Departmental Seminar

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Nickel-Catalyzed Cross Couplings of Alkyl Amine and Alcohol Derivatives

Transition metal-catalyzed cross-coupling reactions have revolutionized organic synthesis, particularly the construction of bonds to sp2-hybridized carbons. However, the discovery of analogous reactions of Csp3 electrophiles have lagged behind, despite their potential to deliver a range of important targets, including chiral molecules in high enantiopurity. Towards solving this challenge in organic synthesis, we have developed a range of nickel-catalyzed cross-couplings of alkyl amine and alcohol derivatives. In particular, we have developed stereospecific, nickel-catalyzed cross couplings of both benzylic amine and alcohol derivatives.1 These reactions utilize starting materials that are readily available in high optical purity; proceed with high levels of stereochemical fidelity; employ air-stable, functional group tolerance coupling partners, such as aryl boronic acids; and display excellent functional group tolerance. This strategy is also effective for the arylation of allylic electrophiles,2 and the use of alternative coupling partners to enable borylations.3 These reactions provide a range of highly enantioenriched products with tertiary and quaternary stereocenters, including molecules important for their biological activity. We have also developed nickel-catalyzed cross-couplings of alkyl amine derivatives with nonactivated alkyl groups (non-benzylic, non-allylic). This exciting new chemistry is particularly useful for late-stage functionalization of alkyl amines. The optimization, scope, and mechanistic studies of these reactions will be presented.