

Structural and Antimicrobial Studies of Cu(II) Macrocylic Complexes

JITENDRA AMBWANI*, N.L. BANSAL† and KSHAMA KAUSHIK
Department of Chemistry, Government. Girls College, Morena, India

Two new macrocyclic complexes of Cu(II) with the composition $\text{Cu}[\text{DPAIDAH}](\text{BF}_4)_2$ and $\text{Cu}[\text{DPADTPH}](\text{BF}_4)_2$ (where $[\text{DPAIDAH}]$ = diphenyl diacetic acid-2,2'-imino diacetic acid dihydrazone and $[\text{DPADTPH}]$ = diphenyl diacetic acid-2,2'-dithio dipropionic acid dihydrazone have been synthesized. The complexes have been characterized on the basis of elemental studies, IR spectral analysis and electronic spectra. The *in vitro* antimicrobial studies revealed that the macrocyclic complexes are potentially active against a few bacteria and fungi and exhibit greater biocidal effect as compared to the ligand fragments.

INTRODUCTION

The study of macrocyclic ligands and their metal complexes constitute a very active area of research¹⁻⁴. Macrocyclics, due to their intriguing ligating properties, have opened up a new area of coordination chemistry. The past few years have witnessed an increasing interest in the synthesis of macrocyclic products using metal ion template procedure⁵⁻⁸.

The growing need for macrocyclic ligands and their metal-complexes has stimulated research efforts of efficient preparations⁹. A broad spectrum of biological activity is reported to be associated with a number of heterocyclic compounds¹⁰. It has also been established that biological activity of ligand enhances manifold on its coordination with suitable metal-ions¹¹.

With a view to correlate the widely applicable synthetic macrocyclic ligands and their Cu(II) complexes with the naturally occurring macrocycles, some new macrocyclic complexes of Cu(II) were previously synthesized by the condensation of the di-hydrazides of imino diacetic acid/pyridine-2,6-dicarboxylic acid with 2,6-diacetyl pyridine and 2,6-pyridine dicarbonyl dichloride. These complexes were found to have octahedral geometry and exhibited antimicrobial activity against bacterial and fungal species¹².

†Department of Chemistry, Govt. P.G. College, (Jiwaji University, Gwalior), Morena (M.P.), India.

EXPERIMENTAL

All the metal acetates and chemicals used in the present work were of AR grade. All the solvents were purified by distillation.

Synthesis of metal complexes: Equimolar amounts of imino diacetic acid dihydrazide (0.01 M), copper acetate (0.01 M) and diphenyl diacetic acid (0.01 M) 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 and ether and then dried in vacuum over anhydrous CaCl_2 in a desiccator.

The other complex was also synthesized by similar procedure.

RESULTS AND DISCUSSION

The complexes are found to be coloured. They are insoluble in water and alcohol, but are soluble in DMF and DMSO. The results of the elemental analysis indicate 1 : 1 metal-to-ligand stoichiometry (Table-1). The molar conductance of 1 mmole solution of the complexes in DMSO falls in the range $102.50\text{--}104.30 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ reveals the non-electrolytic nature of these complexes.

TABLE-1
ANALYTICAL DATA OF LIGAND FRAGMENTS AND Cu(II) MACROCYCLIC COMPLEXES

Compound (colour) [m.f.]	m.p. (°C)	% Analysis, found (calcd.)			
		C	H	N	Cu
[DADH] (Yellowish white) [C ₄ H ₁₁ N ₅ O ₂]	125	29.21 (29.81)	6.67 (6.83)	42.75 (43.47)	—
[DTADH] (White) [C ₆ H ₁₄ O ₂ N ₄ S ₂]	120	29.93 (30.25)	5.78 (5.88)	22.95 (23.50)	—
Cu[DPAIDAH](BF ₄) ₂ (Dark green) Cu[C ₂₀ H ₂₁ N ₅ O ₄](BF ₄) ₂	278	37.74 (38.06)	3.10 (3.33)	10.82 (11.10)	9.99 (10.07)
Cu[DPADTPH](BF ₄) ₂ (Greenish-blue) Cu[C ₂₂ H ₂₄ O ₂ N ₄ S ₂](BF ₄) ₂	284	37.21 (37.31)	3.21 (3.39)	7.76 (7.91)	8.51 (8.97)

In the IR spectrum of imino-di acetic acid dihydrazide and thio-dipropionic acid dihydrazide, sharp and prominent bands were observed in the range of $3190\text{--}3180$, $1715\text{--}1710$ and $1630\text{--}1620 \text{ cm}^{-1}$. These were assigned to the presence of $\nu(\text{NH})$, $\nu(\text{C}=\text{O})$ and $\nu(\text{NH}_2)$ groups, respectively.

In the IR spectra of metal complexes, the peak due to $\nu(\text{NH})$ did not show any

shift (3050 cm^{-1}) ruling out the coordination of nitrogen of (NH) with central metal atom. On the other hand, the peak due to $\nu(\text{C}=\text{O})$ underwent a lowering and $\nu(\text{NH}_2)$ disappeared indicating coordination of oxygen of (C=O) with central metal atom and elimination of (NH₂) group respectively. The spectra of metal complexes exhibited additional bands at $1570\text{--}1560$, $430\text{--}425$, $495\text{--}490$ and $370\text{--}360\text{ cm}^{-1}$ assignable to $\nu(\text{C}=\text{N})$, $\nu(\text{Cu}\text{--}\text{O})$, $\nu(\text{Cu}\text{--}\text{N})$ and $\nu(\text{Cu}\text{--}\text{S})$ respectively (Table-2).

The electronic spectra of Cu(II) complexes show a broad band at $12,323\text{--}11,500\text{ cm}^{-1}$ and charge transfer band at $24,500\text{--}23,400\text{ cm}^{-1}$. The first band is assignable to the ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$ transition characteristic of a tetragonally distorted octahedral stereochemistry^{13, 14}. The latter band can be attributed to L—M charge transfer band (Table-3).

TABLE-2
IR SPECTRAL DATA (cm^{-1}) OF THE COMPOUNDS

Functional groups	[DADH]	[DTADH]	Cu[DPAIDAH](BF ₄) ₂	Cu[DPADTPH](BF ₄) ₂
—CH ₂	2880	2870	2830	2825
—NH	3190	3180	3190	3178
>C=O	1710	1715	1650	1655
—NH ₂	1630	1620	—	—
N—N	1240	1230	1180	1175
>C=N	—	—	1560	1570
$\nu(\text{Cu}\text{--}\text{O})$	—	—	425	430
$\nu(\text{Cu}\text{--}\text{N})$	—	—	490	495
$\nu(\text{Cu}\text{--}\text{S})$	—	—	370	360

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

Compounds	Transitions (cm^{-1})	
	${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$	L → M
Cu[DPAIDAH](BF ₄) ₂	12,323	24,500
Cu[DPADTPH](BF ₄) ₂	11,500	23,400

The ligand fragments and the two Cu(II) macrocyclic complexes were screened *in vitro* for their antimicrobial activity using serial dilution method against two bacteria, viz., *E. coli* (gram negative) and *S. aureus* (gram positive) and two fungi *A. niger* and *C. albicans*.

The biological activity data show that antimicrobial activity of ligands enhances several folds on complexation. This increase in antimicrobial activity is probably either due to faster diffusion of metal complexes as a whole through the cell membranes or due to the combined activity effect of the metal and ligand. The 'MIC' values of the compounds have been represented in Table-4.

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

Compounds	Bacteria		Fungi	
	<i>E. coli</i>	<i>S. aureus</i>	<i>A. niger</i>	<i>C. albicans</i>
[DADH]	4.220	4.210	4.085	4.340
[DTADH]	4.210	4.095	4.070	4.250
Cu[DPAIDAH](BF ₄) ₂	0.236	0.240	0.165	0.255
Cu[DPADTPH](BF ₄) ₂	0.251	0.252	0.170	0.290

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