

Annual Report for 56230-ND1

Project Title: Hypervalent Iodine-mediated Transformation of Silyl-substituted Hydrocarbons

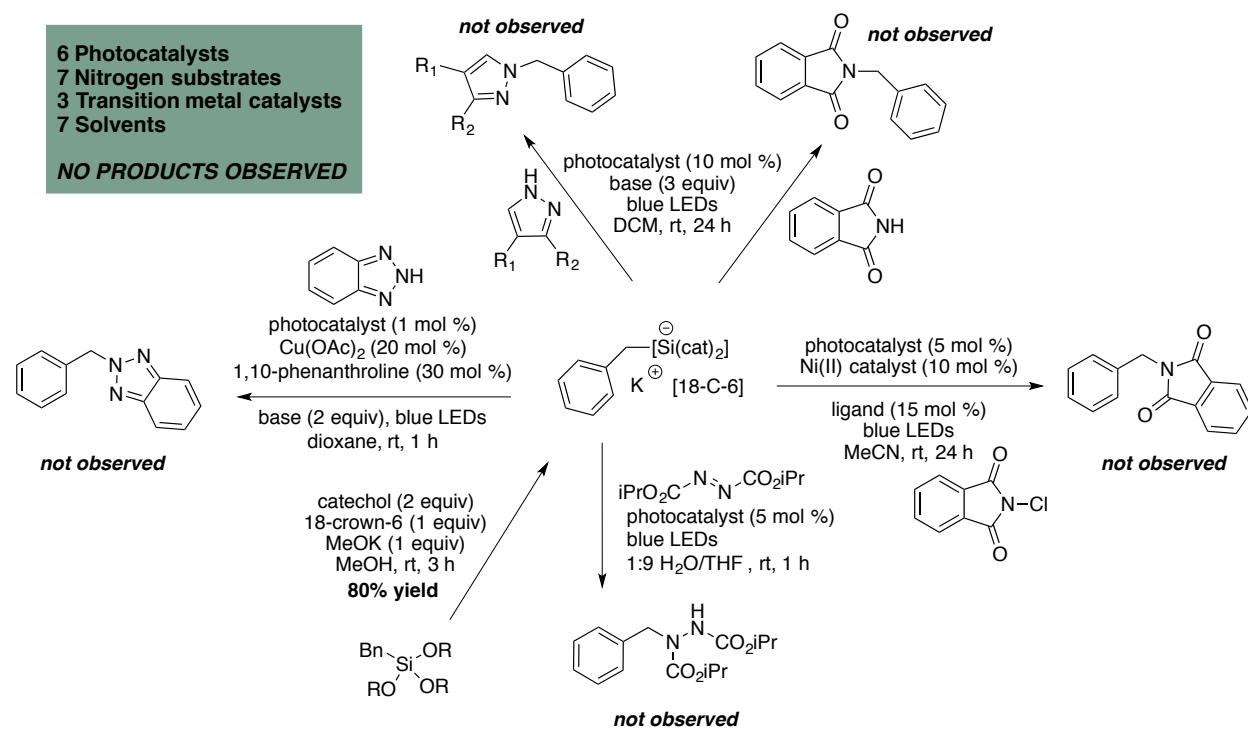
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Progress of the Research

This annual report presents the ongoing work to discover a method to transform a carbon-silicon bond into a carbon-nitrogen bond to access chiral amines in an aza-variant of the Tamao-Fleming reaction, which would provide complementary method to functionalize silyl-containing molecules. To accomplish this goal, our initial work focused on utilizing silylamines with direct activation for alkyl migration with a focus on hypervalent iodine(III) reagents. While our strategy utilizing an oxidation with hypervalent iodide was promising, our efforts using these reagents did not afford the amine product and we decided to investigate alternative mechanistic approaches with azides and Rh-nitrene reagents. Neither the use of amines nor azides as nitrogen-containing substrates was effective in forming a new carbon-nitrogen bond, likely due to the ease with which silicon-nitrogen bonds are hydrolyzed to silanols and amines. Thus, again, a new approach to the desired bond formation was selected: photoredox catalysis. We envisioned that photoredox catalysis, a green and versatile method, could provide access to this synthetically challenging bond conversion. In particular, visible light catalysis in particular is attractive due to its selectivity.

Inspired by the unique reactivity of hypervalent silicon compounds described by Corriu and coworkers, we synthesized bis-catecholato silicates as reagents to access hypervalent reactivity for investigating N-Cl, N-H, and N-N bond-cleavage strategies for C-N bond formation. To evaluate reactivity and potential product formation, all reactions were monitored for product formation using ^1H NMR spectroscopy. The first substrate used in test reactions was N-chlorophthalimide because it is one of the most commonly-used substrates in nitrogen radical chemistry. When bond cleavage of N-Cl bonds was not effective with phthalimide, we shifted the focus to a N-H bond cleavage strategy. Phthalimide, benzotriazole, and three pyrazoles were selected for test reactions due to their successful use in literature examples of radical photoredox-catalyzed C-N bond formation. When both the N-Cl and N-H bond cleavage attempts did not result in any product formation, an N-N bond cleavage was explored using diisopropyl azodicarboxylate (DIAD). Again, no product was observed with any of the photocatalysts used.



Because no single-catalysis approaches were able to produce a C-N bond from a C-Si bond, a dual catalysis was considered as an alternative strategy in which short-lived radicals can be “trapped” by a transition metal catalyst. A photocatalyst, copper(II) acetate, a phenanthroline ligand, and a sterically hindered base were added to

the benzyl silicate and benzotriazole in dioxane for 1h. None of the combinations of photocatalyst or base used in the test reactions resulted in formation of *N*-benzylbenzotriazole as determined using ¹H NMR spectroscopy. Because dual transition metal/photocatalysis is currently a very popular method in organic synthesis, we proceeded to investigate additional additional transition metals and conditions for dual catalysis. Therefore, we next evaluated experiments based upon activation of Ni(II) catalysts instead of utilizing Ni(0) catalysts; our group does not possess a glove box and Ni(0) catalysts are not particularly stable in an oxygen atmosphere. Two varieties of Ni(II) catalysts, three different photocatalysts, and a dipyridinyl ligand were added to the benzyl silicate and *N*-chlorophthalimide. None of the reaction conditions used resulted in product detection in the crude reaction mixture by ¹H NMR spectroscopy.

In summary, the photoredox approach to the bond conversion project has thus far not resulted in successful formation of a C–N bond. Lack of desired product may be a result of poorly-selected carbon or nitrogen substrates, poor overlap between redox potentials of photocatalysts and substrate, and/or absence of the appropriate transition metal catalyst. There are many variables at play in the reaction and either continued investigations or an additional strategies and approaches must be considered. Currently, the benefits and goals remain the same but our methodology must again consider a new strategy.

Impact of the Research on my Career

Receiving an ACS-PRF New Directions grant allowed me to pursue a new direction with more exploratory research that I would not have been able to pursue otherwise. The funding and award also supported my career prior to applying for my promotion to Full Professor. It has prompted me and my group to think more creatively and critically with the potential to obtain preliminary results to further support this research.

Advancing Scientific Education and Student training

To date, this project has contributed to the scientific education and laboratory training of three graduate students, primarily through summer funding support, who have been trained in synthesis, methodology development, and chemical analysis. Students have had the chance to see the development of a new project direction and how to consider new strategies when a project does not work as initially proposed. Students have contributed to brainstorming new strategies.