Arginine Linked Rhenium Wires for Inducible Nitric Oxide Synthase

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We are investigating the catalytic mechanism of mammalian inducible nitric oxide synthase (iNOS), an enzyme that produces L-citrulline and nitric oxide (NO) from L-arginine and O₂. We have designed and synthesized L-arginine based substrates (wires) to characterize intermediates produced by laser-induced electron transfer to the active site. [Re(CO)₃(4,7-dimethyl-phenanthroline)(imidazole-C₈-NH-L-arginine-NO₂)] [BF₄] (1) binds in the protein channel with a K_d = 6 ± 4 µM. A second binding site is observed with a K_d = 17 ± 5 µM; after laser excitation, transient absorption measurements show that Fe(III) is reduced to Fe(II) in less than 10 ns. Rhenium N-hydroxyarginine and N-methoxyarginine wire analogs (2,3) will probe the second turnover of the catalytic cycle with the goal of elucidating the hydrogen source (N-OH versus N⁰-H) as well as determining whether neutral or anionic NO is formed.

![Chemical Structures](image)