

Single Electron Processes to Enable Cross-Couplings

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In the archetypal palladium-catalyzed Suzuki cross-coupling reactions, a three step catalytic cycle mechanistically based on 2-electron processes is employed: oxidative addition of a halide at Pd⁰, transmetalation of an organoboron nucleophile with an organopalladium(II) species, and reductive elimination, which releases the coupled product and regenerates the Pd⁰ catalyst. Although such methods are highly effective for C_{sp2}-C_{sp2} coupling, extension to 2^o and 3^o C_{sp3}-hybridized organoborons has proven challenging owing primarily to lower rates of transmetalation, which is rate limiting in alkylboron Suzuki protocols operating under the traditional mechanistic manifold.

To date, strategies aimed at facilitating the transmetalation of C_{sp3} Suzuki reactions employ excess aqueous base, high temperature, or addition of stoichiometric Cu or Ag salts, thereby eliminating virtually all of the advantages of using organoborons in cross-coupling. Often, the only viable alternative is to abandon the Suzuki approach and utilize more reactive organometallic reagents. The latter not only lack bench stability and severely limit functional group tolerability, but are not configurationally stable and/or are challenging to access in enantiopure form.

The limitations of the transmetalation in the more desirable Suzuki couplings are inherent to the mechanism of this process at the most fundamental level, and thus predispose C_{sp3}-hybridized alkylborons for failure. Described is a novel single electron mechanistic paradigm for cross-coupling that avoids this problem. Thus, dual catalytic cycles are established: a photoredox catalytic cycle, generating radicals from nucleophilic species, and a cross-coupling catalytic cycle that funnels these radicals into a base metal catalytic cycle that effects the cross-coupling.

