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Research paper

Green Synthesis and Antimicrobial Studies of Ni(II) and Zn(II) Dinuclear Schiff Base Complexes

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Abstract

A series of tetradentate Zn(II) and Ni(II) Schiff base complexes derived from N,N-Bis-(2-hydroxyl-5-methoxybenzaldehyde)-m-phenylenediamine was synthesized using microwave assisted synthesis approach for 5-15 minutes. The confirmation of the ligand as well the respective complexes has been elucidated through physiochemical and spectroscopy analyses. The studies show that two metal ions formed bridges connecting two Schiff base ligands. The nitrogen and oxygen atoms in each ligand served as coordination sites for the metal ions. The Schiff base ligand and complexes were screened for antimicrobial properties using Disc diffusion method against Escherichia coli, Bacillus subtilis, Enterobacter cloacae, and Klebsiella pneumoniae. The screening shows that both Zn(II) and Ni(II) complexes give signif-icant inhibition towards the bacteria tested.

Keywords: *Antimicrobial activities; Dinuclear; Metal complex; Microwave assisted synthesis; Schiff base.*

1. Introduction

Microwave assisted synthesis has now becoming the new non-conventional method in organic and inorganic synthesis, replacing the classical reflux that proves to be eco-friendly, clean and conven-ient [1]. The uses of microwave irradiation as heat source not only shorten the reaction time but also enhanced product yield as well as enhanced the purities by reducing unnecessary side reaction [2].

The condensation reaction of primary amines with active carbonyl compounds led to the formation of Schiff bases compounds. Schiff base compounds are considered as "privileged ligand" by many due to its stability and structural design [3]. The azomethine (C=N) group found in Schiff base compound are known to be biological active. Thus, it received significant attention in chemistry and biolo-gy for it various application such as antitumor [4], antifungal [5] and antimicrobial [6], [7].

Schiff base derived from diamine compound are valuable precursors for multinuclear complexes. The condensation between phenylenediamine with salicylaldehyde, resulting in the formation of N2O2 donor-type ligand. This type of ligand is interesting because of its capability to coordinate with either one or more metal ion, depending on the positional relation between two amino groups in precursor [8].

The current research work describes the synthesis of Ni(II) and Zn(II) Schiff base complexes using microwave irradiation. The ligand and its complexes were characterized using physiochemical and spectroscopic technique. All compound undergoes antimicrobial screening against *Escherichia coli*, *Bacillus subtilis*, *Enterobacter cloacae*, and *Klebsiella pneumoniae*.

2. Experimental

2.1 General

The chemicals used in this investigation were of analytical grade. 2-hydroxyl-5-methoxybenzaldehyde, *m*-phenylenediamine (MPD), nickel(II) acetate tetrahydrate, and ninc(II) acetate dihydrate, were purchased from Sigma Aldrich without any further purification. The reactions were carried out using Anton Paar Monowave 450 in G30 boron silicate vials. Elemental microanalysis (carbon, hydrogen and nitrogen) were performed on a Thermo Flash EA 110 Elemental Analyzer. Molar conductance of the complexes was recorded in acetonitrile at room temperature using Mettler Toledo 730 Series conductivity meter. Melting points were measured with a *Stuart* Melting Point SMP10 The IR spectra were recorded as KBr discs in the range of 4000-400 cm^{-1} using Perkin-Elmer FT-IR 1600 spectrometer .^{1}H NMR spectra were recorded on Bruker Avance 300 MHz dissolved in DMSO-d6. NMR spectrometer.

2.2 Synthesis of N, N-Bis-(2-hydroxyl-5-methoxy benzaldehyde)-*m*-phenylenediamine, (HLa)

The Schiff base ligand HLa was synthesized by condensation of 2:1 ratio of 2-hydroxy-5-methoxybenzaldehyde (10mmol) with m-phenylenediamine (5mmol) in 10mL methanol. The reaction mixture was heated in the microwave reactor at 150ºC for 5 minutes. Reddish-orange precipitates were filtered off and washed several times using cold methanol. The precipitate was then dried over anhydrous silica gel. Yield: 1.83g, 97%. m.p: 140ºC. Anal. Calcd for $C_{22}H_{20}N_2O_4$ (%): C, 70.20; H, 5.36; N,7.44. Found: C, 70.02; H, 5.55; N, 7.85. IR (λ max cm^{-1}) (KBr): 1617 (C=N), 1273 (C-O phenolic).

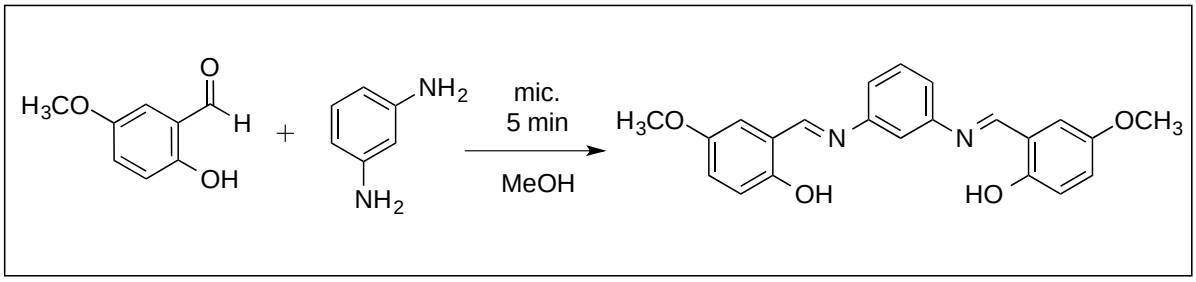

Fig. 1: Synthesis of HLa ligand

2.3 Synthesis of Ni(HLa)

The Ni(HLa) complex was prepared by the addition of 2mmol of $Ni(CH_3COO)_2 \cdot 4H_2O$ and free ligand HLa dissolved in about 10ml ethanol in molar ratio (1 : 1). The mixture was heated heated in the microwave reactor at 150°C for 15 minutes. Yellow precipitate was filtered and wash with cold methanol. The precipitate was then dried over anhydrous silica gel. Yield: 0.94g, 51%. m.p: >300°C. Anal. Calcd for $C_{46}H_{39}N_4Ni_2O_{10}$ (%): C, 59.72; H, 4.25; N,6.06. Found: C, 56.11; H, 4.46; N, 6.42. IR (λ max cm^{-1}) (KBr): 1605 (C=N), 1245 (C-O phenolic), 542 (M-N), 441 (M-O).

2.4 Synthesis of Zn(HLa)

Similar method above was used in preparing Zn(HLa) complex by replacing the metal salt to $Zn(CH_3COO)_2 \cdot 2H_2O$. Orange precipitate was collected and rinsed with cold ethanol. The precipitate was left dried over anhydrous silica gel. Yield: 1.05g, 59%. m.p: >300°C. Anal. Calcd for $C_{44}H_{36}N_4O_8Zn_2$ (%): C, 60.09; H, 4.13; N,6.37. Found: C, 60.23; H, 4.21; N, 7.20. IR (λ max cm^{-1}) (KBr): 1602 (C=N), 1242 (C-O phenolic), 525 (M-N), 425 (M-O).

2.5 Antibacterial test

Antibacterial test of pathogens was carried out by using the disc diffusion method [9]. The bacteria from stock culture were lightly inoculated into the Mueller Hinton Broth (MHB) and let grow overnight at 37°C in an ambient air incubator. The culture was diluted with new MHB in order to achieve optical density of 0.1 at wavelength of 625nm in the spectrophotometer. Later, a sterile cotton swab was dipped into the broth culture and inoculated on the Mueller Hinton Agar (MHA). Sterile paper discs with 6 mm diameter were placed on the agar at equal distance. Subsequently, 10 mL aliquot Ni(II) and Zn(II) complexes at concentration of 0.2M in DMSO were dispensed individually to each of the discs. The agar plate was incubated at 37°C overnight. For each plate, Gentamicin acted as positive control, while DMSO was used as negative control. The diameter of inhibition zone on the plate was recorded and measured in milimeter (mm).

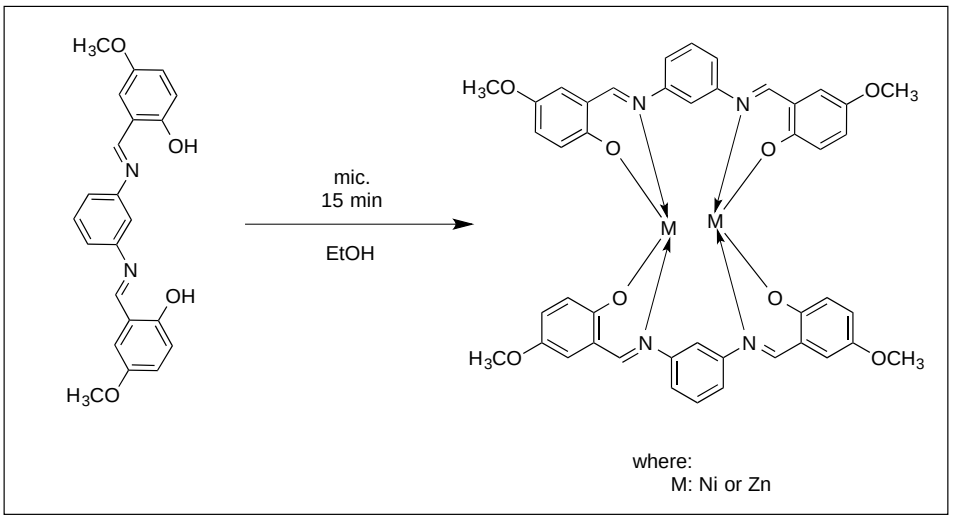

Fig. 2: Synthesis of Ni(II) and Zn(II) metal complex

3. Results and Discussion

3.1. Synthesis

Analytical data suggest a ratio of 1:1 (Metal:Ligand) for the dinuclear metal complexes. The synthesis of HLa ligand and its respective complexes using microware irradiation resulting in solid product that dissolves well in DMSO and DMF, but dissolves partially in chloroform. The molar conductivity corresponding to the Ni(II) and Zn(II) complexes presents low values suggesting a non-electrolyte complexes can be assigned [10].

3.2. Infrared spectra

The infrared spectra of the synthesized free HLa Schiff base ligand and its complexes were taken in range 4000 - 400 cm^{-1}. It reveals that the complexes show a sharp absorption peak of the ν(C=N) shifted 7 – 13 cm^{-1} to lower frequency than its parent ligand indicating the involvement of azomethine N in the complexation [11]–[13]. The ν (C-O) phenolic at 1273 cm^{-1} in ligand also shows a band shifting in the spectra of the complexes. This shifting frequency attributed to the deprotonation of phenolic due to coordination with the metal ions as a result of complexation. The involvement of azomethine N and phenolic O was further confirmed by the appearance of a new absorption peak of ν(M-N) and ν(M-O) stretching mode at range 525 – 542 and 424 – 441cm^{-1} respectively.

3.3. ^{1}H Nuclear Magnetic Resonance

The ^{1}H NMR data for HLa are characterized by four types of signal assigned to phenolic, azomethine, phenyl and methoxy proton. The peak indicating O-H, N=C-H, and OCH_3 signal was appeared at 12.35, 9.02 and 3.76 ppm, respectively. The hydroxyl proton was appeared as small singlet peak, while peak methoxy was appeared as sharp singlet peak. Multiplet peak of aromatic proton was observed to be at range 6.94-7.56 ppm. Upon complexation, the phenolic hydrogen peak was disappeared and the shifting of azomethine (C=NH) to upperfield region in Zn(II) complexes, indicates the coordination of metal ion took place at the phenolic and azomethine hydrogen once it was deprotonated[14]. N.i(HLa) was unable to be analyze using NMR spectroscopy due to its paramagnetic properties.

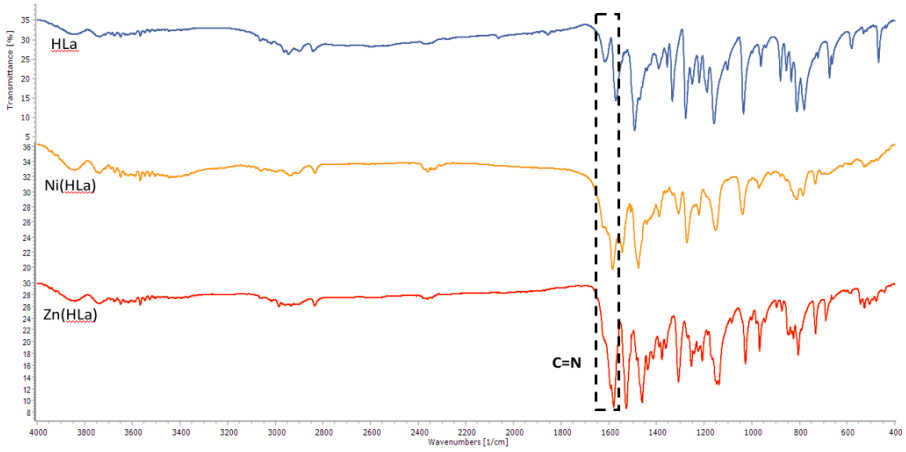

Fig. 3: The IR spectra of HLa ligand and its metal complexes

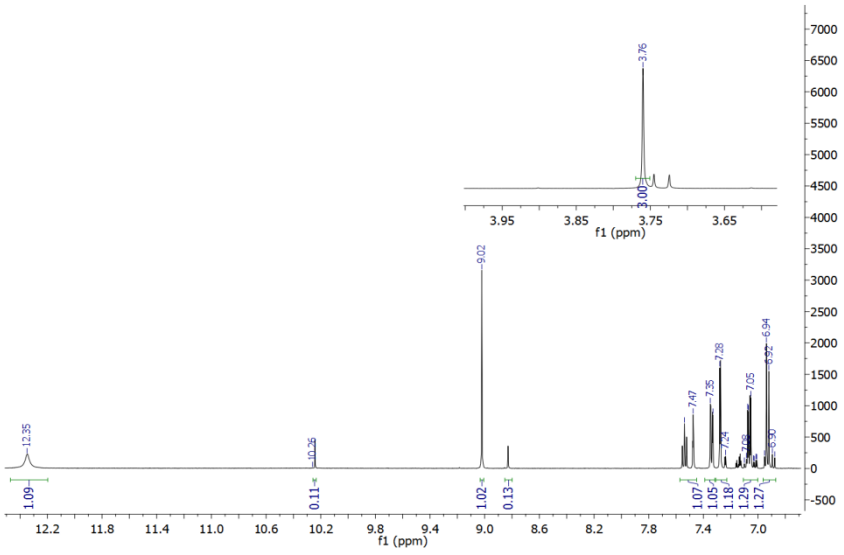

Fig. 4: ^{1}H NMR spectra of HLa ligand

3.4. Antibacterial Activities

Table 1: Relative diameter of inhibition zone of Escherichia coli, Bacillus subtilis, Enterobacter cloacae, and Klebsiella pneumoniae exhibit by ligands and their respective complexes

Sample	Diameter of inhibition (mm)			
	E. coli	B. subtilis	E. cloacae	K pneumoniae
HLa	-	-	-	-
Ni(HLa)	-	14	-	9
Zn(HLa)	-	16	-	11
Gentamicin (positive control)	26	18	21	24

Based on the screening result, the complexes showed higher antibacterial activities than the free ligands, although it only shows moderate activity against tested bacteria. Ni(HLa) and Zn(HLa) work best against *Bacillus subtilis*. This increased activity results from coordination and could be explained by Overtone's concept and Tweedy's theory [15], [16]. According to Overtone's concept of cell permeability, liposolubility is an important factor that governs the antimicrobial activity of antibacterial agents. Chelation reduces the polarity of the metal ions to a greater extent due to the overlap of the ligand orbitals and partial sharing of positive charge of metal atom with donor groups. Besides, it increases the delocalization of π electrons over the whole chelate ring and increases the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into the lipid membrane and increases their antibacterial activities.

4. Conclusion

5-methoxysalicylaldehyde (HL_a) Schiff base ligands and their respective Ni(II)and Zn(II) complexes were synthesized and characterized. Upon complexation, ligand HLa coordinates to a single metal ion while HLb coordinates to two metal ions. All complexes chelated via azomethine-N and phenolic-O of the ligands. The antibacterial screening shows that Ni(II) and Zn(II) complexes provide moderate inhibition towards *Klebsiella pneumoniae* and *Bacillus subtilis* respectively.

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