_6O_4S_2$	2.0776	2.1722	2.1091	2.2190
$C_{16}H_{10}CuN_8O_{10}S_2$	2.0882	2.2086	2.1283	2.3650

Ligand field parameters

Various ligand field parameters were calculated and listed in **Table 2**. The Nephelauxetic parameter β was readily obtained by using the relation $\beta = B$ (complex)/B (free ion), where B (free ion) for Co(II) is

1120 cm^{-1} and Ni(II) is 1041 cm^{-1} . The values of β lie in the range 0.41–0.65. These values indicate the covalent character in metal ligand "σ" bond [27]. On the basis of the above spectral data, following structures have been proposed for metal complexes **1–6 (Fig.2).**



$M = Co(II), Ni(II), Cu(II)$ and $X = Cl^-, NO_3^-$

Figure 2: Proposed structures of metal complexes

Antibacterial studies

The antimicrobial screening data show that the compounds exhibit moderate antimicrobial properties. It has also been proposed that concentration plays a vital role in increasing the degree of inhibition; as the concentration increases, the activity increases [28].

The activity order for *Escherichia coli* was found to be: (**Table 4**)
Gentomycin > 1>2>5>4>6>3

With *Pseudomonas striata.* the order of activity was:
Gentomycin > 2>1>4>3>5>6

Table 4: Antibacterial data of macrocyclic complexes

Complexes	**Bacterial species**	**Diameter (mm) of compounds at concentrations (μgml^{-1})**	
		500	**1000**
1	*E.coli*	30	32
	P.striata	26	28
2	*E.coli*	27	30
	P.striata	29	31
3	*E.coli*	-	14
	P.striata	20	23
4	*E.coli*	22	29
	P.striata	21	25
5	*E.coli*	23	29
	P.striata	17	21
6	*E.coli*	19	22
	P.striata	-	15
Gentomycin	*E.coli*	32	35
	P.striata	30	31

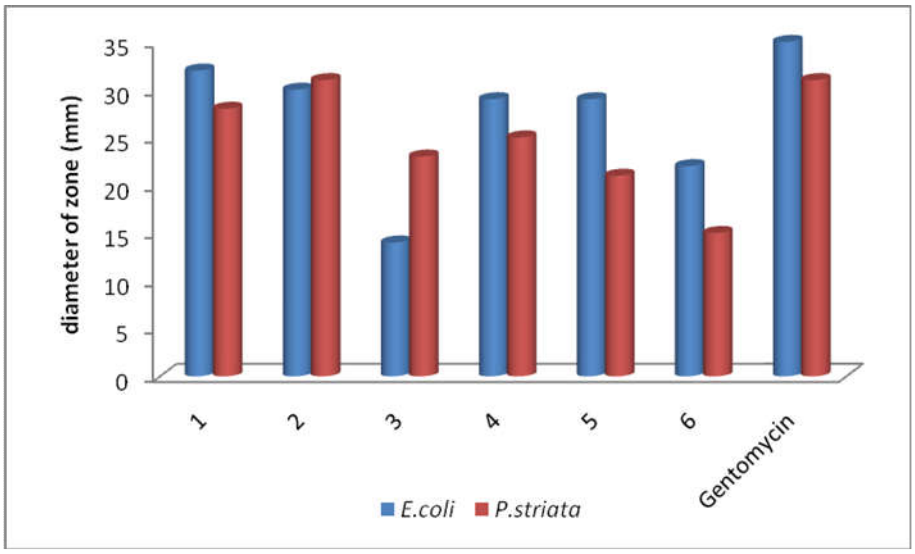


Figure 3: Antibacterial activity of the complexes at 1000 ppm against *E. coli* and *P.striata*

CONCLUSION

Macrocyclic complexes of Co(II), Ni(II) and Cu(II) metal ions were synthesized using thiourea and2,6 pyridine di carboxylic acid by template method.The analytical and physico-chemical analyses confirmed the composition and the structure of the obtained complex combinations. On the basis of the spectral studies Co(II) and Ni(II) complexes were found to have an octahedral geometry whereas Cu(II) complexes were found tetragonal geometry. In vitro antibacterial screening of the synthesized complexes were evaluated against the bacterial species. Cu(II) complexes were found more active against both the bacterial species.

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