Dearomative Alkaloid Synthesis

Abstract: Biologically active alkaloids continue to serve as a means of biomedical discovery in addition to serving as forcing functions for the invention of new chemical transformations. Structurally, many of these natural products and rationally designed drugs also contain one or more piperidine rings, making it the most common nitrogenous heterocycle amongst approved small-molecule therapeutics. Thus, the concise redox-economic construction of these heterocycles in the context of target-oriented synthesis has become a recent research focus in our lab. In particular, leveraging controlled and selective dearomatization reactions has enabled the concise synthesis of several natural products and approved pharmaceuticals from simple feedstock pyridines. Our lab’s recent synthetic efforts related to alkaloids from the lupin, ergoline, aspidosperma, morphinan and manzamine families of alkaloids will be discussed, articulating the breadth of targets that can be accessed by this strategic approach. In addition, both fundamental and translational opportunities afforded by our work in this area will be highlighted.