



Microwave Synthesis and Antimicrobial Activity of Some Copper (II), Cobalt (II), Nickel (II) and Chromium (III) Complexes with Schiff Base 2, 6-pyridinedicarboxaldehyde-Thiosemicarbazone

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ABSTRACT

Some novel Schiff base metal complexes of Cr(III), Co(II), Ni(II) and Cu(II) derived from 2, 6-pyridinedicarboxaldehyde-Thiosemicarbazone (PDCTC) was synthesized by conventional as well as microwave methods. This compound was characterized by elemental analysis, FT-IR, Mass, molar conductance and magnetic susceptibility measurements analyses. Analytical data revealed that all the complexes exhibited 1:1 (metal: ligand) ratio with a coordination number of six. The IR data showed that the ligand coordinates with the metal ions in a hexa-dentate manner. The solid state electrical conductivity of the metal complexes was also measured. Solid state electrical conductivity studies reflected a semi-conducting nature of the complexes. The Schiff base and metal complexes displayed good activity against the Gram-positive bacteria *Staphylococcus aureus*, the Gram-negative bacteria *Escherichia coli* and the fungi *Aspergillus niger* and *Candida albicans*. The antimicrobial results also indicated that the metal complexes displayed better antimicrobial activity as compared to the Schiff bases.

Key words: Microwave method; Hexa-dentate ligands; Biological activities.

INTRODUCTION

Microwave irradiation now a day is an accepted tool for accelerating the organic and inorganic reactions. It leads to the higher reaction selectivity and utilization of the inexpensive reagents. In addition to providing an eco-friendly "green chemistry" approach to the reaction, it is free of environmental impacts¹⁻⁵. The application of microwave irradiation towards the acceleration of

wide range of organic and inorganic reactions has received considerable attention⁶⁻¹¹. It also allowed a greener approach¹².

Schiff base of an important class of ligands in coordination chemistry and have many applications¹³, in different fields. The chemistry of Schiff base complexes continues to attract many researchers¹⁴⁻¹⁶ because of their wide application in food industry, dye industry, analytical chemistry

catalysis, antimicrobial activity, agro-chemical activity¹⁷ and pharmacological applications¹⁸. Semicabazones of aromatic and unsaturated carbonyl compounds have anticonvulsant properties and their advantage over the analogous Thiosemicarbazone is their lesser neurotoxicity¹⁹. Semicabazones have an inhibitory effect on nitric oxide synthesis, which protect the vascular system²⁰.

It is well known that various organic ligands possess strong antibacterial, herbicidal, insecticidal and fungicidal properties²¹. It has also been reported that the activity of bio metals is very often altered through the formation of chelates with different biological relevant ligands²²⁻²⁵. It is suggested that the compounds having antimicrobial activity may act either by killing the microbe or blocking their active sites²⁶⁻²⁸. In addition to this the antimicrobial activity of the compounds also depends upon the nature of the microorganisms.

MATERIALS AND METHODS

All the chemicals used were of AR grade and used without further purification. The infrared

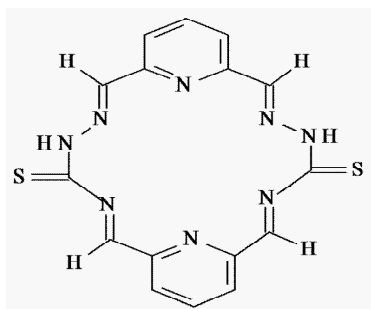


Fig. 1: Structure of Ligand – (PDCTC)

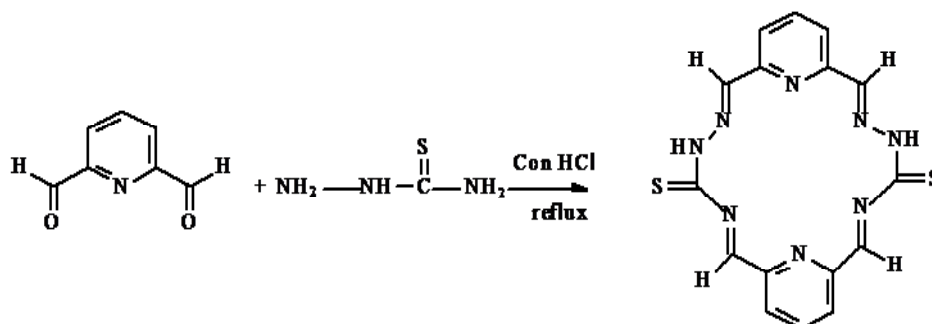


Fig. 2: Preparation of Ligand –PDCTC

spectra were recorded in the range 4000-180 cm^{-1} with a Perkin Elmer 983 G spectrophotometer. The electronic spectra were recorded with Cary model 2390 spectrometer. The molar conductance of complexes in DMF ($\sim 10^{-3}$ M) was determined at $27 \pm 20^\circ\text{C}$ using a Systronic 303 direct reading conductivity bridge. The magnetic susceptibility measurements were made using a vibrating sample magnetometer (VSM) operating at field strength of 5 KG. The ^1H NMR spectra was recorded on varian XL-300 MHz high resolution instrument in CDCl_3 solvent. The mass spectra were recorded using Fanning Mat 8230 Mass spectrometer.

Microwave assisted synthesis were carried out in open glass vessel on a modified microwave oven model 2001 ETB with rotating tray and a power source 230V, microwave energy output 800W and microwave frequency 2450MHz. A thermocouple device was used to monitor the temperature inside the vessel of the microwave. The microwave reactions were performed using on/off cycling to control the temperature.

Conventional method for the synthesis of Schiff bases

The reaction mixture containing 2, 6-Pyridinedicarboxaldehyde, (2g, 0.01183mol in 20ml of methanol) Thiosemicarbazone (1.0787g, .01183 mole in 20ml of methanol dissolved in hot condition) was taken in 250-ml round bottom flask and refluxed for 10h. On cooling the reaction mixture, light yellow colored product was formed. It was collected by filtration and washed with hot water and 50 % cold methanol. This compound was recrystallized from ethanol and dried in vacuo, yield 65% ; m. p. 257°C . (Fig. 2)

Microwave method for the synthesis of Schiff bases

The equimolar (1:1) ratio of methyl isobutyl ketone with 2, 6-Pyridinedicarboxaldehyde, and Thiosemicarbazone with isonicotinic acid hydrazide were mixed thoroughly in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3-4mL of dry ethanol as a solvent. The reaction was completed in a short time (4-5min) with higher (light yellow) yields. The resulting product was then recrystallized with ethanol, finally dried under reduced pressure over anhydrous CaCl_2 in a desiccator. The progress of the reaction, purity of the product was monitored by TLC using silica gel G (yield: 85%).

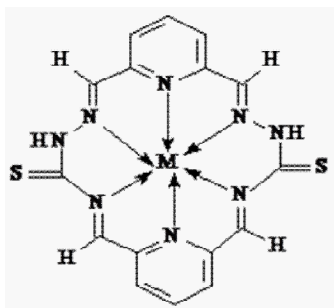


Fig. 3: Proposed Structure of Ligand-Metal complexes $M=\text{Cu}^{2+}, \text{Co}^{2+}, \text{Ni}^{2+}, \text{Cr}^{3+}$

Conventional method for the synthesis of metal complexes

The metal complexes (Figs. 3) was prepared by the mixing of equal moles of metal salts dissolved in the methanol was added followed by 1 ml of 1M NaOAc was added, in 1:1 (metal: ligand) ratio. The resulting mixture was refluxed on water bath for 6- 8h. A coloured product appeared on standing and cooling the above solution. The precipitated complex was, filtered washed with ether and recrystallized with ethanol several times and dried under the reduced pressure over anhydrous CaCl_2 in a desiccator. It was further dried in electric oven at 50-70°C (yield: 65-70%).

Microwave method for the synthesis of metal complexes

The ligand and the metal salts was mixed in 1:1 (metal: ligand) ratio in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3-4mL of dry ethanol as a solvent. The reaction was completed in a short time (5-9min)

Table 1: The comparative results of conventional and microwave methods-Analytical Data of PDCTC and their metal complex

Compound / complex (colour)	M.P t. ^o C	Reaction period CMM(h.)	MM(min.)	CM	Yield %	Mol. Wt.	Elemental Analysis Found (calculated)				
							C %	H%	N%	S%	M%
PDCTC(light-yellow colour)	257	10	5	65	84	380.5	50.4 (42.3)	3.1 (2.6)	29.4 (24.7)	16.8 (14.1)	-
PDCTC - Co(Light brown colour)	215	8	9	70	85	439.4	43.6 (37.1)	2.7 (2.3)	25.4 (21.6)	14.5 (12.3)	13.4 (11.3)
PDCTC -Cu(black colour)	210	6	8	55	84	444	43 (36.2)	2.7 (2.2)	25.2 (21.1)	14.4 (12.1)	14.3 (12)
PDCTC -Ni (light green colour)	230	8	5	61	85	439.4	43.6 (37.1)	2.7 (2.3)	25.4 (21.6)	14.5 (12.3)	13.3 (11.3)
PDCTC -Cr (yellowish green colour)	270	7	6	64	82	432.5	44.3 (36.4)	2.7 (2.2)	25.8 (21.2)	14.7 (12.1)	12 (9.8)

with higher yields. The resulting product was then recrystallized with ethanol and ether and finally dried under reduced pressure over anhydrous CaCl₂ in a desiccator. The progress of the reaction and purity of the product was monitored by TLC using silica gel G (yield: 80-85%).

RESULTS AND DISCUSSION

The analytical data for all the complexes are given in Table-1. The molar conductivity data (Table-3) of the complexes are consistent with the non-electrolytic nature³⁰⁻³¹ of the complexes. The ligand and complexes were characterized by elemental analysis to determine percentage of C, N, S and H. The observed and calculated percentages of the elements are in good agreement and support one ligand to a metal ion. The number of coordinated

ligands to metal determined by Job's continuous method and Mole ratio method established 1: 1 metal to ligand ratio.

IR and ¹H NMR Spectral Analysis

The reagents have been characterized by IR and ¹H NMR spectral data. The infrared spectra of PDCTC show bands at 1697 cm⁻¹ for νC=N; 722 for νC-S; 1540 for νC=S; indicating the Schiff base formation. The lowering of νC=N of azomethine group to the extent of 30-50 cm⁻¹ in all the complexes suggests the participation²⁷⁻²⁹ of azomethine nitrogen in complexation. On coordination, this band is shifted to lower frequency suggests that the ligand is coordinated to metal ion via azomethine nitrogen in all complexes. This change in shift is due to the drift of the lone pair density of azomethine nitrogen towards metal atom³². In the far IR spectral region,

Table 2: Selected IR bands (cm⁻¹) with tentative assignments

Compound	νC=N	νC-S	νC=S	νM-N	νM-S
PDCTC	1697	722	1540	-	-
Cu-PDCTC	1615	650	1560	420	355
Co- PDCTC	1608	708	1550	415	352
Ni- PDCTC	1610	707	1540	412	340
Cr- PDCTC	1623	712	1545	405	325

Table 3: Molar conductance data of metal complexes of PDCTC

PDCTC – Complex	Conductance (Ohm ⁻¹ Cm ² mol ⁻¹)
Cu-PDCTC	26
Co- PDCTC	24
Ni- PDCTC	22
Cr- PDCTC	36

Table 4: Molar conductance data of metal complexes of PDCTC

PDCTC – Complex	Magnetic Momentum (B.M)
Cu- PDCTC	2.24
Co- PDCTC	2.05
Ni- PDCTC	3.73
Cr- PDCTC	2.12

additional medium to strong bands at 405-420 and 325-355 cm⁻¹ are assigned to νM-N and νM-S modes (31,32) respectively. ¹H NMR spectra of PDCTC (CDCl₃ + DMSO-d₆) showed signals at 2.27, (1H,s); 8.15-8.32 (1H), 7.10, 7.86 (4H,s) 3.25 (1Hs) due to C=N(C₅H₄N), NH.

The magnetic moment (Table-4) value of Cu-PDCTC was 2.24 BM indicates one electron

paramagnetism. This value is higher than the spin-only value of 1.73 BM for one unpaired electron. The higher value of the magnetic moment indicates that complexes are monomeric in nature and there is no metal-metal interaction along the axial position in the complex and have distorted octahedral environment³⁵⁻³⁷. The magnetic moment of Co-PDCTC was found to lie in 2.05 BM. Monomeric cobalt complexes have lower magnetic moment values than would be

expected for pure octahedral complexes suggesting flattening towards planar arrangement³⁸⁻⁴². The magnetic moments of Ni (II) complex was observed at 3.73 BM. This value is in the range reported earlier for octahedral complexes⁴³. Cr(III) complex was observed at 2.12 BM.

Antimicrobial activities

The *in-vitro* Antimicrobial activity of the synthesized Schiff base ligands and their corresponding metal complexes on selected bacteria *E. coli* and *S. aureus* and two fungi *A. niger* and *C. albicans* was carried out. All of the tested compounds showed good biological activity against microorganism. On comparing the biological activity of the Schiff base and its metal complexes with the standard bactericide and fungicide, it is shown that some metal complexes have good activity as

compared to the standard but all the complexes are more active than their respective ligands. The higher inhibition zone of metal complexes than those of the ligands can be explained on the basis of Overtone's concept and Chelation theory. On chelation, the polarity of the metal ion will be reduced to greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelating ring and enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. There are other factors which also increase the activity are solubility, conductivity and bond length between the metal and ligand⁴⁴⁻⁴⁷. The bactericidal and fungicidal investigation data of the compounds are summarized in Tables 5 and 6. The results of

Table 5: Antibacterial screening data for the ligands and their complexes

Compound	<i>E. coli</i>						<i>S. aureus</i>					
	Diameter of inhibition zone (mm)			% Activity index			Diameter of inhibition zone (mm)			% Activity index		
	25	50	100	25	50	100	25	50	100	25	50	100
PDCTC	10	15	18	45	60	62	12	16	19	63	64	76
Cu-PDCTC	13	16	20	59	64	68	13	15	20	68	71	80
Co-PDCTC	14	17	21	63	68	72	12	14	18	63	66	72
Ni-PDCTC	16	19	23	72	76	79	11	15	18	57	71	72
Cr-PDCTC	17	20	24	77	80	82	10	16	20	52	76	80
Streptomycin (Standard)	22	25	29	100	100	100	19	21	25	100	100	100

Table 6: Antifungal screening data for the ligands and their complexes

Compound	Diameter of inhibition zone (mm); Concentration in ppm					
	<i>A. niger</i>			<i>C. albicans</i>		
	25	50	100	25	50	100
PDCTC	12	15	21	13	16	20
Cu-PDCTC	14	18	23	14	19	24
Co-PDCTC	15	20	24	15	18	22
Ni-PDCTC	16	19	23	14	17	21
Cr-PDCTC	15	21	25	18	20	25
Miconazole (Standard)	22	25	32	24	26	30

the investigations account for the anti-pathogenic behavior of the compounds and this efficacy is positively modified on complexation.

$$\% \text{Activity index} = \frac{\text{Zone of inhibition by test compound (diameter)}}{\text{Zone of inhibition by test standard (diameter)}} + 100$$

CONCLUSION

In the present research studies, our successful efforts are synthesis of some newly compounds from the conventional as well as microwave methods. These synthesized compounds have been characterized by various physicochemical, VSM and spectral analyses. In the result of microwave-assisted synthesis, it has been observed that the reaction time decreased

from hours to minutes and availability of the product within better yields compared to the classical method. Electrical conductivity data suggest that all the complexes fall in the semiconducting range. The antimicrobial data show that the metal complexes to be more biological active compared to those parent Schiff base ligand against all pathogenic species. The compounds also inhibit the growth of fungi and bacteria to a greater extent as the concentration is increased. The Schiff base ligands were found to be biologically active and their metal complexes displayed enhanced antimicrobial activity against one or two strains. Chelation tends to make the ligand act as more powerful and potent bactericidal agent. Further chelation can help in MDR problems.

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