

Mechanism-Based Design and Development of Nickel-Catalyzed Reactions Stereospecific Cross-Coupling Reactions

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Transition metal-catalyzed cross-coupling reactions have revolutionized the synthesis of natural products and medicinal agents and provided rapid synthetic access to a diverse range of molecules for biological testing. Important challenges remain, however, particularly in reactions that form C–C bonds between sp3 hybridized carbons. We are developing methods for stereospecific alkyl-alkyl cross coupling, where transposition of stereochemical information from the electrophilic starting material to the product occurs. Cross-coupling reactions typically occur with inversion at the reactive center. Stereodivergent reactions, where choice of achiral ligand determines whether the reaction occurs with retention or inversion, will also be presented. The expansion of stereospecific nickel-catalyzed reactions to include ring-contraction of 3-halotetrahydropyrans for stereospecific synthesis of cyclopropanes will also be presented. These methods have been applied in synthesis of bioactive di- and triarylmethanes, enabling identification of new lead compounds with anti-cancer activity.

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