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Solvent-free Synthesis, Characterization and Biological Activity of Transition Metal Complexes of Schiff Base Ligand Derived from 2-Amino Benzimidazole with 4, 4'Dibromobenzil

Sadashiv N. Sinkar [1], Mahesh G. Undegaonkar [2], Sharad P. Moharir [3], Sunil R. Mirgane [4,*]

1 Department of Chemistry; MSS'S Arts Science and Commerce College Ambad, Dist. Jalna, India
2 Department of Chemistry; Arts Science and Commerce College Badanapur, Dist. Jalna, India
3 Department of Chemistry; Siddharth Arts Science and Commerce College Jafrabad, Dist.Jalna, India
4 PG & Research Department of Chemistry; J.E.S. College Jalna, India
* Correspondence: mirganesunil@gmail.com (S.RM);

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Abstract: Microwave-assisted synthesis and characterization of Schiff base ligand complexes of transition metals such as Mn(II), Fe(III), Co(II), Ni(II),Cu(II), Zn(II) Cd(II), and Ag(I) (using Schiff base) prepared by irradiation of 2-Amino benzimidazole with 4,4'dibromo benzil. The Synthesized transition metal complexes and Schiff base ligand have been representatively characterized by elemental analysis and spectral methods such as UV, IR, ^{1}H-NMR, LC-MS, and Thermal analysis. The synthesized ligand and its complexes were also screened for their biological activities, such as antibacterial activity against bacterial species *Staphylococcus aureus*, *Escherichia coli*, and *Salmonella Typhi*. The result indicated that the complexes exhibited octahedral geometry.

Keywords: microwave synthesis; Schiff base; thermal study; biological activity.

1. Introduction

The microwave-induced enhancement of organic reactions is currently a focus of attention for chemists due to the decreased reaction time, improved yields, and easier work up than conventional methods [1]. In microwave synthesis, low boiling, toxic and poisonous solvents are often avoided to avoid accidents [2]. The use of the microwave for the synthesis of organic compounds has proved to be an efficient, safe, and environmentally benign technique with a shorter reaction time [3]. Schiff's bases are compounds having an azomethine (C=N) group. Schiff's base ligands were synthesized by the microwave irradiation of primary amines and active carbonyl groups [4,5]. Microwave irradiated reactions under solvent-free or fewer solvent conditions are attractive results in reduced pollution, low cost, and offer high yields together with safety in processing and handling [6-8]. Benzimidazole derivatives are related to several varieties of pharmacokinetic and pharmacodynamics properties[9]. Specifically, this nucleus is a constituent of vitamin B12. The medicinal activities of the benzimidazole containing moiety have been well familiar Albendazole, Mebendazole[10]. Benzimidazole nucleus is one of the bioactive heterocyclic compounds that exhibit a wide range of biological activities.These biological activities include anti-cancer [11-13],

bactericidal [14], fungicidal [15-17], analgesic [18,19] and anti-viral properties. [20-22] some have Anti-hypertensive activity [23], while some derivatives have been synthesized and evaluated for inhibition of HIV-1 infectivity [24].

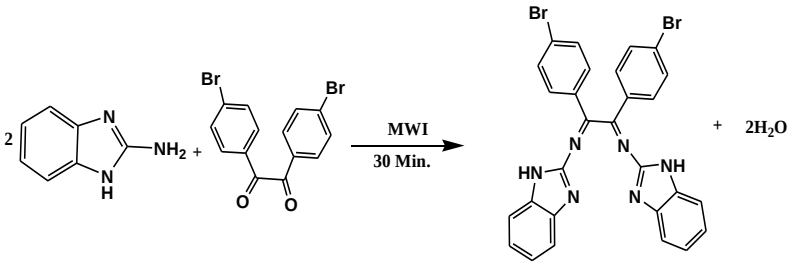
Schiff bases are well known for their biological applications as antibacterial, antifungal, and antiviral agents, plant growth inhibitors insecticidal, antidepressant, anti-inflammatory, anti-tuberculosis, and antimicrobial and anticonvulsant drug activity[25]. We have synthesized Schiff base from 2-amino benzimidazole and 4,4'dibromo benzil under microwave irradiation in the present study. We planned the synthesis of new Schiff bases using microwave irradiation due to ease to workup, improved yield, and completion of the reaction time, less [26].

2. Materials and Methods

All the synthetic grade, analytical grade reagents as well as chemicals were purchased from Sigma Aldrich, Loba Chem., Merck chemicals. All newly synthesized compounds' melting point was found using an electrothermal digital apparatus and uncorrected. ^{1}H-NMR, spectral data were recorded on a Bruker (400 MHz, 100 MHz) spectrometer. Chemical shift (ppm) was referred to as the internal standard Tetramethyl silane (TMS). The synthesized compounds find out the molecular weight using LC-MS. The reaction was monitored by thin-layer chromatography.

2.1. Synthesis of Schiff base ligand.

The Schiff base has been synthesized by reacting 2-Aminobenzimidazole (0.28gm, 0.02mmol) and 4,4 dibromo benzil (0.37gm, 0.01mmol). The reaction was carried out in a microwave oven for 30 minutes. The irradiated product was washed with dry ether and filtered. The final product was recrystallized from ethanol to give pale yellow crystals. The purity of the product was monitored by the use of TLC, using n-hexane and ethyl acetate (7:3). Yield 82%, M.P.198℃.



2-Amino Benzimidazole 4,4 dibromo benzil N-((E)-2-(1H-benzo[d]imidazol-2-ylimino)-1,2-bis (4-bromophenyl)ethylidene)-1H-benzo[d]imidazol-2-amine

2.2. Synthesis of metal complexes.

The Schiff base ligand and metal salts were mixed in a grinder 1:1 (metal: ligand) ratio. The reaction mixture was then irradiated in a microwave oven. The reaction was completed in a short time, between 30-150 sec. The progress of the reaction and purity of the product was monitored by TLC plate. Each product was recrystallized from ethanol and ether, and finally, different colored crystals were obtained. (Yield: 84-98%)

3. Results and Discussion

In the present study of the microwave-assisted synthesis, it was observed that the reaction time had been drastically reduced with a better yield of the products. The difference

was observed probably due to the strong microwave effect and the high enhancement of reaction rate. The conformation of results was also checked by repeating the synthesis process[27]. The microwave irradiation technique was completed with 30-150 Sec. and yield 84-98%. All the metal complexes are colored, solid and stable towards air and moisture at room temperature. They possess a sharp melting point. The complexes are soluble in dimethylformamide and dimethyl sulfoxide but insoluble in common organic solvents3.1. Elemental analysis.

Table 1. Elemental analysis of Schiff base ligand.

Molecular formula (Novel ligand)	Mol.Wt.	Found (Calculated) (%)			
		C	H	N	Br
$C_{28}H_{18}N_6Br_2$	598	54.66 (56.18)	3.71 (3.01)	15.90 (14.05)	25.73 (26.76)

3.2. Physical properties.

Table 2. The details of the physical properties of the novel Ligand and its metal complexes.

Sr.No.	Formula of Ligand/Complex	Colour	M.P.(℃)	Yield (%)
1	$C_{28}H_{18}N_6Br_2$	Pale yellow	198	82
2	[Mn $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Light Green	120	95
3	[Fe $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Brown	188	92
4	[Co $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Brown	138	98
5	[Ni $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Light Green	>300	84
6	[Cu $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Green	>300	85
7	[Zn $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Greenish Yellow	190	93
8	[Cd $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Bright Yellow	259	96
9	[Ag $C_{28}H_{18}N_6Br_2(H_2O)_2$]	Dark Yellow	217	87

3.3. Infrared spectra.

The IR spectrum of the ligand is compared with that of the complexes to determine the changes that might have occurred during the complexations. IR spectrum of the Schiff base ligand exhibit the most characteristic band at υ(C=N, azomethine), 1668 cm^{-1}[28-30]. The metal complexes of Ni(II) and Cu(II) show broadband at 3304-3321 cm^{-1} due to the benzimidazole ring's N-H stretching frequency. A medium intensity band at 831and 819 cm^{-1} in Ni (II), Cu (II), respectively, suggests the presence of coordinated water in these complexes. In the low-frequency region, the band of weak intensity was observed for the complexes in the region 466-467cm^{-1} to (M–N) [31]. The infrared spectral data of the novel ligand and its metal complexes have been presented in Table 3.

Table 3. Selected Infrared frequencies (cm^{-1}) of ligand and its complexes.

Ligand/Complexes	υ(C=N)Azomethine	υ(N-H) Imidazole	υ(C-Br)	υ(M-N)	υ(H_2O)
$C_{28}H_{18}N_6Br_2$	1668	3379	744	-	-
[Ni(L) $(H_2O)_2$]	1587	3321	727	466	3603,819
[Cu(L) $(H_2O)_2$]	1588	3304	738	467	3545,831

^{1}H-NMR spectra.

The ^{1}H-NMR spectra of the Schiff base ligand were recorded in DMSO. The chemical shifts (δ) are given in ppm downfield from tetramethylsilane. The spectrum also shows peaks between 7.16 to 7.08 ppm C-H proton of substituted benzene and N-H proton of benzimidazole

ring at 6.08 ppm. Two aromatic protons of the benzimidazole ring appear doublet in the proton range at δ = 8.02 to 7.16 ppm [32].

3.5. Mass spectra.

The mass spectra of the ligand showed the molecular ion peak at m/z = 598, which correspond to its molecular formula [$C_{28}H_{18}N_6Br_2$].

3.6. Electronic spectra.

The electronic spectra of π-π* and n-π* transition of metal complexes were recorded in DMSO solution in the region of 200 to 800 nm [33]. Ni(II) complex shows three bands at 36,364 cm^{-1}, 43,478cm^{-1}, 48,309cm^{-1} corresponding to the transitions $^3A_{2g} \rightarrow {}^3T_{2g}$ (F) (υ_1), $^3A_{2g} \rightarrow {}^3T_{1g}$ (F) (υ_2), $^3A_{2g} \rightarrow {}^3T_{2g}$ (P) (υ_3), respectively [34]. This suggests octahedral stereochemistry around Ni(II) complex.

UV spectrum of Cu(II) complex showed three bands, 36,232 cm^{-1}, 36,765 cm^{-1} and 43,478 cm^{-1} corresponding to $^2B_{1g} \rightarrow {}^2A_{1g}$ (υ_1) , $^2B_{1g} \rightarrow {}^2B_{2g}$ (υ_2), and $^2B_{1g} \rightarrow {}^2E_g$ (υ_3) transition in octahedral (Figure 1) geometry [35]. The electronic spectral data obtained for both the metal complexes are presented in table 4.

Table 4. Electronic spectral data of Ni (II) and Cu (II) complexes.

Complexes	Frequency (cm^{-1})	Assignment	Geometry
[$NiC_{28}H_{18}N_6Br_2(H_2O)_2$]	36,364 cm^{-1}	$^3A_{2g} \rightarrow {}^3T_{2g}$(F) ($\upsilon_1$)	Octahedral
	43,478 cm^{-1}	$^3A_{2g} \rightarrow {}^3T_{1g}$ (F) (υ_2)	
	48,309 cm^{-1}	$^3A_{2g} \rightarrow {}^3T_{2g}$ (P) (υ_3)	
[Cu $C_{28}H_{18}N_6Br_2(H_2O)_2$]	36,232 cm^{-1}	$^2B_{1g} \rightarrow {}^2A_{1g}$($\upsilon_1$)	Octahedral
	36,765 cm^{-1}	$^2B_{1g} \rightarrow {}^2B_{2g}$ (υ_2)	
	43,478 cm^{-1}	$^2B_{1g} \rightarrow {}^2E_g$ (υ_3)	

3.7. DSC analysis of metal complexes.

The DSC analyses of Ni (II) and Cu (II) metal complexes were conducted from room temperature to 360℃. The DSC curves were obtained under a dynamic nitrogen atmosphere with a flow rate of 80 ml min^{-1} and a heating rate of 10℃ min^{-1}. The thermal data obtained from the thermogram of each metal complex is summarized in Table 5.

The Ni (II) complex undergoes decomposition in two stages as per the data obtained from the thermogram. The peak data may be explained as follows. The first stage occurred in the temperature range of 211.59℃ to 239.39°C with a peak temperature of 227.15°C. This corresponds to the dehydration process with the loss of coordinated water molecules. The second stage occurred in the temperature range of 259.63 °C to 276.44 °C with a peak temperature of 244.33 °C. These endothermic peak values correspond to the decomposition of the ligand and the formation of Stable NiO. These two peak areas gave value of ΔH = 255.07 Joules/g, ΔH= -9.73Joules/g, respectively [36,37].

The Cu (II) complex undergoes decomposition in three stages as per the data obtained from the thermogram. The peak data may be explained as follows. The first stage occurred in the temperature range of 97.97 °C to 139.39 °C with a peak temperature of 118.02°C. This corresponds to the dehydration process with the loss of coordinated water molecules. The second stage occurred in the temperature range of 171.88 ℃ to 223.37 ℃ with a peak temperature of 197.27 °C. These endothermic peak values correspond to the partial

decomposition of the ligand. The third stage occurred in the temperature range of 220.51 °C to 235.98 °C with a peak temperature of 231.22 °C. These endothermic peak values show the partial decomposition of the ligand. The fourth stage occurred in the temperature range of 269.74 °C to 300.84 °C with a peak temperature of 286.37 °C. These endothermic peak values show the decomposition of ligand and formation of Stable CuO. These four peak areas gave value of ΔH =-56.11Joules/g, ΔH = 237.44 Joules/g, ΔH = 23.24 Joules/g, ΔH= 8.32 Joules/g respectively [38,39].

Table 5. Differential Scanning Calorimetry (DSC) analyses of metal complexes.

Sr. No	Complex	Onset Temp. in ℃	Peak Temp. in ℃	End set Temp. in ℃	Transition Enthalpy (ΔH) Joules/g	Sample Mass in mg
1	Ni-L_B	211.59	227.15	239.39	255.07	2.50
		259.63	244.33	276.44	-9.73	
2	Cu-L_B	97.97	118.02	139.39	-56.11	2.56
		171.88	197.27	223.37	237.44	
		220.51	231.22	235.98	23.24	
		269.74	286.37	300.84	8.32	

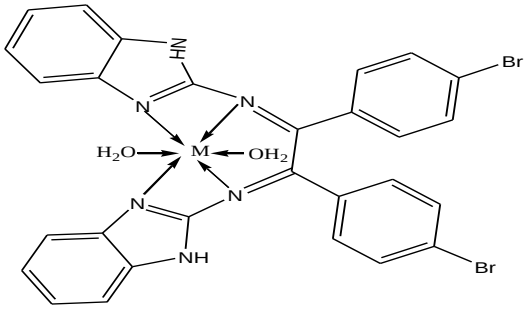


Figure 1. The proposed structure of the complexes when M=Mn(II),Fe(III),Co(II),Ni(II),Cu(II), Zn(II), Cd (II) and Ag(I).

3.8. Antibacterial activity.

Antibacterial activity of Schiff base ligand and its complexes have been tested against bacteria, such as *Escherichia coli*, *Staphylococcus aureus*, and *Salmonella typhi*, which were grown overnight at 37℃ temperature [40,41]. The standard strains were obtained from MTCC Chandigarh. Determination of minimum inhibitory concentrations (MIC) by Micro Broth Dilution Method was used to measure inhibition concentration wavelength at 475nm was evaluated against test bacteria for the concentration ranging between 0.4µg/ml to 100µg/ml [42]. DMSO and compared with antibiotics viz. Streptomycin [43]. All the investigated compounds showed remarkable biological activity against bacteria in (Table.5). The obtained results reflect that; (1)The Co(II) and Ni(II) complexes exhibited very good antibacterial activity against *Escherichia coli*; (2) The Schiff base ligand, Ni(II), and Zn (II) complex showed good activity against *Staphylococcus aureus* bacteria ; (3)The ligand and Co(II), Cu(II) complex exhibited excellent antibacterial activity against *Salmonella typhi*. The parent ligand shows excellent antibacterial activity against *Salmonella typhi*.

Table 6. Antibacterial activity of the ligand and their metal complexes.

Sr. No.	Compounds	Minimal inhibition Concentration (µg/ml)		
		E. coli	***S. aureus***	***S. typhi***
1	Ligand	250	100	50
2	Mn(II)	250	125	500

Sr. No.	Compounds	Minimal inhibition Concentration (µg/ml)		
		E. coli	*S. aureus*	*S. typhi*
3	Fe(III)	250	125	250
4	Co(II)	100	125	100
5	Ni(II)	100	100	250
6	Cu(II)	250	125	125
7	Zn(II)	500	100	500
8	Cd (II)	500	500	250
9	Ag (I)	500	125	500

4. Conclusions

In the present work, we successfully designed and developed N-((E)-2-(1Hbenzo[d]imidazol-2-ylimino)-1,2-bis (4-bromophenyl) ethylidene)-1Hbenzo[d]imidazol-2-amine and its metal complexes. The ligand and its complexes have been characterized by various spectral analyses. Obtained results were in good agreement with the proposed structure. The microwave method has been considered a green chemical route. As the result of microwave-assisted synthesis, it has been observed that reaction time decreased from hours to minutes, and availability of product better yield. This method is simple, mild, and eco-friendly from a green chemistry point of view. Based on the electronic spectra, thermal study data octahedral geometry has been suggested for Ni (II), Cu (II) complexes.

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Conflicts of Interest

There is no conflict of interest of any kind of the authors involved in this work.

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