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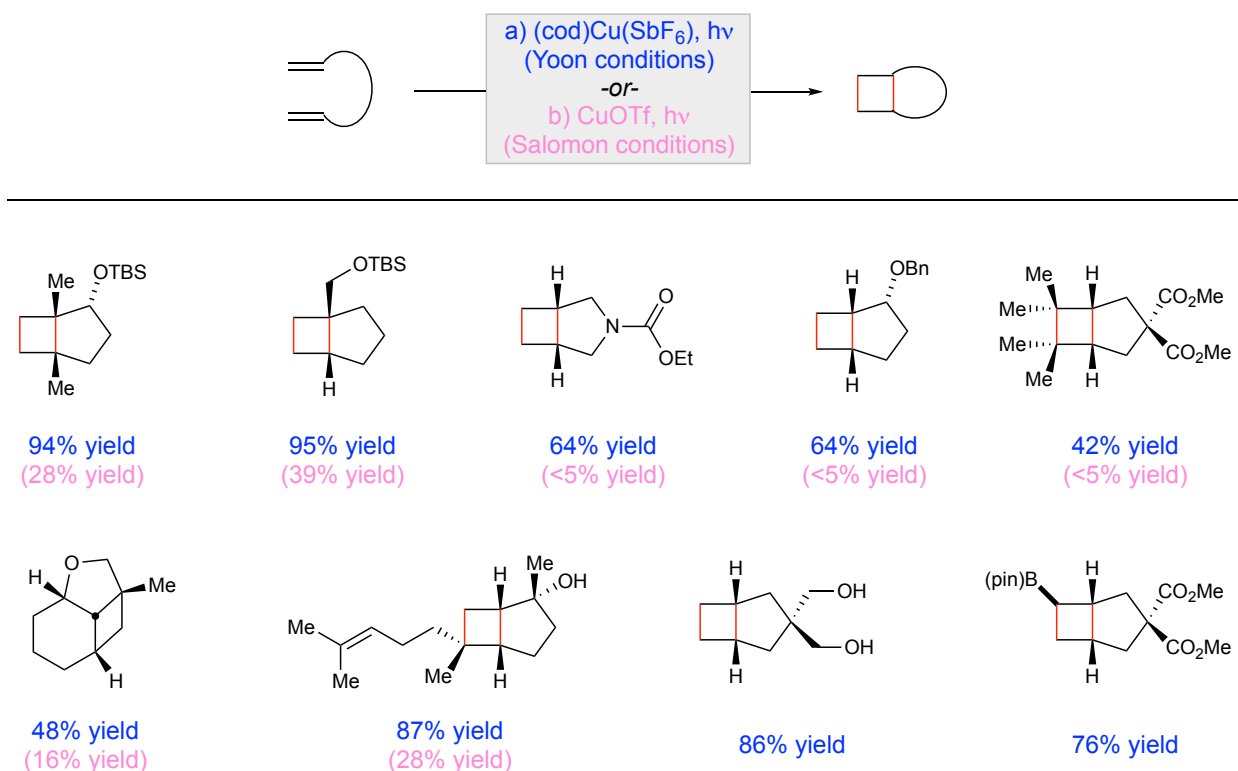
“Copper-Catalyzed Photochemistry with Simple Alkenes”

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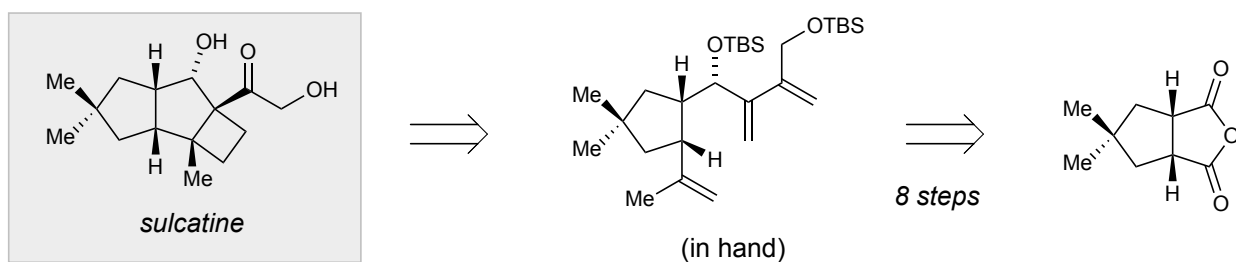
Cycloaddition reactions are widely considered to be among the most powerful transformations in synthetic chemistry. They are valued for their ability to convert simple alkene-containing building blocks into complex bicyclic structures with the simultaneous construction of multiple new bonds and stereocenters. Our laboratory has long recognized that photocycloadditions represent a broad class of unique cycloaddition methods whose development has lagged behind other, “thermal” cycloaddition strategies.

In particular, we have been studying copper-catalyzed [2+2] photocycloaddition, first discovered by Kochi and Salomon in 1973. This remains the only existing reaction that enables the photocycloaddition of unconjugated alkenes, the products of which are simple aliphatic cyclobutanes, which are common in terpene natural products and are increasingly incorporated into drug candidates in the pharmaceutical industry. We have discovered that by manipulating subtle counteranion effects, we can dramatically increase the reactivity of this system, enabling the construction of sterically crowded, densely substituted cyclobutanes.

The past year has focused on two goals. First, we have completed an exploration of the scope of this reaction, and a direct comparison to the Kochi-Salomon conditions shows that the rate increase for a variety of substrates is dramatic, often enabling reactions that were not possible under the original conditions:



Second, in the process of we realized that a concise total synthesis highlighting this method would make a more convincing case for the need for this method. We have worked out all but the final few steps of a synthesis of a terpene natural product called sulcatine G, the key step of which is uniquely amenable to the conditions we have developed for similarly challenging cyclobutane syntheses. We hope to publish the manuscript describing these results within the first few months of 2019.



Finally, in an unexpected development, we have found that the use of chiral ligands can influence the stereochemistry of the copper-catalyzed [2+2] photocycloaddition, in direct contradiction to previous reports attempting the same transformation. While the enantioselectivities observed to date are modest, this is an exciting development that seems to demand further interrogation from both a mechanistic perspective and as a new direction for synthetic methodology development in my laboratory.

This project contributed to the training of a senior graduate student and an exceptional URM undergraduate student who has recently begun his PhD program in chemistry at Cornell.