A computational chemistry study towards rationalization of the iNOS-recognizing properties of Re(I) complexes

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Nitric Oxide Synthase (NOS) is the enzyme that catalyzes the biosynthesis of Nitric Oxide (NO) and L-citrulline from L-Arg. Imaging of NOS *in vivo* by nuclear techniques (SPECT/PET) could provide an insight into NO/NOS-related diseases. Aiming to find $^{99m}Tc(CO)_3$-based probes with pendant iNOS inhibitors, namely N^{ω}-NO_2-L-Arg derivatives, for targeting NOS, we have synthesized and characterized the $^{99m}Tc(I)$ complexes **Tc1** and **Tc2**, and the respective non-radioactive surrogates **Re1** and **Re2**. The matched pairs **Tc1/Re1** and **Tc2/Re2** are stabilized by a pyrazolyl-diamine or diamino propionate chelator, respectively (Fig. 1).[1] Enzymatic studies with the inducible NOS isoform (iNOS) have shown that **Re1** (K_i = 6 μM) presented an higher inhibitory potency than the close analogue **Re2** (K_i = 258 μM).[1] Therefore, to shed some light on the structural parameters of the metal complexes responsible for the different iNOS-recognizing properties, we have applied a computational approach, which included molecular docking and molecular dynamics simulation studies. Herein, we will describe those studies as well as the proposed structural modifications to provide metal complexes with improved affinity for iNOS.

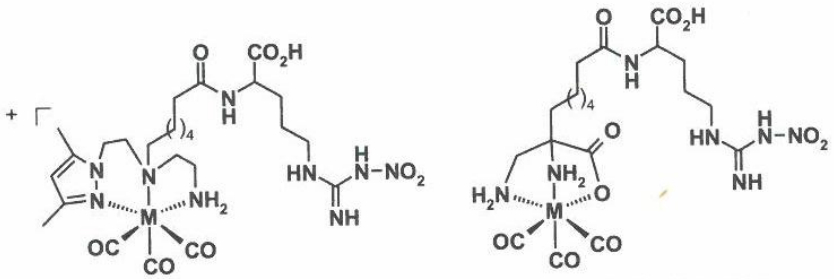

Figure 1

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References:

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