Synthesis, Characterization and EPR Study of Some Transition Metal Complexes with N-O Donor Lewis Base of Isonozide.

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Abstract
A series of new complexes of the type [Cu(L)2]Cl2 (1), [Ni(L)Cl2].H2O(2), [Co(L)2(H2O)2]Cl2 (3), [Mn(L)2(H2O)2] (4), [Zn(L)2Cl2] (5), where L is N-(phthalimidyl) isonicotinamide have been synthesized and characterized by magnetic moment, molar conductivity UV, and (FT-IR) and some of them were characterized by EPR spectroscopy. Ligand was characterized by FT-IR, 1HNMR and 13CNMR spectroscopy. The spectroscopic data indicated that the isonazide ligand act as bidentate N,O donors and the complexes (2-5) are paramagnetic and the complex(6) diamagnetic. The optimization of their structures indicated that the geometry of complex (1) is square planar and tetrahedral for complex (2) and octahedral for complexes (3-5). [DOI: 10.22401/ANJS.00.1.02]

Keywords: cyclic imide, phthalimide, isoniazid, tuberculosis.

1- Introduction
Tuberculosis is one of the most important problems affecting health. It is classified as the second leading cause of death in the world among infectious disease [1]. In 2013, 9 million people were diagnosed with TB, 1.5 million of whom died from the disease. Isoniazid (INH) is the best choice for the treatment of TB and it plays a vital role in effective control of TB,[2].

Hydrazones belong to the azomethane class of compounds have attracted the attention of many chemists because of their broad spectrum of drug activity properties with structural flexibility and associative behavior.

Hydrazones are known as compounds containing two interrelated R1,CN-NR2 nitrogen atoms, as they could act as antimicrobial, antitubercular and antitumor agents [3-6]. After the cornerstone of anti-TB therapy has been used for more than half a century, much has been learned about biochemistry and multifaceted ways to act as isoniazid front-line drugs. In fact, with the massive world TB burden and the alarming rise in the number of clinical isolates that show drug resistance or increased virulence [7-10]. Isoniazid has become the most researched anti tubercular agent, [11-13].

Isonicotinoylhydrazide (INH) is considered one of the strongest and best anti-TB drugs and works to kill M. tuberculosis. Isonicotinoylhydrazone derivatives containing heterogeneous components have been found to possess the best anti-TB activity [14,15].

The clinical benefit of isoniazid (isonicotinic acid hydrazide) was discovered in the 1950’s when its high anti-tuberculosis efficacy was first observed [16], higher than any other compound used at the time [17-20]. INH is indeed particularly active against Mtb with a minimum concentration for inhibiton (MIC) of 0.05 mg/mL [18]. Imides of aromatic dicarboxylic acids are important in the construction of macromolecules 1,2 as well as supramolecular assembly [21-24]. As cancer cells are highly proliferative tissues, one of the most promising biological targets to decrease tumor cell growth is the DNA. Naphthalimide derivatives was among the few compounds that interact with DNA and it Has gained considerable interest based on the properties of the DNA- intercalating and topoisomerase-poisoning activities, [25].

Cyclic imides have great importance because their various compounds have a wide range of biological activities, [26,27].

This work aimed to synthesize a potential ligand containing both, isonicotinoylhydrazide and phthalimidyl moieties and synthesis of new transition metal complexes from this ligand. Thus, the present investigation throw light on synthesis,
characterization, EPR study of novel N-(phthalimidyl) isonicotinamide complexes.

2- Experimental
2-1 chemicals
Chemicals used in this work are supplied from BDH and Fluka companies and are used without further purification.

2-2 Physical measurements
Gallenkamp apparatus were used for determine melting points of prepared compounds and were uncorrected. FTIR spectra were recorded in Baghdad University on SHIMADZU FTIR-8400 Fourier Transform Infrared spectrophotometer using KBr discs. $^1$HNMR and $^{13}$CNMR spectra were recorded on Bruker 500MHz-Avance III instrument using DMSO-d$_6$ as a solvent and TMS as internal reference in the university of Jordan faculty of science. EPR spectra of Cu(II) and Ni(II) complexes were recorded as poly crystalline sample in the DMF solution on convential X-band Bruker Elexsys E 500 CW-spectromwter in En-shams university laboratories.

2-3 Synthesis of ligand
In 250 mL Glacial acetic acid a mixture of (0.013 mole, 0.493g) of phthalic anhydride and (0.013 mole, 0.457g) of isoniazid was reflexed for 6 h. then cooled to room temperature and pour into ice water. The white precipitate of the ligan Fig. (1) was separated, washed with 5% sodium bicarbonate and recrystallized from ethanol. Yield: 90%, m.p.: 220-222 °C, [28,29].

2-4 Synthesis of [Cu(L)$_2$]Cl$_2$
(0.002 mole, 0.53 g) of ligand was dissolved in 25 mL absolute ethanol. To this solution the ethanolic solution of copper salt (CuCl$_2$.2H$_2$O) (0.001 mole, 0.17 g) was added. The mixture was refluxed with stirring for 2h. After cooling to room temperature a green complex of cupper (II) precipitated out. It was filtered, washed with ethanol and dried over P$_4$O$_{10}$ under vacuum. Yield : 83% , m. p.: 276-278 °C, [30].

2-5 Synthesis of [Ni(L)Cl$_2$.H$_2$O]
(0.001 mole, 0.27 g) of ligand was dissolved in 25 mL absolute ethanol. To this solution the ethanolic solution of corresponding salts (0.001 mole) was added. The pH of solution was adjustment to 7 with sodium carbonate then the mixture was refluxed with stirring for 2h. After cooling to room temperature a colored complex precipitated out. It was filtered, washed with ethanol and dried over P$_4$O$_{10}$ under vacuum. Yield: 80%, m. p.: 263-265 °C.

2-6 Synthesis of [Co(L)$_2$(H$_2$O)$_2$]Cl
The complex of Co(II) was synthesized following the same procedure in (2-5), but by using the ratio of 2:1 from ligand to salt. Yield: 78%, m. p.:322-324 °C.

2-7 Synthesis of [Mn(L)$_2$(H$_2$O)$_2$]
The complex of Mn(II) was synthesized following the same procedure in (2-5), but by using the ratio of 2:1 from ligand to salt. Yield: 75% , m. p.: 257-259 °C.

2-8 Synthesis of [Zn(L)$_2$Cl$_2$]
The complex of Zn(II) was synthesized following the same procedure in (2-5), but by using the ratio of 2:1 from ligand to salt. Yield: 76% , m.p.:347-349 °C. Physical properties of prepared compound are listed in Table (2).

3- Result and discussion
3-1 FT-IR, $^1$HNMR and $^{13}$CNMR spectra
FT-IR spectrum of the ligand Fig.(2) showed strong absorption bands at 1724 cm$^{-1}$ and 1687 cm$^{-1}$ assigning to ν (C=O) of phthalimide and ν (C=O) of amide respectively. The vibration of (N–H) group was showed at 3271 cm$^{-1}$. [31].

![Structure of ligand](image)

Fig.(1) Structure of ligand.
$^1$HNMR spectrum for ligand Fig.(3) showed characteristic signals at $\delta = (7.87-8.02)$ ppm due to aromatic protons (a, b, c), at $\delta = (8.85)$ ppm belong to aromatic protons (d) of pyridine ring, at $\delta = (11.7)$ ppm belong to (NH) proton. $^{13}$CNMR spectrum for ligand Fig.(4) showed characteristic signals at $\delta = (121.9, 124.45, 129.89, 135.97, 138.18, 151.23)$ ppm due to aromatic carbons (c, b, a, h, i, d) respectively, at $\delta = (164.66, 165.51)$ ppm belong to amide carbonyl (g) and imide carbonyl (f), respectively.
The FT-IR spectra of all metal complexes exhibited remarkable changes in the positions and intensities of carbonyl and imine moieties. The manganese (II) complex [Mn(L)$_2$(H$_2$O)$_2$]Cl$_2$ showed a broad band around 3564 cm$^{-1}$ assigning the ν (OH) group of coordinated water [32]. As well as, the lowering in the stretching frequency of (C=O) to (1647-1627) cm$^{-1}$ assigning the bonding of oxygen atom of carbonyl with Mn (II) ion.

The solid complex of copper (II) exhibited strong absorption bands (1745-1706) cm$^{-1}$ and (1616-1556) cm$^{-1}$ confirmed the depression of ν (C=O) upon coordination with copper (II) complex which is square-planer symmetry [33-35].

The nickel (II) and zinc (II) complexes showed strong absorptions around (1652-1631) cm$^{-1}$, (1734-1685) cm$^{-1}$, (1595-1515) cm$^{-1}$, due to ν (C=O). However, The weak absorption at (325-286) cm$^{-1}$ and (273-300) cm$^{-1}$ which are assigned to ν (Ni-Cl) and ν (Zn-Cl), respectively. These data confirmed the presence of chloro ligands in the constructions of these complexes. All the metal complexes, Table (1) showed medium to weak bands in the region of (401-586) cm$^{-1}$, and (379-497) cm$^{-1}$, which are belong to the coordination bonds of (M-N) and (M-O) respectively, [32]. However, the bending of δ(OH) for coordination water in manganese (II) and cobalt (II) complexes were appeared at (833-1095) cm$^{-1}$. FT-IR spectral data for ligand and complexes are listed in Table (1).

**Table (1)**

<table>
<thead>
<tr>
<th>No.</th>
<th>Compound</th>
<th>ν (C=O)</th>
<th>ν (NH)</th>
<th>M–O</th>
<th>M–N</th>
<th>M–Cl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L</td>
<td>1724(imide)</td>
<td>1687(amide)</td>
<td>3180-3338</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2</td>
<td>[Cu(L)$_2$]Cl$_2$</td>
<td>1706-1745</td>
<td>3166-3226</td>
<td>422-497(w)</td>
<td>524</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>[Ni(L)Cl$_2$]H$_2$O</td>
<td>1631-1652</td>
<td>3305-3205</td>
<td>447</td>
<td>501</td>
<td>325-268(m)</td>
</tr>
<tr>
<td>4</td>
<td>[Co(L)$_2$(H$_2$O)$_2$]Cl$_2$</td>
<td>1631-1649</td>
<td>3413-3415</td>
<td>366(m)</td>
<td>401-4018</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>[Mn(L)$_2$(H$_2$O)$_2$]</td>
<td>1627-1647(sh)</td>
<td>1596(s)</td>
<td>424-442</td>
<td>586</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>[Zn(L)$_2$]Cl$_2$</td>
<td>1734-1685(s)</td>
<td>1793(w)</td>
<td>3564(s)</td>
<td>379-404</td>
<td>528-561</td>
</tr>
</tbody>
</table>
2- Magnetic moment and Electronic spectra

The free ligand (L) spectrum was estimated the it’s UV-visible in (0.001M ethanol), displayed two transitions at 235 nm and 260 nm assigning to chromophore transitions $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ respectively. The solution of metal complexes in (DMSO $10^{-4}$M) showed remarkable changes in the uv-visible spectra compared with the spectrum of ligand. The yellow solution of Mn(II) complex displayed two absorption at 253 nm and 353 nm which are assigned to MLCT and $\pi \rightarrow \pi^*$ transition respectively; thereby supports the octahedral structure around manganese (II) ion. [36].

The pal brown solution of Co (II) in DMSO sowed high intestine bands at 258 nm, 259 nm, and 360 nm assign by the same way no d→d transitions in involving in the structure of ligand (isonozide) Lewis base. By the same way no d→d transitions band for Ni(II) complex, which it’s green solution showed three absorption bands around 245 nm, 259 nm, and 360 nm assigned to $\pi \rightarrow \pi^*$, n→$\pi^*$ and MLCT respectively. The solid complex of Co (II) exhibited increasing in the magnetic moment around 4.2 BM due to orbital contribution in the $(t_2g)^5(eg)^2$ configuration, ascribed the octahedral geometry.

Furthermore, the increasing in $\mu_{\text{eff}}$ for copper (II) complex to 2.7 BM due to high spin of dx$^2$-y$^2$ in the structure of square-planer complexes of Cu(II) ion. The high spin character present in Mn (II) complex due to magnetic moment of 5.3BM supposed the octahedral geometry of sp$^3$d$^2$ hybridization. The normal value of Ni (II) complex in the region of 2.5 BM support the regular tetrahedral structure around Ni(II) ion, since the presence of two odd electrons in the $(eg)^3(t_2g)^4$ configuration, Table (2).

EPR- Discussion

EPR spectra of Ni(II) and Cu(II) complexes were recorded as poly crystalline sample and for DMF solution. The $g_1$, $g_2$, $g_3$, factors observed from Fig.(5) for nickel (II) and from Fig.(6) for copper (II) complexes have increased as the magnetic field (H) increased. The presence of two odd electrons in Ni(II) (3d$^8$) [sp3 tetrahedral] configuration led to $m_l = 3/2, 1/2, -1/2$ and $-3/2$ respectively; with length hedral 0°, 45° and 90°, respectively in the first and second derivatives of EPR for high spin complexes of nickel (II).

The EPR spectrum of copper (II) showed one derivative at $g = 2.0037$ with increasing of magnetic field, from ($H = 3612$ to 3619 G), investigating the presence of $B_1g_2^2$ term of square planer symmetry since the 3d$^9$ in higher energy of dx$^2$-y$^2$ orbital. The $B_1g_2^2$ were estimated by calculation of $g_1$ and $g_{III}$: $g_1 = 2[1-(\lambda/\Delta L)]$, $g_{III} = 2[1-(4\lambda/\Delta L)]$. Where $\Delta L$ represent the energy observed from digital of device, [30], [38-40].

<table>
<thead>
<tr>
<th>No.</th>
<th>compound</th>
<th>color</th>
<th>Yield %</th>
<th>m.p.</th>
<th>$\lambda_{max}$</th>
<th>$\lambda_{max}$ cm$^{-1}$ mol$^{-1}$</th>
<th>$\mu_{\text{eff}}$ (BM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>L</td>
<td>white</td>
<td>90</td>
<td>220-222</td>
<td>235,260</td>
<td>5</td>
<td>---</td>
</tr>
<tr>
<td>2</td>
<td>[Cu(L)$_2$]Cl$_2$</td>
<td>Light blue</td>
<td>83</td>
<td>276-278</td>
<td>896,293</td>
<td>85</td>
<td>2.2</td>
</tr>
<tr>
<td>3</td>
<td>[Ni(L)Cl$_2$.H$_2$O</td>
<td>Light green</td>
<td>80</td>
<td>263-265</td>
<td>245,259,360</td>
<td>12</td>
<td>2.8</td>
</tr>
<tr>
<td>4</td>
<td>[Co(L)$_2$(H$_2$O)$_2$]Cl$_2$</td>
<td>Light brown</td>
<td>78</td>
<td>322-324</td>
<td>258,360</td>
<td>78</td>
<td>4.2</td>
</tr>
<tr>
<td>5</td>
<td>[Mn(L)$_2$(H$_2$O)$_2$.Cl$_2$</td>
<td>Faint yellow</td>
<td>75</td>
<td>257-259</td>
<td>258,353</td>
<td>73</td>
<td>5.5</td>
</tr>
<tr>
<td>6</td>
<td>[Zn(L)$_2$Cl$_2$]</td>
<td>white</td>
<td>76</td>
<td>347-349</td>
<td>239,264</td>
<td>10</td>
<td>Diama-gnetic</td>
</tr>
</tbody>
</table>
Conclusion

The infrared spectra and the resonance spectrum of the proton and carbon demonstrated the agreement of prepared ligand with the proposed structure. Molecular conductivity measurements, magnetic resonance, FT-IR, $^1$HNMR, $^{13}$CNMR, EPR spectra, showed that the shapes of the prepared complexes was square planer with copper (II) ion and the tetrahedral with nickel (II) and octahedral with both, cobalt (II), manganese (II) and zinc (II). Fig.(7) shows the proposed shapes of prepared complexes.
**References**


