

A Novel Ni(II) Complex: Synthesis, Spectral and Biological Activity Determination Studies

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Abstract – A new Ni(II) metal complex of the ligand ((E) methyl 6-benzyl-2-(4-(benzoxy)benzylideneamino)-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-3-carboxylate), derived from (methyl 2-amino-6-benzyl-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-3-carboxylate) and 4-benzoxybenzaldehyde, has been obtained. Standard spectroscopic techniques were used to elucidate the structural features of the ligand and its nickel (II) complex (elemental analysis, Fourier transform infrared (FT-IR) spectra, ¹H-NMR (proton nuclear magnetic resonance), elemental analysis, molar conductance, UV–Vis (ultraviolet-visible) spectra, magnetic susceptibility, LC-Mass spectrometry, and TGA (thermogravimetric analysis). The analytical data showed that the Ni(II) complex is located in the ligand: metal ratio (1:1). Spectral studies revealed that the ligand bonds bidentate to the Ni metal ion via the nitrogen atom of the CH=N (azomethine) group and the oxygen atom of the C=O (carbonyl) group. A distorted octahedral structure can be suggested for the Ni(II) complex from electronic spectrum data and magnetic susceptibility values. The in vitro antioxidant and enzyme inhibition activities of Ni(II) complex were investigated. Acetylcholinesterase enzyme inhibition potential of the synthesized Ni(II) complex was found to be close to the standard tacrine compound. The Ni(II) complex was evaluated for its in vitro antioxidant activity according to the DPPH (1,1-Diphenyl-2-picrylhydrazyl) free radical scavenging activity and CUPRAC (cupric ions reducing capacity) in vitro bioanalytical methods. The synthesized Ni(II) complex showed effective antioxidant activity according to the both CUPRAC and DPPH method.

Keywords – Biological Activity, Ni(II) Complex, FRAP, Spectroscopy Technique, Schiff Base

I. INTRODUCTION

Schiff bases are organic compounds that contain the imine or azomethine (-C=N-) functional group in their molecular structure. First identified by Hugo Schiff in 1864, they are synthesized by the condensation of primary amines with carbonyl compounds (aldehydes or ketones). They are widely used as intermediates in organic synthesis (cyclization, enantioselective oxidation, cycloaddition), dyes, pigments and in the synthesis of coordinate compounds. Due to their flexible electronic structure, Schiff bases have an incredible tendency to coordinate with transition metals, forming stable complexes. Transition metals play an

important role in the physiochemical activity of living organisms due to their unique properties such as different electrochemical behavior, coordination tendencies in different modes and reactivity towards organic nucleophiles. This enhances the functionality of the Schiff bases and increases their biological activity. Schiff bases are also known to have a wide range of bioactivities. These include antioxidant, anti-bacterial, anti-fungal, anti-tumour, anti-malarial, anti-fever and anti-inflammatory properties. Their use as ligands in complexes is related to their versatile applications such as enhancing biological or catalytic activity, providing higher thermal stability, obtaining porous

coordination compounds (1D, 2D or 3D) or even as corrosion inhibitors [1-5].

The coordination chemistry of the Schiff base complexes of Ni, Co, Cu and Zn is of great importance, for biological applications. Cu and Co complexes can mimic the active sites of metalloenzymes. They show an important function in bioinorganic chemistry. Schiff base complexes of Ni and Co show promising antimicrobial activities. These complex compounds are potential candidates for designing and developing novel antibiotics. A number of Cu and Zn Schiff base complexes have shown photocatalytic activity. These can be used in the purification of water and the conversion of solar energy [6,7].

Schiff bases and their metal complexes are major antioxidative agents. Free radicals are donated hydrogen and electrons. Schiff base compounds could be coordinated to different metals. This is due to the fact that they have different binding properties to metals. Metal complexes that enhance the antioxidant activity of ligands have very important biological activities.

The treatment of various health problems is often associated with the enzyme inhibitory properties of compounds. Many Schiff bases and their transition metal complexes have been investigated for their enzyme inhibitory activities. Significant results have been obtained [8].

This work intention to synthesize novel Ni(II) complex prepared using 1:1 (M:L) molar ratio with nickel(II) metal ion. The structures of Ni(II) complex was characterized by different spectroscopic methods including proton NMR ($^1\text{H-NMR}$), UV-Vis, FT-IR, microanalysis (CHN), conductivity, mass spectra, magnetic moments, and Thermogravimetric analysis (TGA). The novel Ni(II) complex was structurally characterized using various analytical and spectroscopic methods. The antioxidant capacities of the complexes were determined by 1,1-diphenyl-2-picryl hydrazyl (DPPH) free radical scavenging assay and Cupric Reducing Antioxidant Capacity (CUPRAC) methods. Ni(II) complex was also tested for acetylcholinesterase (AChE) enzyme inhibition potential. It was found that the Ni complex of the Schiff base had significant AChE enzyme inhibitory activity and antioxidant activity.

II. MATERIALS AND METHOD

Elemental analysis of the synthesized compounds was performed using an ELEMENTAR Vario EL III CHNS analyzer. A Perkin Elmer 65 FT-IR spectrophotometer with KBr pellets was used to record infrared spectra for each compound. UV-visible spectra were measured in the wavelength range 200-800 nm using a Shimadzu UV-1800 spectrophotometer. Mass spectrometric analysis was recorded on a SCIEX Triple TOF 5600 spectrometer using acetonitrile as solvent. The $\text{Hg}[\text{Co}(\text{SCN})_4]$ calibrant was used to perform the magnetic moments of the complex on a Gouy balance. Thermogravimetric analysis was measurement at a heating rate of 10 °C/min. rate using alumina as standard on a Perkin Elmer Diamond TG/DTA thermogravimetric analyzer in a high purity argon atmosphere at a flow rate of 20 mL/min.

A. Synthesis and characterization of Nickel Complex

To a hot ethanolic solution of the ligand (0.5 g, 1.0 mmol), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ (0.27 g, 1.0 mmol) was slowly added to the solutions in a 1:1 ratio of ligand to metal under reflux conditions for 7 h. Both the purity of the products and the progress of the reaction were monitored by TLC. After washing with diethyl ether, the resulting product was dried over anhydrous CaCl_2 in a desiccator at reduced pressure.

$[\text{NiLCl}_2(\text{H}_2\text{O})_2]1.5\text{H}_2\text{O}$. Light brown powder, Yield: 80%, M.p.: 242 °C. Anal. Calc. for $\text{C}_{30}\text{H}_{35}\text{N}_2\text{O}_{6.5}\text{SNiCl}_2$ (689.23 g/mol): C, 52.23; H, 5.07; N, 4.06; S, 4.65. Found: C, 53.21; H, 5.05; N, 4.10; S, 4.70%. FT-IR Data (KBr, ν cm^{-1}): 3377 ($-\text{OH}/\text{H}_2\text{O}$)_{br}, 3062, 3009 (Ar. $-\text{CH}$), 2948 (Alip. $-\text{CH}$), 1686 (C=O), 1670 (CH=N), 1596, 1575, 1508 (Ar. C=C), 832 (H_2O), 745 (C-S-C), 573, 514 (M-O), 480, 460 (M-N). UV-Vis. (λ_{max} , nm): UV-Vis. (λ_{max} , nm): 227, 233, 246, 254, 266, 279, 286, 297, 302, 319, 369, 410, 412. ESI-MS (m/z): 691.23 (calc.), 691.30 (found) $[\text{M}+2\text{H}]^{2+}$. μ_{eff} (B.M.): 3.70. Λ_{M} : 13.60 $\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$.

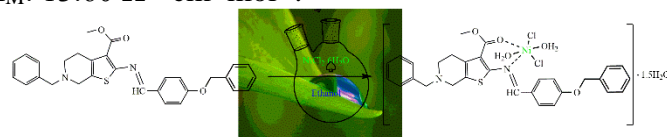


Fig. 1 Structure of the ligand and its Ni(II) complex

B. Acetylcholinesterase Enzyme Activity

AChE activity of the complex was determined according to a slight modification of the Ellman's method [9,10].

C. Antioxidant Methods

DPPH (1,1-Diphenyl-2-picrylhydrazyl) free radical scavenging activity and CUPRAC (cupric ions reducing capacity) in vitro bioanalytical methods were used to evaluate the antioxidant activity of the synthesized Ni(II) complex [11,12].

III. RESULTS AND DISCUSSION

A. Acetylcholinesterase Enzyme Activity

AChE activity of the Ni(II) complex was determined to be close to the standard tacrine compound. According to the results, 60.8% of the AChE activity was inhibited by the standard tacrine, whereas 50.0% the AChE activity was inhibited by the Ni(II) complex at 15 μM concentration (Fig 4). In the Fig. 2 the decreasing enzyme activity can be seen clearly, by increasing the concentration of the complex and standard compound.

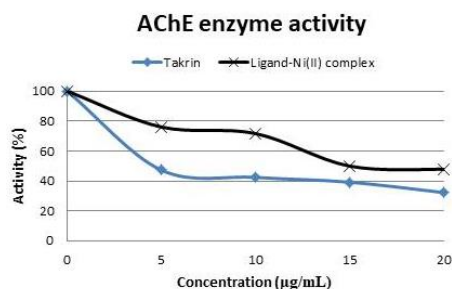


Fig. 2. AChE activity of the Ni(II) complex of the ligand

B. Antioxidant Activity

The synthesized Ni(II) complex was found to have good antioxidant activity according to the CUPRAC method.

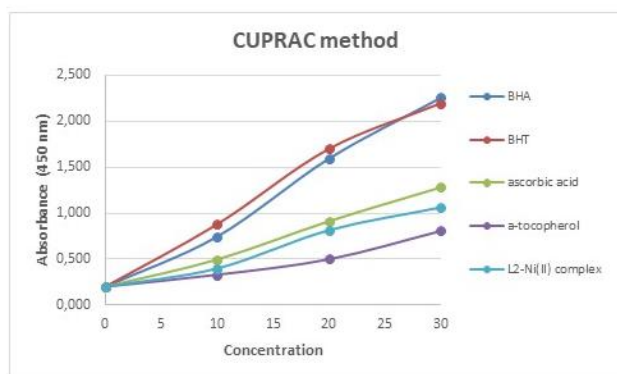


Fig. 3. CUPRAC reducing antioxidant activity of the Ni(II) complex of the ligand

DPPH method's results showed that, the Ni(II) complex had effective DPPH radical scavenging activity compared to the standard antioxidants (Fig. 4).

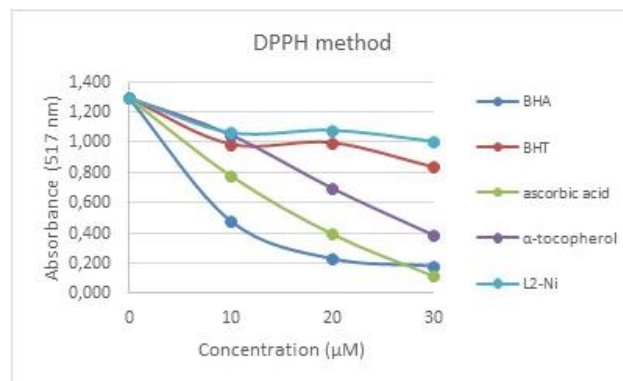


Fig. 4. DPPH radical scavenging activity of the Ni(II) complex of the ligand

C. Characterization

The unique infrared bands of the Schiff base in the ground state ($4000\text{--}450\text{ cm}^{-1}$, KBr) in comparison to the Ni(II) complex provided valuable information about the binding sites of the important groups that were changed, especially the Schiff base.

The free Schiff base shows a broad signal in the IR spectrum at 1696 cm^{-1} , attributed to the carbonyl group, which shifted to 1686 cm^{-1} in the spectral data of the metal complex. Similarly, a signal at 1600 cm^{-1} appeared due to the azomethine $\nu(\text{CH}=\text{N})$ group, this band shifted to 1676 cm^{-1} in the Ni(II) complex. Thus, the frequency shifted to lower and higher values after complexation due to participation of azomethine nitrogen and carbonyl carbon in coordination. The appearance of a broad signal in the IR region $3430\text{--}3490\text{ cm}^{-1}$ showed the presence of coordinated H_2O in the spectra of the Ni complex. Two new signals were ascribed to Ni-O and Ni-N, respectively, in the regions $514\text{--}573\text{ cm}^{-1}$ and $460\text{--}480\text{ cm}^{-1}$ [13-15].

The electronic spectra of the Schiff base confirmed two types of transitions. The first one occurred below 300 nm and can be assigned to the $\pi\text{--}\pi^*$ transition, due to transitions involving molecular orbitals located on the benzene ring and the carbonyl chromophore. This shows that the coordinating site is the azomethine nitrogen and carbonyl oxygen. The second type of transitions appeared at $305\text{--}400\text{ nm}$. These transitions were assigned to the $n\text{--}\pi^*$ transition due to the $\text{CH}=\text{N}$

(azomethine) group and the benzene ring of the ligands. These bands are also altered in the spectra of the Ni(II) complex. This indicates the involvement of the N atom of the CH=N group in coordination with the central Ni(II) atom. Furthermore, there is a band in the region of 412-319 nm which is ascribed to LMCT (ligand-to-metal charge transfer).

The magnetic moment measurement of 3.70 B.M. confirms the octahedral geometry of the Ni(II) complex [2,16].

In the temperature range 50-1000 °C, the thermogram of the complex $[\text{NiLCl}_2(\text{H}_2\text{O})_2] \cdot 1.5\text{H}_2\text{O}$ shows four stages of decomposition. The first stage, between 50-110 °C, corresponds to the dehydration process. The experimental loss of mass of 6.44% is in good agreement with the calculated loss of mass of 6.53%. The second stage of decomposition is associated with the combustion of the loose $\text{C}_7\text{H}_7\text{OCl}$ and coordinated water molecules and takes place in the range of 110-410 °C. This fact is supported by the experimental weight loss value of 28.09% and the calculated mass loss value of 28.42%. The third stage within the temperature range of 410-535 °C corresponds to releasing the $\text{C}_{16}\text{H}_{16}\text{N}$ organic moiety. This is supported by experimental weight loss 32.23% and calculated mass loss 32.74%. The final stage corresponds to the release of the C_2H_2 organic moiety within the temperature range of 535-600 °C. This fact is supported by the experimental weight loss value of 5.51% and the calculated mass loss of 5.25%. The final product obtained is $\text{C}_4\text{H}_3\text{NOS}$ and NiO .

IV. CONCLUSION

The synthesis and characterisation of the Schiff base ligand and the Ni(II) complex are reported in this study. UV-Vis, infrared, mass spectrometry, magnetic susceptibility, TGA and elemental analysis were used to determine the structure of the Ni(II) complex. The thermal stability and degradation steps of the Ni(II) complex were investigated by TGA. Spectroscopy of Ni(II) complexes indicated that they are bidentate ligands, coordinated to metal ions through nitrogen of azomethine group and oxygen of carbonyl group. The geometry of the Ni(II) metal complex was proposed to be octahedral from the structure of the complex based on UV-Vis, elemental analysis and mass spectra. The antioxidant and enzyme inhibition activities of these compound were also

investigated. The compounds exhibited very good free radical scavenging activity and reducing activity, thus showing strong antioxidant activity. Also, the Ni(II) had effective inhibition properties against the AChE enzyme.

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