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Research Article

Microwave Synthesis and Antimicrobial Activity of Novel Metal-Complexes with Schiff Base 2, 5-Thiophene Dicarboxaldehyde-Thiosemicarbazone

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Abstract: Some novel Schiff base metal complexes of Cr(III), Co(II), Ni(II) and Cu(II) derived from 2,5- Thiophene dicarboxaldehyde-Thiosemicarbazone (TDATC) 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 analysis. Analytical data revealed that all the complexes habited 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.
Keywords: Microwave method, Hexa-dentate ligands, Biological activities

INTRODUCTION

Now a day microwave irradiation is an accepted tool for accelerating the organic and inorganic reactions. It leads to the higher reaction selectivity and utilization of the inexpensive reagents [1-2]. In addition to providing an eco-friendly "green chemistry" approach to the reaction, it is free of environmental impacts [3]. The application of microwave irradiation towards the acceleration of wide range of organic and inorganic reactions has received concealable attention [4-6]. It also allowed a greener approach [7].

Schiff base of an important class of ligands in coordination chemistry and have many applications [8], in different fields. The chemistry of Schiff base complexes continues to attract many researchers because of their wide application in food industry, dye industry, analytical chemistry catalysis, antimicrobial activity, agro-chemical activity and pharmacological applications [9]. Semicabazones of aromatic and unsaturated carbonyl compounds have anticonvulsant properties [10] and their advantage over the analogous Thiosemicarbazone is their lesser neurotoxicity [12]. Semicabazones have an inhibitory effect on nitric oxide synthesis, which protect the vascular system [13].

It is well known that various organic ligands possess strong antibacterial, herbicidal, insecticidal and fungicidal properties. It has also been reported that the activity of bio metals is very often altered through the formation of chelates with different biological relevant ligands [13]. It is suggested that the compounds having antimicrobial activity may act either by killing the microbe or blocking their active sites [14-15]. In addition to this the antimicrobial activity of the compounds also depends upon the nature of the microorganisms[16].

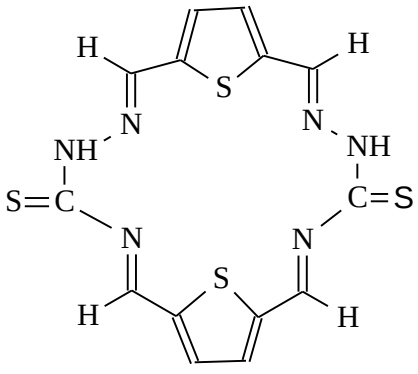

Fig. 1 Structure of Ligand – (TDATC)

MATERIALS AND METHODS

All the chemicals used were of AR grade and used without further purification. The infrared 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 (~ 10-3 M) was determined at 27± 20 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 ^{1}H 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, 5- Thiophene dicarboxaldehyde, (2g, 0.0141 mol in 20ml of methanol) Thiosemicarbazone (1.291g, 0.0141 mol in 20ml of methanol dissolved in hot condition) was taken in 250-ml round bottom flask and refluxed for 8h. On cooling the reaction mixture, dark yellow coloured product was formed. It was collected by filtration and washed with hot water and 50 percent cold methanol. This compound was recrystallised from ethanol and dried in vacuo, yield 65%, m .p. 86 °C (Fig. 2).

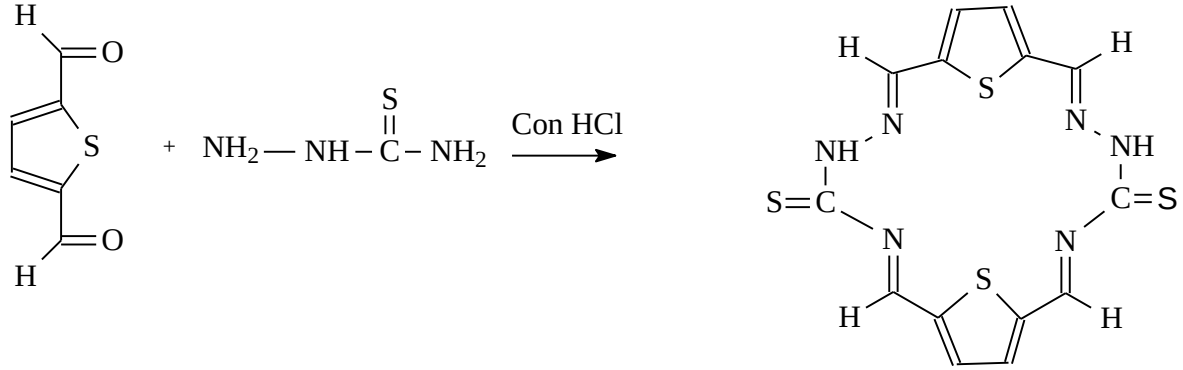

Fig. 2: preparation of Ligand –TDATC

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%).

Conventional method for the synthesis of metal complexes

The metal complexes (Fig. 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) with higher yields. The resulting product was then recrystallized with ethanol and ether and finally dried under reduced pressure over anhydrous $CaCl_2$ in a desiccator. The progress of the reaction and purity of the product was monitored by TLC using silica gel G (yield: 80-85%).

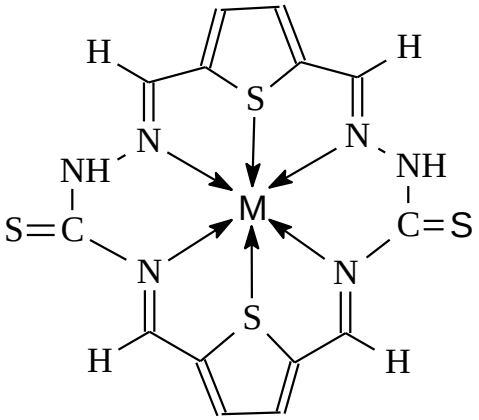

Fig. 3: Proposed Structure of Ligand –Metal complexes (M=Cu^{2+}, Co^{2+}, Ni^{2+}, Cr^{3+})

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 nature (28, 29)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 ^{1}H NMR Spectral Analysis

The reagents have been characterized by IR and ^{1}H NMR spectral data. The infrared spectra of TDATC show bands at 1697 cm^{-1} for VC=N; 722 for VC-S; 1540 for VC=S; indicating the Schiff base formation. The lowering of VC=N of azomethine group to the extent of 30-50 cm^{-1} in all the complexes suggests the participation 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 atom. In the far IR spectral region, additional medium to strong bands at 405-420 and 325-355 cm^{-1} are assigned to VM-N and VM-S modes respectively. ^{1}H NMR spectra of PDCTC ($CDCl_3$ + DMSO-d_6) showed signals at 2.27, (1H,s); 8.15-8.32(^{1}H),7.10,7.86(4H,s) 3.25(^{1}Hs)due to C=N(C_5H_4N),NH.

The magnetic moment (Table 4) value of Cu-TDATC was 1.80 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 environment[. The magnetic moment of Co-TDATC was found to 4.75 BM. Monomeric cobalt complexes have higher magnetic moment values than would be expected for pure octahedral complexes suggesting flattening towards planar arrangement[17]. The magnetic moments of Ni (II) complex was observed at 3.13 BM. This value is in the range reported earlier for octahedral complexes. ·Cr(III) complex was observed at 3.81 BM.

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

Compound / complex (colour)	M.P. (^{0}C)	Reaction period		Yield %		Mol. Wt.	Elemental Analysis Found (calculated)				
		CMM (hr.)	MM (min.)	CM	MM		C %	H%	N%	S%	M%
TDATC (Light-yellow colour)	86	8	5	65	84	390	43	2.5	21.5	32.8	-
							(43.3)	(2.6)	(21.7)	(32.9)	-
TDATC-Co (Light pink colour)	272	8	9	70	85	449	37.4	2.2	18.7	28.5	13.1
							(37.6)	(2.3)	(18.9)	(28.8)	(13.3)
TDATC-Cu (Black colour)	>300 (d)	8	8	55	84	453.5	37	2.2	18.5	28.2	14
							(37.2)	(2.2)	(18.7)	(28.3)	(14)
TDATC -Ni (Light green colour)	280	8	5	61	85	448.7	37.4	2.2	18.7	28.5	13
							(37.6)	(2.3)	(19)	(28.3)	(13.3)
TDATC-Cr (Yellowish green colour)	265	10	6	64	82	442	38	2.2	19	28.9	11.7
							(38.4)	(2.2)	(19.8)	(29.1)	(11.8)

Table 2: Selected IR bands (cm^{-1}) with tentative assignments

Compound	*v*C=N	*v*N-H	*v*C-S	*v*C=S	*v*M-N	*v*M-S
TDATC	1690	3379	724	1535	-	-
Cu-TDATC	1610	3378	660	1555	415	360
Co- TDATC	1605	3376	700	1550	420	350
Ni- TDATC	1612	3378	710	1545	415	335
Cr- TDATC	1616	3373	705	1540	408	340

Table 3: Molar conductance data of metal complexes of TDATC

TDCTC – Complex	Conductance($Ohm^{-1}Cm^2mol^{-1}$)
Cu-TDATC	12
Co- TDATC	33
Ni- TDATC	19
Cr- TDATC	121

Table 4: Magnetic moment data of metal complexes of TDATC

TDATC- Complex	Magnetic Momentum(B.M)
Cu- TDATC	1.80
Co- TDATC	4.75
Ni- TDATC	3.13
Cr- TDATC	3.81

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 show that the 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[18-19]. 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 ligand (42-45).The bactericidal and fungicidal investigation data of the compounds are summarized in Tables 5 and 6. The results of the investigations account for the anti-pathogenic behavior of the compounds and this efficacy is positively modified on complexation.

$$\% \text{ Activity index} = \frac{zone\ of\ inhibition\ by\ test\ compound\ (diameter\ )}{zone\ of\ inhibition\ by\ standard\ (diameter\ )} X100$$

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

Compound	*E .coli*						*S. aures*					
	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
TDATC	10	12	18	50	60	62	12	16	20	66	76	80
Cu-TDATC	13	15	19	65	65	70	13	17	21	72	81	84
Co-TDATC	14	17	21	70	74	78	12	14	18	66	67	72
Ni-TDATC	17	20	24	85	87	89	11	15	18	61	71	72
Cr-TDATC	16	20	24	80	87	89	10	14	20	55	66	80
Streptomycin (Standard)	20	23	27	100	100	100	18	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					
	A .nizer			*C.albicans*		
	25	50	100	25	50	100
TDATC	11	14	20	12	15	21
Cu-TDATC	12	16	22	15	20	22
Co-TDATC	16	21	23	14	19	20
Ni-TDATC	15	19	22	15	16	22
Cr-TDATC	14	21	25	16	19	24
Miconazole (Standard)	22	25	32	24	26	30

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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