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Novel Ni(II) and Zn(II) complexes coordinated by 2-arylaminomethyl-1Hbenzimidazole: Molecular structures, spectral, DFT studies and evaluation of biological activity

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Abstract

 $[NiL^{1,2}Cl_2(OH_2)_3] \cdot zH_2O$ and $[ZnL^{1,2}(CH_3CO_2)_2]$ (L¹ = (1H-benzimidazol-2-ylmethyl)-N-phenyl amine, z = 0 and L² = 2-[(1H-Benzimidazol-2-ylmethyl)-amino]-benzoic acid methyl ester, z = 1) complexes have been synthesized and characterized by a variety of physico-chemical techniques. The central Ni(II) ion is coordinated by only the pyridine-type nitrogen (N_{py}) of benzimidazole ring, three water molecules and two chlorido ligands forming a distorted octahedral geometry. Five coordinated zinc complexes were obtained, where the coordination sphere of zinc ion is made up of secondary amino group (NH_{sec}), N_{py} and two acetate groups, one acts as a unidentate and the other as a bidentate. A theoretical DFT/UB3LYP method combined with LANL2DZ basis set shows that all the metal-ligand bonds are of the L \rightarrow M type. Electronic structures have been calculated using TD-DFT method. The antibacterial activity of NiL^{1,2} complexes decreases by the introduction of COOCH₃ group in the ortho-position of the aniline moiety

Key Words: Benzimidazole; Hydrogen bond; TD-DFT; NBO; Antimicrobial

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1. Introduction

Benzimidazole nucleus is a crucial pharmacophore in drug discovery. Pharmaceutical properties including antitumor [1-2], anti-HIV [3], anti-Parkinson [4] antimicrobial [5] and anti-HCV NS3/NS4A serine protease [6] are unique characteristics known for benzimidazole derivatives. Moreover, benzimidazoles were used extensively as corrosion inhibitors for metal and alloy surfaces [6]. A considerable number of metal benzimidazole complexes including Cr, Mn, Fe, Co, Ni, Zn, Pd, Pt, Au, and Re has been reported [7-9]. Metal complexes containing benzimidazole-based ligands are subject of intensive researches not only owing to their rich coordination chemistry, but also due to a number of established and potential application areas e.g. production of efficient orange light emitting devices (OLEDs), with enhanced stability and efficiency. Metal complexes of biologically important ligands were sometimes more effective than free ligands [10]. These different applications have attracted many experimentalists and theorists to investigate the spectroscopic and structural properties of benzimidazole and some of its derivatives.

Recently, structural studies, antimicrobial activity, *in vitro* cytotoxicity, and structure-activity relationship for some derivatives of 2-arylaminomethylbenzimidazole and their Pd(II) and Pt(II) complexes have been reported **[8-9]**. In the earlier studies, it was found that, the Pd(II) complexes were inactive against all the tested microorganisms, whatever the nature of the substituent on the para-position of the aniline ring **[11]**. As a continuation of our recent studies on synthesis, biological studies, and density functional theory (DFT) calculations of some benzimidazole metal complexes **[8-9,11]**, the main aspects of the present work are: (i) discussing the coordination modes of bi- and tridentate 2-arylaminomethyl-1H-benzimidazoles (L^{1,2}) ligands (Fig. 1) towards Ni(II) and Zn(II) ions, (ii) how far the introduction of methyl ester group in aniline moiety affects geometry and biological activity of the titled complexes, (iii) discussing theoretically the molecular geometries, vibrational spectra and, electronic absorption spectra, as well as natural bond orbital (NBO) analysis, and frontier molecular orbital (FMO).

2. Experimental

2.1. Synthesis and characterization

One mmole hot ethanolic solution of ligands $L^{1,2}$ [11-13] was added to one mmole hot ethanolic solution of either NiCl₂·6H₂O or Zn(CH₃CO₂)₂·2H₂O, and refluxed for 6 h, whereupon the complexes precipitated. The low conductance values of NiL^{1,2} complexes (10⁻³ M, DMF) indicated their non-electrolytic nature, while zinc complexes are insoluble in most common solvents such as DMSO and DMF. The elemental analyses data are in a good agreement with those calculated for the suggested formula.

- Data for NiL¹ (C₁₄H₁₉Cl₂N₃NiO₃) (1). Color: Buff. Yield: 68%. MS: M⁺ = 407 (calcd. 406). Anal. Calcd. %C, 42.32; %H, 4.71; %Cl, 17.42; %N, 10.33; %Ni, 14.42. Found: %C, 42.97; %H, 4.56; %Cl, 18.08; %N, 10.59; %Ni, 14.56. FT IR: 3399, v(NH)_{sec}; 3054, v(C-H)_{Ar}; 2922, v(C-H)_{Aliph}; 1602, v(C=N) + v(C=C); 1499, v(C=C); and 1429 cm⁻¹, β (NH)_{sec}. Molar Cond. (10⁻³ M, DMF): 8.22 Ω^{-1} cm² mole⁻¹. μ_{eff} = 3.82 B.M.. UV-Vis. (DMF): 274, 280, 351, 456, 608, and 824 nm.
- Data for ZnL¹ (C₁₈H₁₉N₃O₄Zn) (2). Color: Yellow. Yield: 50%. MS: M⁺ = 406 (calcd. 406). Anal. Calc. %C, 53.15; %H, 4.71; %N, 10.33; %Zn, 16.08. Found: %C, 52.98; %H, 4.58; %N, 10.26; %Zn, 15.97. FT-IR: 3070, v(C-H)_{Ar}; 2975, v(C-H)_{Aliph}; 2924, v(C-H)_{Aliph}; 1602, v(C=N) + v(C=C); 1545, v_{ass}(COO⁻); 1494, v(C=C); 1431, v(C=C); 1470, v_{ass}(COO⁻); 1385, v_{ss}(COO⁻); 1277, v_{ss}(COO⁻), 938, 828, and 640 (COO unidentate deformation) and 596 cm⁻¹ [π(CO₂)].

- Data for NiL² (C₁₆H₂₃Cl₂N₃NiO₆) (3). Color: Pale yellow. Yield: 62%. MS: M⁺ = 477 (calcd. 477). Anal. Calc. %C, 39.79; %H, 4.80; %Cl, 14.68; %N, 8.70; %Ni, 12.15. Found: %C, 39.41; %H, 4.56; %Cl, 15.12; %N, 8.68; %Ni, 12.06. FT IR: 3564, v(NH)_{im}; 3363, v(NH)_{sec}; 3061, v(C-H)_{Ar}; 1682, v(C=O); 1610, v(C=N); 1582, v(C=C); 1510, v(C=C), and 1269 cm⁻¹; v(C-O). Molar Cond. (10⁻³ M, DMF): 17.57 Ω^{-1} cm² mole⁻¹. μ_{eff} = 3.41 B.M.. UV-Vis. (DMF): 276, 281, 342, 457, 609, and 824 nm.
- Data for ZnL² (C₂₀H₂₁N₃O₆Zn) (4). Color: White. Yield: 70% MS: M⁺ = 464 (calcd. 464). Anal. Calc. %C, 51.68; %H, 4.55; %N, 9.04; %Zn, 14.07. Found: %C, 51.59; %H, 4.51; %N, 8.97; %Zn, 13.99. FT IR: 3587, v(NH)_{im}; 3361, v(NH)_{sec}; 2951, v(C-H)_{Aliph}; 1687, v(C=O); 1634, v_{ass}(COO⁻); 1580, v(C=C); 1513, v(C=C); 1438, v_{ass}(COO⁻); 1264, v_{ss}(COO⁻), 920, 697 and 616 cm⁻¹ (COO unidentate deformation).

2.2. Instruments

Infrared spectra (4000-200 cm⁻¹) were recorded in KBr discs using *FTIR-460 plus, JASCO*. Thermogravimetric analysis was carried out in dynamic nitrogen and air atmospheres (20 mL min⁻¹) with a heating rate of 10 °C min⁻¹ in platinum crucible using *DTG-60H SIMULTANEOUS DTA-TG APPARATUS-SHIMADZU*. Mass spectra were recorded at 70 eV using *SHIMADZU QP-2010 plus* mass spectrometer. Elemental microanalyses were performed at Micro-analytical Center, Cairo University. The analyses were repeated twice to check the accuracy of the obtained data. The metal content was determined complexometry [**13**]. X-ray powder diffraction patterns were studied over $2\theta = 5-60$ ° range using Philips X-ray diffractometer model PW 1840. Radiation was provided by copper anode (K_a, $\lambda = 1.54056$ Å) operated at 40 kV and 25 mA. Spectrophotometric measurements were carried out using UV-Vis. *SHIMADZU Lambda 4B*. Magnetic measurements were carried out on a *Sherwood Scientific* magnetic balance using Gouy method [**14**]. Diamagnetic corrections were made by Pascal's constant and Hg[Co(SCN)₄] was used as a calibrant. Digital *Jenway 4330* Conductivity-pH meter with (1.02) cell constant was used for pH and molar conductance measurements.

2.3. Computational details

Gas phase geometries of [NiL^{1,2}Cl₂(OH₂)₃] and [ZnL^{1,2}(CH₃CO₂)₂] complexes were optimized by DFT/B3LYP method **[15]** combined with LANL2DZ basis set **[9]** using Gaussian 03 package **[16]**. The optimized geometries were verified by performing frequency calculation. Vibrational modes were analyzed *via* Gaussview software **[17]**. Electronic spectra were obtained by using timedependent density functional theory (TD-DFT) **[18]** method. Net atomic charges had been obtained

using natural bond orbital (NBO) analysis of Weinhold and Carpenter [19]. Frontier molecular orbitals (FMO) were performed at the same level of theory.

2.4. Biological studies

The antimicrobial activities of the tested samples were determined by a modified *Kirby-Bauer disc diffusion method* **[20]** under standard conditions using *Mueller-Hinton* agar medium (tested for composition and pH), as described by NCCLS **[21]**. The antimicrobial activities were carried out using culture of *Bacillus subtilis, Staphylococcus aureus,* and *Streptococcus faecalis* as Grampositive bacteria and *Escherichia coli, Pseudomonas aeruginosa,* and *Neisseria gonorrhea* as Gramnegative bacteria. The solution of 20 mg/ml of each compound (free ligand, metal complexes and standard drug *Tetracycline*) in DMSO was prepared. Centrifuged pellets of bacteria from a 24 h old culture containing approximately 10⁴-10⁶ CFU/ml (colony forming unit) were spread on the surface of *Mueller Hinton* Agar plates. Then the wells were seeded with 10 ml of prepared inocula to have 10⁶ CFU/ml. Petri plates were prepared by pouring 100 ml of seeded nutrient agar. DMSO (0.1 ml) alone was used as control under the same conditions for each microorganism. The antimicrobial activities could be calculated as a mean of three replicates.

3. Results and discussion

3.1. Geometry optimization and NBO analysis

3.1.1. [NiL^{1,2}Cl₂(OH₂)₂] complexes

The fully optimized geometries of $[NiL^{1,2}Cl_2(OH_2)_3]$ complexes and numbering of atoms are shown in Fig. 2. Selected bond distances and angles are listed in Table 1. The molecular structures of these complexes show a distorted octahedral geometry around Ni(II) centre as revealed from the spreading in their calculated bond distances (1.907-3.126 Å), and bond angles (89.79-107.40°). As shown in Fig. 2, the benzimidazoles L^{1.2} interact with metal ion through only the pyridine-type nitrogen (N11) as the aniline moiety is bent out of the coordination plane and becomes far from the Ni(II) ion. Table 1, summarizes the details of H-bond interactions. Two types of H-bond are known **[22]**, the first one is the conventional, defined as A-H...B where A, and B are electronegative atoms such as nitrogen, oxygen or halogen. Another type of H-bonding is the blue-shifting hydrogen bond, usually C-H...B, where B is either an electronegative atom carrying lone pair or a region of excess electron density (π electrons of an aromatic system). Each water molecule in the axial position of octahedral structure is involved in three H-bonds of different strength, and this leads to a distorted geometry. For example, (O33H₂) in NiL¹ complex interacts with the methylene proton (H24) and two chlorine atoms (Cl31 and Cl38) with D...A distances 2.12, 2.38, and 2.76 Å, respectively

(Table 1). It is seen that C14-H24...O33 interaction is the strongest one (155.8 °) among the latter interactions, since the angle of interaction approaches linearity **[23]**. It is worthy to mention that the H25 proton of NH_{sec} (N21) group in NiL² is participated in H-bond with the oxygen atom (O43, - 0.668e) of the ester group **[13]**, while the imidazolic proton (H22) interacts with the nitrogen atom (N21) of NH_{sec} group through another H-bond with distance of 2.51 Å.

Natural bond orbital (NBO) analysis [**19**] and second order perturbation theory analysis of Fock Matrix provide details about the type of hybridization, nature of bonding and strength of the interactions between metal ion and donor sites [**24**]. According to NBO results, the electronic configuration of Ni in NiL² (as representative example) is: [core]4s^{0.34}3d^{8.72}4p^{0.33}4d^{0.01}5p^{0.20}, 17.996 core electrons, 9.573 valence electrons, and 0.018 Rydberg electrons with 27.587 electrons as a total electrons that is in agreement with the calculated natural charge (+0.413e) on nickel atom. The strength of interaction between Ni(II) and active binding sites has been assigned by second order interaction energy (E^2). The E^2 values are 2.77, 1.20, 0.64, 0.44, 1.81, and 1.57 kcal/mol for LP(1)N11 \rightarrow RY*(9)Ni, LP(2)Cl31 \rightarrow σ^* (Ni-Cl31), LP(2)O32 \rightarrow σ^* (Ni-Cl31), LP(2)O33 \rightarrow σ^* (Ni-Cl31), LP(4)Cl38 \rightarrow RY*(9)Ni and LP(2)O39 \rightarrow RY*(9)Ni, respectively. In addition, the lone pair interaction (~29 kcal/mol) of oxygen (O43) atom of the carbonyl group with anti-bonding σ^* (C42-O43) anti-bonding orbital in the aniline ring and this leads to a strong π -electron delocalization with an energy difference ~ 220 kcal/mol.

3.1.2. [ZnL^{1,2}(CH₃CO₂)₂] complexes

The fully optimized geometries of $[ZnL^{1,2}(CH_3CO_2)_2]$ complexes and numbering of atoms are shown in Fig. 3 and their selected geometric parameters are listed in Table 1. The local coordination environment of Zn(II) ion can be described as a distorted square pyramidal completed by two N atoms, N11 and N21, and two oxygen atoms of a bidentate acetate group in the base of the pyramid and an oxygen atom from a monodentate acetate in the axial position. This geometry prevents the participation of COOCH₃ group in the coordination sphere of ZnL² complex as was experimentally found [**12**]. It was found that, C13N11 and C14N21 bond lengths in ZnL¹ complex were increased upon the coordination of N11 and N21 to metal ion. In ZnL¹ complex, the bond length of ZnN11 (2.091 Å) is in agreement with the average zinc-imidazole bond distances (2.02-2.08 Å) [**25**]. On the same manner, the bond distance of ZnN21 (2.36 Å) is comparable to the average value of 2.27 Å which was previously observed for *sec*-NH donors in five-coordinated zinc(II) complexes [**25**]. The Zn-O32 and Zn-O38 bond distances of the bidentate acetate anion are 2.126 and 2.222 Å,

respectively [26]. Zn-N21 bond length in ZnL^2 complex is longer than that of ZnL^1 due to participation of NH_{sec} in H-bond. The unidentate acetate interacts with methylene group forming H-bond with D...A distances, 2.085, and 2.115 Å, for $ZnL^{1,2}$ complexes. According to NBO, the electronic configuration of Zn in ZnL^1 is [core]4s^{0.30}3d^{9.98}4p^{0.31}: 18 core electrons, 10.59 valence electrons (on 4s, 3d, and 4p atomic orbitals), and 0.0078 Rydberg electrons with 28.605 as a total electrons and +1.395e as a natural charge. The E^2 values were found to be 32, 12, 20, 36, and 10 kcal/mol for LP(1)N11 \rightarrow RY*(6)Zn, LP(1)N21 \rightarrow RY*(6)Zn, LP(2)O32 \rightarrow RY*(6)Zn, LP(2)O37 \rightarrow RY*(6)Zn and LP(2)O38 \rightarrow RY*(6)Zn, respectively [27].

3.2. Electronic structure, frontier molecular orbitals and magnetic susceptibility

Frontier molecular orbitals play an important role in electric and optical properties **[28]**. The frontier orbital gap can be used to characterize the chemical reactivity and kinetic stability of the molecule. Fig. 4 shows the electronic distributions and energy levels of HOMO and LUMO orbitals for the titled complexes. The values of the energy gap between HOMO and LUMO are 0.84, 0.51, 4.75 and 3.48 eV for NiL^{1,2} and ZnL^{1,2} complexes, respectively.

The absorption spectra of many octahedral Ni(II) complexes can be easily interpreted using Tanabe-Sugano diagram for d⁸ electron configuration [**29**]. The electronic ground state is ${}^{3}A_{2g}$ and spin-allowed transitions to three triplet-excited states are expected and can be easily observed in solution absorption spectra. The most important excited states for octahedral Ni(II) complexes are ${}^{1}E_{g}$, ${}^{3}T_{2g}$, and ${}^{3}T_{1g}({}^{3}F)$ [**30**]. The ${}^{3}T_{2g}$, and ${}^{3}T_{1g}({}^{3}F)$ excited states are close in their energy at all ligand-field strengths. The energy of the first singlet excited state ${}^{1}E_{g}$ is almost independent of ligand-field strength as it arises from the same $t_{2g}{}^{6}e_{g}{}^{2}$ electronic ground state. Here, the two bands between 275 and 282 nm in NiL^{1,2} are assigned to $\pi - \pi^{*}$ in benzimidazole ring [**8-9**], while the band at 342 nm is attributed to intra-molecular H-bond ring [**13**] (Fig. S1, supplementary materials). The three bands at 457, 608 and 824 nm, are assigned to ${}^{3}A_{2g} \rightarrow {}^{3}T_{2g}$ (v₁), ${}^{3}A_{2g} \rightarrow {}^{3}T_{1g}$ (${}^{3}F$) (v₂) and ${}^{3}A_{2g} \rightarrow {}^{1}E_{g}$ (v₃), respectively.

The values of the effective magnetic moment (μ_{eff}) of NiL^{1,2} complexes at 296 K were found to be 3.82 and 3.41 B.M. with orbital angular momentum contribution (spin-orbital coupling) **[30]** for octahedral Ni(II) complexes. Generally, experimental values differ from the spin-only ones (2.83 B.M.), usually being somewhat greater. This is because the orbital motion of the electrons also contributes to the magnetic moment. The theoretical magnitude of spin only μ_{eff} (μ_s) for an octahedral nickel complex is 2.83 B.M., whereas orbital contribution (μ_{s+L}) raises this value to 4.47

B.M. **[31]**. In the present work, it was found that the observed values of μ exceed μ_s , but are not high as μ_{s+L} **[31]**. This is because the electric fields of other atoms, ions, and molecules surrounding metal ion in its compounds which can restrict the orbital motion of the electrons so that the orbital angular momentum and hence the orbital moments are partially quenched.

To gain detailed insight into the charge transitions, TD-DFT calculations were performed. The absorption spectra were simulated using *GAUSSSUM* software [**32**] based on the obtained TD-DFT results. Each excited state was interpolated by a Gaussian convolution with the full-width at half-maximum (FWHM) of 3000 cm⁻¹. The calculated d-d excitation wavelengths of the nickel complexes and their assignments are given in Table 2 as representative example, while those of zinc complexes are included in supplementary material section (Table S1). The intensity of these transitions has been assessed from the oscillator strength (*f*). The d-d transitions are forbidden and their oscillators' strengths are very small (close to 0.0) [**33**].

3.3. Vibrational assignments

The theoretical FT IR spectra of the titled complexes were obtained at B3LYP/LANL2DZ level of theory. The calculated harmonic frequencies were found to be higher than the experimental values due to electron correlation approximate treatment, anharmonicity effects and basis set deficiencies, etc. [34-35]. Scale factors were introduced [8] to overcome these shortcomings. Herein, a *uniform* scaling method with a value of 0.970 has been introduced. Benzimidazoles (L^{1,2}) have a strong intermolecular hydrogen bond [13] with a broad band (3500-2200 cm⁻¹) in their vibrational spectra [11-13]. Therefore, it is experimentally difficult to assign the benzimidazolic NH (N12) band. In complexes, this group remains intact and is observed at 3566 and 3564 cm⁻¹ in NiL^{1,2} and at 3587 cm⁻¹ in ZnL². This is theoretically confirmed, since the position of $v(NH_{Bz})$ band remains virtually unaltered in $L^{1,2}$ and their complexes. The sharp bands at 3427 (L^{1}) [11] and 3345 cm⁻¹ (L^{2}) [13] are assigned to v(NH_{sec}). The discrepancy between the latter values is attributed to intra Hbond. For NiL¹, the NH_{sec} group is not involved in chelation, but it participates in H-bond with axial chlorido atom (Fig. 2) giving a band at 3399 cm⁻¹. Alternatively, the NH_{sec} of L² in NiL² remains also intact, but it is liberated from the effect of intra H-bond and is shifted to a higher value (3363 cm^{-1}) with respect to the free ligand. On the same manner, the scaled v(NH_{sec}) mode (NiL²) is assigned at 3381 and 3367 cm⁻¹ in NiL² and L², respectively. On the other hand, the v(NH_{sec}) mode is observed at low wavenumber, 3350 cm⁻¹ in ZnL¹ complex and becomes broad indicating its involvement in coordination sphere. For ZnL^2 complex, the NH_{sec} group suffers from two antagonistic effects, the withdrawal effect of the nitrogen atom, as a result of complex formation,

and the intra H-bond. These two effects compensate each other, lead to appearance of this group at higher wavenumber than that of the free ligand, 3361 cm^{-1} [12].

The v(C=N) mode is observed at 1682 cm⁻¹ [**11**] in L¹. In complexes, this group is shifted to low frequencies and is overlapped with C=C bands to give a band at 1601 cm⁻¹ in NiL¹ and ZnL¹. In L², the v(C=N) is overlapped with v(C=O) and v(C=C) modes due to H-bond [**13**]. In complexes, the C=N group is liberated from H-bond with increasing of double bond characters and is observed at 1634 cm⁻¹ (ZnL²), while it is overlapped with v(C=C) giving a band at 1610 cm⁻¹ in NiL². Moreover, the band at 1674 cm⁻¹ in L² is assigned to v(C=O). In complexes, the carbonyl group is not involved in chelation, since its stretching mode is located at a higher wavenumber, 1682 and 1687 cm⁻¹ for NiL² and ZnL², respectively.

Deacon and Phillips [36] studied and assigned three binding modes of the carboxylate group in the IR spectra of many acetates and trifluoroacetates complexes, and arrived the following conclusions according to the value of Δv , $\Delta v = [v_{ass}(COO^{-}) - v_{ss}(COO^{-})]$: (i) unidentate complexes exhibit $\Delta v > 200$ cm⁻¹ that are much greater than ionic complexes. (ii) chelating (bidentate) complexes exhibit $\Delta v < 100 \text{ cm}^{-1}$ that are significantly less than ionic values. (iii) the Δ values for bridging complexes (Δv) are greater than those of chelating (bidentate) complexes, and close to the ionic values. Here, the new bands at 1591-1419 cm⁻¹ and 1385-1250 cm⁻¹ in the ZnL^{1,2} are assigned to asymmetric and symmetric stretching vibrations of coordinated carboxylate group, respectively [37]. For ZnL¹ complex, the $v_{ass}(COO^{-})$ and $v_{ss}(COO^{-})$ modes of the unidentate acetate group appear at 1545 and 1277 cm⁻¹, respectively. The lower values of these modes may be attributed to participation of this group in intra H-bond with methylene group of ligand (Fig. 3). In addition, this complex exhibits three bands (COO deformation) of the unidentate acetate group at 933, 828 and 640 cm⁻¹ and $[\pi(CO_2)]$ at 596 cm⁻¹ [37]. Also, this complex shows new bands corresponding to bidentate acetate group at 1470 and 1385 cm⁻¹ ($\Delta v = 85$ cm⁻¹). Similarly, ZnL² complex exhibits $v_{ass}(COO^{-})$ and $v_{ss}(COO^{-})$ modes at 1634 and 1264 cm⁻¹ for unidentate group, while the band at 1438 cm⁻¹ is assigned to $v_{ass}(COO^{-})$ of bidentate group. The bands at 920, 794, and 616 cm⁻¹ are allocated to COO deformation of the unidentate group. The detail assignments of the remaining bands in the theoretical vibrational spectra of the studied complexes are shown in Table S2 as supplementary materials.

3.4. Mass spectrometry

The mass spectrum of NiL¹ complex (1) gives rise to M^+ at m/z 407 due to [NiL¹Cl₂(OH₂)₃] with two fragmentation pathways (scheme S1, supplementary materials). The first route is traced by a peak (m/z 371) due to removal of 2H₂O from M^+ followed by loss of 2 Cl to offer a fragment at m/z 301 ([NiL¹(OH₂)]) and then loss H₂O to give peak at m/z 281, [NiL¹]. The second way involves loss of 2Cl to provide a fragment at m/z 336, [NiL¹(OH₂)₃]. It was found that the involvement of C=N_{py} in chelation introduces a weakness point through which the benzimidazole ring decomposes to imidazole moiety with a fragment at m/z 181, [(imidazole)NiCl(OH₂)] [9]. The NiL² complex (3) has a strong M⁺ peak at m/z 477 corresponding to [NiLCl₂(OH₂)₃]·H₂O and decomposes through four fragmentation routes (scheme S2, supplementary materials). There were no evidences revealed the participation of carbonyl group in chelation.

The mass spectra of $Zn-L^{1,2}$ complexes give rise to M⁺ at m/z 406 and 464, respectively due to $[ZnL^{1,2}(CH_3CO_2)_2]$. For Zn-L¹ complex (2), (scheme S3, supplementary materials), the first pathway involves removal of CH₃ to give a fragment at m/z 391, followed by loss of oxygen atom (m/z 375) and then CH₃CO to provide a peak at m/z 331. The second route is typical as ligand itself with fragments due to L¹ (m/z 223), 2-methylene benzimidazole (m/z 131), and benzimidazole (m/z 118). Fragmentation pattern of Zn-L² complex (4) goes under four complicated fragmentation routes as demonstrated in (scheme S4, supplementary materials). The peak at m/z 242 confirms the presence of two acetate groups around metal ion, [(Benzimidazole)Zn(CH₃CO₂)].

3.5. Thermal analyses and kinetics studies

The thermal degradation of NiL¹ (1) proceeds *via* four main stages maximized at 160, 325, 445, and 570 °C in nitrogen atmosphere. The 1st stage is assigned to elimination of 2H₂O with a mass loss amounts to 8.78 % (calcd. 8.85 %). The 2nd event is attributed to removal of 2HCl molecules with a mass loss 18.26 % (calcd. 17.95%). The 3rd and 4th stages are assigned to decomposition of L¹ giving NiO as a final residue with a total mass loss, 72.96% (calcd. 73.20%). Regarding the TG curve constructed for ZnL¹ complex (2), one can observe mainly one peak maximized at 514 °C. This stage is attributed to elimination of L¹, C₂H₆, CO and CO₂ leaving ZnO with overall mass loss amounts to 80.27 % (calcd. 80.05 %).

For NiL² complex (**3**), the thermal degradation starts at 100 °C, with two peaks at 331 and 409 °C in nitrogen atmosphere with overall mass loss amounts to 68.96% (calcd. 84.48 %) assuming NiO as a final residue as no other nickel compounds can present at 1200 °C. Similar, degradation of ZnL^2 complex (**4**) is also incomplete [**38**] up to 1200 °C with four peaks at 75, 289, 418, and 550 °C

and total mass loss amounts to 64.18% (calcd. 82.87 %) with ZnO as residue. This behavior [9] reflects the high stability of these complexes comparing with those of ligand L¹. However, the thermal decomposition of ZnL² complex in air shows two degradation stages at 289 and 458 °C with overall mass loss amounting to 82.62%. Coats-Redfern equation [39] was used to calculate the thermo-dynamic parameters from TG curves (Table S3 as supplementary materials). The positive ΔH^* values mean endothermic processes, while the negative ΔS^* values indicate that the complexes are spontaneously formed and are highly ordered in their activated states [8]. The activation energies of the decomposition stages were found to be in the range of 40-666 kJ/mole indicating the high stability of these complexes in terms of their H-bonds.

3.6. X-ray powder diffraction

Single crystals of the reported complexes could not be obtained since these complexes are amorphous in their nature. The X-ray powder diffraction patterns were recorded over $2\theta = 5-60^{\circ}$ range in order to obtain an idea about the lattice dynamics of these compounds. The values of 2θ , interplanar spacing d (Å) and the relative intensities (*l/I*°) were tabulated in (supplementary material, table (S4)). The comparison between the obtained XRD patterns of the title complexes (supplementary material, figure S2), revealed that the pronounced effect of metal type on the crystallinity of these compounds. The identification of the complexes was done by the known method [9]. There are five strong diffraction peaks in NiL² complex at 6.73°, 19.88°, 21.08°, 26.72°, and 28.98° and the interstices of the corresponding crystal faces are 13.12, 4.46, 4.21, 3.33, and 3.07 Å, respectively. The interstice 6.73 Å at $2\theta = 13.12^{\circ}$ is the interlayer spacing of NiL² complex. Moreover, the similarity between nickel complexes, with an interlayer spacing at 6.73 Å, suggests that both complexes have the same phase structure. This behavior has been also found between the zinc complexes with nearly the same interstice 10.74 Å at $2\theta = 8.24^{\circ}$.

3.7. Biological activity

The antimicrobial activity data of NiL^{1,2} complexes were compared with those of the free ligands and the corresponding Pd(II) and Pt(II) complexes **[11,13]**. The results revealed the capacity of the titled complexes for inhibiting the metabolic growth of the investigated bacteria to different extents and especially the *Staphylococcus aureus* (Fig. 5). The variation in the effectiveness of the studied compounds against different organisms depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells. Here, the nickel complexes are active against both types of the bacteria, which may indicate broad-spectrum properties **[40]**.

It was found that NiL^1 complex is more toxic against the tested organisms than NiL^2 that is in agreement with the previously reported data of the free ligands [11,13] as the introduction of COOCH₃ in the aniline ring decreases distinctly the antibacterial activity of NiL^2 complex. As shown in Fig. 5, the nickel complexes exhibit slightly lower toxicity than their free ligands. This may be attributed to their inability to chelate metals, which are essential for the metabolism of microorganisms, low lipophilicity and/or to form hydrogen bonds with the active centers of cell structures, resulting in an interference with the normal cell cycle. Finally, the nickel complexes are toxic than the inactive palladium complexes [11,13] at the same concentration. This may be interpreted in terms of the strength of the M-L bonds, besides other factors such as size of the cation, receptor sites, diffusion, and a combined effect of the metal and the ligands for inactivation of the bio-molecules.

4. Conclusion

Better approaches to the synthesis of Ni(II) and Zn(II) complexes coordinated by 2-arylaminomethylbenzimidazole derivatives as potential antimicrobial agents have been developed. The reasonable agreement between the theoretical and experimental data reflects to great extent the suitability of the applied basis set, LANL2DZ for this type of work and confirms the suggested structures. The obtained results seem to suggest the different ligational behavior of such ligands towards the metal ion. TD-DFT calculations help to assign the electronic transitions. Vibrational assignments revealed the presence of two types of coordinated acetate groups in the zinc complexes. The calculated values of the second order interaction energy showed strong coordination bonds between the ligands and metal ions. The EI mass spectra indicated the involvement of pyridine-type nitrogen in chelation and decomposition of benzimidazole ring into imidazole moiety. The introduction of substituent in the ortho-position of the aniline ring decreases markedly the antibacterial activity of the investigated nickel complexes. The strength of the M-L bonds, besides other factors such as size of the cation, receptor sites, diffusion, and a combined effect of the metal and the ligands affect the biological activity of this type of compounds.

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Figure-caption list

Figure (1): The optimized structures of benzimidazole ligands $L^{1,2}$.

Figure (2): The optimized structures of (a) $Ni-L^{1}$ (1) and (b) $Ni-L^{2}$ (2) complexes.

Figure (3): The optimized structures of (a) $Zn-L^{1}$ (1) and (b) $Zn-L^{2}$ (2) complexes.

Figure (4): Molecular orbital surfaces and energy levels of (a) Ni-L¹, (b) Ni-L², (c) Zn-L¹ and (d) Zn-L² complexes.

Figure (5): Antibacterial activities of L^{1,2} and their Ni-L^{1,2} complexes and tetracycline against *B. subtilis, S. aureus*, and *S. faecalis* as Gram-positive, *P. aeruginosa, E. coli*, and *N. Gonorrhea* as Gram-negative bacteria.





(a)



(b) Figure (2) 3



(b) Figure (3)



(a)(HOMO, -5.90 eV)

(LUMO, -5.06 eV)





(b)(HOMO, -5.92 eV)

(LUMO, -5.41 eV)





(c) (HOMO, -6.11 eV)







(d)(HOMO, -8.91 eV)

ACC



Figure (4)



Table (1): Selected bond lengths (Å), angles (°) and charge (e) for the titled complexes								
$[NiL^{1}Cl_{2}(OH_{2})_{3}](1)$		$[ZnL^{1}(CH_{3}CO_{2})_{2}](2)$		$[NiL^2Cl_2(OH_2)_3]$ (3)		$[ZnL^{2}(CH_{3}CO_{2})_{2}](4)$		
Bond lengths (Å)	Bond Angles (°)	Bond lengths (Å)	Bond Angles (°)	Bond lengths (Å)	Bond Angles (°)	Bond lengths (Å)	Bond Angles (°)	
N11Ni = 1.907	N11NiCl32 = 91.5	N11Zn = 2.090	N11ZnN21 = 75.7	N11Ni = 1.908	N11NiCl31 = 91.0	N11Zn = 2.084	N11ZnN21 = 74.9	
Cl32Ni = 2.258	N11NiO40 = 89.8	N21Zn = 2.360	N11ZnO37 = 118.6	Cl31Ni = 2.255	N11NiO32 = 105.3	N21Zn = 2.385	N11ZnO36 = 111.8	
Cl37Ni = 2.298	Cl32NiCl39 = 95.8	O37Zn = 1.942	N21ZnO37 = 92.3	Cl38Ni = 2.287	Cl31NiCl38 = 95.6	O36Zn = 1.950	N21ZnO36 = 107.1	
O33Ni = 2.841	N11NiO33 = 103.4	O32Zn = 2.126	O32ZnO37 = 128.2	O32Ni = 2.883	N11NiO33 = 101.0	O31Zn = 2.091	O31ZnO36 = 62.2	
O34Ni = 3.072	N11NiO34 = 107.4	O38Zn = 2.221	O38ZnO37 = 111.8	O33Ni = 3.126	N11NiO39 = 90.1	O37Zn = 2.240	O36ZnO37 = 110.9	
O40Ni = 1.943		C14H23O31 = 2.085	O32ZnO38 = 61.9	O39Ni = 1.952		C14H23O30 = 2.115	O36ZnO31 = 119.6	
H-bond								
Cl24H24O33		C14H23O31	C14H23O31 =	Cl24H24O33	C14H24O33		N21H25O46 =	
= 2.120		= 2.085	137.9	= 2.121	= 155.8		142.0	
O33H37Cl31				O33H37Cl31	O33H37Cl31		C14H23O30 =	
= 2.379				= 2.381	= 142.0		140.4	
O33H36Cl38				O33H36Cl38	O33H36Cl38			
= 2.761				= 2.764	= 128.7			
N12H22N21				N12H22N21	N12H22N21			
= 2.510				= 2.518	= 97.17			
Charge (e)								
N11 = -0.553		N11 = -0.6/3		N11 = -0.563		N11 = -0.673		
$N_1 = 0.426$		N21 = -0.750		$N_1 = 0.413$		N21 = -0.756		
C132 = -0.436		Zn = 1.394		C131 = -0.416		Zn = 1.399		
033 = -0.983		0.32 = -0.827		032 = -0.984		031 = -0.816		
0.34 = -0.984		037 = -0.881		033 = -0.991		030 = -0.8/8		
C139 = -0.483		038 = -0.771		C138 = -0.4/8		03/=-0.7/3		
0+00.200				0.570.707				

1						
f	Composition					
0.0001	HOMO-1→LUMO (98%)					
0.0	HOMO-3 \rightarrow LUMO (63%), HOMO-11 \rightarrow LUMO (16%)					
0.0	HOMO-7→LUMO (21%), HOMO-6→LUMO (18%)					
0.0005	HOMO-8 \rightarrow LUMO (28%), HOMO-16 \rightarrow LUMO (23%)					
0.0004	HOMO \rightarrow LUMO (92%)					
0.0097	HOMO-2→LUMO (77%)					
0.0027	HOMO-7 \rightarrow LUMO (34%), HOMO-8 \rightarrow LUMO (25%)					
0.0804	HOMO→LUMO+1 (93%)					
	9					
0.0002	HOMO-1→LUMO (91%)					
0.0	HOMO-4→LUMO (59%), HOMO-12→L (19%)					
0.0001	HOMO-6→LUMO (46%), HOMO-9→LUMO (15%)					
0.0002	HOMO-7→LUMO (26%), HOMO-3→LUMO (22%), HOMO-18→LUMO (21%),					
0.0005	HOMO→LUMO (99%)					
0.0111	HOMO-2 \rightarrow LUMO (53%), HOMO-3 \rightarrow LUMO (34%)					
0.0021	HOMO-3→LUMO (34%), HOMO-2→LUMO (27%), HOMO-7→LUMO (23%),					
0.0019	HOMO-5→LUMO (88%)					
C						
	f 0.0001 0.0 0.0005 0.0004 0.0097 0.0027 0.0804 0.0002 0.0 0.0001 0.0002 0.0005 0.0111 0.0021 0.0019					

Table (2): Selected computed d-d excitation energies (eV), electronic transition configurations, and oscillator strengths (f) of the studied nickel complexes

General significance of the obtained results:

- $[NiL^{1,2}Cl_2(OH_2)_3]$ and $[ZnL^{1,2}(CH_3CO_2)_2]$ benzimidazole complexes were synthesized.
- Biological activity is affected by the nature of the substituent on aniline ring.
- Two types of coordinated acetate groups are assigned in zinc complexes.
- Strong coordination bonds between ligands and metal ions as revealed by E^2 values.

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Best regards Yours

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Graphical abstract

The obtained results confirmed the different coordinating mode of the studied benzimidazole ligands towards Ni(II) and Zn(II) metal ion; [NiLCl₂(OH₂)₃] and [ZnL(CH₃CO₂)₂]