Investigating the reaction mechanisms for ligand exchange in diruthenium complexes with biomedical applications

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INTRODUCTION: Diruthenium (II,III) tetracarboxylates complexes in the form [Ru2(RCOO)4(L)x]n+, in which L is a Lewis base, x={1,2} is the number of ligands, and n the charge of the complex, have potential interest in supra-molecular chemistry, catalysts and antitumoral drugs. These compounds have delocalized unpaired electrons in their most common electronic states and a tendency to form paddle-wheel geometries[1]. Given their unique electronic structure and physical properties, theoretical calculations and molecular simulations are valuable approaches to study their reactivity. **OBJECTIVES:** Here we employ computations to study the axial ligand (L) exchange of diruthenium tetracarboxylates for a series of biomolecular models in order to probe the possible mechanisms of coordination to biological targets. **MATERIALS AND METHODS:** Electronic structures, geometry optimizations, solvent and thermo-chemical contributions, and reaction paths of the diruthenium coordinated to different ligands were calculated using the program Gaussian 09. We employed DFT with the hybrid functional B3LYP, and the LanL2DZ effective basis set. Ligands tested were L= Cl-, H2O, CH3SH and CH3S-. The last two compounds model cysteine side-chains. **RESULTS AND DISCUSSION:** Calculated geometries for L=Cl- and x=2 are in good agreement with geometries determined by X-ray crystallography. Reaction energies and barriers for ligand exchange vary considerably between the different ligands when the first axial ligand is exchanged but have a small shift when the second axial ligand is exchanged. Solvent and thermo-chemical contributions must be included for quantitative comparisons with experimental equilibrium and rate constants, which are available in the literature for these ligand reactions[2]. **CONCLUSIONS:** The conformational freedom of diruthenium tetracarboxylates can be modeled with DFT methods to good accuracy. The same method was employed to model the reactivity of axial ligand exchange and reasonable results were obtained in comparison to experimental equilibrium and rate constants. Thus, the exchange mechanisms determined in this study may be reliable to understand the complexation of diruthenium metallodrugs in biological media.

Keywords: computational simulations, diruthenium complexes, metallodrugs
Supported by: CNPq

References:

1. R.L.S.R. Santos; R. Van Eldick; Denise de Oliveira Silva. Thermodynamics of Axial Substitution and Kinetics of Reactions with Amino Acids for the Paddlewheel Complex Tetrakis(acetato)chloridodiruthenium(II,III). 2012. Inorganic Chemistry, 51, 6615-6625.

2. Castro, M.A.; Roitberg, A.E; Cukiernik, F.D. Theoretical and Experimental Studies of Diruthenium Tetracarboxylates Structure, Spectroscopy, and Electrochemistry. 2008. American Chemical Society. Inorganic Chemistry, 47, 4682-4690.