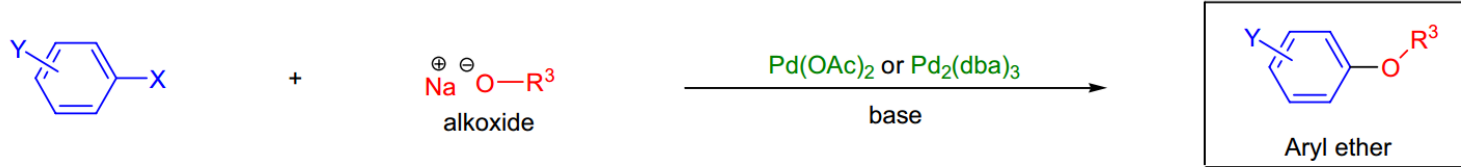
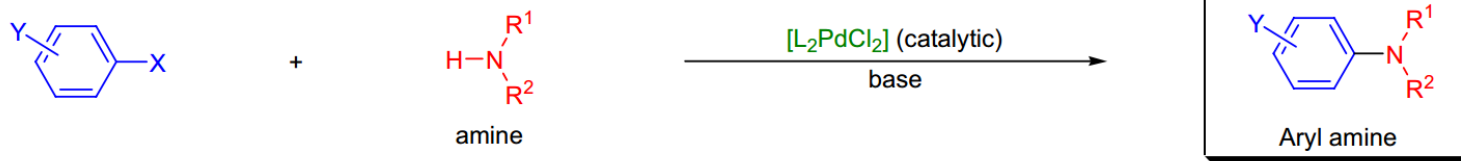


Buchwald–Hartwig Cross-Coupling

Introduction

The direct Pd-catalyzed C-N and C-O bond formation between aryl halides or trifluoromethanesulfonates and amines (1° and 2° aliphatic or aromatic amines; imides, amides, sulfonamides, sulfoximines) or between aryl halides or triflates and alcohols (aliphatic alcohols and phenols) in the presence of a stoichiometric amount of base is known as the Buchwald-Hartwig cross-coupling.

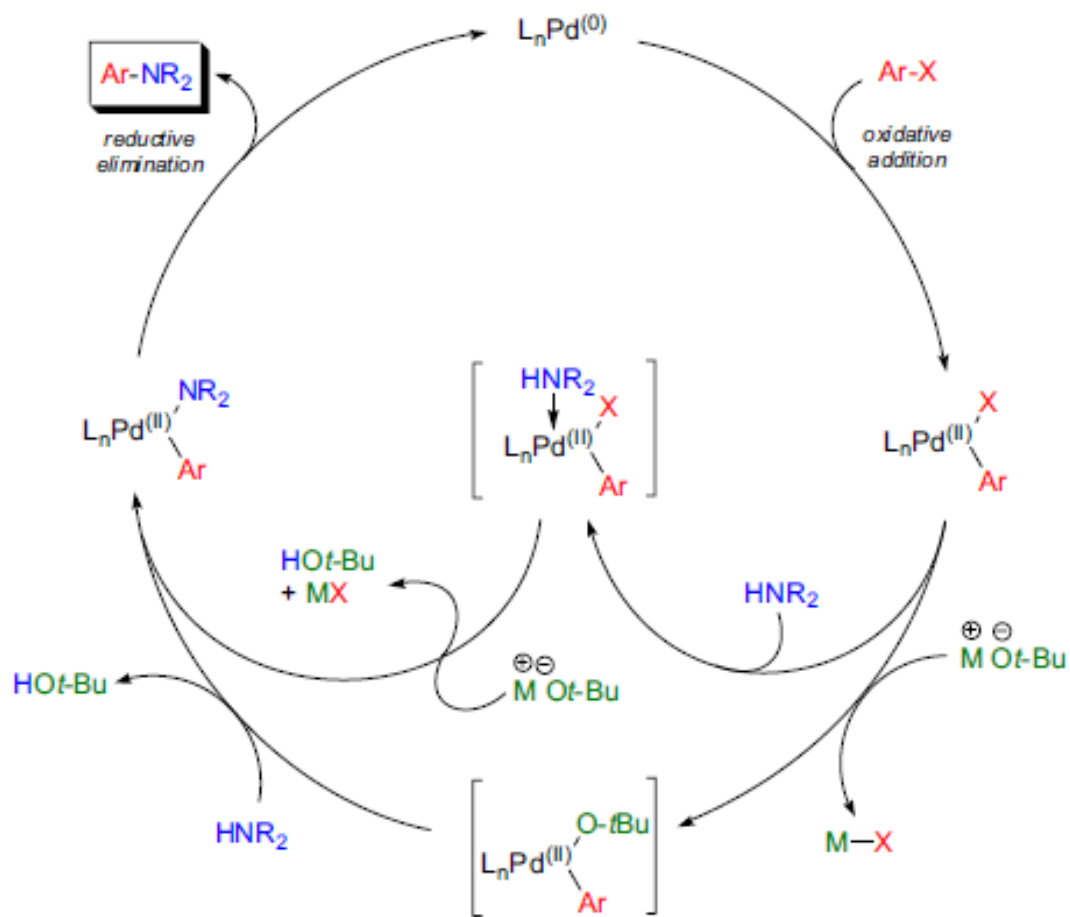


$X = \text{Cl, Br, I, OTf}; Y = o, m \text{ or } p\text{-alkyl, phenacyl, amino, alkoxy}; R^{1-2} = 1^\circ \text{ or } 2^\circ \text{ aromatic or aliphatic}; R^3 = 1^\circ, 2^\circ, \text{ or } 3^\circ \text{ aliphatic or aromatic}; L = \text{P}(o\text{-Tol})_3, \text{BINAP, dppe, dba}; \text{base: NaOt-Bu, LHMDS, K}_2\text{CO}_3, \text{Cs}_2\text{CO}_3$

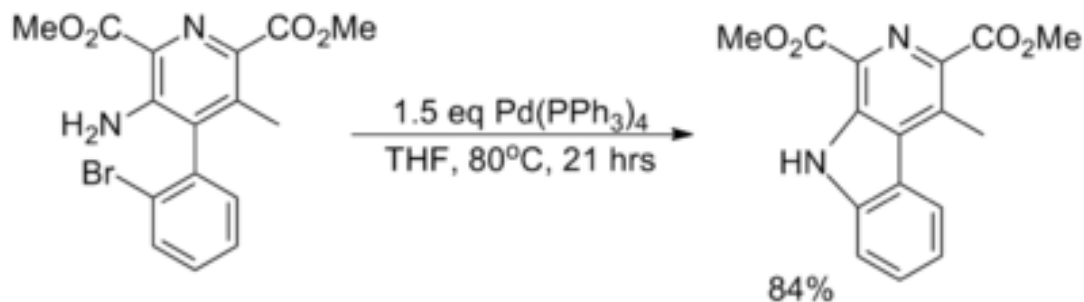
Mechanism

The first step in the catalytic cycle is the oxidative addition of Pd to the aryl halide (or sulfonate). In the second step the Pd(II)-aryl amide can be formed either by direct displacement of the halide (or sulfonate) by the amide via a Pd(II)-alkoxide intermediate. Finally, reductive elimination results in the formation of the desired C-N bond and the Pd(0) catalyst is regenerated. Below is the catalytic cycle for the formation of an arylamine.

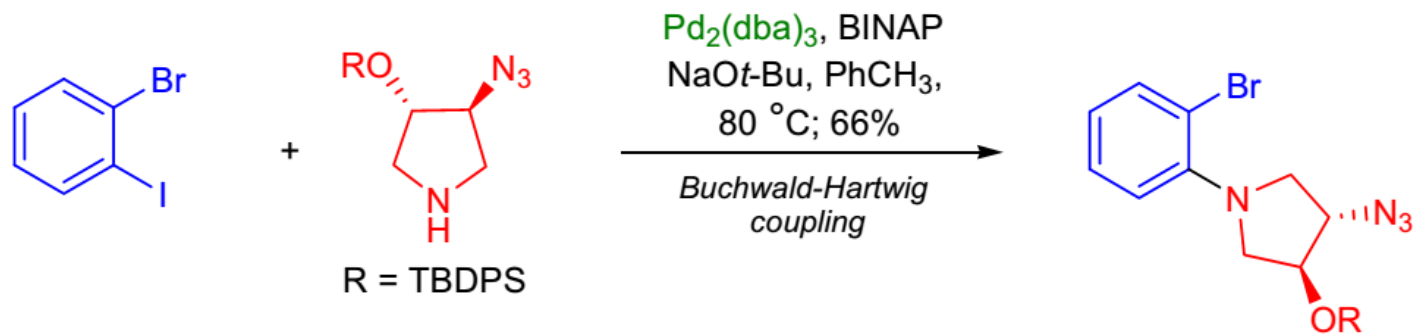
Mechanism



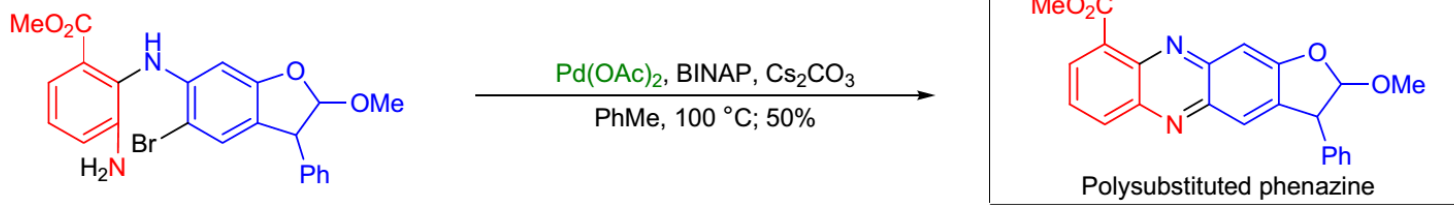
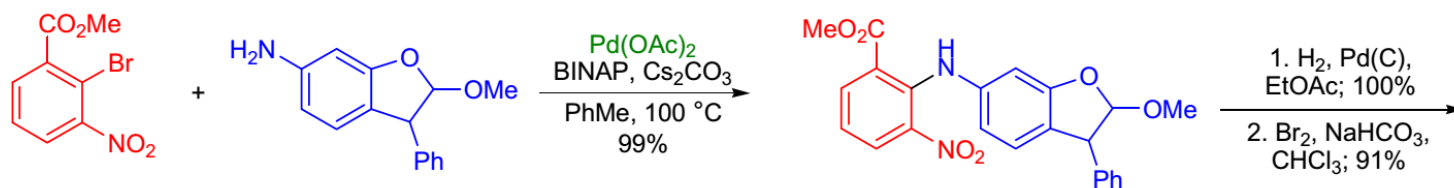
Then, in 1984, Dale L. Boger and James S. Panek reported an example of Pd(0)-mediated C–N bond formation in the context of their work on the synthesis of lavendamycin which utilized stoichiometric Pd(PPh₃)₄. Attempts to render the reaction catalytic were unsuccessful.



Synthetic Applications



Synthetic Applications



A scenic view of a lake with a building in the background and trees on the shore. The text "Thank you" is overlaid in a stylized, purple and blue font.

Thank you