

Theoretically understanding the exchange of NO and the nature of the Ru-NO bond in ruthenium-nitrosyl metallic complexes.

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Abstract: Specially after its discovery as a signaling molecule in the cardiovascular system[1], which led to the 1998 Nobel Prize in Physiology, nitric oxide (NO) has been shown to be involved in numerous other physiological functions such as modulation of the immune and endocrine response, cardiovascular control, neurotransmission, induction of apoptosis, among others[2-4]. Therefore, NO has been the focus of various studies in the past decades, many of them aiming at developing compounds capable of controlling NO's concentration in the body. As example, ruthenium-NO complexes have shown promising results for this purpose and thus, they are subject of great study in the literature [5-7]. However, despite the progress in synthesis, characterization and biological studies, there are much to be understood about the release of NO by metallic complexes, such as the reaction mechanism, the oxidation forms of the released NO and how it stays in the body after dissociation. Regarding these objectives, in this work density functional theory was used to investigate the electronic structure, reduction potentials and nitric oxide ligand exchange reactions in a series of ruthenium-nitrosyl model complexes of form $[Ru^{II/III}(X)(L)(NO)](X = salen or NH_3; L = Cl-, NH_3, L = CL-, NH_$ pyridine, P(OEt)₃, OH, H₂O). For instance, Natural Bond Orbital and Charge Decomposition Analysis studies revealed the key influence of the axial ligand in the electronic population of nitrosyl and NO⁺/NO⁰ character, as well as in the strength and electronic donation/backdonation of the Ru-NO interaction. As an example, strong π receptors in the axial position, trans to the NO, tend to weaken the Ru-NO backdonation and thus, weakening the Ru-NO bond. General aspects from the aqueous solvation of the complexes were also investigated through Monte Carlo statistical mechanical simulations. They showed that the complexes may be involved in strong hydrogen bonds with water, in particular the amino-complexes, which can form H-bonds with average energies up to -22.4 ± 0.4 kcal mol⁻¹. Calculations also show that while Ru^{II} complexes have only one thermically accessible spin state, Ru^{III} complexes may have excited spin states lying very close to the ground state (less than 30 kcal mol⁻¹) depending on the ligands coordinated to the metallic center, suggesting that the mechanism of NO ligand exchange, which is a spin-forbidden reaction, may vary across the different complexes. To investigate these observations, we constructed Potential Energy Surfaces (PES) for reactions of exchanging NO. The PESs showed the presence of one or multiples Minimum Energy Crossing Points (MECP) between the singlet and



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triplet species of the Ru^{III}-NO complexes. For instance, the NO release for the $[Ru(NH_3)_5NO]^{3+}$ is more favorable in the triplet state, with activation barriers seven times smaller (~6 kcal mol⁻¹) than in the singlet state[8]. High level Complete Active Space Self Consistent Field (CASSCF) calculations were also done in located MECPs geometries, revealing in some complexes the presence of strong spin-orbit coupling, with coupling constants larger than 500 cm⁻¹.

Key-words: nitric oxide, ruthenium, coordination complexes, dft, spin-forbidden reactions, cda, nbo.

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