

CARBON-NITROGEN BOND FORMATION VIA TANDEM CARBON-HYDROGEN (C-H) AND NITROGEN-HYDROGEN (N-H) BOND FUNCTIONALIZATION

The oxidative cross-coupling of carbon-hydrogen (C-H) and nitrogen-hydrogen (N-H) bonds to form carbon-nitrogen (C-N) bonds is an important synthetic advance, as amine and amide functional groups are ubiquitous in biologically active molecules. This technique is orthogonal to conventional amination techniques, which rely on electrophilic nitration/reduction strategies or metal catalyzed coupling of pre-functionalized arenes.

This seminar is mainly focused on the development of oxidative methods for constructing *N*-arylamines and amides via tandem C-H/N-H bond activation and increasing synthetic efficiency for total synthesis of an inhibitor of botulinum neurotoxin via direct C-H functionalization.

The first project “Metal-Free Intermolecular Oxidative C-N Bond Formation via Tandem C-H and N-H Bond Functionalization” is focused on the development of a novel intermolecular oxidative amination reaction, a synthetic transformation that involves the simultaneous functionalization of both an N-H and C-H bond. The process, which is mediated by an I(III) oxidant and contains no metal catalysts, provides a rapid and green method for synthesizing protected anilines from simple arenes and phthalimide.

The second project “I(III)-Mediated Regioselective C-H Bond Amination of 2-Arylpyridine Derivatives” is focused on developing a novel, useful and economical process for the direct amination of 2-phenylpyridine derivatives. This process requires cheap and commercially available copper triflate and works for a variety of different 2-phenyl- pyridine derivatives.

The third project “Increasing synthetic efficiency via direct C-H functionalization: formal synthesis of an inhibitor of botulinum neurotoxin,” is focused on designing an efficient scheme for the synthesis of one of the best known inhibitors of botulinum neurotoxin serotype A (BoNTA). The synthetic route involves two palladium catalyzed C-H functionalization reactions, formally activating three C-H bonds.