THESIS ABSTRACT

The thesis entitled "***Nickel(0)-Catalyzed Intra- and Intermolecular Coupling of Aldehydes with Unsaturated Systems***" is divided into five chapters.

Chapter 1 summarizes the literature on reductive coupling of aldehydes with other unsaturated systems (alkenes, dienes, allenes, alkynes, enynes, and diynes), with a focus on Ni^0-catalysis. Activated by a Lewis acid, Ni^0 could undergo oxidative cyclization with aldehydes and π-bonds of unsaturated systems to form a five-membered oxanickelacycle, which was selectively cleaved by reducing agents to yield diverse reductive coupling products. Oxidative cyclization governs regio- and stereoselectivity, influenced by the stereoelectronic factors of the ligand and the substrates. The chapter highlights key developments of reductive coupling and identifies critical gaps in current methodologies, setting the stage for the research described in subsequent chapters.

Chapter 2 presents our work on the catalytic intramolecular reductive coupling of *O*-allyl salicylaldehydes to afford exclusive *syn*-chromanols using a bench-stable Ni^{II} salt as a Ni^0 precursor. By applying this strategy, we achieved the formal synthesis of a series of potential drug molecules based on s*yn*-chromanol frameworks.
[*Org. Lett.* **2024**, *26*, 4024-4029]

Chapter 3 describes Ni^0-catalyzed reductive coupling of alkene-tethered indole-carbaldehydes to access tricyclic indole scaffolds, including all relevant [1,2]-, [2,3]-, [3,4]-, and [1,7]-fusion patterns under a single set of reaction conditions. The ring size was further modulated by varying the alkene chain length.
[*Manuscript in Preparation*]

Chapter 4 unveils the Ni^0-catalyzed regiocontrolled intramolecular sila-alkenylation of aldehydes, featuring selective *β*-hydride elimination as the key step. The stereoelectronic properties of silane controlled the selectivity in the *β*-hydride elimination step. Several control experiments and kinetic studies supported the conclusion that *syn*-oxanickelacycle formation is the rate-determining step. The methodology serves as an efficient alternative for the Lewis acid-mediated intramolecular hydroalkenylation of aldehydes and alkenes.
[*Org. Lett.* **2025**, *27*, 12549-125548]

Chapter 5 presents the Ni-catalyzed reductive coupling of 1,3-diynes with unactivated aldehydes, enabling the regioselective synthesis of various enyne alcohols. A wide range of alkyl- and aryl diynes were efficiently coupled with aliphatic and aromatic aldehydes. Further, we aim to develop an enantioselective version of the reaction using a chiral ligand.
[*Manuscript in Preparation*]

Overall, this thesis demonstrates efficient, modular, and *syn*-selective intramolecular alkene-aldehyde reductive coupling strategies to access *syn*-chromanols and tricyclic indoles in a broad range, serving as core building blocks for numerous natural product and bioactive molecules. The diyne-aldehyde reductive coupling provides various enyne alcohols that can be further functionalized.