**Austin Ventura**

**3rd Year Medicinal Chemistry Student Seminar**

**Title:**

Strategic Catalytic Reactions for the Synthesis of Biologically Active Chemical Motifs for Small Molecule Drugs

**Abstract:**

Alkanes, aldehydes, alkyl amines and ethers are abundant chemical feedstocks that have versatile uses as fuel, lubricating oils, and raw materials in the chemical and pharmaceutical industry. Existing methodologies for metal-catalyzed cross-couplings of these commodity chemicals typically rely on preinstallation of reactive functional groups on both reaction partners. In contrast, C–H functionalization approaches offer promise in simplification of the requisite substrates and have recently been developed to afford value-added C(*sp2/3*)−C bonds that have demonstrated potential applications in drug development and late-stage modification of peptides and polymers; however, challenges from low reactivity and similar reactivity of various C–H bonds introduce considerable complexity. This work describes the optimization and initial mechanistic investigations of three unique Ni-catalyzed C–C bond forming reactions using an unusual reaction medium that incorporates the simultaneous use of di-*tert*-butyl peroxide as an oxidant and hydrogen-atom-transfer (HAT) agent and zinc metal as a reductant. The first reaction is an oxidative cross dehydrogenative coupling of *N*-heterocycles with aldehydes to forge a-amino ketones, a highly desired chemical motif in medicinal and synthetic chemistry. The second reaction is a simplified and cheap approach to direct methylation of of C(*sp3*)–H bonds which can be used for late-stage modification of active pharmaceutical ingredients (APIs) to explore the potential benefits of the ”magic methyl effect”. Lastly, the third reaction highlights the synthesis of a broad range of ketones via direct C–H functionalization of aldehydes with alkyl and aryl carbon electrophiles as coupling partners. In total, these reactions showcase the utility and compatibility of nickel catalysis under thermal redox conditions to provide value-added CC bonds that are of high importance to both medicinal and synthetic chemists, alike.

Zoom Link: <https://umich.zoom.us/j/95885862464?from=addon>

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