

Syntheses, Characterization and *in vitro* biological potent of 2-aminobenzothiazole moiety with Ce(III) metal complexes

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Abstract

The New bioactive metal complexes have been synthesized by reaction of Ce(III) salt in 1:2 molar ratio with ligands L¹ and 3-(ethoxymethylene)-2,3-dihydro-*IH*-indolo-[2,3-*b*]-phenazin-4(*5H*)-ylidene)benzathiazole-2-amine (L²) in methanol. The metal complexes and ligands have been characterized by molar conductance, element analysis, melting point, FT-IR, ¹HNMR, TGA, and XRD analysis and were screened for pathogenic organisms *Bacillus subtilis*, *Staplococcus aureus* (as gram positive bacteria), *Escherichia coli* (as gram negative bacteria) and *Candida tropicalis* and *Aspergillus niger* (as fungi species) were compared to known antibiotics amoxicillin. The complexes are more potent than ligands as antimicrobial and antioxidant agent.

Keywords: Schiff base, antimicrobial, antioxidant, conductivity etc.

Introduction

Oxidative stress, an imbalance toward the pro-oxidant side of the pro-oxidant/antioxidant homeostasis, occurs in several human diseases [1]. Schiff bases are important ligands and can be easily synthesized and coordinated with a variety of metal ions [2] complexes exhibit more effective antioxidant activity than the ligand alone. In this paper, we report syntheses, structural determination of two novel Ce(III) complexes and their biological activities [3-8].

2. Experimental

2.1. Experimental and instrumentation

C, H, N, and S (CHNSO) were estimated by elemental analyzer (Perkin Elmer 2400 Series-II). Multinuclear magnetic resonance spectra ¹H NMR was recorded on a Jeol delta 2 - NMR and Bruker advance II 400 NMR spectrometer respectively. Thermal studies were carried out by using Perkin Elmer TGA-4000. All commercial reagents were procured chemically pure and were of analytical reagent grade.

2.2. Syntheses of ligands

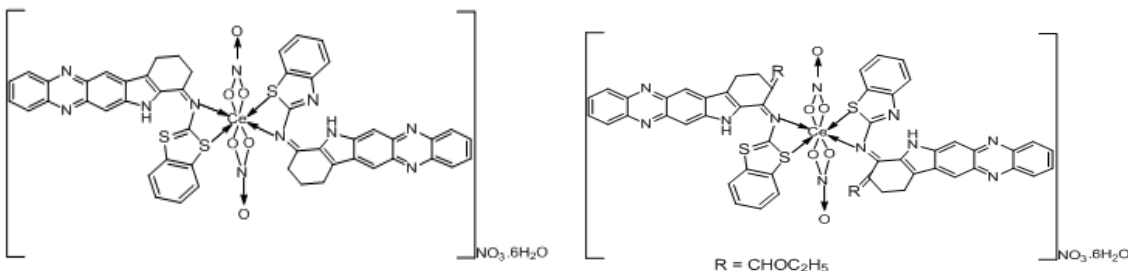
Syntheses of ligands (L^1 and L^2)

Ligands (L^1) and (L^2) were prepared by following literature [9].

Syntheses of complexes

2.3. Syntheses of $[Ce(L^1)_2(NO_3)_2NO_2].6H_2O$ and $[Ce(L^2)_2(NO_3)_2NO_2].6H_2O$

The calculated amount of 0.043 g (0.0001 mol) $Ce(NO_3)_3.6H_2O$ and 0.84 g (0.0002 mol) ligand (L^1) in 1:2 molar ratio dissolved in methanol stirred for 6 min under microwave irradiation at pH 7–8. The progress of the reaction and purity of the product was monitored by TLC using silica gel. By adopting the same synthetic strategy, we were also successfully synthesized second cerium complex in Scheme 1.



Scheme 1. Structure of $Ce(L^1)_2(NO_3)_2NO_2].6H_2O$ and $[Ce(L^2)_2(NO_3)_2NO_2].6H_2O$.

2.4. DPPH & H_2O_2 radical-scavenging activity and Antimicrobial assay

The scavenging of stable DPPH radical is usually applied for the assay of antioxidant activities of compounds across a short time scale.

3. Results and discussion

3.1. Elemental analyses, Magnetic properties Molar conductance

Elemental analyses of Ce(III) complexes of Schiff base ligands are reported 1:1 electrolyte natures of the complexes [10]. Magnetic moment recorded for Ce(III) complex is due to the presence of one unpaired electron [11].

3.2. Spectral Characterization

3.2.1. Electronic spectra

A broad band observed at the 254–252 nm for azomethine group with associated $\pi - \pi^*$, and complexes are attributed decrease 225–222 nm to ligand to metal charge transfer (LMCT). The

electronic spectra of cerium metal complexes show high intensity band in the near UV region at 325–301 nm [12] related $\pi - \pi^*$ and $n - \pi^*$ shifting for due to $4f \rightarrow 5d$ transition for bathochromic shifting and S and N atom participating of complexes formation in Fig. 1.

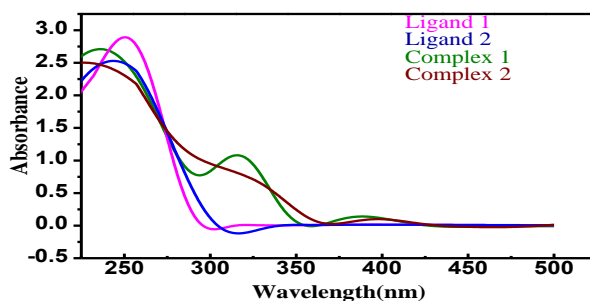


Fig. 1. UV spectra of ligands and Ce metal complexes.

3.3.2 FT-IR spectra

The IR spectra of ligands exhibit strong band in the range of $1636\text{--}1629\text{ cm}^{-1}$ assigned to $\nu(>\text{C}=\text{N})$ group which is shifted to the lower frequencies around $1615\text{--}1610\text{ cm}^{-1}$ upon complexation shows ligand attach with metal complex and results are well agreed with previous reports [13]. This shift shows that $\nu(>\text{C}=\text{N})$ involving in the coordination. Strong absorption bands in the regions $1415\text{--}720\text{ cm}^{-1}$, in the metal complexes confirmed that the nitrate acts as bidentate ligands. $463\text{--}418\text{ cm}^{-1}$ and $407\text{--}402\text{ cm}^{-1}$ which could be assigned to the vibration of $\nu(\text{Ce}\text{--}\text{N})$ and $\nu(\text{Ce}\text{--}\text{S})$, respectively [14] in Fig. 2.

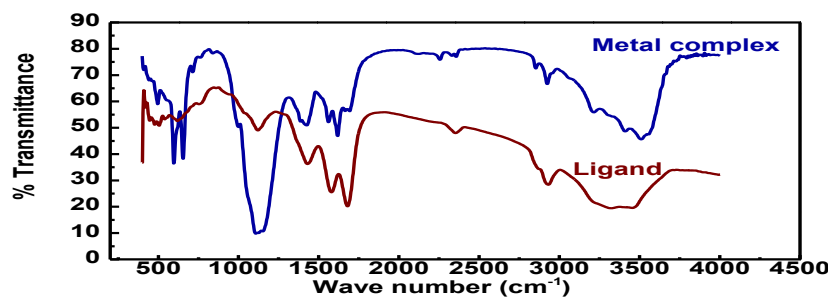


Fig. 2. FT-IR spectra of ligand (L^1) and $[\text{Ce}(L^1)_2(\text{NO}_3)_2]\text{NO}_3 \cdot 7\text{H}_2\text{O}$ complex.

3.3.3. NMR analysis

^1H NMR spectrum of ligand (L^1) (400 MHz, $\text{DMSO-}d_6$): $\delta = 8.5$ ppm (s, 1H, -NH, indole), $\delta = 7.69\text{--}7.03$ ppm (m, 10H, Ar-H), $\delta = 3.3$ ppm (solvent peak), $\delta = 5$ ppm (solvent residual peak), $\delta = 2.49$ ppm (s, 6H, methylene) ^1H NMR spectrum of metal complex (1:2) ($\delta = 8.85$ ppm

(s, 1H, -NH), $\delta = 7.67 - 7.32$ ppm (s, 6H, Ar-H), $\delta = 3.3$ ppm (solvent peak), $\delta = 5-4.9$ ppm (solvent residual peak), $\delta = 2.49-2.06$ ppm (s, 6H, methylene) in Fig. 3 and 4.

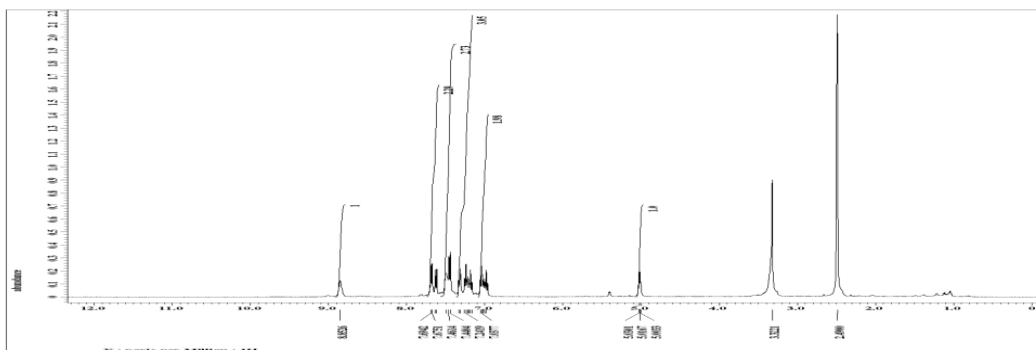


Fig. 3. ^1H NMR spectrum of L^1 ligand.

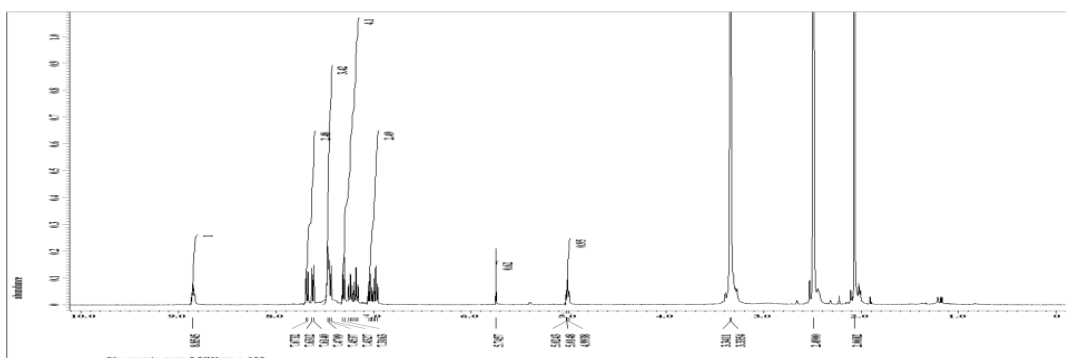


Fig. 4. ^1H NMR spectrum of $[\text{Ce}(L^1)_2(\text{NO}_3)_2\text{NO}_3] \cdot 6\text{H}_2\text{O}$ complex.

3.3.6. X-ray diffraction analysis

The unit cell of complex yielded values of lattice constants, $a = 4.8200 \text{ \AA}$, $b = 4.8200 \text{ \AA}$, $c = 4.8200 \text{ \AA}$. In concurrence with these cell parameters, the conditions such as $a = b = c$ and $\alpha = \beta = \gamma = 90^\circ$, required to be crystal system in Fig. 5.

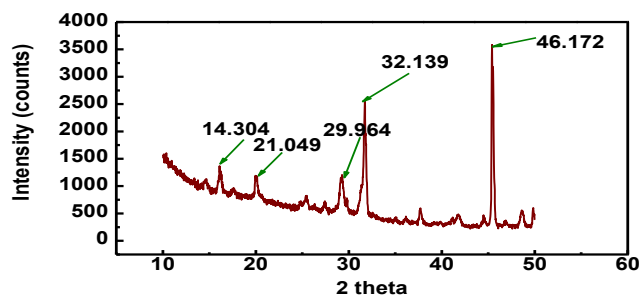


Fig. 5. XRD spectra of $[\text{Ce}(L^1)_2(\text{NO}_3)_2\text{NO}_3] \cdot 6\text{H}_2\text{O}$

3.3.7 Thermal analysis

The first degradation step occurs at the temperature range 130–220 °C corresponding to weight loss 9.15% of six water molecules. The loss of coordinate loss of nitrate weight 10.51% at the temperature range 220–240 °C. Third step occurs at the temperature range 240–590 °C corresponding to weight loss 5.25% of one crystalline nitrate molecule. 35.51% in temperature range 590–670 °C is concluded the loss of ligand moiety from the metal complexes. The final decomposition 14.89% continues until the final residue CeO₂ is left in Fig. 6.

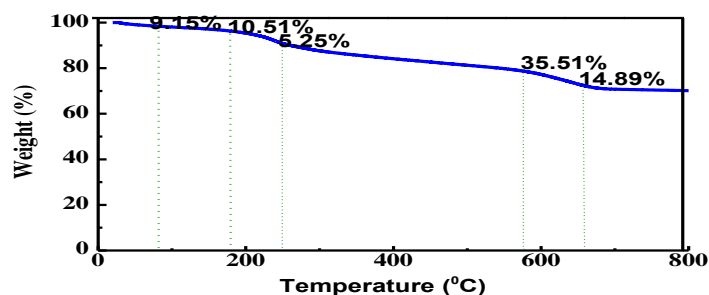


Fig. 6. XRD spectra of $[Ce(L^1)_2(NO_3)_2NO_3] \cdot 6H_2O$

3.4. Biological activities

Antioxidant activities

Hydrogen peroxide scavenging activity

This is the powerful tools of antioxidant activity H₂O₂ is based upon the ability of a compound to convert H₂O₂ into water and was used for the determination of the H₂O₂ scavenging power Figs. 7a and b.

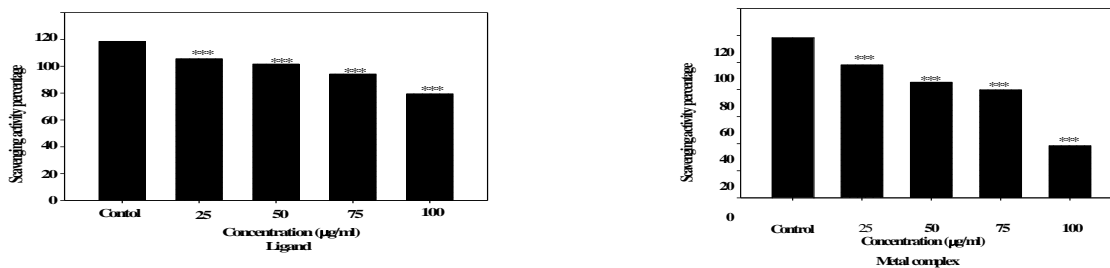
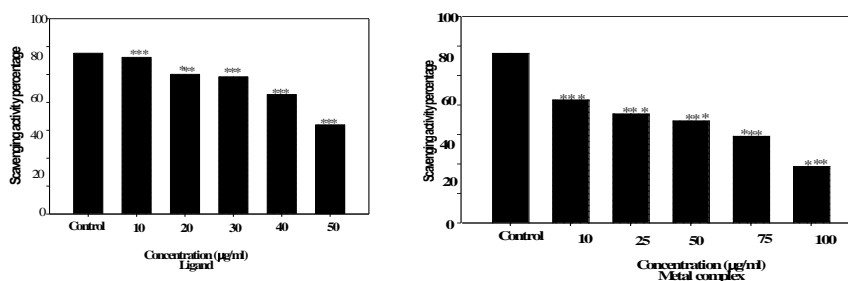


Fig. 7a and 7b. The percent H₂O₂ scavenging activity of L¹ and $[Ce(L^1)_2(NO_3)_2]NO_3 \cdot 6H_2O$.

DPPH radical-scavenging activity

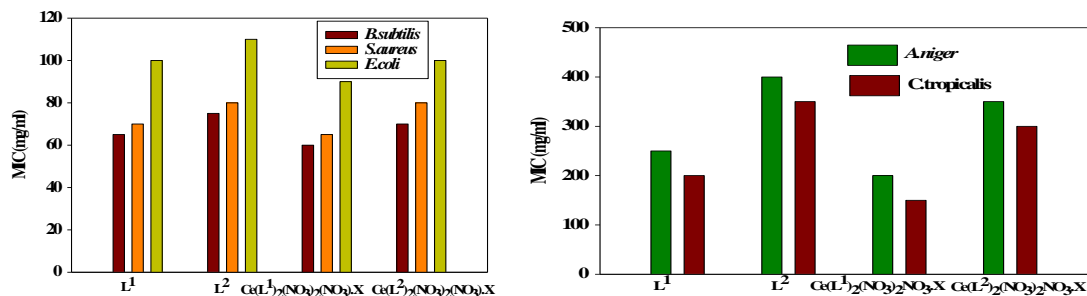
The use of a stable DPPH radical (due to extensive delocalization of the unpaired electron has the advantage of being less affected by side reactions, such as enzyme inhibition and metal chelation [15-17]. The values of DPPH radical scavenging activities of the ligand, and complex are given in Figs. 8a and b.



Figs. 8 a and b. The percent DPPH scavenging activity L^1 and $[Ce(L^1)_2(NO_3)_2]NO_3 \cdot 6H_2O$.

Antimicrobial activities

Gram positive bacteria *B. subtilis* ATCC 6633 and *S. aureus* ATCC 6538P, gram negative bacteria *E. coli* ATCC 25922 and yeast like fungi *A. niger* MTCC 282 and *C. tropicalis* ATCC 13803. Increased activity of the metal chelates can be explained on the basis of chelation theory [18]. Ligands and partial sharing of positive charge of metal ion with donor groups of the Schiff base ligand [19, 20].



Figs. 8 a and b. Antibacterial and antifungal activity against ligands and their metal complexes.

4. Conclusion

The Schiff bases derived from the condensation between heteroaryl ketone and 2-aminobenzothiazole in 1:1 molar ratio, series of bidentate ligands synthesized 1:2 molar ratio and complexes showed bicapped octahedral geometries. The studied complexes represent efficient

antimicrobial agents. The study revealed that the ligand (L¹) and [Ce(L¹)₂(NO₃)₂]NO₃.6H₂O is more potent for antioxidant activity than ligand (L¹).

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