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Synthesis and Characterization of Zn(II) Schiff Complex Derived from Pyrazole

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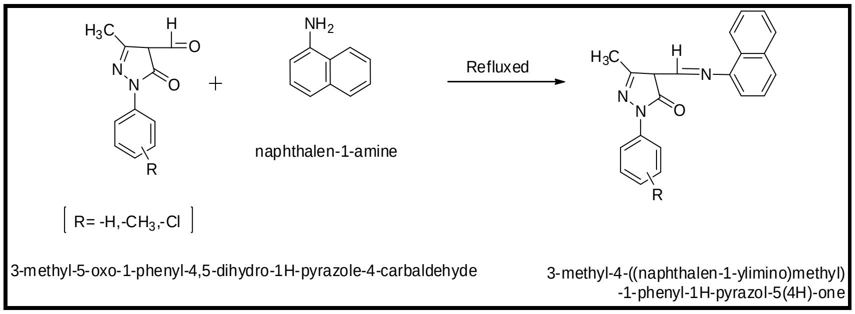
ABSTRACT

A series of novel Schiff base ligands and its Zn(II) coordination compounds were synthesized, characterized and evaluated for antibacterial and antioxidant activity. All the synthesized ligands and complexes were characterized by spectroscopic techniques and Electronic spectra. The in-vitro antimicrobial Schiff base complexes bear polar and nonpolar properties together; this makes them suitable for permeation to the cells and tissues, it enhances the activity against the bacteria and fungi. The antioxidant properties were measured with DPPH (1,1-diphenyl-2-picrylhydrazyl). These properties were due to the unique feature of ligands such as highest lipophilicity, lowest electron withdrawing power and highest polarizability.

Graphical Abstract



Synthesis of Schiff base ligands

Keywords: Schiff base pyrazolone, Zn(II) complexes, Antibacterial, Antioxidant.

INTRODUCTION

Research in chemistry-synthesis Schiff base and their metal complexes has attracted many attentions. Pyrazolone, as a prominent structural motif is found in numerous biologically active compounds. Typical pyrazole derivative are pyrazole -3-ones (pyrazolones) whose synthesis, reactivity and numerous application are well documented. Due to the trouble-free preparation and its rich biological activity of broad spectrum antibacterial action, antipyretic and analgesics, antitumor, anti-tuberculosis, antidepressant and anticonvulsant activities [**1**], pyrazolone and its complexes have both received considerable attention in coordination chemistry and medicinal chemistry [**2**].

However to very little has appeared on the antioxidant properties of Schiff base pyrazolone coordination compounds, and its suitability against bacteria and fungus. Many reports about the antioxidant and antimicrobial activity of antipyrine base derivatives.

Zinc have also a critically important metal for wide variety of cellular events, indeed no life form is possible without the presence of this element. Due to the large structural variability, biological importance and our interest in this area is focused for a considerable time on the investigation of coordination chemistry of transition metal with using pyrazolone based ligands [**3**], initiate us to design Zn (II) Schiff base complexes and evaluate systematically their antimicrobial and antioxidant activity [**4**]. The aim of this work is to evaluate and come across the suitability of these coordination compounds for antioxidant and antimicrobial activity [**5**]

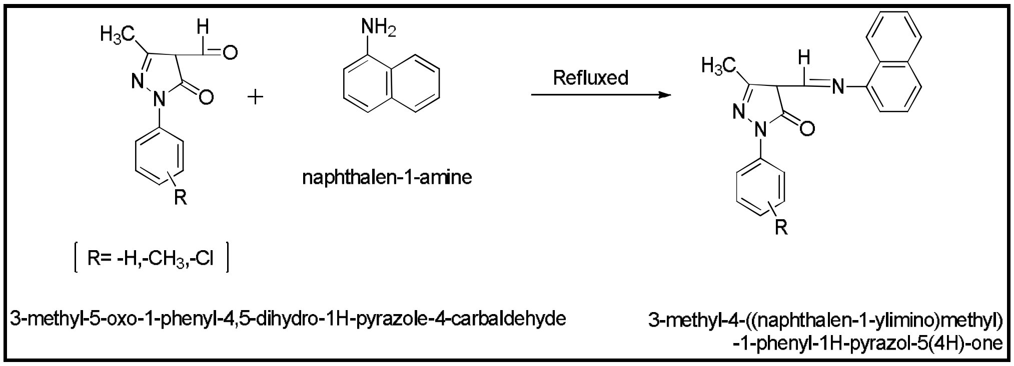
MATERIALS AND METHODS

The solvents were used after purification using the standard method described in literature. 1-Phenyl-3-methyl-2-pyrazoline-5-one (E-Merck); ethylenediamine (BDH); *o*-phenylenediamine (Aldrich) and $ZnCl_2 \cdot 6H_2O$, (Aldrich) were used as received.

Infrared spectra were recorded with a Perkin-Elmer IR spectrophotometer (4000-50 cm^{-1}) using KBr pellets. ^{1}H-NMR spectra of the compound was recorded with Bruker-400 using $CDCl_3$ as a solvent and TMS as an internal reference. Mass spectra (EI) obtained on a JEOL D-300 mass spectrometer, The FAB mass spectra were recorded on a JEOL SX 102 mass spectrometer using Argon/Xenon (6 kV, 10mA) as the FAB gas [**6-8**]. The accelerating voltage was 10 kV and the spectra were recorded at room temperature with using *m*-nitrobenzyl alcohol (NBA) as matrix. Electronic spectra in the 200–800 nm range were obtained in acetone on a “SHIMADZU” UV 160A using quartz cell of 1 cm^3. Magnetic measurements were carried out at room temperature by the Gouy method using $Hg[Co(SCN)_4]$ as calibrant. Molar conductance of the Schiff base complexes was determined on Systronics direct reading conductivity meter type CM - 82T. TGA was carried out on universal V3.0G TA instrument in the range 0–700°C at a heating rate of 10°C min^{-1} under nitrogen. DSC was carried out on universal V3.0G TA instrument in the range 0-300°C. The Mossbauer spectra were collected using a Cryophysics MS-1 microprocessor-controlled spectrometer operating in the constant acceleration mode [**9**]. The source was 25 mci- ^{57}Co/Rh and spectra were fitted using a standard non-linear least square package. X-ray structure analyses Powder diffraction diagrams were obtained on a Philips PW 1710 diffractometer (Cu/Ka; scan rate 1° min^{-1}) with a graphite monochromator.

Synthesis of Schiff base ligands: 1 mmol of PMP was dissolved in methanol solvent. This solution was added in a solution of 1mmol of 1-aminonapthalene in 50 mL, this reaction mixture was refluxed for 5 h. then cooling a crystalline compound was separated (Scheme 1). The compound was filtered and washed with water then dried in vacuum oven [**10**]. The suitable crystals for single crystal X-ray study were grown in ethyl acetate [**11, 12**].

LigandH_2L^1
(H17 PMP) L: Yield :81%, m.p.:160-162°C, ^{1}H NMR (DMSO, 400 MHz, MS): d 2.35(s, 3H), 7.16-7.20(t, 1H), 7.43-8.11(m, 11H), 8.90-8.93(d, 1H), 12.39-12.42(d, 1H), IR spectra (KBr, cm_1): 3749, 3063, 1651(C=O), 1497(C=N_{cyclic}, 1350, 1281, 748; EI-MS m/z: ---M+ (calculated = 327).

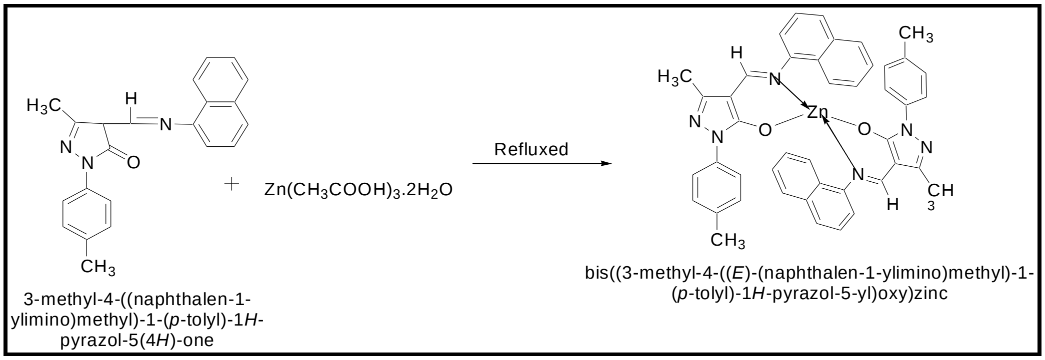


Scheme 1. Synthesis of Schiff base ligands

LigandH_2L^2

(H17 PM_PMP) L_2: Yield :81%, m.p.:155-157°C, ^{1}H NMR (DMSO, 400 MHz, MS): d 2.32(s, 3H), 2.33(s, 3H), 7.23-7.25(d,2H), 7.61-7.68(m, 2H), 7.74-7.79(m, 1H), 7.85-7.87(d, 1H), 7.91-7.93(m, 3H), 8.04-8.10(m, 2H), 8.87-8.90 (d, 1H), 12.40-12.43(d, 1H), IR spectra (KBr, cm_1): 3742, 3055, 1651(C=O), 1512(C=N_{cyclic}, 1342, 1288, 771; EI-MS m/z: --- M+ (calculated = 341).

Synthesis of Zn(II) Complexes: Complexes of Schiff bases were prepared by the following method. All the Zn(II) complexes of Schiff bases were prepared by the following method [13]. Metal salt (1.0 mmol) was dissolved in minimum amount of water and the solution was added to a hot methanolic solution of the corresponding Schiff base (2.0 mmol). The reaction mixture was refluxed for 5 h. A crystalline solid was formed which was filtered, washed with hot distilled water and then from ethanol and dried under vacuum [14].



RESULTS AND DISCUSSION

IR Spectra: H_2L^2 (H17 PM-PMP): 3-methyl-4-((naphthalen-1-ylimino)methyl)-1-(p-tolyl)-1H-pyrazol-5(4H)-one.

The infrared spectra of the ligand show a broad band in a region 3100-3600 cm^{-1}, which may be due to υ(OH). Free υ(OH) is generally observed in between 3500- 3600 cm^{-1}. The low value of this band is due to intermolecular or intramolecular H-bonding, which suggests the presence of keto-enol tautomeric form, at least in the solid state. The same is also inferred from its NMR signal at about δ~10.52 ppm due to an enolic proton. The phenyl group shows υ(CH) at 3060 cm^{-1} and υ (C=C) at 1540 cm^{-1}. The bands at ~1640, ~1594, and ~1300 cm^{-1} may be assigned to υ(C=N) (azomethine), υ(C=N) (pyrazoline ring), and υ(C–O), respectively.

The ligands as well as its corresponding complexes show absorptions in the regions 3000-2800 cm^{-1} which may be due to υ(C–H). The Schiff base ligand of the present study shows a strong band due to δ(O–H) in the region 1210-1270 cm^{-1}. Although all of the metal complexes show this band, its intensity is found to be lower than that of ligand. This may be due to the deprotonation of the 5-OH group of the ligand [15, 16]. All of the metal chelates show bands in the region 3100–3600 cm^{-1}, which may be due to the presence of water molecules. As shown by TGA of all the metal chelates, this band may be assigned to the one coordinated water molecules, which can be also inferred from bands at ~710 cm^{-1}, and may be due to the bending modes of vibrations of the water [17].

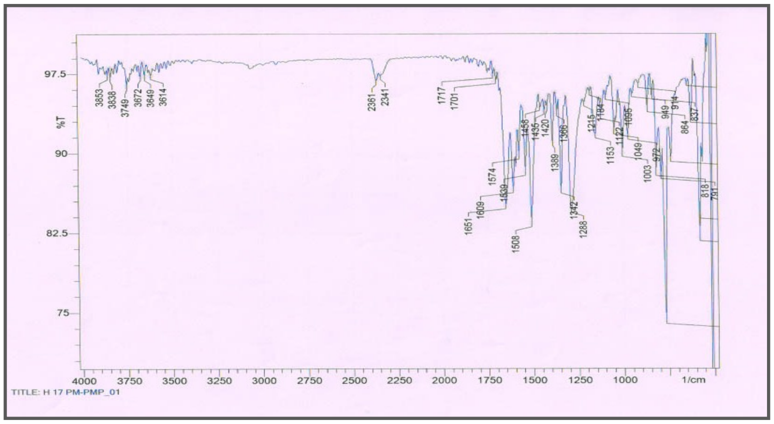


Figure 1. IR Spectra 3-methyl-4-((naphthalen-1-ylimino)methyl)-1-(p-tolyl)-1H-pyrazol-5(4H)-one.

A characteristic band of intermediate intensity is found at ~1300 cm^{-1}, which may be due to υ(C–O). On coordination, this band is shifted towards higher frequency indicating that the oxygen of the 5-OH group of the pyrazoline ring of the ligand has taken part in the coordination. The observed low-energy shift of υ(C=N) (azomethine) in the metal chelates suggests nitrogen coordination [18]. While υ(C=N) (cyclic) observed at the same energy in the chelates indicates the non-participation of the cyclic nitrogen in the coordination [19]. The Zn–N stretching vibration for complexes was observed at 258 cm^{-1}, and that for Zn–Cl is seen at 381 cm^{-1} in the anion species [20, 21]. The stretching vibrations of Zn–N in complexes are consistent with the high spin character of these complexes. Low spin frequencies for Zn–N appear around 50–70 cm^{-1} higher frequency to that of high spin complexes.

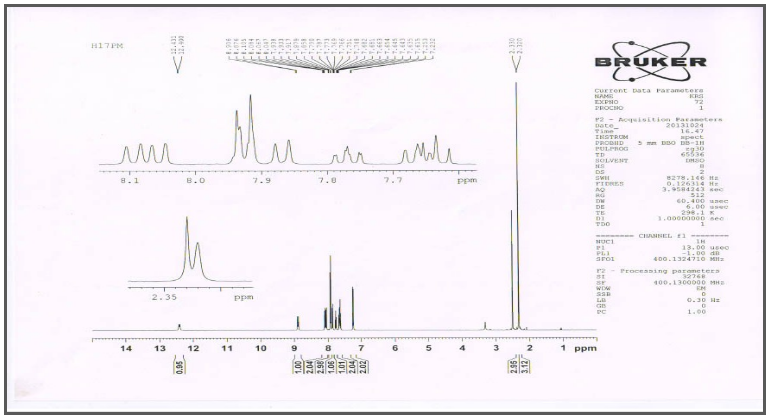


Figure 2. ^{1}H-NMR spectra of Schiff base ligands of H_2L^1 and H_2L^2.

^{1}H NMR:H_2L^2 (H17 PM- PMP): 3-methyl-4-((naphthalen-1-ylimino)methyl)-1-(p-tolyl)-1H-pyrazol-5(4H)-one.

The ^{1}H-NMR spectra of Schiff base ligands H_2L^1, H_2L^2 were carried out in DMSO-d_6 at room temperature (Fig 2). Ligands H_2L^1 and H_2L^2 show two singlet's with integration of six protons near the δ~2.35 and ~2.79 ppm for methyl group attached to pyrazolone ring and phenyl ring, respectively [22, 23]. Ligands H_2L^1 and H_2L^2 shows triplet at ~1.5 ppm for methylene proton of ethylenediamine. The enolic nature of all Schiff base ligand shows broad singlet at δ~10.52 ppm, due to rapid exchange interaction of keto-enol tautomerism. The sharp singlet at δ~8.91 ppm, observed due to aldehydic proton in all Schiff base ligand. The phenyl multiplet observed in the range of δ~7.31-7.98 ppm. From the NMR data it's observed that ligands shows keto-enol tautomerism.

APPLICATIONS

Antibacterial activity: In vitro activates of *B. subtillis* (MTCC-619), *S. aureus* (MTCC- 96), *E. coli* (MTCC-722) and *K. pneumonia* (MTCC-109) bacteria and the fungus *C. albicans* (ATCC-90028) were carried out for ligands and corresponding Zn(II) complexes [24]. The susceptibilities of certain strains of bacteria and a fungus to the ligands and their corresponding Schiff base complexes were evaluated by measuring the minimum inhibitory concentration at which no growth was observed was taken as the MIC values [25]. The results are given in table 1 for all the compounds. Comparison of MIC values (in µg cm^{-3}) of Zn (II) complexes and standard drugs against different bacteria are presented in table 1. The tetradentate Schiff base ligands shows antibacterial activity starting from 150 to 35 µgcm^{-3} against three bacteria, the activity increase with an increase in the concentration [26]. It is very interesting that Zn (II) complexes show higher activity as compared with Schiff base (azomethine) ligands [27], because Zn (II) Schiff base complexes bear polar and nonpolar properties together [28] this makes them suitable for permeation to the cells and tissue.

Table 1. Minimum inhibitory concentration of Antibacterial and Antifungal activity

Compounds	Minimum inhibitory concentration, MIC µg mL^{-1}, Zone of inhibition (mm)					
	Gram positive		Gram negative		Average (%)	Scavenging activity (%)
	MTCC-619	MTCC-96	MTCC-722	MTCC-109		
H_2L^1	26	24	27	32	27.5	59
H_2L^2	28	29	30	34	30.25	41
H_2L^3	38	34	35	33	35	66
H_2L^4	41	46	42	48	44.25	48
$[Zn(L^1)(Cl)(H_2O)]$	52	55	57	65	57.25	57
$[Zn(L^2)(Cl)(H_2O)]$	50	54	52	58	53.5	48
$[Zn(L^3)(Cl)(H_2O)]$	56	56	58	60	57.5	69
$[Zn(L^4)(Cl)(H_2O)]$	57	53	54	58	55.5	51
Ref.	27	33	38	44	40.5	49

Average of zone of inhibition of ligands [H_2L^1 -H_2L^4] =34.25mm; Average of zone of inhibition of complexes=55.93mm, MTCC-619- Bacillus subtilis, MTCC-96 - Staphylococcus aureus, MTCC-722- Escherichia coli,MTCC-109- Klebsiella pneumonia.

Antioxidant activity: There are different methods used to evaluate the *in vitro* antioxidant capacity of isolated compounds, mixtures of compounds, biological fluids, tissues and synthetic compounds which involve different mechanisms of determination of antioxidant activity [29], for example: chemical methods based on scavenging of ROS or RNS such as peroxynitrite [30], the hydroxyl radical and superoxide. Other methods measure the disappearance of free radicals using spectrophotometry [31, 32], such as ABTS•+ (2,2´-azinobis-(3-ethyl-benzothiazoline- 6-sulphonate) cation radical) DPPH (2,2-diphenyl-1-picrylhydrazyl). Other assays to determine the total antioxidant power include techniques such as the Magnesium reducing/antioxidant power method use the insitu electrochemically generated bromine [33, 34]. The results in the measurement of antioxidant capacity depend on the method used.

In the present paper we have carried out scavenging effect on DPPH. 1.5 mL methanolic solution of the synthesized compounds (0.2 mM) was added to 1.5 mL (0.2 mM) solution of DPPH radical in methanol (final concentration of DPPH and synthesized compounds was 0.1 mM). The mixture was shaken vigorously and allowed to stand for 30 min. after this the absorbance at 517 nm was determined and the percentage of scavenging activity was calculated using the formula shown below. Ascorbic acid was used as the reference compound. All tests and analyses were undertaken on three replicate and the results were averaged (Table 1).

CONCLUSION

The newly synthesized Schiff base Zn(II) complexes are proposed various application. The Schiff base ligands are behaving as O, N, N, O donor tetradentate ligands. Also the chloride and coordinated water is coordinated with metal ion confirmed from FT-IR, thermal study. Electronic spectra, Mossbauer spectra study evidence the fact of octahedral arrangement around Zinc(II). Moreover biological screening state this Schiff base complexes enhance the activity against the bacteria and fungi due to Schiff base complexes bear polar and nonpolar properties together; this makes them suitable for permeation to the cells and tissues. The antioxidant properties of ligands are due to highest lipophilicity, lowest electron withdrawing power and highest polarizability, increase the activity of metal complexes.

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