Research on Biological Properties of Ruthenium (III) Heterocyclic Schiff Base Complexes

K. Sampath, S. Sathiyaraj, P. Indhumathi, M. Shanmugaprakash

Abstract. A set of ruthenium complexes of +3 oxidation state were synthesized with the available ruthenium precursors and the synthesized Schiff base ligands. The complexes are formed by the substitution of the ligand in the octahedral metal precursors. Samples are characterized using analytical as well as spectroscopic techniques. To ascertain pharmacological properties binding study with DNA were carried out. Further, cleavage studies were performed with gel electrophoresis. The in vitro antitumor property was analysed in HeLa tumor cell lines.

Key words: Ruthenium, complexes, +3 oxidation State, Antitumor.

I. INTRODUCTION

In the last few decades, the metal complexes have extensively studied as DNA footprints.1,2 A significant role plays in biomolecules by the metal complexes and can bind with DNA intercalation, groove-binding, etc.2,3 Hence, the metal complexes were investigated to act as chemotherapeutic agents.4,5 Notably, platinum based complexes, i.e., cisplatin and carboplatin, are already identified to be a potential anticancer drugs.6 Schiff bases are potential antitumor candidates.7

The metal complexes containing heterocyclic compounds are of current interest due to the remarkable biological properties, since, it possesses the hetero atoms, S and O, etc.8 Because of the ligand exchange property and resemblance to iron in binding to certain biomolecules, ruthenium complexes are potent candidates in medical applications.9

From these investigation, we designed a ruthenium(III) complexes containing Schiff bases of thiazole derivatives. The bio-property of complexes was analysed by DNA binding and anticancer activity with HeLa cancer cells.

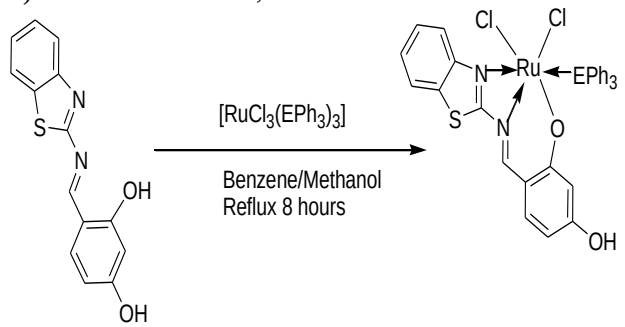
II. EXPERIMENTAL

Reagents and Methods. The AR and Reagent grade chemicals was used as purchased. The solvents are used in all the methods were purified.10 The Schiff base ligand was synthesized based on the reported literature.11 Mass spectrum of the complexes was at SAIF, IITM, Chennai. The EPR spectrum of the complexes were recorded at the SAIF, IIT Bombay. Melting points of the samples were recorded on Veego The [RuCl3(PPh3)3]12 and [RuCl3(AsPh3)3]13 were used for ligand substitution reactions were synthesized by reported literature.

Synthesis of Schiff base ruthenium(III) complexes. The metal precursors, [RuCl3(EPh3)3] (E= P/As), were dissolved in benzene whereas the Schiff base (in methanol) was slowly added with stirring and were refluxed to about 8 h. Evaporation of solvents in the reaction mixture gave a colored precipitate.

[RuCl2(PPh3)(L1)] (1). Yield 65%, Colour: Brown and M.P.: 279 oC. CHNS Calc for C32H24Cl2N2O2PRuS is C, 54.63; H, 3.44; N, 3.98; S, 4.56 and found: C, 54.50; H, 3.61; N, 4.11; S, 4.73. IR (cm-1): 1606 ν(C=N), 1260 ν(Ph-CO), 1590 ν(C=N thiazole ring). UV-vis, nm: 308, 366, 414, 447, 481, 529, 584. EPR, g value: 2.20. μeff: 1.97 μB. EI-MS, m/z (M+): Calculated = 703.56; Found = 704.

[RuCl2(AsPh3)(L1)] (2). Yield 61%; Colour: Brown and M.P.: 292 oC. CHNS Calc for C32H24Cl2N2O2AsRuS is C, 51.42; H, 3.44; N, 3.75; S, 4.29 and found: C, 51.01; H, 3.70; N, 3.93; S, 4.54. IR (cm-1): 1594 ν(C=N), 1284 ν(Ph-CO), 1575 ν(C=N thiazole ring). UV-vis, nm: 306, 368, 409, 440, 582. EPR, g value: 2.24. μeff: 1.92 μB. EI-MS, m/z (M+): calculated = 747.50; Found = 748



Scheme Synthesis of complexes, where, E= P or As.

DNA interaction experiment. DNA interaction experiments were carried by the methods available.10,14,15

Anticancer activity. Anticancer study was carried out on HeLa cancer cells and The MTT assay was used for cell viability test. The experimental procedures were followed according to the reported literature.15

III. RESULTS AND DISCUSSION

The thiazolyl Schiff base substituted ruthenium(II) complexes are air stable and non-hygroscopic. The calculated data were comparable with elemental analysis and other analytical data found which confirms the molecular formulae (Scheme) proposed for the complexes.

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Ir Spectral Studies

The FT-IR spectroscopy is one of the important technique used to elucidate the structure of the compounds, Also, It helps to found out the mode of co-ordination of the ligands with the ruthenium atom. A very strong band, C=N of Schiff base, showed at 1635 cm−1 which was shifted to 1594-1606, in complexes, confirms the coordination of N atom of ligand with ruthenium.16-18 The phenolic ν(C-O) band found at 1254 cm-1 in Schiff base.18 This band shifted to 1260-1284 cm-1 confirms the second coordination via phenolic oxygen. The oxygen and nitrogen mode is also supported by a band, 442-460 cm−1 and 510-545 cm−1 for ν(M-O) and ν(M-N)19, respectively, complexes analyzed. The other characteristic bands of triphenylphosphine and AsPh3 are also appeared in predictable regions.20

Uv-Visible Spectra

All the Ultra violet - Visible spectrum of the compounds were dissolved in dimethylsulfoxide and recorded. The uncoordinated ligand showed two bands at 309 and 368-448 nm. These bands due to the π-π* & n-π* transitions in the aromatic ring and imine chromophore.21 In ligand substituted complexes, the ligand centered bands were shifted. It reveals the coordination to the metal precursors. The charge transfer bands appeared at 306-584 nm. For ruthenium(III), 2T2g is the ground state whereas 2A2g and 2T1g are the first excited doublet levels from t2g4 eg1 configuration.22 The spectral features are comparable to other ruthenium(III) octahedral complexes.23-25

Ei-Mass Spectra

EI-mass spectral fragments of ligand substituted ruthenium(III) complexes are in good agreement with the proposed structure. Figure 1 shows the mass spectrum of the complex 1. The M+ ion peak appeared at m/z = 704 for 1 and 748 for 2, confirms the proposed structure.

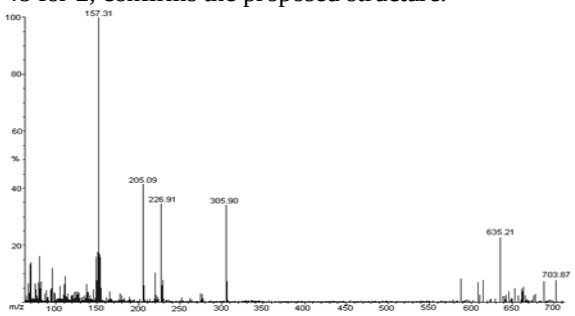

Figure 1 EI-Mass spectrum of the complex [RuCl(PPh3)2(L1)] (1)

Magnetic Moment

The complexes have shown magnetic susceptibility value in the range of μeff = 1.92-1.97 BM reveal that they are paramagnetic and in low-spin 4d5 configuration. This is respect to a single unpaired electron. It confirms the +3 oxidation state of ruthenium.

Epr

The X-band EPR spectrum were recorded in solid state at ordinary temperature. Figure 2 shows the EPR spectrum of complex 1. It is a characteristic spectrum of an axially system with g□ 2.23 and g|| around 2.16, for a tetragonally distorted (gx=gy≠gz) octahedral field. It indicates the tetragonal distortion in the complexes. The complex 2 exhibited the g value of 2.24 due to spin exchange in the intermolecular molecules. The nature and position of peaks are comparable to other reported octahedral ruthenium complexes.24,20

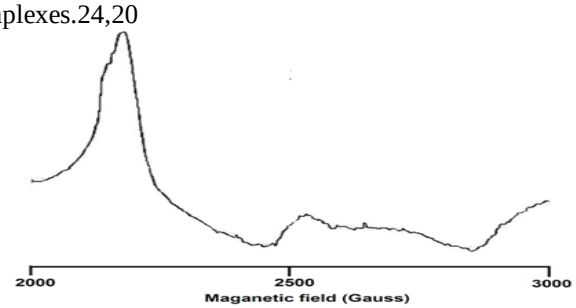

Figure 2 EPR spectrum of the complex [RuCl(PPh3)2(L1)] (1)

Dna Binding Study

UV Visible spectroscopy i.e., absorption spectroscopic technique is universally accepted technique, used to find out binding properties of samples with DNA. When increasing DNA concentration into the complex solution, the change in absorption spectral features is shown in Figure 3. At 257-272 nm, a hyperchromic effect was observed with 2-3 nm hypsochromism. This confirms a binding between DNA and complexes. These result inferred a non-intercalative binding.

The binding constant (Table 1) of the ligand (reported value) and complexes were, 0.84 X 104 M-1, 8.3 X 104 M-1 (1), 4.8 X 104 M-1 (2), of the order 1 > 2 > HL. The binding constant values indicates that the complex 1 showed better binding than other complexes.

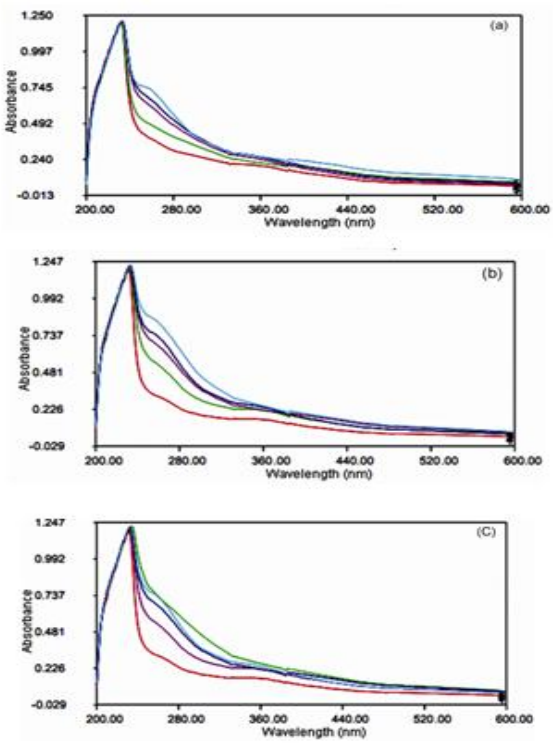

Figure 3 UV-Visible spectra of the compounds in Tris HCl-NaCl buffer, (a) HL1, (b) complex 1 and (c) complex 2 with change in DNA concentration.

Cytotoxic activities. Cytotoxic activity was tested in Human cervical cancer cell line. The IC50 of the complexes was obtained in the concentration range, 1-100 μM. The IC50 values are 139 ±2, 21± 4 and 58 ± 3 for the ligand, complex 1 and complex 2, respectively. The result reveals that the complex 1 showed more cytotoxicity than the complex 2. The ligand does not register significant activity.

IV. CONCLUSION

Bezothiazolyl – substituted salal Schiff base substituted Ruthenium(III) complexes were synthesized. These ligand substituted complexes were characterized with (CHNS), FT-IR, UV-vis, magnetic susceptibility, EPR and Mass. The characterization results reveals an octahedral geometry to the ruthenium(III) complexes. DNA - binding study by absorption titration technique indicates electrostatic interaction with DNA surface. The Kb values reveal the strong binding of the complexes containing PPh3 with CT-DNA than AsPh3 complexes. The cytotoxicty activity shows the complex 1 has higher antiproliferative effect than the complex 2 and ligand.

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