Novel Synthesis of Important Pharmaceutical Compounds using Visible Light and a Photocatalyst

Zhang, Jason (School: The Carol Martin Gatton Academy of Mathematics and Science in Kentucky)

In the past decade, photocatalysts have been used to create important biomolecules by facilitating electron transfers between different compounds in the presence of visible light like sunlight. Photocatalysts function similar to chlorophyll pigments, which absorb sunlight to excite and transfer electrons in photosynthesis. In 2016, the Nicewicz group reported that alkenes can undergo single-electron oxidation in the presence of a photocatalyst and sunlight to form alkene radical cation intermediates, which further reacts to create essential biomolecules. However, the application of using photocatalysts to oxidize alkynes had not been successful due to considerably higher oxidation potential of alkynes than alkenes. In this work, we present a novel strategy of lowering this barrier by reacting alkynes with the compound 2,6-lutidine N-oxide and a photocatalyst under blue light to synthesize a variety of useful bicyclic amides. These nitrogen-containing bicyclic compounds are crucial intermediates of many biological drugs like the antidepressant milnacipran. Previous synthesis of these compounds requires harsh reaction conditions and precious metal catalysts, a pharmaceutical concern as some metal residuals may remain in the drugs. However, this research presents the metal-free and sustainable synthesis of these important biomolecules. The structures and purities of our synthesized compounds have been verified by Nuclear Magnetic Resonance (NMR) spectroscopy. In addition, factors affecting the yields of these photocatalytic reactions, including solvent effects and substituent effects, have been analyzed. This research represents an efficient, metal-free and sustainable synthesis of a variety of important pharmaceutical precursors using visible light.

Awards Won:
Second Award of $2,000