Development of Caged-Complexes for Studying Zn^{2+} Signaling and Homeostasis

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Zn^{2+} has many well-understood structural and catalytic functions of in biology; in addition, current research suggests that free Zn^{2+} may function as a neurotransmitter and have a role in the pathology of several neurological diseases. While fluorescent sensors can be used to image endogenous metal ions, directly correlating fluorescence signals to specific biological events can be difficult. In order to elicit a physiological response, Zn^{2+} can be released from synaptic vesicles by electrical stimulation, or applied exogenously. Although observations made using these techniques may suggest certain functions, the concentration of Zn^{2+} used to initiate the activity may not be physiologically relevant. Caged compound can circumvent this problem by allowing controlled release of the analyte. Caged compounds are metal ion chelators that release analytes when exposure to light of a specific wavelength. We are interested in developing several classes of caged-complexes for Zn^{2+} based on classic nitrobenzyl-based photochemistry. Two general strategies have been pursued successfully to realize the primary goal of making caged complexes: (**1**) placing a nitrobenzyl group onto an aniline ring such that photolysis weakens an aniline nitrogen-zinc interaction and (**2**) integrating a nitrobenzyl group on the backbone of a zinc chelator so that uncaging fragments the ligand. We have devised several new synthetic strategies for these two classes of ligands known as ZinCast and ZinCleav respectively and have conducted detailed binding and photochemical studies with the Zn^{2+} complexes.