Synthesis, spectroscopic, and quantum-chemical analysis of mononuclear Ru(II)-naphthylhydrazine complex

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Abstract: *Ruthenium(II) complexes have become increasingly recognized and utilized as potent anticancer agents in recent years. These compounds possess unique capabilities in targeting cancer cells and interfering with vital cellular processes, offering new hope in the relentless battle against cancer. This research study focuses on the characterization of a newly synthesized Ru(II)-naphthylhydrazine complex by IR and NMR spectroscopies. NMR spectral data have revealed the presence of different chemical environments within **1** based on the chemical shifts observed in the ^{1}H and ^{13}C NMR spectra. The infrared spectra were recorded in the region ranging from 400 cm^{-1} to 4000 cm^{-1}, capturing a comprehensive range of vibrational modes of the studied compound with the main chemical groups outlined. The quantum-chemical optimization of **1** at B3LYP/6-31+G(d,p)(H,C,N,Cl)/LanL2DZ(Ru) level of theory allowed the prediction of structural parameters and analysis of intramolecular interactions governing stability through Natural Bond Orbital approach. The future biological investigation of this compound is advised.*

Keywords: Ru(II), DFT, IR, NMR

2. Introduction

Ruthenium, a transition metal in group 8, exists in oxidation states of Ru(II) and Ru(III), with the possibility of Ru(IV) compounds, which are usually unstable due to higher oxidation states. Ruthenium ions have a hex-coordinated structure with octahedral coordination geometries and Ru(II) complexes are more stable [1]. Ruthenium complexes disrupt critical cellular processes in cancer cells, like apoptosis, by forming coordination bonds with essential biomolecules, such as nucleic acids [2]. First-generation ruthenium compounds ([η^6-arene]ruthenium(II) complexes) in the 1980s showed promise as anticancer agents [3]. Later, drugs like NAMI-A and KP1019 demonstrated remarkable potential in clinical trials against solid tumors, selectively accumulating in tumor tissues while managing toxicity [4]. This research includes

synthetic procedure and spectral characterization of ruthenium(II)-naphthylhydrazine complex, **1**, along with the quantum-chemical optimization.

2. Materials and methods

*2.1. Procedure for synthesis of **1***

The ruthenium salt [{$RuCl_2(\eta^6$-*p*-cymene)}$_2$] was dissolved in methanol and stirred in a nitrogen atmosphere for 15 minutes until fully dissolved. Then, lithium hydroxide and the ligand were added, followed by 15 minutes of stirring in a nitrogen atmosphere. The mixture was left to stir overnight (20 hours). The next day, the solution was placed in a freezer at -25°C for 2 hours, filtered, and washed off with 10 ml of diethyl ether. The filtrate appeared bright ocher yellow.

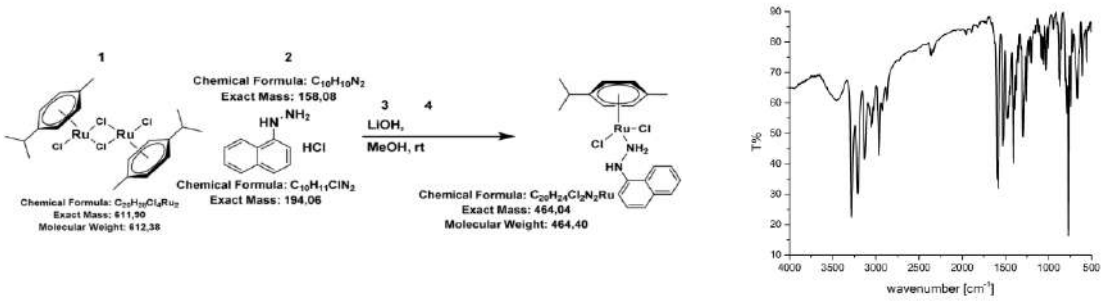

Figure 1. Synthesis of **1** (left) and IR spectrum of **1** (right).

2.2. Analytical methods

The infrared (IR) spectrum was obtained using the FTIR spectrometer - Avatar 370, Thermo Nicolet, covering the range from 400 cm^{-1} to 4000 cm^{-1}. The procedure involved recording a blank sample spectrum with a KBr pellet, followed by the **1** spectrum using a sample pellet containing 100 mg of KBr powder and 1 mg of the complex.

NMR spectra were acquired using a Bruker AvanceTM 400 MHz spectrometer with a Bruker wide bore magnet operating at 300 MHz, referencing chemical shifts to tetramethylsilane. The analysis used 6 mg of the ruthenium complex dissolved in 3 ml of deuterated chloroform.

2.3. Theoretical analysis

The structure of **1** was optimized in the Gaussian 09 Program Package at B3LYP/6-31+G(d,p)(H,C,N,Cl)/LanL2DZ level of theory. The optimization was performed without any geometrical constraints and the absence of imaginary frequencies proved that the stable structure was obtained. The intramolecular interactions were analyzed by the Natural Bond Orbital theory approach.

5. Results and Discussion

*4.1. Analysis of IR and NMR spectra of **1***

Infrared spectroscopy was utilized for the qualitative structural analysis of a newly synthesized ruthenium complex. Figure 1 presents the IR spectrum of **1**. The IR spectrum of **1** shows bands at 3452 and 3284 cm^{-1}, indicating free and associated stretching N-H vibrations of amines. A strong band at 1595 cm^{-1} is assigned to the deformation vibrations of amines. Also, a peak at 1296 cm^{-1} with moderate intensity corresponding to the stretching vibration of C-N bond is noticed. The spectrum contains bands of sp^3 hybridized C-H vibrations at 2964 cm^{-1}. The existence of an aromatic ring and sp^2 hybridized C-H groups are shown at 3051 cm^{-1}. A peak at 1473 cm^{-1} corresponds to CH_2 group vibrations. At lower wavenumbers (665 cm^{-1}) band associated with Ru-Cl vibration is observed.

The ^1H NMR spectrum of **1** exhibits distinct peaks representing specific proton environments with unique chemical shifts (Figure 2). Doublet at 1.33 ppm belongs to hydrogen atoms of isopropyl moiety. Peaks at 2.29 ppm and 3.03 ppm correspond to protons of methyl group and CH group of isopropyl moiety. A peak at 5.56 ppm denotes hydrogen atom of NH group. The rest of peaks are located between 6.9 and 8.1 ppm which is characteristic of the hydrogen atoms within aromatic rings. Distinct carbon environments are observed in the ^{13}C NMR spectrum (Figure 2). Isopropyl and methyl groups display the lowest shifts (22.16, 22.41, and 30.97 ppm). Chemical shifts of the other carbon atoms are between 108.94 and 134.05 corresponding to the carbon atoms of the aromatic ring. The highest value of chemical shift was observed for the carbon atom attached to the hydrazine group (143.76 ppm) which is expected due to the electronegativity of the mentioned group. The most intense signal at 77.03 ppm corresponds to deuterated chloroform, the solvent used.

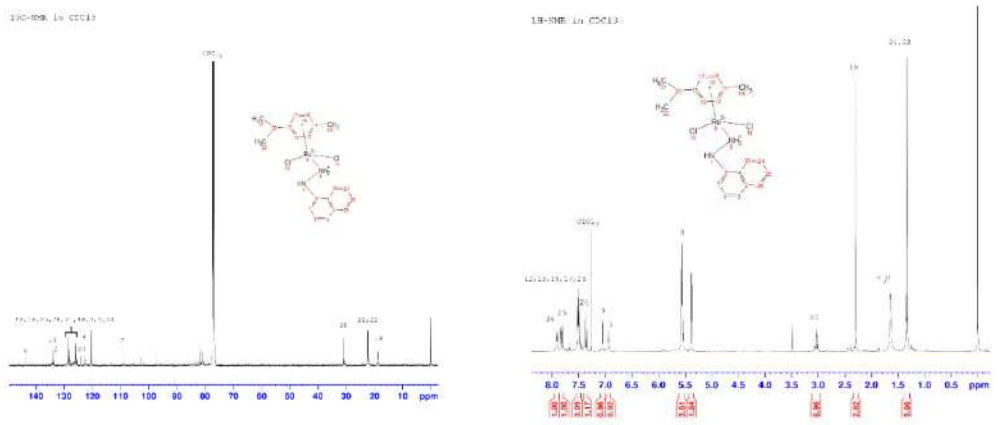

Figure 2. ^1H (left) and ^{13}C (right) NMR spectra of **1.**

*4.2. Optimized structure of **1** and intramolecular interactions*

The optimized structure of **1** is shown in Figure 3. The structure consists of a p-cymene moiety directly attached to Ru(II), naphtylhydrazyl moiety and two chlorido

ions. The Ru-Cl bonds are 2.441 and 2.453 Å which is in the expected range based on the comparison with similar compounds. The Ru-N bond length is 2.176 Å. The angle Cl-Ru-Cl is 90.479°. The optimization of the compound restores the pseudo-octahedral geometry as three positions are occupied by p-cymene moiety. The most abundant interactions include π(C-C)→π*(C-C) of *p*-cymene and napthylhydrazyl rings with energies between 30.6 and 33.1 kJ mol^{-1}. Different stabilization interactions are formed between the aromatic ring and hydrazine group through positive resonant effect of nitrogen atoms. The electron donation from chlorido ligands is very strong, LP(Cl)→LP*(Ru) with a stabilization energy of 350 kJ mol^{-1}. The rest of interactions with the metal ion are much weaker.

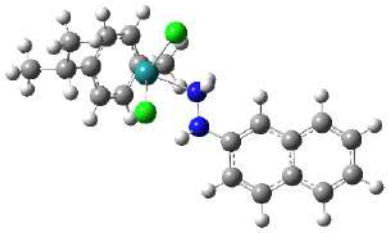

Figure 3. Optimized structure of 1 (at B3LYP/6-31+G(d,p)(H,C,N,Cl)/LanL2DZ(Ru) level of theory)(hydrogen-white, carbon-grey,nitrogen-blue, chlorine-green, ruthenium-teal).

3. Conclusions

This research study focused on characterizing the newly synthesized Ru(II)-naphthylhydrazine complex, **1**, using NMR and IR spectroscopies. The IR spectrum showed characteristic vibrational modes of functional groups, including amines, aromatic rings, and halogens. The NMR allowed the elucidation of the structural properties of 1. The most important stabilization interactions include π(C-C)→π*(C-C) and interactions between donor atoms and Ru.

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