A Retro-Staudinger Cycloaddition: Mechanochemical Cycloelimination of a β-Lactam Mechanophore

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Polymer mechanochemistry enables a variety of unique chemical reactions including the ring-opening of spiropyran, activation of latent catalysts, and even formally forbidden transformations like the disrotatory electrocyclic ring-opening of benzocyclobutene. Diversifying the scope of mechanochemical transformations remains a key goal in this emerging field, particularly for applications such as self-healing materials. We recently discovered the mechanically facilitated [2+2] cycloelimination reaction of a β-lactam mechanophore to generate ketene and imine functional groups—the reverse reaction of the eminent Staudinger cycloaddition. The mechanochemical reactivity of the β-lactam unit was predicted by DFT calculations and confirmed experimentally through a combination of kinetic analyses, UV-vis absorption measurements, and polymer end-group analysis using ^{1}H and ^{13}C NMR spectroscopy. This work introduces a new mechanophore that provides a promising platform for the realization of materials with inherent self-healing characteristics.

Towards Reaction-Based Fluorescent Probes for Reactive Carbonyl Species

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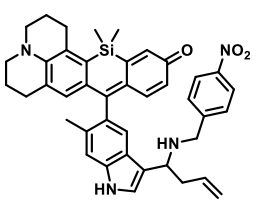
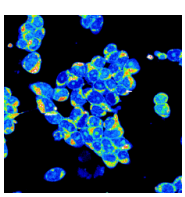
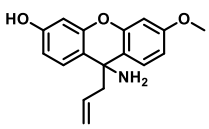
Reactive oxygen species, in particular reactive carbonyls, play an important role in the maintenance and preservation of essential cellular functions. For instance, formaldehyde (FA), in the 0.2 to 0.4 mM range, is produced and maintained endogenously via enzymatic pathways. At these levels, FA can promote cell proliferation, as well as mediate memory formation. Once elevated, FA stress is known to induce cognitive impairments, memory loss, and neurodegeneration owing to its potent DNA and protein cross-linking mechanisms. Optical imaging is a powerful non-invasive approach used to study FA in living systems; however, biocompatible chemical probes for FA are currently lacking. We report the design, synthesis, and biological evaluation of Formaldehyde Probe 1 (FP1), a new fluorescent indicator based on the 2-aza-Cope sigmatropic rearrangement. The remarkable sensitivity, selectivity, and photostability of FP1 has enabled us to visualize FA in live HEK293TN and Neuroscreen-1 cells. Additionally, we are developing two-photon variants which will allow for the imaging of FA in biological tissues. We envision that FP1 and the two-photon variants will find widespread applications in the study of FA associated with normal and pathological processes.



FP1





Two-Photon