

Synthesis, spectroscopic, and theoretical analysis of Ru(II)-phenylhydrazine complex

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DOI: 10.46793/ICCBIGK23.395A

Abstract: In recent decades, metal-based chemotherapeutics have attracted considerable attention and excitement within the oncology research community, with ruthenium(II) complexes emerging as a particularly promising class of anticancer agents. In this study, the synthesis of a new ruthenium complex was performed, followed by its structural characterization using NMR and IR spectroscopy. The compound's infrared spectrum reveals characteristic bands corresponding to N-H and C-H stretching vibrations from sp² and sp³ hybridized carbon atoms, vibrations of aromatic rings and additional vibrations related to CH₃, C-N, and chloride species at various wavenumbers. The ¹H NMR spectrum of the Ru140 complex reveals distinct peaks corresponding to different atomic environments, including protons attached to sp³ hybridized C-atoms, nitrogen atoms, and protons involved in aromatic rings, as well as signals from deuterated chloroform and water. The ¹³C NMR spectrum displays peaks for saturated carbon atoms in methyl and isopropyl groups at lower, and aromatic carbons at higher chemical shifts. The structure of the complex was optimized at B3LYP/6-31+G(d,p)(H,C,N,Cl)/LanL2DZ level of theory and intramolecular interactions were analyzed through the Natural Bond Orbital approach.

Keywords: ruthenium, DFT, NBO, NMR

3. Introduction

Ruthenium compounds present promising anticancer agents due to the biocompatibility of ruthenium and its similarity to iron [1]. One of the notable features of ruthenium(II) complexes is their ability to interact with biomolecules, including nucleic acids, which are crucial for the survival and growth of cancer cells. By forming coordination bonds with nucleic acids, ruthenium(II) complexes can disrupt essential cellular processes, resulting in cell cycle arrest and programmed cell death (apoptosis),

specifically in cancer cells [2]. In this study, a Ru(II)-phenylhydrazine complex, **C1**, has been synthesized and characterized by IR and NMR spectroscopies. Density functional theory (DFT) and Natural Bond Orbital (NBO) approaches were used for the theoretical analysis of this compound.

2. Materials and methods

2.1. Procedure for synthesis of **C1**

The synthesis of **C1** is shown in Figure 1. Ruthenium salt, $[\{\text{RuCl}_2(\eta^6\text{-}p\text{-cymene})\}_2]$, was dissolved in chloroform under a nitrogen atmosphere and stirred until a clear and reddish solution was obtained. Phenylhydrazine was added in four portions (33 μl each). Upon the addition of the fourth portion, the solution turned orange and became cloudy. After one hour of stirring in nitrogen, the solution was transferred to a freezer at -25°C and filtered after two hours. The flask was washed with 5 ml of chloroform. The resulting filtrate was bright yellow.

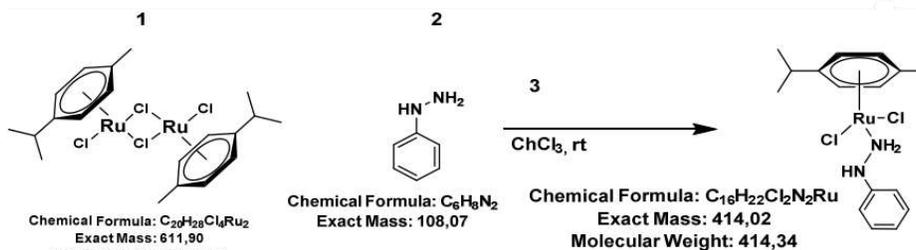


Figure 1. Synthesis of **C1** complex.

2.2. Instrumental methods

IR spectra were recorded on an FTIR spectrometer (Avatar 370 - Thermo Nicolet). The sample was recorded in the form of a potassium bromide (KBr) pellet in the wavenumber range between 400 cm^{-1} and 4000 cm^{-1} . NMR spectra were recorded on Bruker AvanceTM 400 MHz spectrometer with Bruker wide bore magnet at 300 MHz with NMR console Tecmag Apollo. Chemical shifts for ^1H and ^{13}C NMR spectra were referenced to internal standard TMS. The probes were prepared in deuterated chloroform. Peak assignment was done using the MastReNova software.

2.3. Theoretical methods

The structure of **C1** was optimized based on the previously determined level of theory that was suitable for Ru(II)-based compounds, namely B3LYP/6-31+G(d,p)(H,C,N,Cl)/LanL2DZ(Ru), in the Gaussian 09 Program Package. The intermolecular interactions governing the stability of the formed complex were assessed by the Natural Bond Orbital (NBO) approach.

6. Results and Discussion

In the IR spectrum of **C1** (Figure 2), starting from the highest wavenumbers, a band of medium intensity attributed to the stretching vibration of N-H bonds is observed at 3330 cm^{-1} . The presence of aromatic rings in the compound leads to a very intense band at 3180 cm^{-1} . The intense band of C-H stretching vibrations from sp^2 hybridized carbon atoms appears at 3070 cm^{-1} , while the presence of sp^3 hybridized carbon atoms is confirmed by bands at 2990 , 2960 , 2930 , and 2870 cm^{-1} . High-intensity bands corresponding to the deformation vibrations of amine groups are observed at 1600 and 1500 cm^{-1} . Medium-intensity peaks at 1450 and 1390 cm^{-1} are associated with the deformation vibrations of the CH_3 group. Vibrations corresponding to C-N bonds are present at 1280 and 1250 cm^{-1} and are also of medium intensity. Finally, the very intense band at 760 cm^{-1} is characteristic of vibrations associated with chloride species.

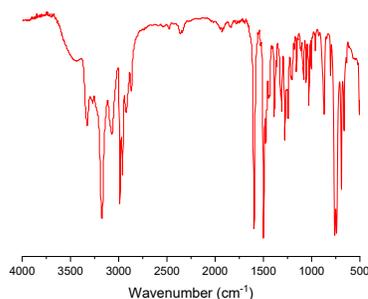


Figure 2. IR spectrum of **C1**

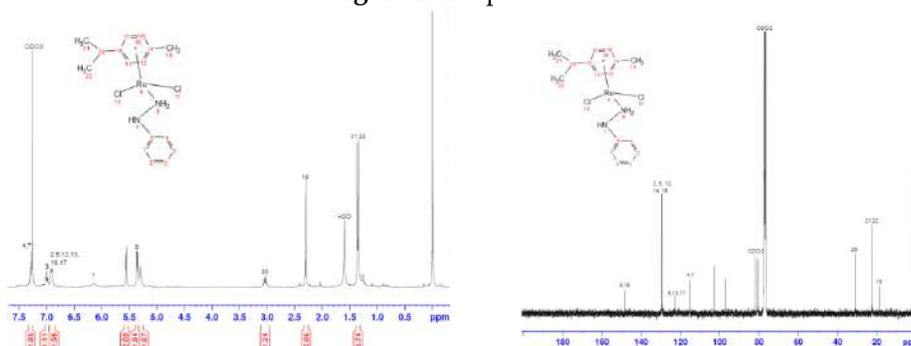


Figure 3. ^1H (left) and ^{13}C (right) NMR spectra of **C1**.

In Figure 3, the ^1H NMR spectrum of **C1** is displayed. The spectrum exhibits doublets at 1.35 ppm , indicating the presence of protons bound to sp^3 hybridized C-atoms. A singlet at 2.30 ppm confirms the existence of an additional methyl group within *p*-cymene moiety. The peak at 3.03 ppm originates from a proton of the CH group. The singlets observed at 5.56 ppm and 6.14 ppm suggest the presence of protons bound to nitrogen atoms. Additionally, the chemical shifts of protons bound to aromatic rings are present in the expected region. The spectrum also shows signals from deuterated chloroform at 7.26 ppm and water at 1.59 ppm . Figure 2 shows the ^{13}C NMR spectrum of **C1**. Singlets at 18.72 , 22.41 , and 30.96 ppm are attributed to carbon atoms of methyl and isopropyl groups. Chemical shifts above 115 ppm are attributed to the presence of aromatic carbons. Additionally, peaks arising from deuterated chloroform, used as a solvent, are seen at 76.70 , 7.02 , and 77.34 ppm .

The optimized structure is presented in Figure 4. It has been previously shown that the selected level of theory can be used for the optimization of the crystal structure of similar compounds and the prediction of IR and NMR spectra. The structure of C1 consists of *p*-cymene moiety in the vicinity of Ru(II), phenylhydrazine that is bound to the metal ion through an amino group and two chlorido ligands. These ligands surround central metal ion in a pseudo-octahedral geometry. The electron donation occurs through π electron cloud and lone pairs on nitrogen and chlorine. Various intramolecular interactions stabilize the structure of C1. The aromatic rings of *p*-cymene and phenyl moieties are stabilized by the interactions between neighboring C-C bonds. The interactions between *p*-cymene and Ru occur through $\pi(\text{C-C})\rightarrow\text{LP}(\text{Ru})$ interactions with stabilization energy of 470 kJ mol⁻¹ which proves the assumption that the *p*-cymene moiety is important for the complex formation. Nitrogen and chlorido ligands form stabilization interactions with Ru with stabilization energies of 370 and 350 kJ mol⁻¹, respectively. Additionally, there is an interaction between chlorido ligand and amino group through a weak hydrogen bond.

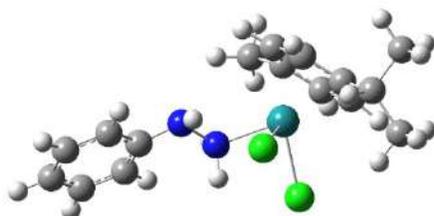


Figure 4. IR spectrum (left) and optimized structure of C1 (at B3LYP/6-31+G(d,p)(H,C,N,Cl)/LanL2DZ(Ru) level of theory)(right).

3. Conclusions

In this study, the synthesis of a new Ru(II)-phenylhydrazyl complex was conducted. The infrared spectrum of the compound confirmed the presence of certain functional groups. The ¹H and ¹³C NMR spectra provided important information about the chemical environment of the atoms, confirming the successful synthesis of the compound. The most important stabilization interactions were determined from the optimized structures. The obtained results confirmed the expected structure of the compound.

Acknowledgment

The authors gratefully acknowledge financial support from the Science Fund of the Republic of Serbia (Serbian Science and Diaspora Collaboration Program: Knowledge Exchange Vouchers: Project TumorSelCoum 6388843).

References

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