

Selective Catalytic Cross-Couplings with Organolithium Reagents

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Catalytic carbon–carbon bond formation based on cross-coupling reactions plays a central role in the production of natural products, pharmaceuticals, agrochemicals and organic materials. Catalysts for coupling reactions with a variety of organometallic reagents have been developed. However, the high reactivity and poor selectivity of common organolithium reagents, which are among the most broadly used reagents in chemical synthesis, have largely prohibited their use as a viable partner in direct catalytic cross-coupling reactions.

In this contribution our strategies for the selective cross-couplings of organolithium reagents will be discussed. More specifically, this presentation will focus on the development of the enantioselective synthesis of tertiary and quaternary stereogenic centers via copper-catalyzed asymmetric allylic alkylation with primary and secondary organolithium reagents. We have found that both the structure of the active chiral catalyst and the nature of the solvent used are the most critical factors in achieving successful asymmetric catalysis with these extremely reactive reagents.¹⁻⁴

This presentation will also focus on our recently developed palladium-catalyzed cross-coupling between a wide range of alkyl-, aryl- and heteroaryl-lithium reagents and aryl- and alkenyl-bromides.⁵ The process proceeds quickly under mild conditions (room temperature) and avoids the notorious lithium halogen exchange and homocoupling. Again, the control of the reactivity and aggregation state of the organolithium reagent by choosing an appropriate solvent and the use of a very active catalyst are key factors for achieving high levels of selectivity.

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