

PRF# 56568-DNI-3

Project Title: Nickel-Mediated Bimolecular Bond Formation and the Applications in the Conversion of Petroleum Products

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With the support of the ACS-PRF, our research group has made significant progress on understanding the fundamental mechanism of Ni-mediated bond activation and formation. In addition, we have applied the insight to develop carbofunctionalization reactions of alkenes. These reactions are useful in upgrading petroleum products, such as vinyl arenes, into value-added products with more complex structures.

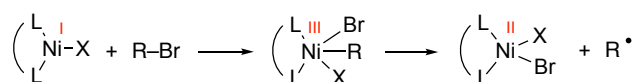
1. Fundamental Study of Ni(I)-Mediated Oxidative Addition of Alkyl Halides

Ni(I)-mediated single-electron oxidative addition of alkyl halides has been extensively proposed as a key step to afford radical intermediates in Ni-catalyzed cross-coupling reactions. There are four mechanisms through which this step could take place: oxidative addition, outer-sphere electron transfer, inner-sphere electron transfer, and concerted halogen-atom-abstraction (Scheme 1). No previous experimental studies have been carried out to distinguish these pathways and elucidate the operative mechanism. We isolated a series of Ni(I)-Ar complexes that selectively activate alkyl halides over aryl halides to eject radicals and form Ni(II) complexes (Scheme 2). Kinetic studies on the steric, electronic, and solvent effects, in combination with DFT calculations, reveal that the alkyl halide activation proceeds via a concerted halogen-atom-abstraction mechanism, which contrasts with previously proposed outer-sphere electron transfer mechanism observed for Ni(0)-mediated aryl halide activation. This mechanistic characterization and the selective activation of alkyl halides relative to aryl halides by Ni(I) provide insight into the overall mechanism of Ni-catalyzed cross-coupling reactions and offer a basis for differentiating electrophiles in cross-electrophile coupling reactions. A manuscript based on this work has been submitted for publication.

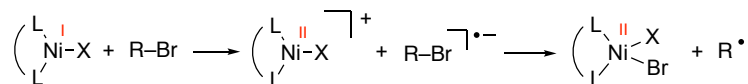
Graduate student, Justin Dicciani, carried out all the experiments in this study. He has focused his graduate study on the fundamental understanding of Ni-mediated bond activation and formation. His outstanding work has earned him several awards, including the Margaret and Herman Sokol Fellowship and the Ted Keusseff Fellowship. Justin will complete his Ph.D. thesis next year. Another graduate student, Luchuan Ju, focuses on probing the ligand effect on Ni-mediated C-C bond formation, and has made important progress on isolating Ni intermediates with catalytically relevant ligand structures. He is currently investigating how chiral ligands control the stereoselectivity in forming new C-C bonds.

Scheme 1. Possible Pathways for Ni(I)-Mediated Radical Formation from Alkyl Halides

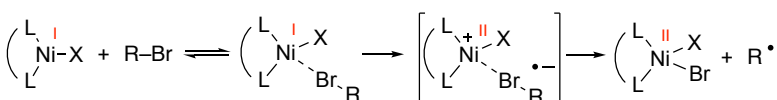
1. Oxidative Addition



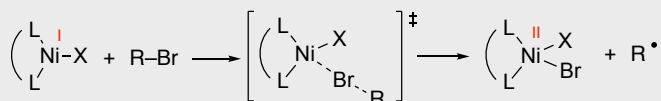
2. Outer-Sphere Electron-Transfer



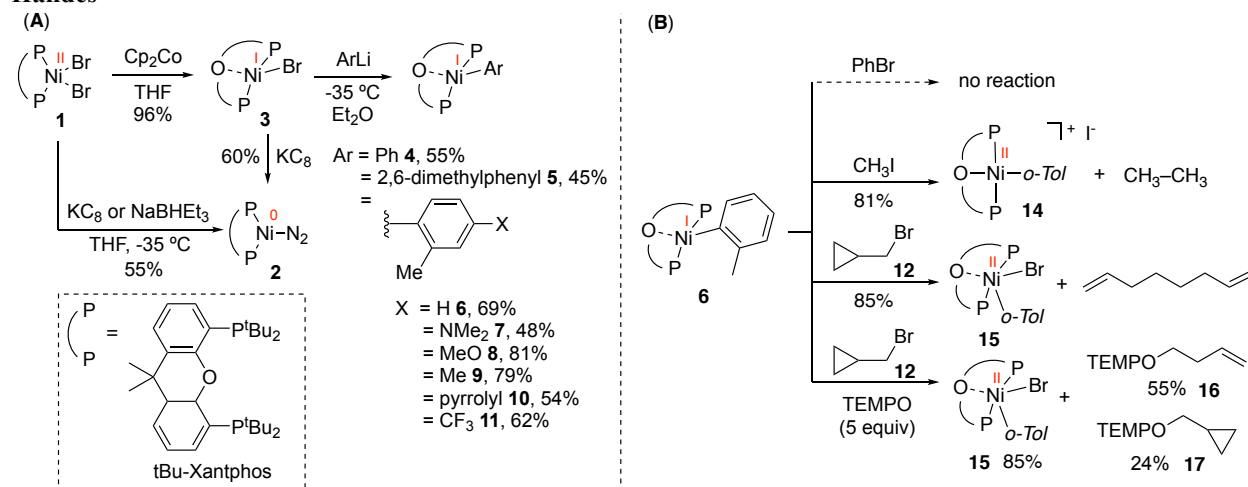
3. Inner-Sphere Electron-Transfer



4. Concerted Halogen Atom Abstraction



Scheme 2. Synthesis of (*t*-Bu-Xantphos)Ni(I) Complexes and Their Reactivity in Activating Aryl and Alkyl Halides



2. Stereoselective Carbofunctionalization of Vinyl Arenes

Alkenes, such as α -olefins and vinyl arenes, are versatile petroleum products that are employed in some of the most successful and well-developed asymmetric catalytic transformations, including hydrogenation and dihydroxylation. Asymmetric alkene carbofunctionalization would enable efficient construction of new C–C bonds while simultaneously introducing stereocenters to afford value-added products. 1,2-Dicarbofunctionalization and hydrofunctionalization of alkenes have emerged as compelling approaches to rapidly increase molecular complexity by forming vicinal di-substitution patterns and tertiary carbon centers, but corresponding asymmetric methods have been restricted to a handful of precedents, with the scope limited to intramolecular and diene substrates. We are developing asymmetric 1,2-dicarbofunctionalization and hydrocarbofunctionalization reactions, using Ni catalysts in combination with chiral ligands. To access a broad scope of applications, we engage electrophilic coupling partners, such as aryl and alkyl halides, under reducing conditions, which can bypass the need for pre-generation of air-sensitive organometallic coupling reagents. Moreover, the greater availability of electrophiles, relative to nucleophiles, can broaden the scope of accessible structures. Despite recent advances in reductive cross-electrophile coupling, only one non-enantioselective example has been reported for the carbofunctionalization of alkenes, and it suffers from a limited scope. Our preliminary data reveal that the development of the new carbofunctionalization reactions of alkenes can enable shorter and more atom-economic synthetic routes to challenging and important targets. Mechanistic studies are also being carried out to answer key questions, in order to form mechanistic rationales for addressing synthetic challenges. This project has taken off with promises to succeed, and will become a major focus of our research group. Postdoctoral researcher, Xiaoxu Qi, focuses on this project, who has made significant progress on identifying new catalyst systems.