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Synthetic and Structural Studies of Some Macrocyclic Complexes of Ni(II) of Bioinorganic Relevance

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Two new macrocyclic complexes have been synthesized by condensing 2,6-diacetyl pyridine/2,6-pyridine dicarbonyl dichoride with dithio-dipropionic acid dihydrazide in presence of Ni(II) ions. The complexes have the formulae Ni[DPDTDH]$(BF_4)_2$ and Ni[DCDTDH]$(BF_4)_2$ (where [DPDTDH] = 2,6-diacetyl pyridine-N-dithio-dipropionic acid dihydrazone and [DCDTDH] = 2,6-pyridine dicarbonyl dichloride-N-dithio-dipropionic acid dihydrazone) have been synthesized. The structure of the complexes has been elucidated on the basis of IR and electonic spectral data, magnetic properties and conductivity studies. All these complexes have been tested for their antimicrobial activity against bacteria *E. coli* and fungal strains *C. albicans* and *A. flavus*. The biological activity of metal chelates was found to be much more as compared to the macrocyclic ligand fragments and individual metal ions.

INTRODUCTION

Macrocyclic compounds, due to their intriguing ligating properties, have opened up a new area of coordination chemistry[1–3]. The amide macrocyclic ligands are of interest because of their metal complexes function similarly to porphyrin analogues in catalysing organic oxidation reactions[4–6]. The Ni(II) complexes are spinfree paramagnetic with nearly octahedral arrangement of the ligand atoms around the metal ions. The amino groups (—NH_2) in the metal complexes of dihydrazides and dihydrazones show strong coordination with metal ions[7–9]. The macrocyclic and clathro complexes of transition metals have been synthesized by the template reaction with aldehydes and ketones. The complexes of the 15 and 16 membered macrocycles L^1 and L^2 have so far been investigated[10–11]. The conjugated and consequently planar 2,7-diketone has presence of Ni(II) to be a structurally versatile ligand containing one metal ion through its N and S donor atoms[12, 13]. The Ni(II) complexes undergo metal-based one and one step reversible reduction and the redox potentials correlate with the ligand field strengths of the macrocycles[14] and the planar conjugated macrocyclic nitrogenous bases, especially phthalocyanine[15]. These complexes were found to have octahedral geometry and exhibited antimicrobial activity against bacterial and fungal species[16].

In continuation of our work, two new macrocyclic complexes have been syntheized by condensing dithio-dipropionic acid dihydrazide with 2,6- diacetyl pyridine/2,6-pyridine dicarbonyl dichloride.

The presence of N—C—S linkage is believed to account for the fungicidal, antibacterial and antiviral activities[17–19]. The changes in solvent structures occur

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through ions in aqueous, nonaqueous and mixed solvent system[20, 21]. The interest in these compounds arises from their various applications in the field of bio-inorganic chemistry[22].

EXPERIMENTAL

Chemicals of AR grade were used for synthesizing the compounds. Dithio-dipropionic acid dihydrazide has been synthesized from its corresponding dimethyl ester of acid and hydrazine hydrate by the reported procedure[23]. Its purity was ascertained by preliminary investigations, *viz.*, melting point and TLC method for single spot.

Both the complexes were synthesized as follows: Equimolar amounts of dithio-dipropionic acid dihydrazide (0.01 M), nickel acetate (0.01 M) and 2,6-diacetyl pyridine (0.01 M) or 2,6-pyridine dicarbonyl dichloride were mixed in ethanol with continuous stirring. The solution thus obtained was refluxed over a water-bath for around 6 h. Subsequently, it was concentrated to one-third of its original volume. Then, a little of sodium tetrafluoroborate was added and the solution was cooled overnight, when black crystals separated out. The crystals were filtered, washed with alcohol, ether and then dried in vacuum over anhydrous $CaCl_2$ in a desiccator.

The magnetic studies of the synthesized complexes were carried out on a Johnson Mathey susceptibility balance. Their elemental analysis and metal contents were estimated by standard procedures.

RESULTS AND DISCUSSION

On the basis of elemental analysis all macrocyclic complexes were assigned a metal to ligand stoichiometry of 1 : 1 : 1. The molar conductivity values of the complexes were found to be 119–112 $ohm^{-1}cm^2 mol^{-1}$ in DMF consistent with 2 : 1 electrolytic behaviour in this solvent. The colour and the crystalline nature of the solid complexes indicate that they are of the same family showing 1 : 1 electrolytic nature in DMSO.

The analytical data of the ligand and metal complexes are presented in Table-1.

TABLE-1
ANALYTICAL DATA OF Ni(II) MACROCYCLIC COMPLEXES

Compound (m.f.)	Colour	m.p. (°C)	% Analysis, Found (Calcd.)			
			C	H	N	Ni
[DPDTDH] [$C_{15}H_{19}O_2N_5S_2$]	Brownish black	220	49.21 (49.31)	5.14 (5.20)	14.10 (14.17)	–
[DCDTDH] [$C_{13}H_{13}O_2N_5S_2Cl_2$]	Green	225	38.30 (38.51)	3.14 (3.20)	17.15 (17.28)	–
Ni[DPDTDH] $(BF_4)_2$ Ni[$C_{15}H_{19}O_2N_5S_2$] $(BF_4)_2$	Black	260	30.11 (30.21)	3.10 (3.18)	11.35 (11.75)	9.75 (9.85)
Ni[DCDTDH]$(BF_4)_2$ Ni[$C_{13}H_{13}O_2N_5S_2Cl_2$] $(BF_4)_2$	Brownish green	265	24.35 (24.53)	1.95 (2.04)	10.85 (11.01)	9.15 (9.23)

In the IR spectra of dithio-dipropionic acid dihydrazide sharp and prominent bands were observed at 3025, 1605 and 1550 cm^{-1}. These were assigned to the presence of ν(NH), ν(C═O) and $\nu(NH_2)$ groups respectively. ν(N—N) transitions were observed around 945 cm^{-1}. Another distinct band was observed in the spectrum of ligand fragment at 1085 cm^{-1} which was characteristic of the ν(C—S) bond.

In the IR spectra of metal complexes, the peak due to ν(NH) did not undergo any shift (3025 cm^{-1}), ruling out the coordination of nitrogen of (NH) with the central metal atom. However, the band due to ν(C═O) shifted to a negative shift by 30–40 cm^{-1}, appearing at 1540 cm^{-1}, while the position of ν(N—N) bond shifted to higher wave numbers (970 cm^{-1}). These observations led to the conclusion that the amide has involved in complexation. The peak due to ν(C—S) bond underwent a lowering. It appeared at 1020 cm^{-1} in the spectra of complexes indicating the coordination of sulphur of C—S with central metal atom. An intense band appeared at 1490 cm^{-1} which was due to the formation of C═N bond in the complexes. This bond was formed due to the condensation of acetyl groups with the dihydrazide. A bond was also seen around 2800 cm^{-1} due to $\nu(CH_2)$ group in the spectra of complexes, which is unaltered as compared to the peak shown by the ligand fragment (Table-2).

TABLE-2

IR SPECTRAL DATA (cm^{-1}) OF THE LIGANDS AND THEIR Ni(II) COMPLEXES

Functional group	DPDTDH	DCDTDH	$Ni[DPDTDH](BF_4)_2$	$Ni[DCDTDH](BF_4)_2$
CH_2	2800	2800	2800	2800
—NH	3025	3025	3025	3025
>C═O	1605	1600	1560	1550
$—NH_2$	1550	1450	–	–
N—N	945	945	1035	1035
>C═N—	–	–	1490	1490
>C═S—	1085	1055	1045	1025
ν(M—O)	–	–	545	560
ν(M—N)	–	–	475	475
ν(M—S)	–	–	315	320

The ligand field spectra of Ni(II) complexes of all the macrocyclic ligands show two bands in the region 11,350–11,200 and 17,500–17,100 cm^{-1} which may be ascribed to $^3A_{2g}$–$^3T_{2g(F)}$ and $^3A_{2g}$–$^3T_{1g(F)}$ transitions, respectively, suggesting[19] an octahedral environment around Ni(II) ions (Table-3).

The ligands and their two Ni(II) macrocyclic complexes were screened for their antimicrobial activity towards *E. coli* and fungal strains *C. albicans* and *A. flavus* (incubation period 24 h at 37°C). Remarkable inhibition of *E. coli* and fungal strains was 40–50% with ligands respectively. The minimum concentration of the test compound showing no visible turbidity was termed the "MIC" value for that compound, *i.e.*, the minimum concentration which is able to prevent any detectable growth of the micro-organism.

TABLE-3
ELECTRONIC SPECTRAL DATA (cm^{-1}) OF THE COMPLEXES

Compounds	Transitions (cm^{-1})	
	$^3A_{2g} \rightarrow {}^3T_{2g}$	L→M
$Ni[DPDTDH](BF_4)_2$	11,200	17,100
$Ni[DCDTDH](BF_4)_2$	11,350	17,500

For bacterial studies

$$Ni[DPDTDH](BF_4)_2 > Ni[DCDTDH](BF_4)_2$$

The reasons for the observed trend of activity may be.

(1) More lipo solubility of the macrocyclic complexes.

(2) More rapid penetration of the complexes as a whole through the cell walls of the micro-organism causing damage to the synthesis of protein and nucleic acids of the microbe.

TABLE-4
MIC VALUES OF THE COMPOUNDS IN MOLAR CONCENTRATION ($\times 10^{-4}$)

Compounds	*E. coli*	*C. albicans*
[DPDTDH]	4.120	4.130
[DCDTDH]	5.110	5.120
$Ni[DPDTDH](BF_4)_2$	2.350	2.450
$Ni[DCDTDH](BF_4)_2$	3.200	3.225

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