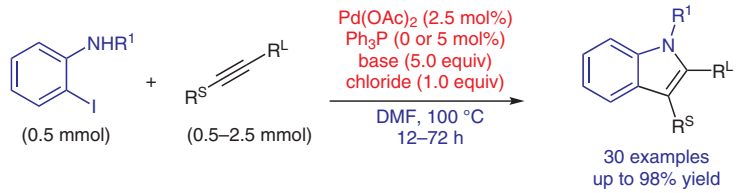
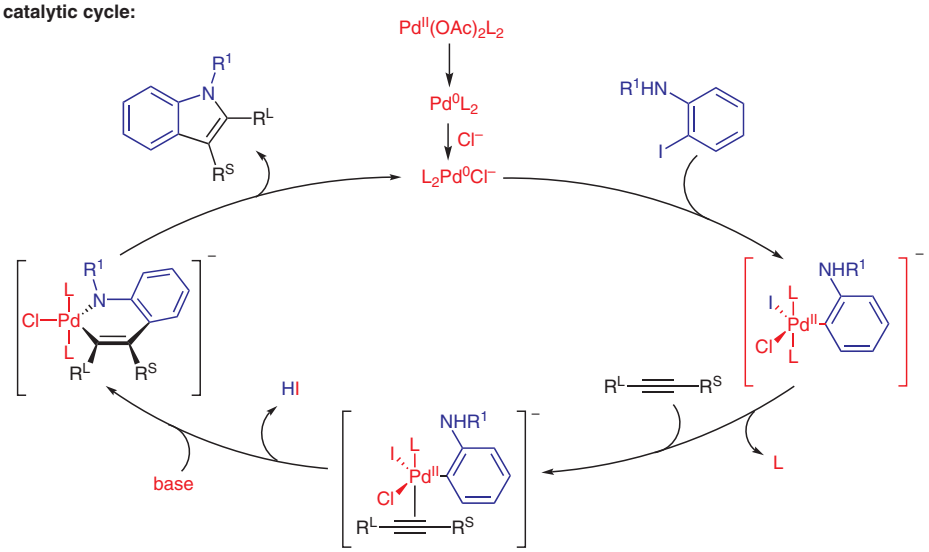
R. C. LAROCK*, E. K. YUM, M. D. REFVIK (IOWA STATE UNIVERSITY, USA)
Synthesis of 2,3-Disubstituted Indoles via Palladium-Catalyzed Annulation of Internal Alkynes
J. Org. Chem. **1998**, *63*, 7652–7662, DOI: 10.1021/jo9803277.

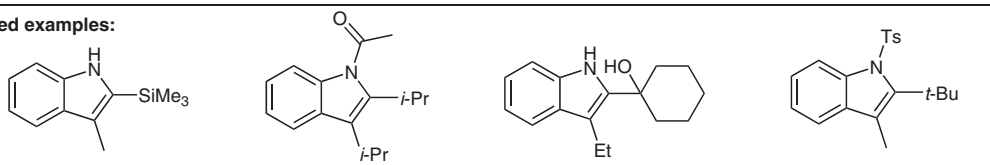
Larock Indole Synthesis



Proposed catalytic cycle:



Selected examples:



98% yield
source of Cl^- = *n*-Bu_4NCl
base = Na_2CO_3
Ph_3P = 5 mol%

91% yield
source of Cl^- = *n*-Bu_4NCl
base = KOAc
Ph_3P = none

85% yield
source of Cl^- = LiCl
base = KOAc
Ph_3P = none

86% yield
source of Cl^- = *n*-Bu_4NCl
base = KOAc
Ph_3P = none

Significance: In 1998, Larock and co-workers reported a palladium-catalyzed coupling of 2-iodoanilines with internal alkynes to afford 2,3-disubstituted indoles; an important heterocyclic scaffold. The reaction proceeds under mild conditions to afford the indole products in good to excellent yields.

Comment: The regioselectivity of the reaction is dependent on both substrate and reaction conditions employed. When more than one equivalent of the chloride is added, the reaction rate is retarded, and there is an increase in the formation of side products.

Review: R. Chinchilla, C. Nájera *Chem. Rev.* **2014**, *114*, 1783–1826.

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Category
Metals in Synthesis

Key words
Larock indole synthesis
palladium catalysis
annulation
regioselectivity
alkyne insertion