

Microwave Assisted Synthesis Of Schiff Base Ligand In Bio Based Solvent And Their Transition Metal Complexes

Amol D. Kale^a, Rajendra P. Phase^a Sanjay S. Kotalwar^a And Vasant B. Jagrut^{b*}

^adepartment. Of Chemistry, Lal Bahadur Shastri. Sr. College, Partur -431501 (Ms) India

^bdepartment Of Chemistry, Swami Vivekanand Senior College, Mantha-431504 (Ms) India

Abstract:

A new series of transition metal complexes have been synthesized by conventional as well as microwave technique from ligand, HL E-N'-(2-hydroxy-4-methoxybenzylidene)-5-methyl-2H-pyrazole-3-carbohydrazide (3) in methanol. The Key intermediate schiff base ligand were prepared by allowing condensation of 2-hydroxy-4-methoxybenzaldehyde (1) with 5-methyl-1H-pyrazole-3-carbohydrazide (2) under microwave irradiation using bio based greener solvent system ethyl lactate: water. The authenticity of these ligands and their Fe(II), Zn(II), Cu(II), Co(II) and Ni(II) complexes were confirmed on the basis of spectroscopic technique such as Mass, IR, ¹H NMR, UV spectroscopy and elemental analyses. The thermal stability of metal complexes was also studied by TGA.

Key Word: Pyrazole schiff-base ligand, Metal Complexes, Ethyl lactate Microwave irradiation.

Date of Submission: 11-07-2024

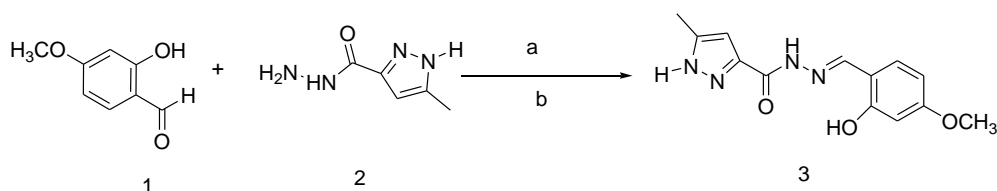
Date of Acceptance: 21-07-2024

I. Introduction

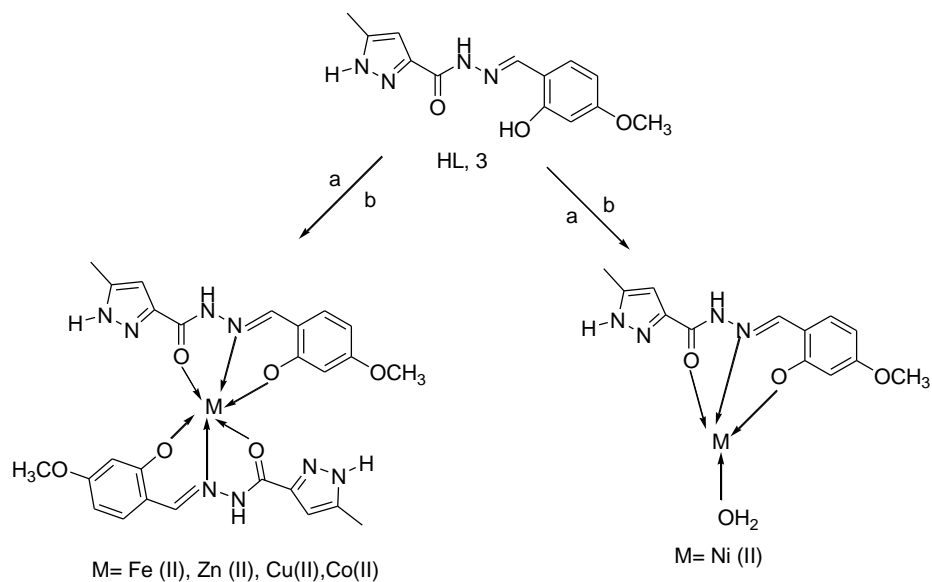
Heterocyclic hydrazones play vital role in pharmaceutical and biological sciences, hydrazones containing molecules have been attracted attention for synthetic and medicinal chemist due to their broad spectrum of pharmacological and biological activities such as antitumor, antineoplastic, antiviral and anti-inflammatory [1-6]. Schiff bases, is an important key intermediate in coordination chemistry because of its ability to coordinate with metal ions, have attracted researchers since their beginning to explore their potential in diverse fields. In recent years' heterocyclic hydrazides are used as generation for schiff bases and their metal complexes with the hope to enhance biological activities of desired compounds. The biological activity and coordination chemistry of N-heterocyclic hydrazides (e.g. iso-nicotinic acid hydrazide, etc.) have also been studied [7]. The study of the transition metal complexes of schiff base ligands has been illustrate considerable concentration because of their remarkable chemistry [8] and biological significance [9]. The well characterized bio functionality of pyrazole (isomeric with imidazoles) derivatives is often associated with the chelating phenomena with trace metal ions [10–15]. Pyrazole resultant metal ion complexes have been broadly studied in recent years owing to their great diversity of biological activity, including antimalarial, antibacterial, antitumor, antiviral etc. [16–25]. Pyrazoles are pi-excessive, better pi-donors and weaker pi-acceptors than six membered heterocycles and can act as a hard donor site [26, 27]. The various range of biological effects exhibited by pyrazole molecules has prepared and acted as a subject of extensive research in medicinal and pharmaceutical studies [28, 29]. Metal complexes incorporating an amide functional group have gained considerable attention too. Amides possess broad biological properties and are utilized as effective chelating agents [30]. Outstandingly, amide groups incorporated into heterocyclic bases such as pyridine and pyrazine have emerged as a rapidly expanding class of ligand scaffolds that efficiently bind metal ions [31]. Traditionally Schiff bases and their metal complexes have been carried out in organic solvent by conventional methods. These methods suffer from various limitations including poor yields, longer reaction time and environmentally harmful solvent. Therefore, attention of chemists directed toward the synthesis of Schiff bases and their metal complexes by using microwave irradiation. Microwave technology is an emerging alternative energy source for chemical transformations in minutes instead of hours or even days. Hence, now a day's increase use of microwave irradiation for enhancing chemical synthesis and increasing their productivity. Literature survey revealed that there is scanty information for the synthesis of metal complexes using microwave irradiation. Recently in 2024 Savita Bargujar demonstrated the microwave synthesis of Schiff base metal complexes under multiple conditions and reported advantage of microwave technique is the extraordinary acceleration in reaction rate when compared to conventional mode [32]. Abhinav Jain and his co-worker establishes the empirical comparison between microwave and alternative synthetic techniques for Schiff base ligands and their metal complexes in terms of kinetic parameters by referencing multiple examples from the current literature [33]. Thus microwave assisted synthesis offers several advantages over conventional heating such as homogeneity, selective heating, shorter reaction time with better yields [34 -37].

Keeping in view and in continuation our work [38], herein we report microwave assisted synthesis of pyrazole based ischiff base and their metal complexes with better yields in shorter reaction time. The key intermediate schiff bases were also synthesized using bio based solvent (ethyl lactate: water solvent system) under microwave conditions. In recent years' ethyl lactate is an emerging bio based greener solvent due to its unique physicochemical properties, therefore it has been successfully used for the organic transformation [39 - 42]. The main goal of this paper is to develop green method techniques with shorter reaction time which is used in the preparation of schiff bases and their metal complexes.

The titled compounds E-N'-(2-hydroxy-4-methoxybenzylidene)-5-methyl-2H-pyrazole-3-carbohydrazide (**3**) was synthesized by allowing condensation of 2-hydroxy-4-methoxybenzaldehyde (**1**) with 5-methyl-1H-pyrazole-3-carbohydrazide (**2**) in ethyl lactate: water solvent system under microwave condition. Compounds (**4a-4e**) were prepared by carried reaction of Schiff base (**3**) with metal nitrate, Fe (II), Zn (II), Cu (II), Co (II) and Ni (II) in methanol using microwave irradiation as well as by conventional method. The reaction sequence is outlined in **Scheme 1 & 2**



Reaction Condition (A) Ethanol, Acetic Acid, Reflux (B) Ethyl Lactate: Water, Acetic Acid, Microwave.
Scheme 1 Synthesis Of Schiff Base Ligand Using Bio Based Solvent Under Microwave Condition.



Reaction Condition (A) Methanol, Metal Nitrate, Reflux (B) Methanol, Metal Nitrate, Microwave.
Scheme 2 Synthesis Of Metal Complexes By Conventional As Well As Microwave Technique.

II. Experimental

Materials & Methods:

All chemicals were obtained from commercial sources and used without any further purification. The melting points were determined in open capillaries and are uncorrected. The IR spectra were recorded on a FT-IR (JASCO FT-IR 4100) Japan. The ¹H and ¹³C NMR was measured on Bruker Avance II 400 MHz FT NMR with low and high temperature in DMSO using TMS as internal reference. Mass spectra were recorded on GC-MS spectrometers. Elemental analyses were performed on a Perkin-Elmer 2400 CHN analyser.

General Procedure

Synthesis of Schiff base(E)-N'-(2-hydroxy-4-methoxybenzylidene)-5-methyl-1H-pyrazole-3-carbohydrazide, HL (3)

Conventional synthetic route

A mixture of 2-hydroxy-4-methoxybenzaldehyde (1) (0.01 mol, 1.52 g) and 5-methyl-1H-pyrazole-3-carbohydrazide (2) (0.01 mol, 1.40 g) was dissolved in ethanol (25 mL). To this solution a few drops of glacial acetic acid were added and the reaction mixture was reflux for 3 h. The reaction was monitored on TLC. After completion, the reaction mixture was poured on ice and the obtained solid was filtered washed with cold water and recrystallized from ethanol-water mixture.

Microwave Irradiation synthetic route

In a conical flask, 5-Methoxy-2-Hydroxy Benzaldehyde (1) (0.002 mol), 5-methyl-1H-pyrazole-3-carbohydrazide (2) (0.002 mol) and catalytic amount of glacial acetic acid was dissolved in ethyl lactate-water system (70 :30). The reaction mixture was irradiated using a microwave at 160 Watt. The progress of the reaction was monitored on a TLC plate. After completion, the reaction mixture was poured in ice cold water and was extracted with EtOAc. The solvent was removed and the crude product was crystallized using ethanol-water mixture.

Analysis of Schiff base HL (3)

M.F. C₁₄H₁₆N₄O₃ Yield 92%; M.P. 283; yellow powder; FT-IR (KBr, cm⁻¹): 3361 (OH), 3206 (N-H), 1656 (C=O), 1603 (C=N), ¹H NMR (400 MHz, DMSO-d₆) = δ 2.96 (3H, s, CH₃), δ 3.32 (3H, s, OCH₃), δ 6.88 (2H, dd, Ar-H), δ 7.44 (1H, s, Ar-H), δ 7.91 (1H, s, Py-H) δ 8.44 (1H, s, CH=N), δ 10.58 (1H, s, Py-NH), δ 12.40 (1H, s, CONH), δ 13.88 (1H, s, Phenolic OH) ¹³C NMR (400 MHz, DMSO, ppm) 168.20 (Phenolic carbon), 163.72 (amide carbon), 160.43 (azomethine carbon), 154.74-101.36, (Pyrazole & aromatic carbon), 55.65 (methoxy carbon) 15.39 (methyl carbon); Elemental analysis found (%) C, 58.95; H, 5.96; N, 18.93; O, 15.80 calculated for, C₁₄H₁₆N₄O₃: C, 58.32; H, 5.59; N, 19.43; O, 16.65; MS (m/z): 288 (M⁺).

Preparation Of Complex (4a-E)

Conventional synthetic route

Metal nitrate in methanol was added to methanolic solution of (E)-N'-(2-hydroxy-4-methoxybenzylidene)-5-methyl-1H-pyrazole-3-carbohydrazide, (3) at hot condition in 1:1 / 1:2 (metal:ligand) molar ratio and reaction mixture slightly adjusted to basic. Then the reaction mass was refluxed for 3 h. The progress of reaction was monitored by TLC and after completion of reaction colored precipitates were obtained. The obtained solid product was filtered, washed with hot methanol and dried.

Microwave Irradiation synthetic route

In a conical flask, Metal nitrate and (E)-N'-(2-hydroxy-4-methoxybenzylidene)-5-methyl-1H-pyrazole-3-carbohydrazide, (3) dissolved in methanol. The solution of reaction adjusted slightly to basic. Then this reaction mass was irradiated using a microwave at 160 Watt. The progress of the reaction was monitored on a TLC plate. After completion, the reaction mixture was poured in ice cold, coloured precipitates. The obtained solid was filtered, washed with hot methanol and dried.

Analysis of metal complex [Fe (C₁₄H₁₅ N₄O₃)₂] (3a)

M.F.C₂₈H₃₀FeN₈O₆Yield 80%; M.P. >300; Black powder; FT-IR (KBr, cm⁻¹): 3200 presence of Amide (N-H), 1621 due to carbonyl assembly (C=O), 1603 endorsed to (C=N), 502 (M-O), 472 (M-N); ¹H NMR (400 MHz, DMSO-d₆) = δ 2.98 proton of methyl group (6H, s, (CH₃)₂), δ 3.77 exposed to presence of methoxy proton (6H, s, (OCH₃)₂), δ 6.46 (4H, dd, Ar-H), δ 7.80 (2H, s, Ar-H), δ 8.16 (2H, s, Py-H) δ 8.45 accredited to azomethine proton (1H, s, CH=N), δ 10.11 (2H, s, Py-NH), δ 12.07 this shift distinguished as a amide proton (1H, s, CONH); Elemental analysis found (%) C, 52.85; H, 3.98; Fe, 8.86; N, 18.15; O, 15.85 calculated for C₂₈H₃₀FeN₈O₆: C, 53.34; H, 4.80; Fe, 7.89; N, 17.77; O, 15.23.

Analysis of metal complex [Zn (C₁₄H₁₄ N₄O₃)₂] (3b)

M.F.C₂₈H₂₈N₈O₆ZnYield 85%; M.P.>300; Yellow powder; FT-IR (KBr, cm⁻¹): 1621 allowed to carbonyl group (C=O), 1580 attributed by (C=N), 555 (M-O), 478 (M-N); ¹H NMR (400 MHz, DMSO-d₆) δ 2.97 is due to proton of methyl group (6H, s, (CH₃)₂), δ 3.41 showed to presence of methoxy proton (6H, s, (OCH₃)₂), δ 6.92-7.33 presence of aromatic proton (6H, m, Ar-H), δ 7.88 (2H, s, Py-H), δ 8.55 recognized to azomethine proton (1H, s, CH=N), δ 10.09 (2H, s, Py-NH), Elemental analysis found (%) C, 53.20; H, 4.90; Zn, 11.10; N, 18.09; O, 14.81 calculated for C₂₈H₃₀FeN₈O₆: C, 52.71; H, 4.42; Zn, 10.25; N, 17.56; O, 15.05.

Analysis of metal complex [Ni (C₁₄H₁₇O₄N₄)] (3c)

M.F.C₁₄H₁₆N₄NiO₄Yield 87%; M.P.>300; Orange powder; FT-IR (KBr, cm⁻¹): 3308 is due to coordinated water (H₂O), 1619 permissible to carbonyl group (C=O), 1563 licensed to (C=N), 561 (M-O), 476

(M-N); ¹H NMR (400 MHz, DMSO-d₆) = δ 2.98 due to proton of methyl group (3H, s, CH₃), δ 3.38 attributed by methoxy proton (3H, s, OCH₃), δ 6.15 presence of aromatic proton (2H, dd, Ar-H), δ 7.71 (1H, s, Py-H), δ 8.39 (1H, s, Py-NH), δ 9.72 predictable to azomethine proton (1H, s, CH=N); Elemental analysis found (%) C, 45.78; H, 3.98; Ni, 16.73; N, 14.22; O, 18.15 calculated for C₂₈H₃₀FeN₈O₆: C, 46.32; H, 4.44; Ni, 16.17; N, 15.43; O, 17.63.

III. Result And Discussion

Initially the ligand HL, **3** was synthesized by carrying the condensation reaction of pyrazole-3-carbohydrazide (**2**) with 2-hydroxy-4-methoxy benzaldehyde (**1**) in ethanol under reflux condition for 5 h. according to literature [43]. When we carried the same reaction using 100 % ethyl lactate using microwave irradiation it gave a good result, as compared to conventional methods. (Table-1). In addition, the polarity of the solvent was tuned by using water as a co-solvent with ethyl lactate in different percentages. It observed that 70 % ethyl lactate in water produced the more polar solvent in which the product obtained in a shorter time with better yield (Table 2). Ethyl lactate: water solvent system attributes more polar a reaction mixture, has greater ability to couple with the microwave energy and accelerate the rate of reaction compared with conventional heating. Therefore, this method can be considered as an ideal tool for efficient green synthesis of schiff base ligand

Table 1 Optimization of reaction conditions of Schiff base ligands (**3**)

Entry	Solvent	Synthetic methods	Time	Yield (%) ^a
1	Ethanol	Conventional	3 h	65
2	100 % Ethyl lactate	Microwave	4 m	70

^a Isolated yield

Table 2 Effect of solvent polarity on the yield for the synthesis of Schiff base ligands (**3**)

Entry	Solvent System	Synthetic Method ^b	Time (m)	Yield (%) ^a
1	100 % Ethyl lactate	M W	4	70
2	70 % Ethyl lactate in water	M W	4	92
3	40 % Ethyl lactate in water	M W	4	75
4	20 % Ethyl lactate in water	M W	4	70

^aIsolated yield, ^bAll the reactions were carried out under microwave condition

The synthesized ligand (**3**) used for the formation of metal complexes (**4a-4e**). Initially complexes were synthesized by refluxing the mixture of metal nitrate and ligand in 1 :1 and 1 : 2 molar proportion in methanol for 3 h it gives moderate yields. When the same complexation reaction was carried under microwave conditions, it was observed that an increased rate of reaction with better yields as compared to conventional methods (**Table 3**). This is because it provides homogeneity of the medium which results in shorter reaction times and increased yields.

Table 4 Optimization condition of metal complexes. (**4a-e**)

Entry	Compound	Conventional			Microwave		
		Solvent	Time (h) ^a	Yield (%)	Solvent	Time (min) ^b	Yield (%)
4a	[Fe(C ₁₄ H ₁₅ N ₄ O ₃) ₂]	Methanol	3	67	Methanol	5	80
4b	[Zn(C ₁₄ H ₁₄ N ₄ O ₃) ₂]	Methanol	3	71	Methanol	5	83
4c	[Cu(C ₁₄ H ₁₅ N ₄ O ₃) ₂]	Methanol	3	69	Methanol	5	82
4d	[Co(C ₁₄ H ₁₅ N ₄ O ₃) ₂]	Methanol	3	70	Methanol	5	83
4e	[Ni(C ₁₄ H ₁₇ O ₄ N ₄)]	Methanol	2	71	Methanol	4	82

^aReaction carried under conventional heating. ^bReaction carried under microwave irradiation

The structure of the ligand and their metal complexes were confirmed on the basis of spectroscopic technique such as FT-IR, ¹HNMR, ¹³CNMR, Mass and UV-Vis spectroscopy. TGA-DTA and elemental analyses also performed for synthesized compounds. The elemental analysis and physical data of prepared compounds are shown in **Table 5**.

Table-5 Physical and Analytical data of Ligand HL (**3**) and Complexes (**3 & 4a-e**)

Compound	M. W.	Color	MPs (°C)	Elemental analysis (%) Calcd. (Found)				
				C	H	N	M	O
C ₁₄ H ₁₆ N ₄ O ₃ (3)	288.0	Yellow	283	58.32 (58.95)	5.59 (5.96)	19.43 (18.93)	---	16.65 (15.80)
[Fe(C ₁₄ H ₁₅ N ₄ O ₃) ₂] (4a)	630.4	Black	≥ 300	53.34 (52.85)	4.80 (3.98)	17.77 (18.15)	7.89 (8.86)	15.23 (15.85)
[Zn(C ₁₄ H ₁₄ N ₄ O ₃) ₂] (4b)	638.0	Yellow	≥ 300	52.71 (53.20)	4.42 (4.90)	17.56 (18.09)	10.25 (11.10)	15.05 (14.81)
[Cu(C ₁₄ H ₁₅ N ₄ O ₃) ₂] (4c)	638.1	Green	≥ 300	52.70 (52.10)	4.74 (4.10)	17.56 (16.90)	9.96 (10.25)	15.04 (14.88)
[Co(C ₁₄ H ₁₅ N ₄ O ₃) ₂] (4d)	633.5	Brown	≥ 300	53.08 (52.85)	4.77 (4.10)	17.69 (17.10)	9.30 (10.10)	15.15 (14.90)
[Ni(C ₁₄ H ₁₇ O ₄ N ₄)] (4e)	363.0	Orange	≥ 300	46.30 (45.78)	4.44 (3.98)	15.43 (14.22)	16.17 (16.73)	17.63 (18.15)

IR Spectra

IR spectra of the free ligand HL exhibited IR bands at 3361, 3206 and 1656 cm⁻¹ for ν(O-H) hydroxyl proton, ν(N-H) of pyrazole carbohydrazide and ν(C=O) group of the pyrazole carbohydrazide respectively. The IR band at 1603 cm⁻¹ attributed by azomethine ν(C=N) [44]. In all complexes (4a-e) absence of IR band for ν(O-H) indicates deprotonation, the disappearance of the signal due to the involvement of phenolic OH in the coordination sphere with the corresponding metal ions [45]. The stretching frequencies of ν(C=O) in all metal complexes shifted to lower wave numbers in the region of 1606-1621. This confirmed the oxygen atom of the carbonyl involved in the coordination [46]. The characteristic band ν(C=N) in all complexes were found to be shifted to a lower wavelength number compared to the ligand HL, these bands appeared in the region of 1603–1563 cm⁻¹. This signifying coordination of the azomethine nitrogen to the central metal ions [47]. In complexes Fe(II), Cu(II) and Co(II) hydrazide N-H bands appeared at 3200, 3202 and 3201 respectively, whereas disappearance of ν(N-H) observed in Ni(II) and Zn(II) complexes, it is due to enolisation and followed by deprotonation [48]. The presence of broad bands in the Ni (II) complex appeared at 3308 cm⁻¹ indicated the presence of water molecules [49]. The IR bands at 502-561 cm⁻¹ and 472-478 cm⁻¹ in the complexes are assignable to ν(M-N) and ν(M-O) indication to the coordination between the metal ions with oxygen and nitrogen atoms, respectively [50-52].

Table 6 FT-IR data of Ligand HL (**3**) Complexes (**3 & 4a-e**)

Compound	Molecular formula [Empirical formula]	Ph-OH	-N-H	C=O	-C=N	M-N	M-O	H ₂ O
3	C ₁₄ H ₁₆ N ₄ O ₃	3361 cm ⁻¹	3206 cm ⁻¹	1656 cm ⁻¹	1603 cm ⁻¹	-----	-----	
4a	C ₂₈ H ₃₀ FeN ₈ O ₆ [Fe(C ₁₄ H ₁₅ N ₄ O ₃) ₂]	-----	3200 cm ⁻¹	1621 cm ⁻¹	1603 cm ⁻¹	502 cm ⁻¹	472 cm ⁻¹	
4b	C ₂₈ H ₂₈ N ₈ O ₆ Zn [Zn(C ₁₄ H ₁₄ N ₄ O ₃) ₂]	-----	-----	1621 cm ⁻¹	1580 cm ⁻¹	555 cm ⁻¹	478 cm ⁻¹	
4c	C ₂₈ H ₃₀ CuN ₈ O ₆ [Cu(C ₁₄ H ₁₅ N ₄ O ₃) ₂]	-----	3202 cm ⁻¹	1616 cm ⁻¹	1548 cm ⁻¹	560 cm ⁻¹	477 cm ⁻¹	
4d	C ₂₈ H ₃₀ CoN ₈ O ₆ [Co(C ₁₄ H ₁₅ N ₄ O ₃) ₂]	-----	3201 cm ⁻¹	1606 cm ⁻¹	1558 cm ⁻¹	558 cm ⁻¹	475 cm ⁻¹	
4e	C ₁₄ H ₁₆ N ₄ NiO ₄ [Ni(C ₁₄ H ₁₇ O ₄ N ₄)]	-----	-----	1619 cm ⁻¹	1563 cm ⁻¹	561 cm ⁻¹	476 cm ⁻¹	3308 cm ⁻¹

¹H-NMR Spectra

In ¹H NMR spectrum of the schiff base, HL. The characteristic signal of the O-H group proton appeared at δ 13.88 (1H, s). The proton of the CONH were observed at δ 12.40 (1H, s), pyrazoline N-H proton appeared at δ 10.58 (1H, s), whereas signal at δ 8.44 (1H, s) attributed by azomethine proton (HC=N). Aromatic protons were resonated in the region δ 6.88-δ 7.99, methoxy protons at δ 3.32 (3H, s) and methyl protons of CH₃ appeared at δ 2.96. The spectrum of the complexes differs from that of the free ligands as explained. In all metal complexes absence of OH signal in ¹H-NMR spectra is attributed by the enolisation and followed by deprotonation during complexation. This result confirmed involvement of oxygen of OH group in coordination sphere with the corresponding metal ions [53, 54] ¹H NMR spectrum of the complex: Fe(II) displayed singlet signals at δ 12.07 which could be attributed by the proton of an amide nitrogen. Whereas The disappearance signal of amide proton observed in complexes Zn(II) and Ni (II), which represents that the ligand coordinated with the metal ion in the enolic form. This may be due to the donation of the lone pair of electrons from O-N-O to the central metal atom resulting in the formation of a coordinated bond [55, 56]. The pyrazoline NH proton appeared at the region of δ 8.45- δ 9.72 in all complexes, suggesting azomethine group coordinated with metal ions [57]. The ¹HNR signal

of methyl and methoxy group in all complexes appeared in the region of δ 2.97-2.98 and δ 3.42-3.77 respectively. According to all spectral data following structure of ligands and their metal complexes are confirmed.

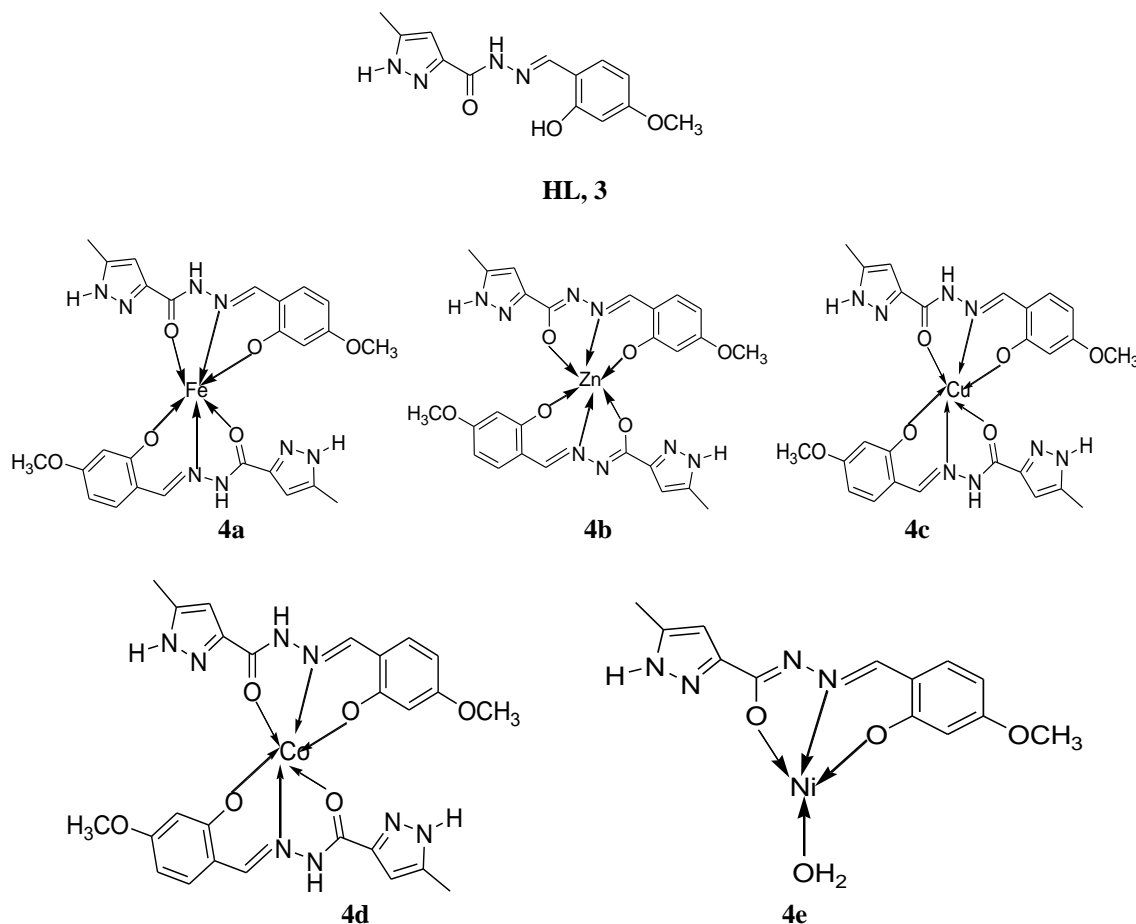


Fig.1. Structure of ligand, HL (3) and metal complexes (4a-e)

UV-Visible Spectra

The electronic absorption spectrum of the free Schiff base ligand was deliberate in DMSO solvent from 200 nm to 900 nm at room temperature. In the UV-Visible absorption spectra of Schiff base ligands, it was possible to observe two sets of bands resultant to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of both the carbonyl moiety and imine bonds, present in the molecules [58]. The electronic spectrum of the free ligand shows a band at 345 nm recognized to the $n \rightarrow \pi^*$ transition of the azomethine group. There is a strong band at 277 nm due to a $\pi \rightarrow \pi^*$ transition [59]. The electronic spectrum of the Ni(II) complex shows two bands in the regions 261, 335 nm, respectively, which can be assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ and 413 nm this band assigned due to the LMCT transition [60] and predictable to ${}^3T_1(F) \rightarrow {}^3T_1(P)$, ${}^3T_1(F) \rightarrow {}^3A_2(F)$, and ${}^3T_1(F) \rightarrow {}^3T_2(F)$ transitions respectively.

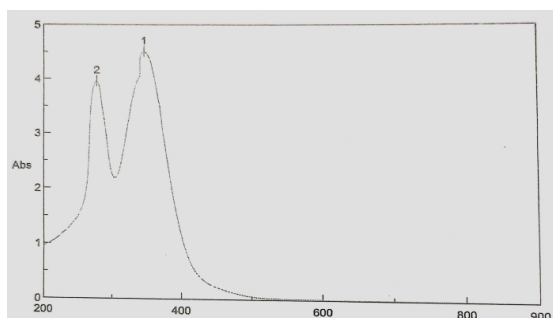


Fig. 2. UV spectra of HL,3

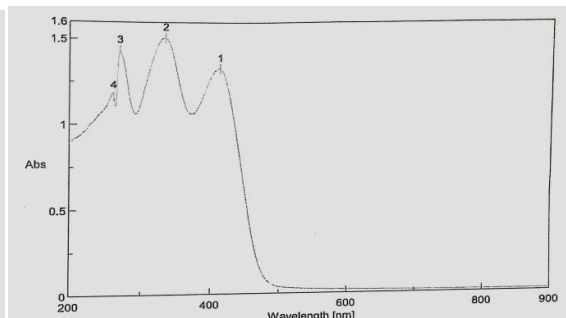


Fig. 3. UV spectra of Ni (II) complex

Thermal Analysis

The thermal performances of the synthesized complexes were analyzed using TG and DTA techniques in a temperature series, 25–900°C under a controlled heating rate and were determining the lattice and coordinated water content in complexes. TG-DTA of the Fe(II), Zn(II), Cu(II), Co(II) and Ni(II) complexes were carried out to study thermal potency, disintegration manners and showed equivalent patterns of thermal decomposition. It is clear that all the metal complexes undergo thermal decay within three or four steps. Within the Ni(II) complexes, Figure 4 illustrates three breakdown stages occurring within the temperature range of 190–760°C. The initial phase is characterized by the removal of a single coordinated water molecule at temperatures around 240°C. The subsequent stage involves the partial loss of the ligand within the temperature range of 370–380°C. Finally, the third phase entails the complete detachment of the ligand at temperatures exceeding 620°C, followed by an oxidation reaction leading to the creation of metal oxide.

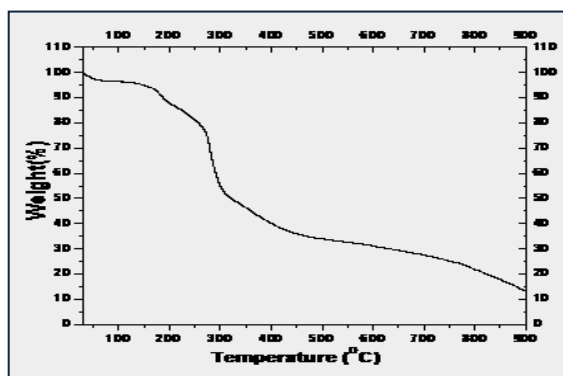


Fig. 4. TGA-DTA Of Ni (II) Complex

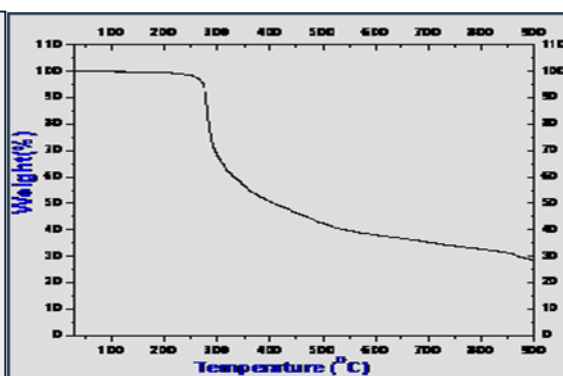


Fig. 5. TGA-DTA Of Zn (II) Complex

IV. Conclusions

The synthesis of Fe(II), Zn(II), Cu(II), Co(II) and Ni(II) was performed by conventional as well as using microwave techniques. The reported microwave method has more advantages compared to conventional methods including clean reaction conditions, shorter reaction time with high yields. The key intermediate Schiff base ligands were also prepared by efficient and eco-friendly synthetic protocol. Herein the rate of formation for ligand accelerated by microwave using bio based greener reaction media, ethyl lactate. This method offers unique features such as reaction complete within a short time, inexpensive and non-toxic green solvent and gives excellent yield of the desired products with simple and easy reaction conditions and workup process. The synthesized ligand (HL) and their metal complexes characterized by spectroscopic technique and the structure of synthesized compounds are well in agreement with all spectral data.

Acknowledgement

The authors are thankful to The Principal, S. V. Sr. College, Mantha and The Principal Davgari College, Aurangabad for providing facilities for research work. Authors are also thankful to The Director, SAIF-RSIC, Panjab University, Chandigarh, India for spectral analyses.

References

- [1] Petering Hg, Buskirk Hh, Crim Ja, The Effect Of Dietary Mineral Supplements Of The Rat On The Antitumor Activity Of 3-Ethoxy-2-Oxobutyraldehyde Bis(Thiosemicarbazone). *Cancer Res* 1967; 27 (6_Part_1): 1115–1121.
- [2] Sartorelli Ac, Agrawal Kc, Tsiftoglou As, Moore Ec, Characterization Of The Biochemical Mechanism Of Action Of A-(N)-Heterocyclic Carboxaldehyde Thiosemicarbazones. *Advances In Enzyme Regulation*. 1977;15:117-139. Doi: [https://doi.org/10.1016/0065-2571\(77\)90012-7](https://doi.org/10.1016/0065-2571(77)90012-7)
- [3] White J, Streptonigrin-Transition Metal Complexes: Binding To Dna And Biological Activity. *Biochemical And Biophysical Research Communications*. 1977;77(1):387-391. [https://doi.org/10.1016/S0006-291x\(77\)80209-X](https://doi.org/10.1016/S0006-291x(77)80209-X)
- [4] Gianni L., Corden Bj, Myers Ce, The Biochemical Basis Of Anthracycline Toxicity And Antitumor Activity, In: E. Hodgson, J.R. Bend, R.M. Philpot (Eds.), *Reviews In Biochemical Toxicology*, Vol.5, Elsevier, Newyork, 1983;1-28.
- [5] Huang Zx, May Pm, Quinlan Km, Metal Binding By Pharmaceuticals. Part 2. Interactions Of Ca(Ii), Cu(Ii), Fe(Ii), Mg(Ii), Mn(Ii) And Zn(Ii) With The Intracellular Hydrolysis Products Of The Antitumor Agent Icrf 159 And Its Inactive Homologue Icrf 192. *Agents And Actions*. 1982; 12:536–542. <https://doi.org/10.1007/Bf01965940>
- [6] Howard Ra, Sherwood E, Erck A, Kimball Ap, Bear JI, Hydrophobicity Of Several Rhodium(Ii) Carboxylates Correlated With Their Biologic Activity. *Journal Of Medicinal Chemistry*. 1977;20(7):943–946. Doi:10.1021/Jm00217a016
- [7] Sinn E, Harris Cm, Schiff Base Metal Complexes As Ligands, *Coordination Chemistry Reviews*. 1969;4(4):391-422. Doi:10.1016/S0010-8545(00)80080-6
- [8] Fei Bl, Sun Wy, Zhang Ya, Yu Kb, & Tang Wx, Synthesis And Crystal Structure Of An Infinite One-Dimensional Chain Containing A Poly-Metallocege Of Mnii With 4,4'-Bis(Imidazol-1-Yl)methyl) Biphenyl. *Journal Of The Chemical Society, Dalton Transactions*, 2000;(14):2345–2348. Doi:10.1039/B002692I

- [9] (A) Davies Mb, Cobalt 1994. Coordination Chemistry Reviews, 1997;(164):27–160. Doi:10.1016/S0010-8545(97)00027-1 (B) Smith, D, Copper 1996, Coordination Chemistry Reviews, 1998;172(1):457–573. Doi:10.1016/S0010-8545(98)00098-8
- [10] Zishen W, Zhiping L & Zhenhuan Y, Synthesis, Characterization And Antifungal Activity Of Glycylglycine Schiff Base Complexes Of 3d Transition Metal Ions. Transition Met Chem, 1993;(18):291–294. <https://doi.org/10.1007/Bf00207949>
- [11] Skipper He, Robins Rk, Thomson Jr, Cheng Cc, Brockman Rw, Schabel Jr. Fm, Structure-Activity Relationships Observed On Screening A Series Of Pyrazolopyrimidines Against Experimental Neoplasms. Cancer Res. 1957;17:579.
- [12] French Fa, Blanz Jr. Ej, Amaral Jr. Do, French, Jda, Carcinostatic Activity Of Thiosemicarbazones Of Formyl Heteroaromatic Compounds. Vi. 1-Formylisoquinoline Derivatives Bearing Additional Ring Substituents, With Notes On Mechanism Of Action. J. Med. Chem. 1970;13(6):1117–1124.
- [13] Cory Jh, Fleischeher Ae, Specific Inhibitors Directed At The Individual Components Of Ribonucleotide Reductase As An Approach To Combination Chemotherapy. Cancer Res. 1979; 39:4600.
- [14] Rice Wg, Turpin Ja, Schaeffer Ca, Graham L, Clanton D, Buckheit Rw, Covell D G, Evaluation Of Selected Chemotypes In Coupled Cellular And Molecular Target-Based Screens Identifies Novel Hiv-1 Zinc Finger Inhibitors. Journal Of Medicinal Chemistry, 1996; 39(19):3606–3616. <https://doi.org/10.1021/Jm960375o>
- [15] Otsuka M, Fujita M, Sugiura Y, Ishii S, Aoki T, Yamamoto T, & Inoue J, Novel Zinc Chelators Which Inhibit The Binding Of Hiv-Ep1 (Hiv Enhancer Binding Protein) To Nf-Kappa.B Recognition Sequence. Journal Of Medicinal Chemistry, 1994;37(25):4267–4269. Doi:10.1021/Jm00051a002
- [16] Torayama H, Nishide T, Asada H, Fujiwara M, & Matsushita T, Preparation And Characterization Of Novel Cyclic Tetranuclear Manganese (Iii) Complexes: Mniii4(X-Salmphen)6 (X-Salmphen2 = N,N'-Di-Substituted-Salicylidene-1,3-Diaminobenzene (X = H, 5-Br). Polyhedron, 1997;16(21):3787–3794. [https://doi.org/10.1016/S0277-5387\(97\)00148-4](https://doi.org/10.1016/S0277-5387(97)00148-4)
- [17] Sakai K, Tomita Y, Ue T, Goshima K, Ohminato M, Tsubomura T, Kawakami K, Syntheses, Antitumor Activity, And Molecular Mechanics Studies Of Cis-Ptcl2(Pzh)2 (Pzh=Pyrazole) And Related Complexes. Crystal Structure Of A Novel Magnus-Type Double-Salt [Pt(Pzh)4][Ptcl4][Cis-Ptcl2(Pzh)2]2 Involving Two Perpendicularly Aligned 1d Chains. Inorganica Chimica Acta, 2000;297(1-2):64–71. Doi:10.1016/S0020-1693(99)00287-X
- [18] Broomhead Ja, Rendina Lm, & Webster Lk, Dinuclear Complexes Of Platinum Having Anticancer Properties. Dna-Binding Studies And Biological Activity Of Bis(4,4'-Dipyrazolymethane-N,N')-Bis[Dichloroplatinum(Ii) And Related Complexes. Journal Of Inorganic Biochemistry, 1993;49(3):221–234. Doi:10.1016/0162-0134(93)80007-V
- [19] Broomhead Ja, & Lynch Mj, The Synthesis And Characterization Of Dinuclear Platinum Complexes Bridged By The 4,4'-Dipyrazolymethane Ligand. Inorganica Chimica Acta, 1995;240(1-2):13–17. Doi:10.1016/0020-1693(95)04644-5
- [20] Onoa Gb, Morenouv, Font-Bardia M, Solans X, Perez Jm, Alonso C, Structural And Cytotoxic Study Of New Pt(Ii) And Pd(Ii) Complexes With The Bi-Heterocyclic Ligand Mepirizole. Journal Of Inorganic Biochemistry, 1999;75(3):205–212. Doi:10.1016/S0162-0134(99)00089-6
- [21] Pons J, Ros J, Llagostera M, Perez Ja, Ferrer M, Spanish Patent No. 01494, 2003.
- [22] Baraldi Pg, Beria I, Cozzi P, Geroni C, Espinosa A, Gallo Ma, Romagnoli, R., Cinnamoyl Nitrogen Mustard Derivatives Of Pyrazole Analogues Of Tallimustine Modified At The Amidino Moiety: Design, Synthesis, Molecular Modeling And Antitumor Activity Studies. Bioorganic & Medicinal Chemistry, 2004;12(14):3911–3921. Doi: 10.1016/J.Bmc.2004.04.045
- [23] Xia Y, Dongb Zw, Zhao Bx, Ge X, Meng N, Shin Ds, & Miao Jy, Synthesis And Structure–Activity Relationships Of Novel 1-Arylmethyl-3-Aryl-1h-Pyrazole-5-Carbohydrazide Derivatives As Potential Agents Against A549 Lung Cancer Cells. Bioorganic & Medicinal Chemistry, 2007;15(22):6893–6899. Doi: 10.1016/J.Bmc.2007.08.021
- [24] Bandgar Bp, Gawande Ss, Bodade Rg, Gawande Nm, & Khobragade Cn, Synthesis And Biological Evaluation Of A Novel Series Of Pyrazole Chalcones As Anti-Inflammatory, Antioxidant And Antimicrobial Agents. Bioorganic & Medicinal Chemistry, 2009;17(24):8168–8173. Doi: 10.1016/J.Bmc.2009.10.035
- [25] Sridhar R, Perumal Pt, Etti S, Shanmugam G, Ponnuswamy Mn, Prabavathy Vr, & Mathivanan N, Design, Synthesis And Anti-Microbial Activity Of 1h-Pyrazole Carboxylates. Bioorganic & Medicinal Chemistry Letters, 2004;14(24):6035–6040. Doi: 10.1016/J.Bmcl.2004.09.066
- [26] Bekhit Aa, Ashour Hma, Abdel Ghany Ys, Bekhit Aeda, & Baraka A, Synthesis And Biological Evaluation Of Some Thiazolyl And Thiadiazolyl Derivatives Of 1h-Pyrazole As Anti-Inflammatory Antimicrobial Agents. European Journal Of Medicinal Chemistry, 2008;43(3):456–463. Doi: 10.1016/J.Ejmech.2007.03.030
- [27] Constable Ec, Steel Pj, N,N'-Chelating Biheteroaromatic Ligands; A Survey. Coordination Chemistry Reviews, 1989;93(2):205–223. Doi:10.1016/0010-8545(89)80016-5
- [28] Reedijk J, In Wilkinson G, Gillard Rd And Mccleverty Ja (Eds), Comprehensive Coordination Chemistry, Pergamon, Oxford, 1987;2:73.
- [29] Cetin A, Kurt H, Synthesis, Antibacterial Activity And Molecular Docking Studies Of New Pyrazole Derivatives. Lett. Drug Des. Discov. 2020; 17:745–756. <http://dx.doi.org/10.2174/1570180816666190905155510>
- [30] Karrouchi K, Radi S, Ramli Y, Taoufik J, Mabkhot Y, Al-Aizarfi F, Ansar M, Synthesis And Pharmacological Activities Of Pyrazole Derivatives: A Review. Molecules 2018; 23:134. <https://doi.org/10.3390/molecules23010134>
- [31] Rajput A, & Mukherjee R, Coordination Chemistry With Pyridine/Pyrazine Amide Ligands. Some Noteworthy Results. Coordination Chemistry Reviews, 2013;257(2):350–368. Doi: 10.1016/J.Ccr.2012.03.024
- [32] Bargujar S, Ratnani S, Jain R, Recent Advances In Microwave Assisted Synthesis Of Schiff Base Metal Complexes. Inorganic Chemistry Communications, 2024;162:112250. <https://doi.org/10.1016/J.Inoche.2024.112250>
- [33] Jain A, De S, Barman P, Microwave-Assisted Synthesis And Notable Applications Of Schiff-Base And Metal Complexes: A Comparative Study, Research On Chemical Intermediates, 2022;48(5):2199-2251. <http://dx.doi.org/10.1007/S11164-022-04708-7>
- [34] Hassan Am, Heakal Bh, Khamis H, El-Naeem G, Marzouk E, Abdelmoaz Ma, And Younis A, Design, Synthesis, Dft Studiesand Anticancer Activity Of Novel Metal Complexes Containing 1,3,5-Triazino[1,2-A]Benzimidazole Moiety Using Microwave As An Approach For Green Chemistry. Egypt. J. Chem., 2021, 64;(1):323-340. 10.21608/Ejchem.2020.29618.2639
- [35] Hassan Am, Heakal Bh, Said Ao, Aboulth Wm, And Abdelmoaz Ma, Comparative Study For Synthesis Of Novel Mn (Ii), Co (Ii), Ni (Ii), Cu (Ii), Zn (Ii) And Zr (Iv) Complexes Under Conventional Methods And Microwave Irradiation And Evaluation Of Their Antimicrobial And Anticancer Activity. Egypt. J. Chem., 2020;63(7):2533-2550. <https://doi.org/10.21608/Ejchem.2020.21048.2255>
- [36] Jain Rk, And Mishra Ap, Microwave Synthesis, Spectral, Thermal, And Antimicrobial Activities Of Some Transition Metal Complexes Involving 5-Bromosalicylaldehyde Moiety. Current Chemistry Letters, 2012;1:163-174. Doi: 10.5267/J.Ccl.2012.7.003