

COMPLEX FORMATION OF COPPER(II) WITH A PROLINE SUBSTITUTED 8-HYDROXYQUINOLINE: SOLUTION STUDIES AND STRUCTURAL CHARACTERIZATION

Inna Safyanova¹, Nóra V. May², Oszkár Csuvi³, Ferenc Fülöp³, István Szatmári³, Eva A. Enyedy¹

¹*Department of Inorganic and Analytical Chemistry, Interdisciplinary Excellence Centre and MTA-SZTE Lendület Functional Metal Complexes Research Group, University of Szeged, H-6720 Szeged, Dóm tér 7, Hungary*

²*Chemical Crystallography Research Laboratory, Research Centre for Natural Sciences, Magyar Tudósok Körútja 2, H-1117 Budapest, Hungary*

³*Institute of Pharmaceutical Chemistry, University of Szeged, H-6720 Szeged, Eötvös u. 6, Hungary*

e-mail: sssafyanova@gmail.com

Abstract

8-hydroxyquinoline and its substituted derivatives are a well-known class of bidentate ligands widely used in bioanalytical and supramolecular chemistry due to wide specter of their applications and high coordination binding activity [1, 2]. 8-hydroxyquinolines and their metal complexes often exhibit anticancer activity [2], and the most prominent example is orally active tris(8-hydroxyquinolato)gallium(III), which is tested under clinical trials phase I and II [3]. The cytotoxicity of 8-hydroxyquinolines is also related to complexation with endogenous metals such as the redox active copper and iron ions [4]. 8-Hydroxyquinolines generally suffer from limited water solubility, and in this work a more water soluble D-proline hybrid molecule, (D)-5-chloro-7-((proline-1-yl)methyl)8-hydroxyquinoline (8HQCl-D-Pro, Fig. 1.a), was developed and its complexation with copper(II) was investigated.

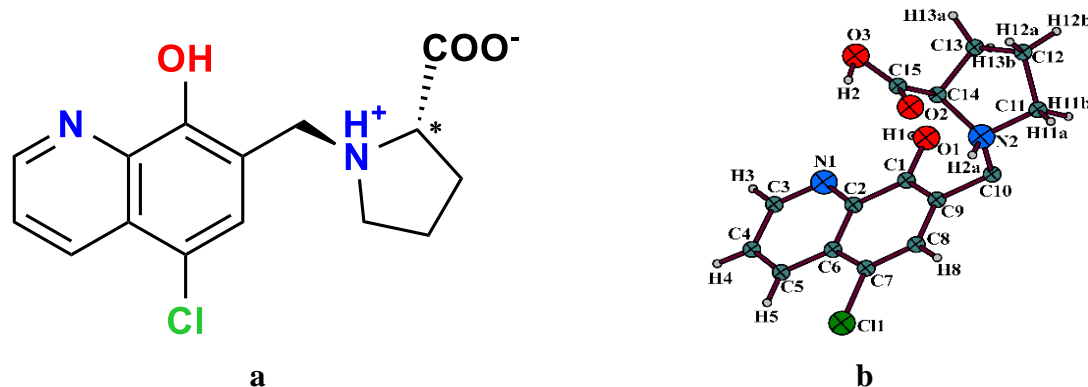


Figure 1. a) Scheme of 8HQCl-D-Pro ligand; b) Crystal structure of 8HQCl-D-Pro.

The ligand was synthesized similarly as the analogous 8HQCl-L-Pro in our previous work [5]. The solution equilibrium processes of 8HQCl-D-Pro, whose crystal structure was obtained and determined by X-ray analysis (Fig. 1.b), with copper(II) was investigated in a 30% (v/v) dmsu/water solvent mixture using pH-potentiometry and UV-visible spectroscopy. A model containing mononuclear $[\text{Cu}(\text{LH})]^+$, $[\text{Cu}(\text{L}_2\text{H})]^-$ and $[\text{Cu}(\text{LH})_2]$ species is proposed (Fig. 2).

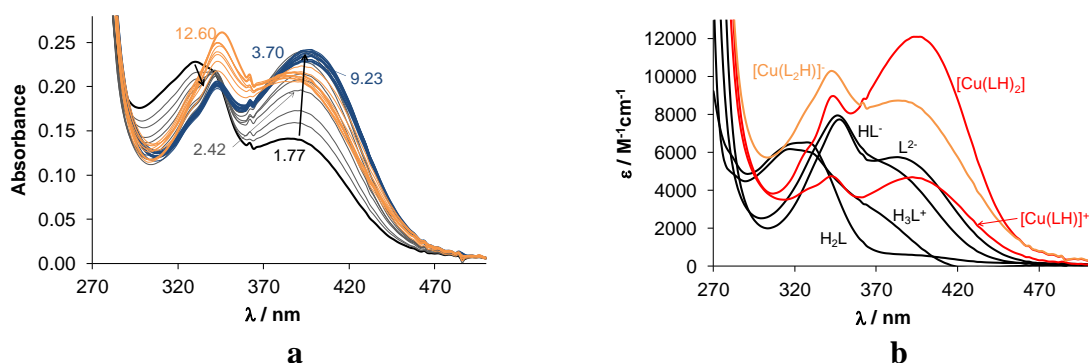


Figure 2. a) UV-visible absorption spectra of 8HQCl-D-Pro at pH range 1.9–12.6 in a 30% (v/v) DMSO/H₂O solvent mixture; b) individual UV-visible absorption spectra of the different complexes (red lines) and ligand species (black lines) calculated for the Cu(II) – 8HQCl-D-Pro system ($c_{\text{ligand}} = 42,5 \mu\text{M}$; $c_{\text{Cu(II)}} = 23 \mu\text{M}$; $T = 25.0 \text{ }^\circ\text{C}$; $I = 0.1 \text{ M (KCl)}$, $l = 1 \text{ cm}$).

Acknowledgements

This work was supported by the National Research, Development and Innovation Office-NKFIA through project GINOP-2.3.2-15-2016-00038 and Ministry of Human Capacities, Hungary grant, TKP-2020. Visegrad Scholarship 52010718 (I. S.).

References

- [1] Y. Song, H. Xu, W. Chen, P. Zhan and X. Liu, *Med. Chem. Commun.* 6 (2015) 61.
- [2] A. R. Timerbaev, *Metallomics.* 1 (2009) 193.
- [3] U. Jungwirth, J. Gojo, T. Tuder, G. Walko, M. Holcman, T. Schöfl, K. Nowikovskyy, N. Wilfinger, S. Schoonhoven, C.R. Kowol, R. Lemmens-Gruber, P. Heffeter, B.K. Keppler, W. Berger, *Mol. Cancer Ther.* 13 (2014) 2436.
- [4] V. Oliveri and G. Vecchio, *Eur. J. Med. Chem.* 120 (2016) 252.
- [5] J. P. Mészáros, J. M. Poljarevic, I. Szatmári, O. Csuvik, F. Fülöp, N. Szoboszlai, G. Spengler, É. A. Enyedy, *Dalton Trans.* 49 (2020) 7977.