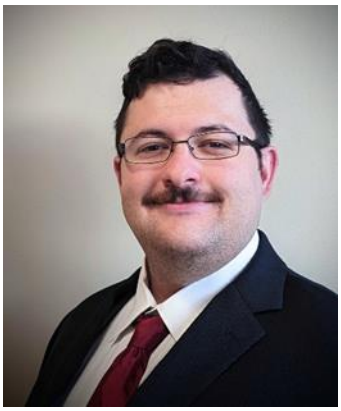
University of Central Florida
Department of Chemistry Seminar Series – Fall Semester 2023
Monday, November 6th, 9:00 AM, Location CB2 105

Insights into Nitric Oxide Reactivity with Iron-Containing Enzymes



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Most proteins belonging to the cytochrome P450 superfamily (CYPs) catalyze the hydroxylation or epoxidation of their substrates through the activation of dioxygen (O_2). A majority of CYPs characterized follow a similar mechanistic pathway en route to a so-called 'Compound I' (Cpd I) intermediate (formally an iron(IV) porphyrin cation radical). However, TxtE, a bacterial CYP found in S. scabiei, utilizes O_2 and nitric oxide (NO) to catalyze the direct nitration of L-tryptophan (Trp). We have shown that the TxtE ferric-superoxo intermediate cannot be further reduced in the presence of Trp—a prerequisite event for the formation of Cpd I and subsequent substrate hydroxylation. Current investigations suggest that decoration of the indole ring of the substrate influences TxtE reactivity, most likely through outer-sphere influences. For example, TxtE appears to hydroxylate halogenated Trp analogs (e.g., 4-F-Trp). To further investigate this, a series of substituted Trp analogues were investigated to determine if the apparent change in reactivity is due to electronic or steric effects introduced by substitutions on the indole. A collection of kinetic assays, electron paramagnetic resonance spectra, and endpoint assays of products will be presented for the wild-type enzyme with the substrate analogs.