Abstract

The arene and heteroarene units are ubiquitous throughout chemistry and the natural world, present in at least one iteration in almost every pharmaceutical or agrochemical. C–C and C–N bonds are among the most common linkages in natural products, pharmaceuticals, agrochemicals, and materials. Over 80% of FDA-approved drugs contain at least one nitrogen atom, often introduced via C–N bond-forming reactions. C-C bond formation can be considered in terms of arylation, alkylation, or the introduction of carbonyl groups. Herein, three strategies are described for the C-C and C-N bond-forming reactions of arenes and heteroarenes.

In Chapter 1, we have developed a novel cascade aminoarylation reaction with an aryl sulfonate tethered aryne precursor. Through the nucleophilic addition of secondary amines and the Smiles-Truce rearrangement of the sulfonate group, the strategy can afford hindered biaryl aminophenols. The reaction is transition-metal-free, can produce highly sterically hindered biaryls, and uses a straightforward base treatment at room temperature to form aryl C-C and C-N bonds.

In Chapter 2, we have developed two strategies for Nickel-catalyzed *ortho*-alkylation and arylation of benzoic acids. This process can successfully tether both primary and secondary simple alkyl groups derived from abundantly available amine-generated redox-active pyridinium salts without the assistance of any β-carbonyl groups, unlike the previously developed method with 4d transition metal. Apart from this, we also report the first nickel-catalyzed ortho-arylation strategy to incorporate a variety of aryl groups and styryl group *ortho* to benzoic acid.

In Chapter 3, we have developed a transition metal-free, mild, and one-pot approach for the 3-formylation of pyridines to access nicotinamide drug analogs. This methodology solves the crucial bond-forming problems in pyridine, e.g., 3-formylation. Many drugs and pharmacological analogs were formylated at late stages using our established approach. This procedure was used to afford the bisindolyl core in a single pot and to perform one-pot sequential functionalization to provide multisubstituted pyridines. We have developed a rearrangement of 2-phenyl pyridine to perform a novel carbonylative phenyl transposition reaction. Our strategy enabled an N-to-C swap reaction of 3-heteroaryl pyridines to afford fused heteroaryl derivatives.