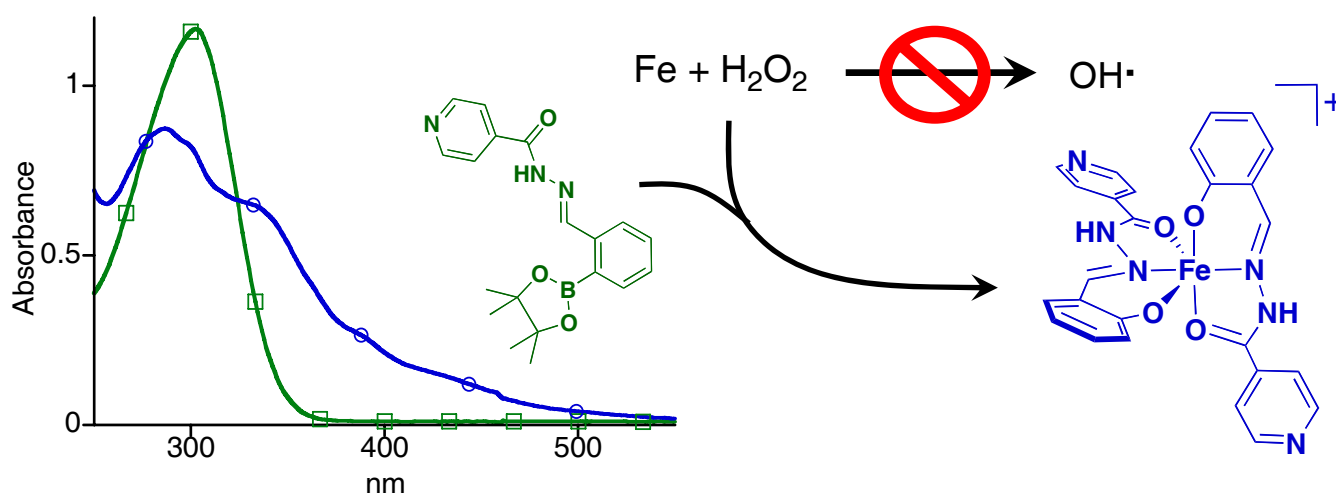


Manipulating Metal-Catalyzed Oxidative Stress with Triggerable Chelating Agents

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Disruption of the complex trafficking networks that regulate cellular metal content and distribution can lead to cellular dysfunction due to metal deficiency, overload, or misappropriation. For example, localized iron overload is implicated in several degenerative diseases, including Parkinson's, Alzheimer's, and age-related macular degeneration, wherein iron-mediated oxidative stress is hypothesized to contribute to cell death. Metal chelators are attractive agents for readjusting cellular metal loads, but targeting a specific metal ion at the exclusion of others and without inhibiting metalloproteins can be challenging. Furthermore, because ligands influence the chemical properties of their coordinated metals, chelating agents used intracellularly can alter not only the location but also the reactivity of metals, especially iron, copper and zinc. Here, we will present our efforts to develop chelating agents that can be triggered by specific stimuli to change their metal binding capacity and reactivity. In particular, we will discuss prochelators that are activated by hydrogen peroxide to bind iron and copper to suppress metal-catalyzed oxidative stress, as well as caged copper complexes that release redox-active copper following light activation.



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