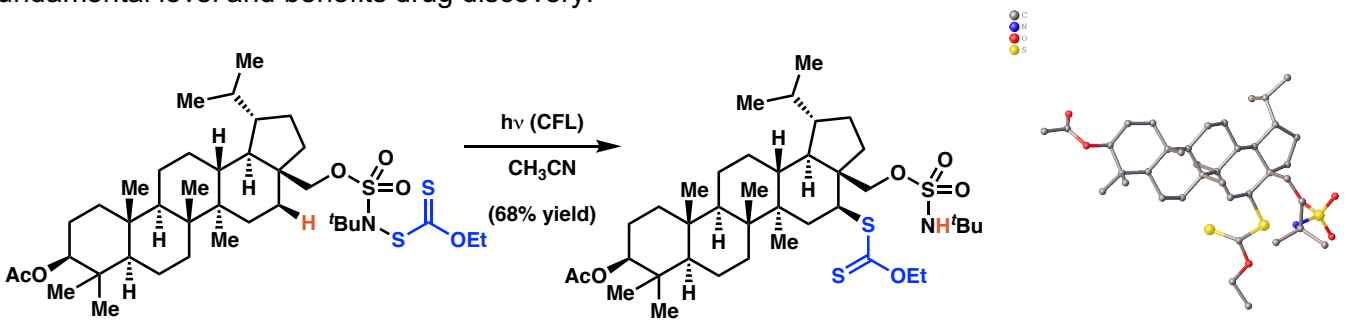
TITLE: Alcohol and Amine Derivatives Guide Position-Selective C–H Functionalization Reactions

ABSTRACT

Free radical reactions represent an important and versatile class of chemical transformations. Nitrogen-centered radical applications remain underexplored due to the lack of convenient methods for their generation. Recent advances have improved access to nitrogen-centered radicals through photoredox-mediated oxidation of two such directing groups: amides and sulfonamides. Guided by this approach, we hypothesized that alcohols, masked as sulfamate esters, and amines, masked as sulfamides, could engage in photoredox-mediated oxidation to furnish nitrogen-centered radicals that could guide C–H functionalization reactions.

Moreover, our directed technology has been inspired by one of the most reliable and powerful known reactions to guide C–H functionalization reactions: the Hofmann–Löffler–Freytag (HLF) reaction, which uses amines or amides as directing groups. Like many of the most robust radical-mediated technologies to direct the activation of tertiary and secondary centers, the HLF reaction is guided through 1,5-hydrogen-atom transfer (HAT) processes, which proceeds through a kinetically-favorable six-membered ring transition state. By contrast, **few reports describe 1,6-HAT with a traceless linker**, such as an alcohol masked as a sulfamate ester or an amine masked as a sulfamide, and there are **no general strategies** to enable masked alcohols or amines to direct functionalization of aliphatic γ-C(sp^3)–H centers. This talk will outline this novel strategy to harness alcohols and amines to replace C–H bonds at γ-C(sp^3)–H centers, which are not generally accessible to directed functionalization. We will demonstrate that C–H abstraction can be robustly coupled with **varied functionalization reactions.** This talk will highlight the first generalizable synthetic strategy to functionalize γ-C(sp^3)–H bonds based on masked alcohols or amines, to push the boundaries of organic chemistry at a fundamental level and benefits drug discovery.



BIOGRAPHY

Jennifer L. Roizen is an Assistant Professor at Duke University and a 2017 Thieme Chemistry Journals Award recipient. She had her first taste of synthetic research with J. Hodge Markgraf and Tom Smith as a Williams College undergraduate, where she advanced syntheses of benzoisocanthenones and contributed to publications on the total synthesis of hennoxazole A (a marine natural product). She moved to the California Institute of Technology to earn a Ph.D. with Brian Stoltz, researching approaches to access the ineleganolide core. These Cope-centric approaches remain the only published strategies to access the all carbon framework of ineleganolide, a small molecule that continues to elude synthetic campaigns. Upon graduation, Dr. Roizen became an NIH postdoctoral researcher and CMAD fellow with Justin Du Bois at Stanford University, where they extended intermolecular amination technologies. Dr. Roizen's laboratory researches total synthesis and the development of cross-coupling and C–H functionalization processes.

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