

Synthesis, characterization, antibacterial activity and molecular modeling studies of Ni(II) and Zn(II) complexes with phenylpyridylformamidine ligand

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Abstract

The Ni(II) and Zn(II) complexes with phenylpyridylformamidine (PhPyF) ligand, [Ni(PhPyF)Cl₂] and [Zn(PhPyF)Cl₂], have been prepared and investigated using different chemical techniques such as elemental analysis, molar conductance, FT-IR, Uv-Vis spectra and magnetic moment. The obtained chemical analysis data showed the formation of 1:1 (metal: ligand) ratio. The square planar and tetrahedral geometry for NiL and ZnL were respectively suggested on the basis of magnetic moment, spectral data and molecular modeling studies. The free ligand and its metal complexes have been tested in vitro against a number of bacteria (Gram-negative and Gram-positive) in order to assess their antibacterial activities.

Keywords: Ni (II) and Zn(II) complexes, phenylpyridylformamidine, molecular modeling.

Introduction

Nitrogen-containing ligands and their metal complexes played an important role in the development of coordination chemistry resulting in an enormous number of publications, ranging from pure synthetic work to physicochemical [1-6] and biochemically relevant studies of metal complexes [7-11].

Formamidines which are an important class of heterocyclic compounds have been widely used in agricultural [12], microbiology [13], catalysts [14] and medicine fields like pharmacological agents [15]. Their use as intermediates in synthetic organic chemistry is quite diversified [16], as protecting groups for primary

amines [17] and supporting linkers in solid phase synthesis [18]. Additionally, since these compounds present donor atoms on their structures, they are also very appealing ligands for the synthesis of coordination compounds [19].

The coordination chemistry of metal complexes containing neutral formamidine and anionic formamidinate ligands has been extensively investigated in recent years [20]. Mononuclear and polynuclear complexes have been reported [21-24]. In the present work, we report the results on the synthesis, characterization, molecular modeling

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and antimicrobial activities of Zn(II) and Ni(II) complexes of PhPyF ligand.

Experimental

Material and methods

All the used reagents and solvents were reagent grade. PhPyF ligand was synthesized according to the literature [25]. Elemental analysis was done using a Perkin-Elmer elemental analyzer. IR spectra were recorded in KBr discs on a JASCO FT/IR-410 spectrometer in the 4000~400 cm^{-1} region. UV-Vis spectroscopies were performed on a JASCO 7850 spectrophotometer. Molar conductances were measured at room temperature in DMF on a Jenway 4510 Conductivity Meter. The room temperature magnetic moment (μ_{eff}) was measured according to the literature [26].

Preparation of Ni(II) and Zn(II) complexes

The ligand (170 mg, 1 mmol) was dissolved in 15 mL of THF. This was slowly added to a methanol solution of $\text{MCl}_2 \cdot \text{XH}_2\text{O}$ (1.00 mmol) ($\text{M} = \text{Zn}, \text{Ni}$). The mixture was stirred for 1 h and the resulting solid was collected by filtration and washed with 20 ml THF. This was dried under vacuum for 1 h. *Anal.* Calc. for $\text{C}_{12}\text{H}_{11}\text{N}_3\text{Cl}_2 \text{ Zn}$: C, 43.22; H, 3.29; N, 12.59 %. Found: C, 43.28; H, 3.51; N, 12.70 %., (Yield: 76%), and for $\text{C}_{12}\text{H}_{11}\text{N}_3\text{Cl}_2 \text{ Ni}$: C, 44.04; H, 3.05; N, 12.04 %. Found: C, 43.9; H, 3.25; N, 12.31 %., (Yield: 70%).

Molecular modeling studies

An attempt to gain a better insight on the molecular structure of metal complexes, geometric optimization and conformational analysis has been performed by the use of Gaussian software [27]. Semi empirical method

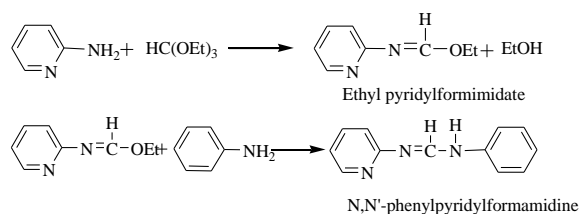
PM3 is then used for optimizing the full geometry of the system.

Antibacterial screening

The biological activities of the complexes/ligand have been studied for antibacterial activities by a previously reported method [28] against Gram-negative bacteria, i.e., *Bacillus subtilis*, *Salmonella typhae* and *Escherichia coli* and Gram-positive bacteria, i.e., *Staphylococcus aureus*. The nutrient agar medium (Peptone, Beef extract, NaCl and Agar- Agar) and 5 mm diameter paper disks (Whatman No.1) were used. The investigated compounds, i.e. ligand and complex, were dissolved in DMF. The filter paper disks were soaked in solutions of ligands as well as complex, dried, and then placed in petri plates previously seeded with the test organisms. The plates were incubated for 24 h at 37 °C and the inhibition zone around each disk was measured in mm. In order to ensure that solvent had no effect on bacteria, a negative control test was performed with DMF and found inactive in culture medium. Disks with the antibacterial drug Tetracycline was applied as positive controls. The obtained results are tabulated in Table 2.

Results and discussion

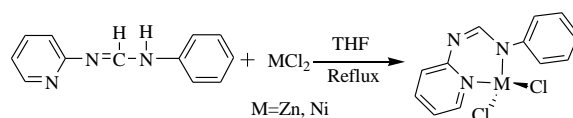
Ligand (PhPyF) was synthesized according to literature [25] in two steps with excellent yield and facile separations. First, reactions of aminopyridine with ethyl orthoformate form pyridyl formimidate and, then, the unsymmetrical formamidine is obtained by reacting the formimidate with the aniline (Scheme 1).



Scheme 1. Synthesis of PhPyF ligand

NiL and ZnL complexes were synthesized by mixing NiCl₂ and

ZnCl₂, and the neutral ligand PhPyF in THF under reflux (Scheme 2).



Scheme 2. Syntheses of NiL and ZnL complexes

The molar conductance data of the complexes in DMF were too low and indicated that the complexes can be regarded as non-electrolyte in nature. The observed values of magnetic moment for complexes are generally diagnostic of the coordination geometry about the metal ions. The μ_{eff} (BM) values of NiL and ZnL complexes reveal their diamagnetic characters. Accordingly, this suggests the NiL has d⁸ complex electronic configuration with a low spin state which adopt a square-planar environment around the Ni(II) ion [29]. However, the Zn(II) complex due to completely filled d-orbital might be either square planar or distorted tetrahedral geometry [30]. The conflict in the ZnL geometry required another technique to show the exact 3D structure, which was clarified by quantum calculations method.

Electronic spectrums of the complexes were taken in DMF solution (Figures 1 and 2). The spectra of the Zn(II) complex are dominated by the the broad band in the region 320-410 nm corresponding to the intra-ligand transition of PhPyF or a charge-transfer transition [31,33,34]. Zn(II) complexes usually do not have d-d absorption bands in the visible region due to the presence of completely filled 3d orbitals [31,35,36].

The electronic spectrum of Ni(II) complex displayed two bands in the region at 325 and 364 nm which are assigned to LMCT transitions [31,37,38]. Two intense bands centered at 225 and 282 nm due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ of ligand center transitions [33,39].

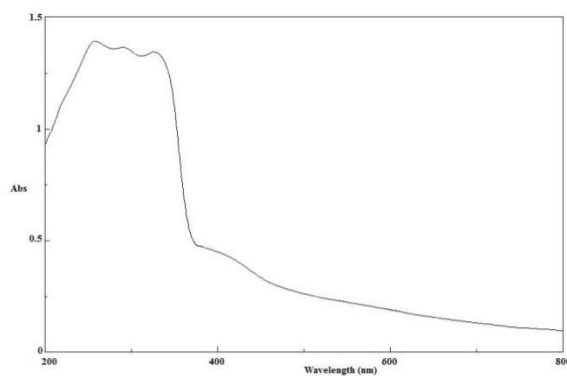


Figure 1. Electronic spectra of Zn(II) complex

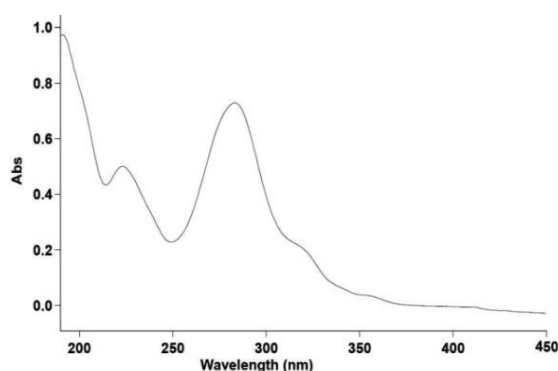


Figure 2. Electronic spectra of Ni(II) complex

The complexes show similar IR spectral features, exhibiting a strong band between 1586 and 1592 cm^{-1} corresponding to $\nu(\text{C}=\text{N})$. This band is shifted to the lower frequencies relative to the free ligand upon the coordination of the nitrogen atoms and indicating the coordination of compound to the metal ions via the azomethine nitrogen [31,32].

A moderately strong peak was observed at 3036 cm^{-1} for aromatic C-H stretching modes for ligands. The signals in region 1460-1600 cm^{-1} are assigned to C=C stretching mode of aromatic ring ligands [40,41]. The weak bands in the rang 485 and 490 cm^{-1} which were attributed to the $\nu(\text{Ni}-\text{N})$ and $\nu(\text{Zn}-\text{N})$ respectively [42].

Since our trials to obtain a single crystals of the metal complexes were unsuccessful so far, and in order to gain a better understanding of geometrical structures of the investigated complexes, molecular modeling studies have been done by means of Gaussian software (semi-empirical / PM6 method) [27]. The advantages of using a more objective method of analyzing geometry have been apparent for many years [42]. Some selected bond lengths and angles are listed in Table 1, the optimized structures, with atom labeling scheme, of complexes NiL and ZnL were represented in Figures. 3 and 4, respectively.

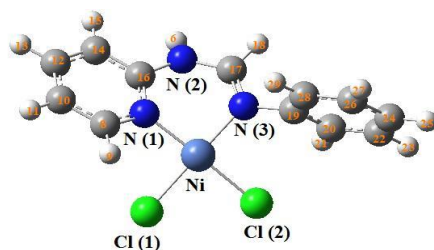


Figure 3. Optimized structures, with atom labeling scheme, of complex NiL

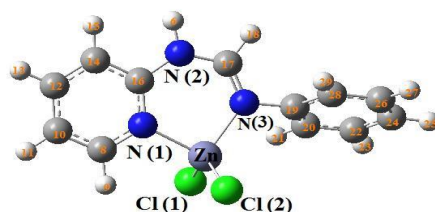


Figure 4. Optimized structures, with atom labeling scheme, of complex ZnL

To further confirm the coordination arrangement of the Ni and Zn complexes, the degree of distortion in the four coordination mode can be calculated from the coordinate geometry index, τ_4 (Eq. 1) [44]:

$$\tau_4 = \frac{[360^\circ - (\alpha + \beta)]}{360^\circ - 2\theta} = \frac{360^\circ - (\alpha + \beta)}{360^\circ - 2(\cos^{-1}(-1/3))} = \frac{360^\circ - (\alpha + \beta)}{141^\circ} \text{ Eq. 1}$$

where: α and β are the two greatest valence angles of coordination center, $\theta = \cos^{-1}(-1/3) \approx 109.5^\circ$, is ideal tetrahedral angle. The degree of distortion, $\tau_4 = 1$ and 0 for perfect tetrahedral and square-planar arrangement, respectively. The NiL and ZnL complexes had $\tau_4 = 0.0599$, and 1.019, respectively. These values supported the 3D modeling results of NiL close to a squareplanar arrangement whereas ZnL was close to a tetrahedral arrangement.

Antimicrobial activity of the PhPyF and corresponding complexes are presented in Table 2. Comparisons of the biological activity of the synthesized compounds with the standard Tetracycline have been carried

out taking usual precautions. From this study, it may be concluded that the complexes have higher activity than ligand but less efficient than antibiotics. The increased activity of metal complexes can be explained on the basis of chelation theory [45]. On chelation, the polarity of the metal ion will be reduced to a 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 chelate ring and enhances the presentation of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganism. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism.

Another interesting result observed here is that the complex of [Zn(PhPyF)Cl₂] show higher activity than the complex [Ni(PhPyF)Cl₂]. These results suggest that the nature of the metal and the coordinated metal ion play significant roles in the inhibition activity.

Table 1. Selected bond angles (°) and bond lengths (Å) of the title complexes

Bond	Angle	Bond	Angle
Cl2-Zn1-Cl3	130.9341	Cl2-Ni1-Cl3	90.16588
Cl2-Zn1-N1	104.4526	Cl2-Ni1-N1	88.0219
Cl2-Zn1-N3	106.8154	Cl2-Ni1-N3	174.8331
Cl3-Zn1-N1	103.9319	Cl3-Ni1-N1	176.7217
Cl3-Zn1-N3	109.4535	Cl3-Ni1-N3	88.3284
N1-Zn1-N3	95.2566	N1-Ni1-N3	93.1253
C8-N1-C16	118.0028	C8-N1-C16	118.2664
C16-N2-C17	129.8518	C16-N2-C17	124.8449
N1-C16-C14	121.679	N1-C16-C14	122.009
N1-C16-N5	121.8881	N1-C16-N5	119.6782
Bond	lengths	Bond	lengths
Zn1-Cl2	2.2159	Ni1-Cl2	2.1349
Zn1-Cl3	2.2225	Ni1-Cl3	2.1267
Zn1-N1	2.0307	Ni1-N1	1.8983
Zn1-N3	1.9911	Ni1-N3	1.8827
N1-C8	1.3724	N1-C8	1.3682
N1-C16	1.3772	N1-C16	1.3774
N2-C16	1.4212	N2-C16	1.4195
N3-C19	1.4551	N3-C19	1.4522
N3-C17	1.3121	N3-C17	1.309
C8-C10	1.3967	C8-C10	1.4006
C14-C16	1.4195	C14-C16	1.4154
C14-C12	1.3908	C14-C12	1.3932
C10-C12	1.3994	C10-C12	1.3988
N2-H6	1.0249	N2-H6	1.0195
C8-H9	1.1088	C8-H9	1.1073
C14-H15	1.088	C14-H15	1.0876
C19-C20	1.4047	C19-C20	1.4058
C19-C28	1.405	C19-C28	1.4043
C26-C28	1.3969	C26-C28	1.3978
C20-C22	1.3967	C20-C22	1.3966
C24-C26	1.399	C24-C26	1.3982
C22-C24	1.3991	C22-C24	1.3996
C28-H29	1.0085	C28-H29	1.0883
C20-H21	1.0977	C20-H21	1.0918

Table 2. Antibacterial data of free ligand (PhPyF) and title complexes (100mgL⁻¹)

Compound for treatment	Inhibition zone in mm			
	<i>Bacillus subtilis</i>	<i>Escherichia coli</i>	<i>Salmonella typhi</i>	<i>Staphylococcus aureus</i>
L	11	10	13	9
ZnL	25	23	27	21
NiL	19	10	21	17
Tetracycline	28	25	30	32
DMF	0	0	0	0

Conclusion

The [Zn(PhPyF)Cl₂] and [Ni(PhPyF)Cl₂] complexes with phenylpyridylformamide (PhPyF) ligand have been prepared and investigated using different chemical techniques. Molecular modeling studies show that NiL was close to a squareplanar arrangement whereas ZnL was close to a tetrahedral arrangement. Antimicrobial activity of [Zn(PhPyF)Cl₂] complex shows higher activity than the complex [Ni(PhPyF)Cl₂].

Acknowledgments

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