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

Structure-Activity Relationship of Cu(II) Complexes With Naftalato-Imine Ligands as Effective Compounds in Scavenging Free Radicals

Nathalia S. de Oliveira[1], Ianka J. Nunes[2], Alecia F. da Silva[1], Tamara dos S. Machado[1], Wesley V. Ferreira[1], Jenifer Saffi[2], Adriana C. Pinheiro[1]

[1] *Centro de Ciências Químicas, Farmacêuticas e de Alimentos, Universidade Federal de Pelotas, Brasil*
[2] *Departamento de Ciências Básicas de Saúde, Universidade Federal de Ciências da Saúde de Porto Alegre, Brazil.*
E-mail: natholiveira95@gmail.com; acpinheiro@ufpel.edu.br

Thematic Area: Biological Inorganic Chemistry

Keywords: Copper complexes, Schiff base, antioxidant activity

Schiff bases, a significant group of materials in the field of inorganic chemistry, are characterized by the presence of the azomethine linkage (-C=N-) [1]. The azomethine functional group has been acknowledged as a flexible pharmacophore for the formulation and advancement of numerous bioactive lead compounds. Importantly, derivatives of Schiff bases and their metal complexes have shown promising results, suggesting their potential applications in pharmaceuticals [2]. Copper complexes with Schiff base ligands are promising for their antioxidant properties [2]. Antioxidants are substances that protect cells from the harmful impact of free radicals. Based on these aspects, our group has focused int the synthesis and characterization of two new copper (II) complexes supported by naphthol–imine ligands (**3** e **4**), **Figure 1**. We have assessed their spectroscopic and electrochemical properties. To investigate pharmacological possibilities for its application, we evaluated radical scavenging activities using *DPPH* and *ABTS assay*. **1** and **2** did not show any DPPH radical scavenging activity. In the $ABTS^{+}$ radical scavenging assay, the pro-ligands had similar results to each other, and the positive control, Trolox (IC_{50} = 17.4 ± 0.9 µM and I_{max} of 97.9 ± 0.1% for **1**; IC50 = 4.31 ± 0.2 µM and I_{max} of 86.7 ± 0.1% for **2**; IC_{50} = 10.8 ± 0.2 µM and I_{max} of 100 ± 0 % for Trolox). Complexes **3** and **4** showed a higher capacity for scavenging DPPH and $ABTS^{+}$ radicals than the pro-ligands. In the DPPH assay, the IC_{50} values of the complexes were similar to Trolox. In the ABTS assay, Cu(II) complexes demonstrated a higher potential for scavenging the ABTS radical than Trolox, with complex **4** showing the best antioxidant potential with IC_{50} = 0.8 ± 0.2 µM. Complex **3** showed IC_{50} = 2.1 ± 0.8 µM, while Trolox had an IC_{50} = 10.8 ± 0.2 µM. Then, these compounds showed potent scavenging activity in studies *in vitro*. The MTT assays were used to evaluate the toxicity of the compounds in V79 cells over 24 h, using concentrations ranging from 1 µM to 100 µM. This complex showed low cytotoxicity in mammalian cells and no cytotoxicity in the antioxidant concentration range. Toxicity studies *in vivo* are being conducted.

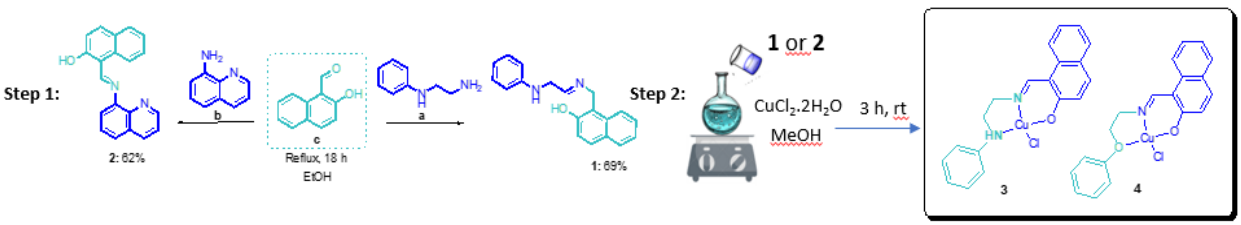

Figure 1. Synthetic route for the preparation of **1** and **2** pro-ligands and their copper complexes.

Acknowledgments: FAPERGS and CNPQ.

References

[1] M.T. Nazeri et al., ACS Comb Sci. 22(8), 361-400 (2020).
[2] I. Tumosienė, et al. Molecules. 25(13), 2980 (2020).