XXI Brazilian Meeting on Inorganic Chemistry
X Brazilian Meeting on Rare Earths
III Workshop on Theoretical Bioinorganic Chemistry
Belo Horizonte, September 12 - 15th 2024

Copper(II) Complex with 3,5-dimethyl-4-(arylselanyl)-1*H*-pyrazole Bisligand: Synthesis, characterization, DFT Studies, Antitumoral and Antioxidant activity

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Thematic Area: Biological Inorganic Chemistry

Keywords: Copper complexes, antitumoral and antioxidant activity, DFT studies

Cancer cells may be a selective target for copper-based agents [1]. Selenium-containing compounds are interesting due to their efficacy and selectivity against cancer cells, exerting their action alone or in combination with other drugs. Herein, we describe the synthesis and characterization of one copper(II) complex formed by pyrazolyl ligand containing the Se group (**Figure 1**). The single crystal X-ray analysis of the **2c** complex revealed that a mononuclear complex co-crystallizes in the solid state. Density Functional Theory (DFT) calculations optimize the complexes' electronic structures. The monomeric nature of **2c** is maintained in solution. The DFT calculations show that the cis form is thermodynamically favored with ΔG = -1.407 kcal.mol^{-1} compared to the trans compound. Additionally, **2c** was characterized as a monometallic species by ESI-HRMS and electron paramagnetic resonance (EPR) analysis. Experiments were conducted to evaluate the synthetic radical scavenging effect of DPPH and ABTS at different concentrations (0.2 to 200 µM) using compounds **1** and **2c**. The results demonstrate that the Cu(II) complex tested in this study effectively produced an antioxidant effect. The antiproliferative activity of compounds **1** and **2c** was assessed against various human tumor cell lines and normal cells over 72h. Compound **2c** exhibited significant cytotoxic activity and selectivity against the HCT116 cancer cell line (IC_{50} = 22 ± 0.9 µM). At a concentration of 10 µM, **2c** induced genotoxicity similar to that of doxorubicin in HCT116 cells. More experiments to further investigate the molecular mechanisms of their biological effects are underway.

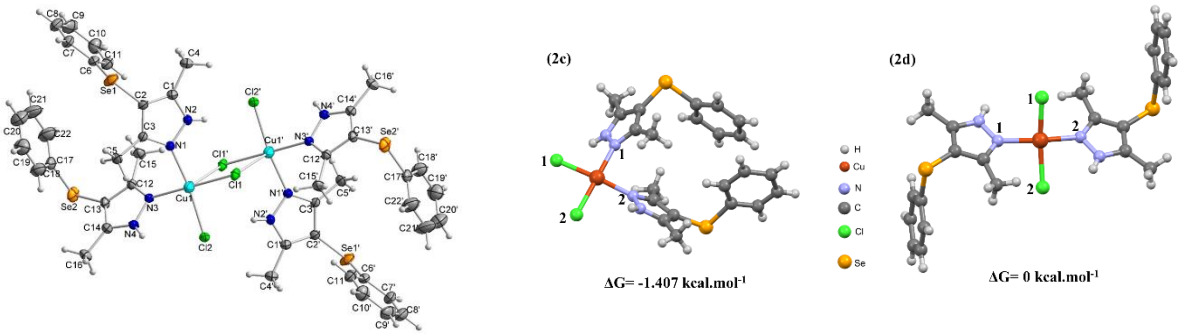

Figure 1. (a) ORTEP drawing of **2c**. Ellipsoids are drawn at the 50% probability level. (b) Ground state optimized structures of **2c (cis)** and **2d (trans)** at the B3LYP/def2-TZVPP/def2-SVP level of theory.

Acknowledgments: CNPQ, FAPERGS, CAPES, PPGQ-UFPel and PPGBio-UFCSPA.

References

[1] Ji, P. et al. Pharmaceuticals 2023, 16, 234.