Kumada Cross-Coupling

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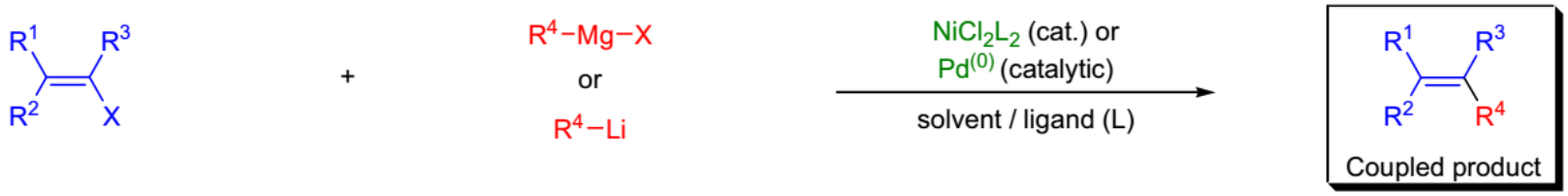
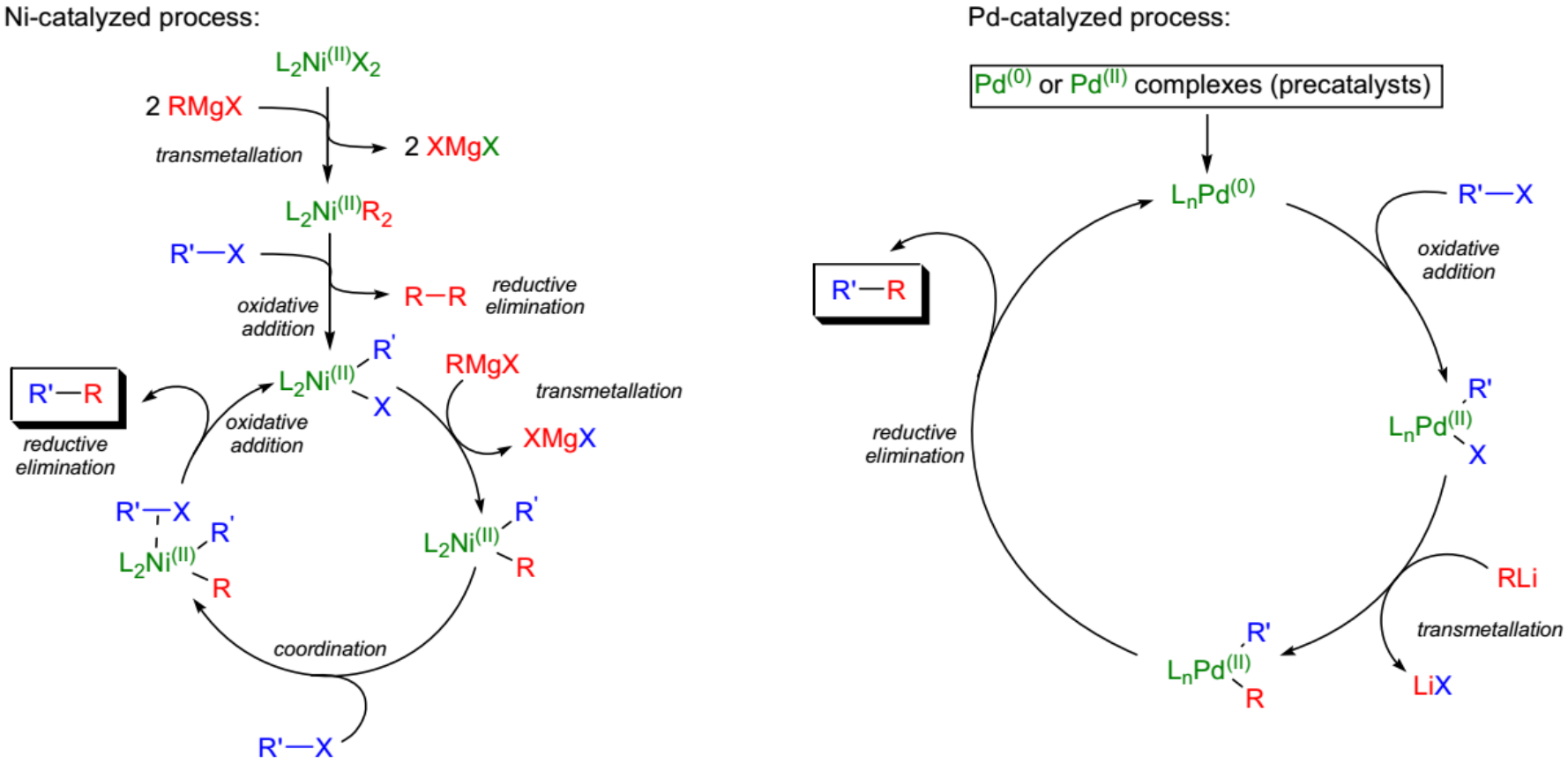
What Is Kumada Cross-Coupling



R^{1-3} = H, alkyl, aryl, alkenyl; X = F, Cl, Br, I. OTf; R^4 = alkyl, aryl, alkenyl; X = Br, I; L = PPh_3 or L_2 = dppp, dppe, dppb

The cross-coupling reaction between alkyl-,aryl- or alkenyl halides and Grignard reagents or organolithium reagents in the presence of Nickel or Pd catalysis is called Kumada cross-coupling.

Mechanism of Kumada Cross-Coupling

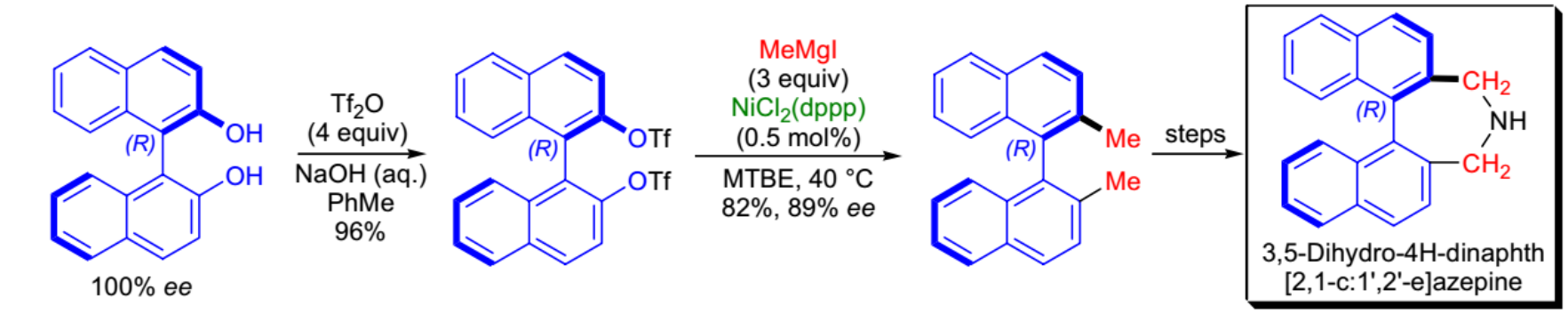


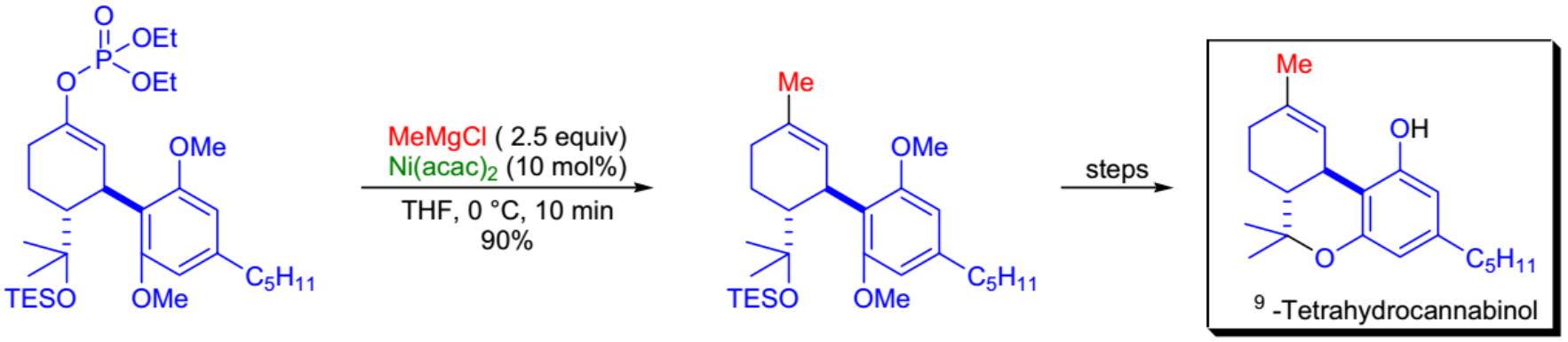
The Difference Between Ni and Pd Catalysis

$R^{1\text{-}3}$ = H, alkyl, aryl, alkenyl; X = F, Cl, Br, I. OTf; R^4 = alkyl, aryl, alkenyl; X = Br, I; L = PPh_3 or L_2 = dppp, dppe, dppb

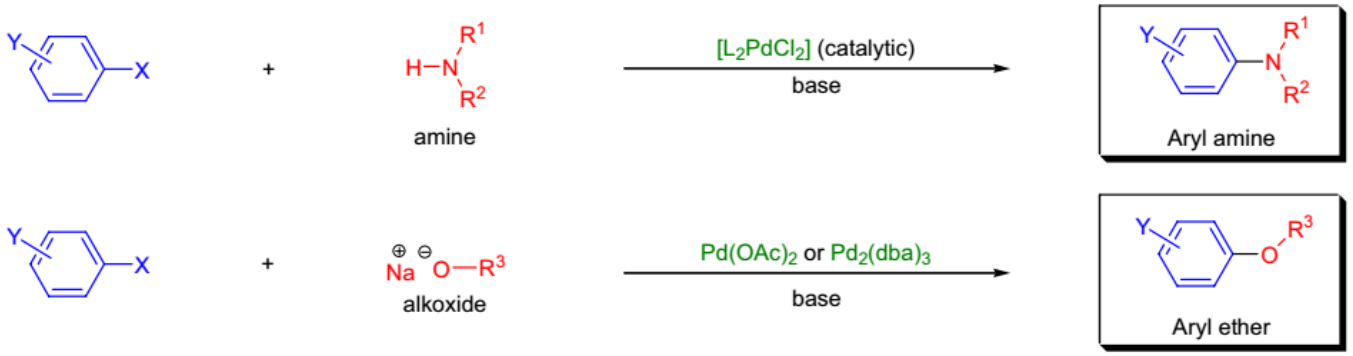
	Ni catalysis	Pd catalysis
Grignard reagents	√	√
organolithium reagents	×	√
aryl chlorides	√	×
aryl bromides and iodides	√	√

Applications of Kumada Cross-Coupling

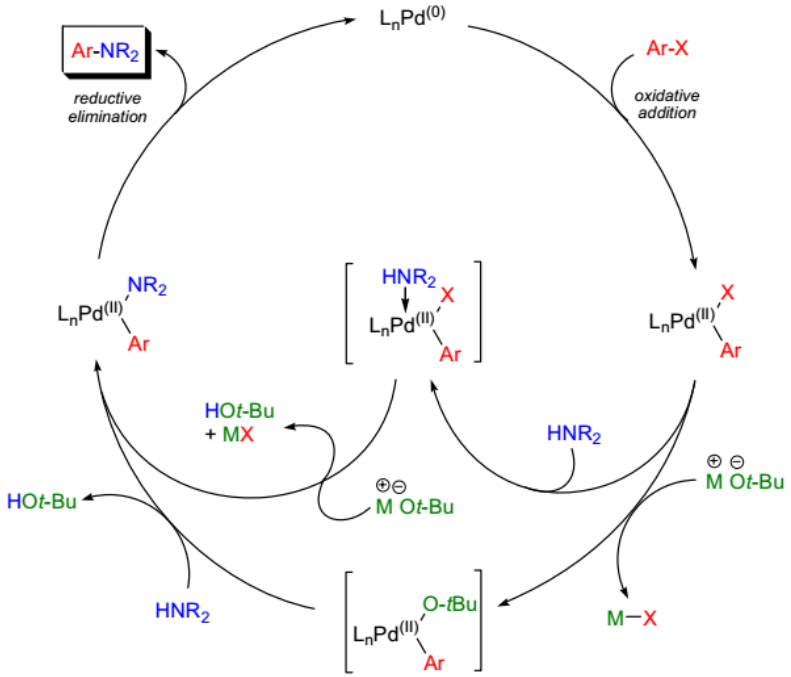




Buchwald-Hartwig Cross-Coupling

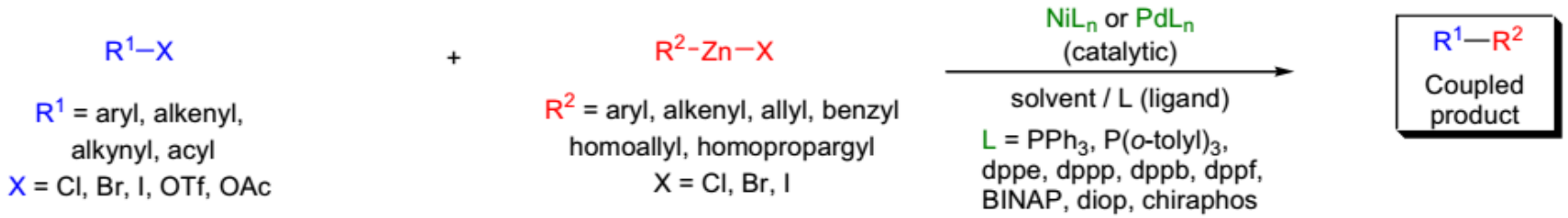


X = Cl, Br, I, OTf; Y = *o, m* or *p*-alkyl, phenacyl, amino, alkoxy; $R^{1\text{-}2}$ = 1° or 2° aromatic or aliphatic; R^3 = 1°, 2°, or 3° aliphatic or aromatic; L = P(*o*-Tol)$_3$, BINAP, dppf, dba; base: NaO*t*-Bu, LHMDS, K_2CO_3, Cs_2CO_3



The direct Pd-catalyzed C-N and C-O bond formation between aryl halides or oTf and amines or between aryl halides or triflates and alcohols in the presence of a stoichiometric amount of base is known as the Buchwald-Hartwig cross-coupling.

Negishi Cross-Coupling

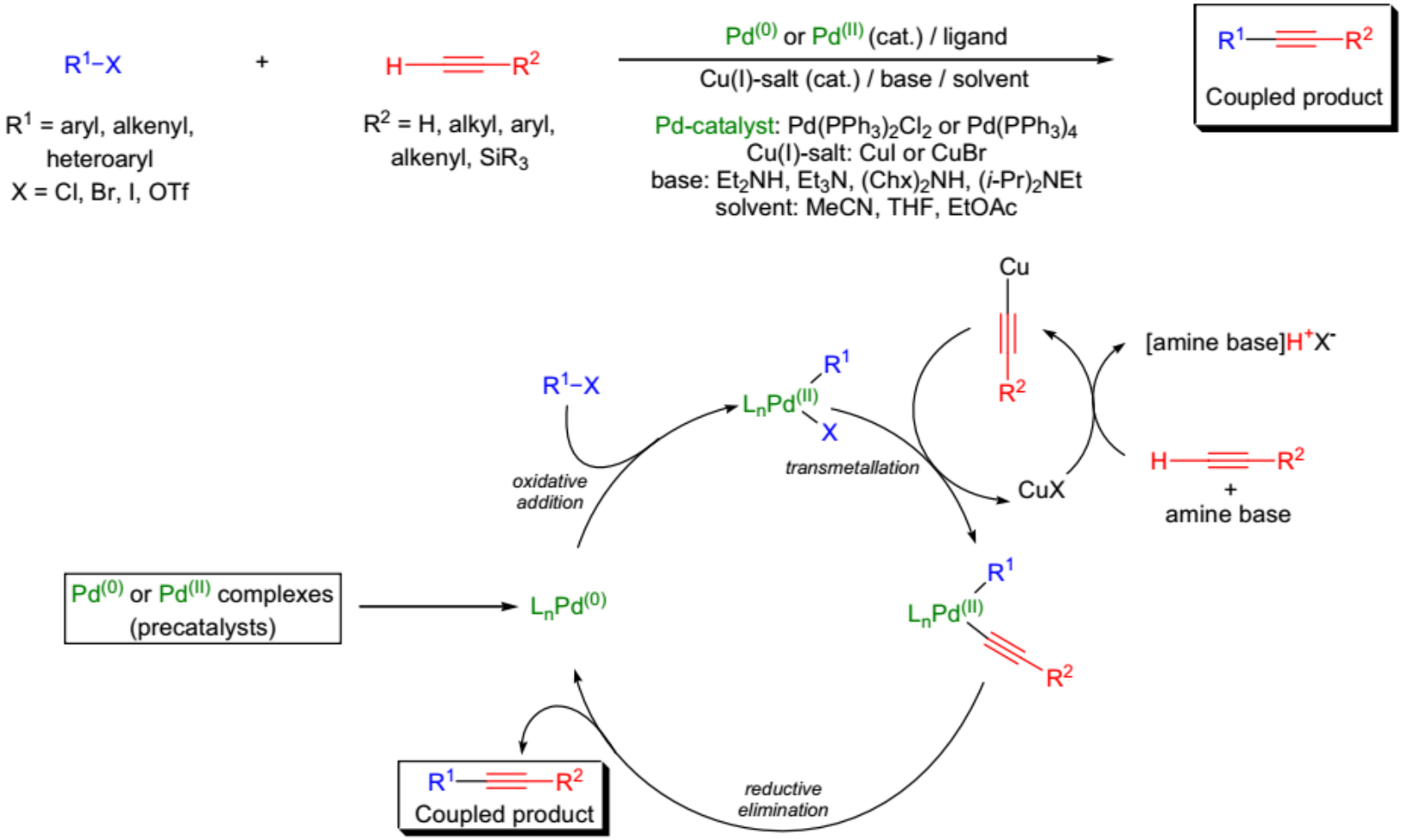


The Pd- or Ni-catalyzed stereoselective cross-coupling of organozincs and aryl-, alkenyl-, or alkynyl halides is known as the Negishi cross-coupling.

Why use organozincs instead of Grignard reagents or organolithium reagents ?

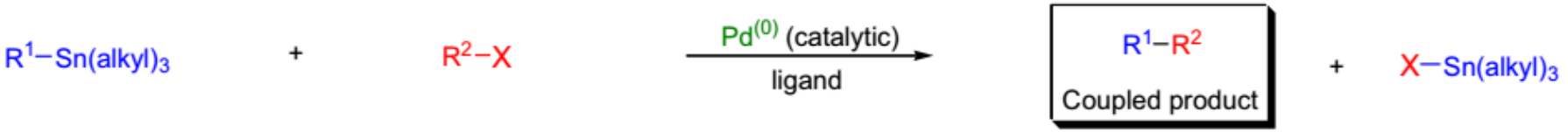
In order to improve the functional group tolerance of the process, the organometallic coupling partners should contain less electropositive metals than lithium and magnesium

Sonogashira Cross-Coupling

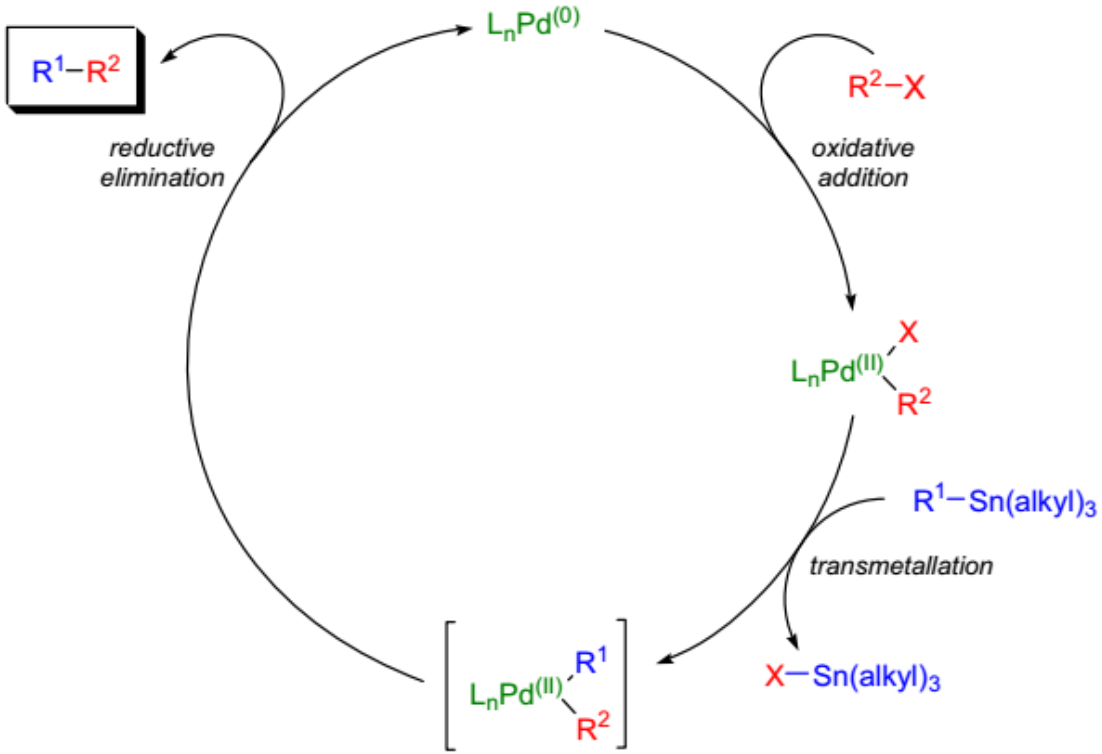


The copper-palladium catalyzed coupling of terminal alkynes with aryl and vinyl halides to give enynes is known as the Sonogashira cross-coupling

Stille Cross-Coupling

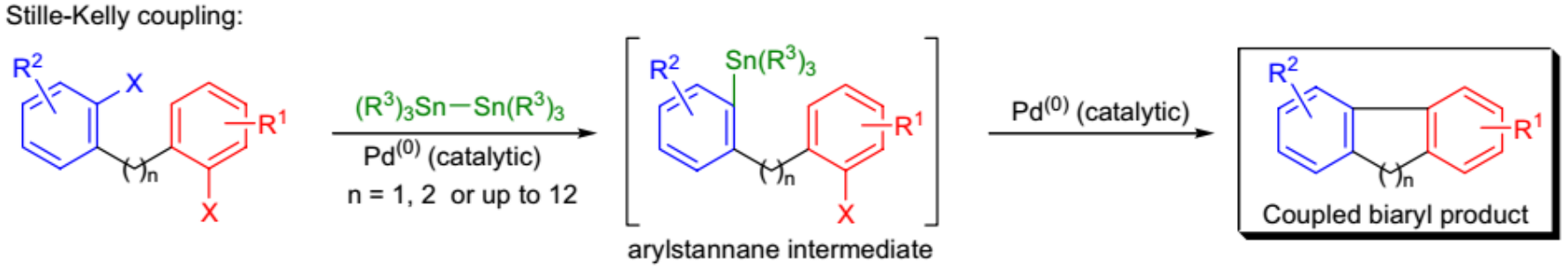


R^1 = allyl, alkenyl, aryl; R^2 = alkenyl, aryl, acyl; X = Cl, Br, I, OTf, $OPO(OR)_2$

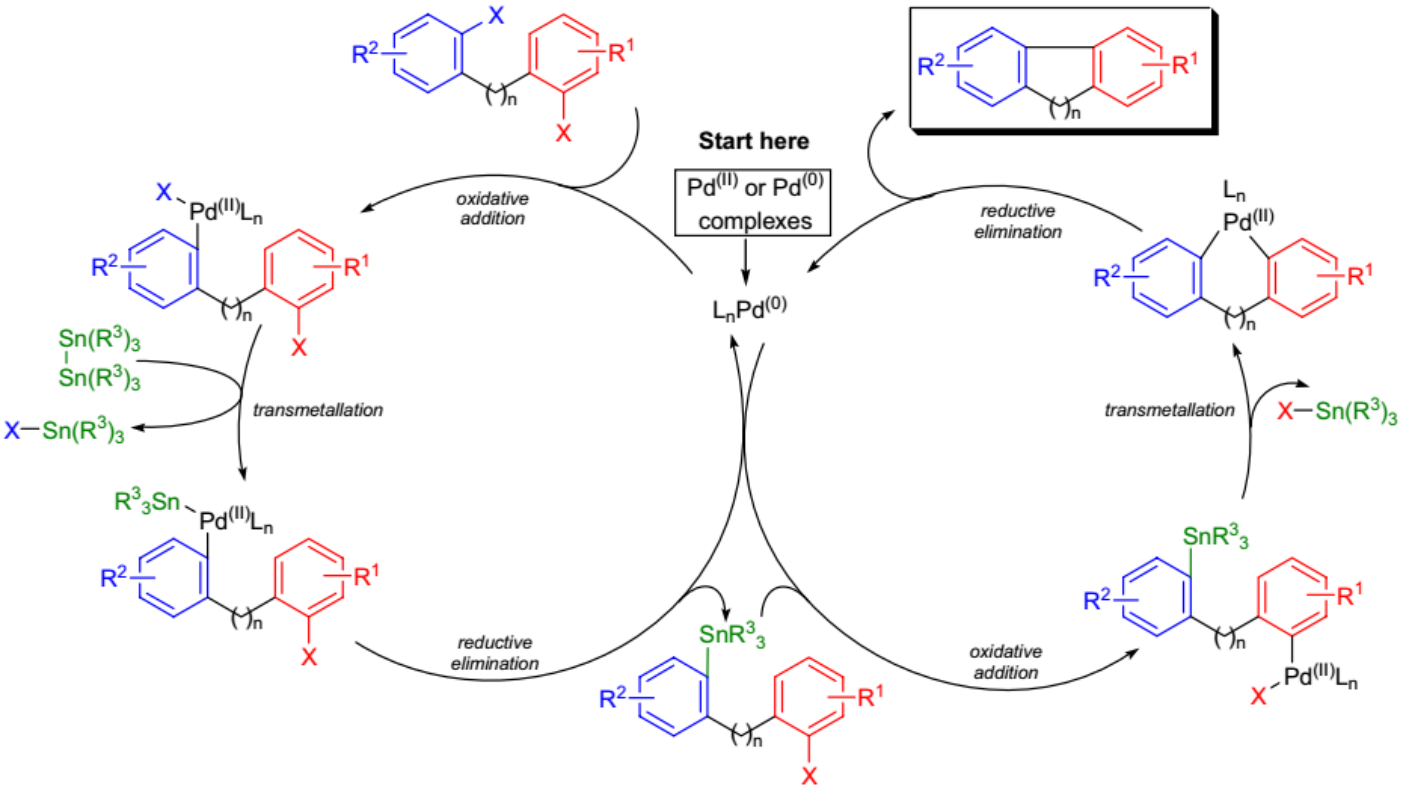


The Pd(0)-catalyzed coupling reaction between an organostannane and an organic electrophile to form a new C-C sigma bond is known as the Stille cross coupling

Stille-Kelly Coupling

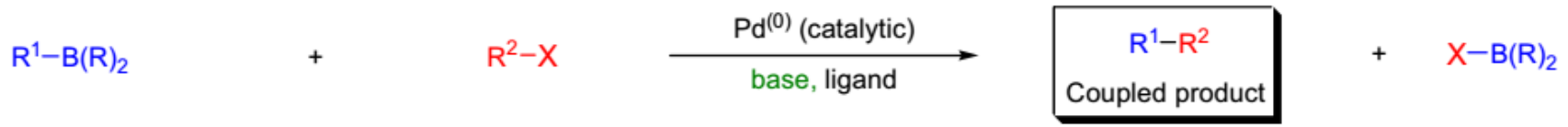


R^1, R^2 = alkyl, aryl, electron-withdrawing or electron-donating; R^3 = Me, *n*-Bu; X = Br, I, OTf

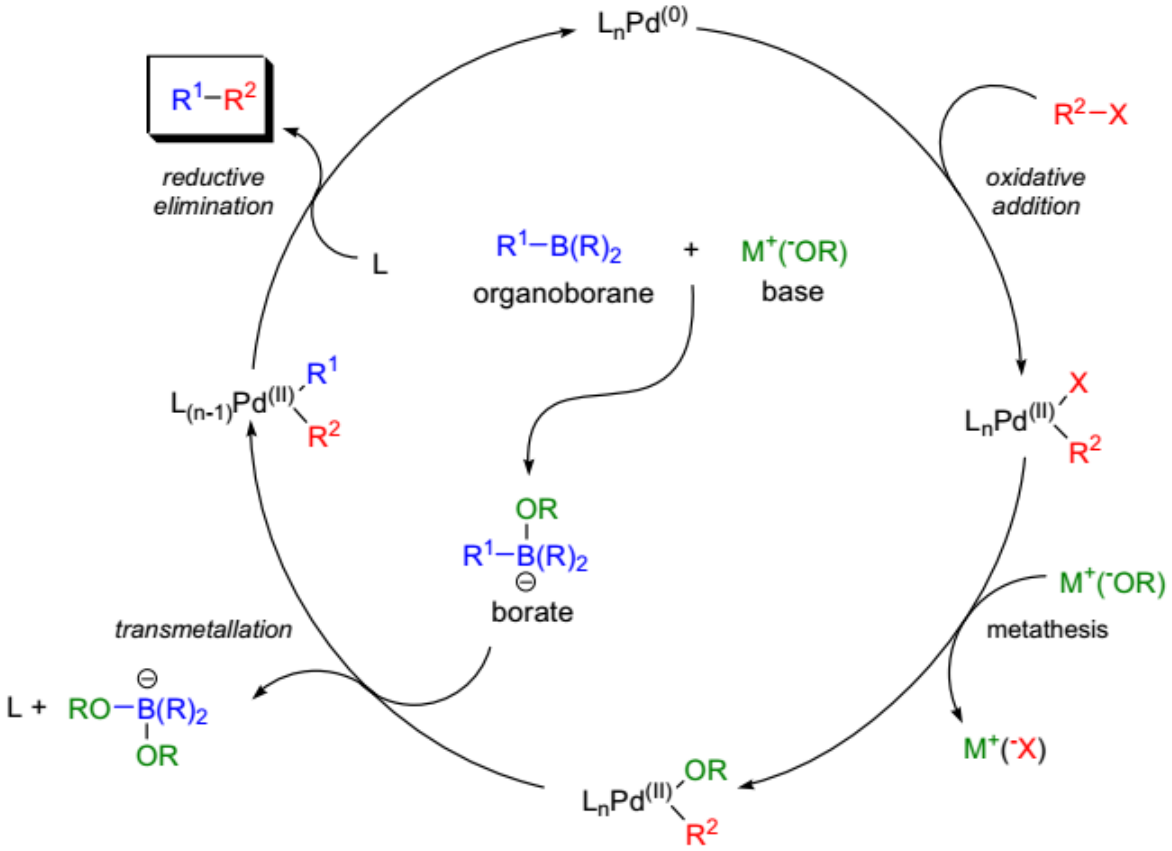


The Pd-catalyzed intramolecular biaryl coupling of aryl halides or aryl triflates in the presence of distannanes is known as the Stille-Kelly coupling.

Suzuki Cross-Coupling



R^1 = alkyl, allyl, alkenyl, alkynyl, aryl; R = alkyl, OH, O-alkyl; R^2 = alkenyl, aryl, alkyl; X = Cl, Br,I, OTf, $OPO(OR)_2$ (enol phosphate);
base = Na_2CO_3, $Ba(OH)_2$, K_3PO_4, Cs_2CO_3, K_2CO_3, TlOH, KF, CsF, Bu_4F, NaOH, $M^+(^-O\text{-alkyl})$



The palladium-catalyzed cross-coupling reaction between organoboron compounds and organic halides or triflates provides a powerful and general method for the formation of carbon-carbon bonds known as the Suzuki cross-coupling.