Ferriheme-nitrite interactions: Linkage Isomerism and Reaction with NO

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X-ray crystallography studies have shown that nitrite binds to the *met* form of human hemoglobin and horse heart myoglobin via the *O*-nitrito mode, which may be contrasted with the *N*-nitrito or "nitro" mode found in synthetic model complexes.[1] To explain the difference, we have studied the different linkage isomers as well as their interconversion pathways (transition states) with extensive DFT model studies.

Heme models of various complexities, ranging from a simple porphin to a 119-atom hemoglobin active site model, helped us quantify the environmental effects that influence on the nitrite binding mode. The distal histidine residue (and its protonation state), in particular, appears to be critical in this regard. Solvation also a significant, but more limited effect.

We have also studied the reaction of ferriheme-nitrite with NO, leading to N_2O_3, which has been proposed as the NO carrier between red blood cells and the endothelium, the site of vasodilation. Highlights from an extensive series of computationally explored pathways will be presented.

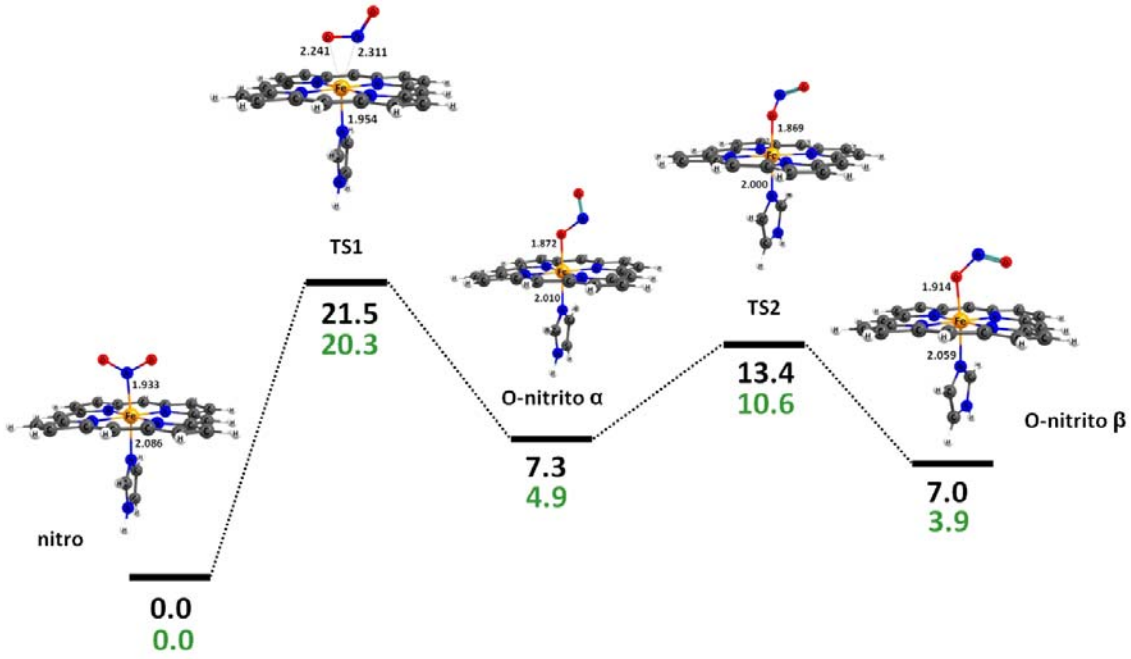

Fig.1. Relative electronic (in black) and Gibbs free (in green) energies in kcal/mol of the 3 heme-nitrite linkage isomers and of the 2 isomerization transition states.

[1] a) Copeland, D.M. & al. *J. Inorg. Biochem.* **2006**, *100* b) Yi, J. & al. *Biochemistry* **2008**, *47*.