

ref : O. Baudoin, *Chem. Eur. J.* **2010**, *16*, 2654-2672.
O. Baudoin, *Chem. Soc. Rev.*, **2011**, *40*, 4902-4911.

Reporter: Tao Cheng
Supervisor: Prof. Yong Huang
2012-09-23

Content

Part I Introduction

Part II Heteroatom-directed C-H arylation

Part III Oxidative addition/metalation-induced C-H arylation

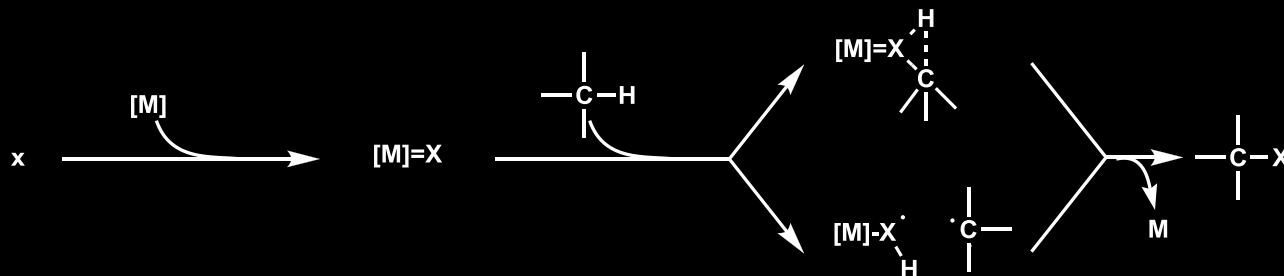
Part IV Non-directed organometallic C-H arylation

Part V Summary

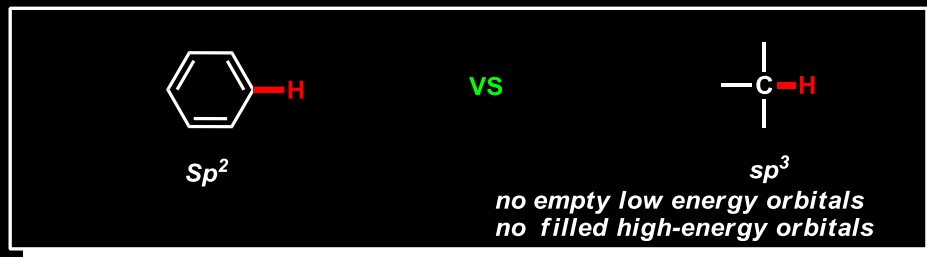
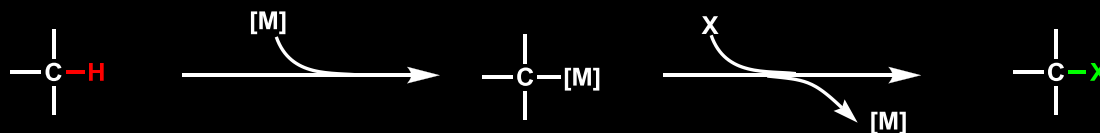
Introduction

Classification of transition-metal-catalyzed C-H functionalization

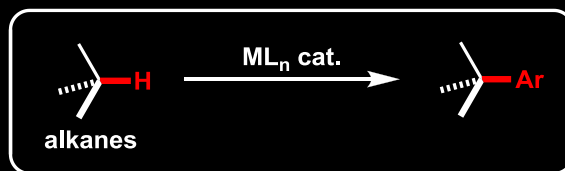
a) Outer-sphere mechanism / coordination chemistry



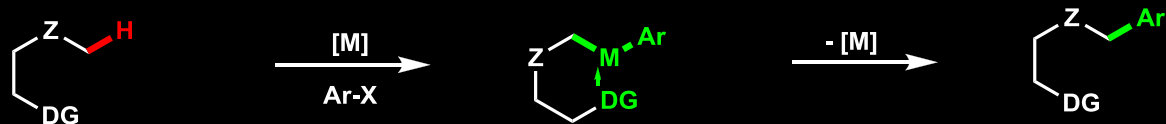
b) Inner-sphere mechanisms / organometallic chemistry: C-H activation



Introduction

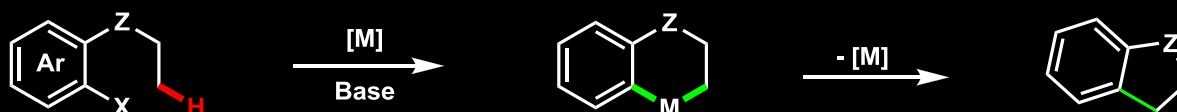


A. Heteroatom-directed C-H arylation

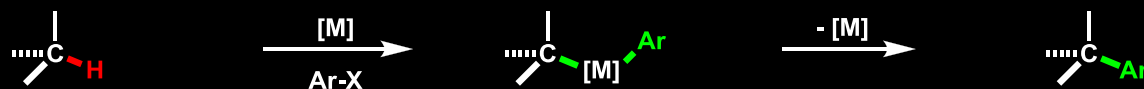


DG = Directing Group

B. Oxidative addition/metalation-induced C-H arylation



C. Non-directed organometallic C-H arylation



Content

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Part II Heteroatom-directed C-H arylation

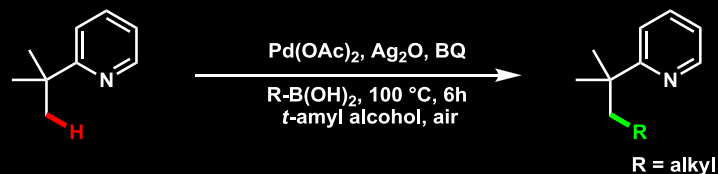
Part III Oxidative addition/metalation-induced C-H arylation

Part IV Non-directed organometallic C-H arylation

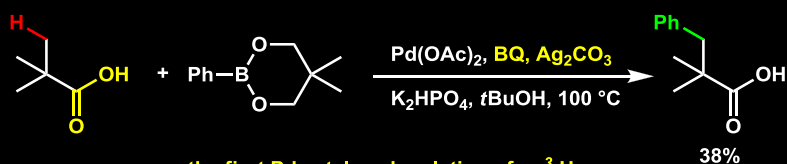
Part V Summary

Heteroatom-directed C-H arylation

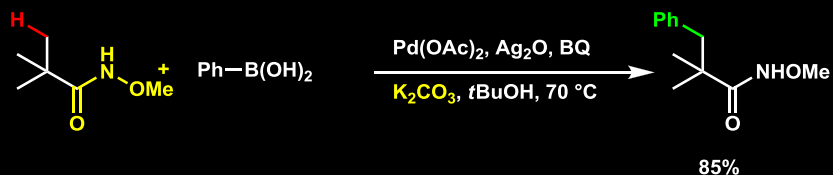
Directed C(sp³)-H arylation with arylboronic reagents



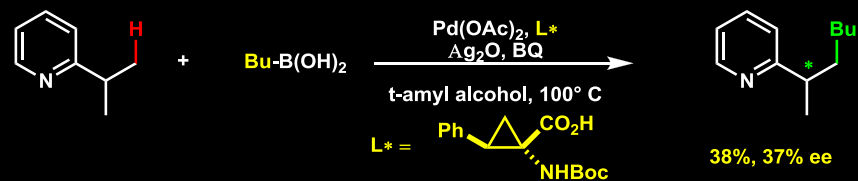
J. -Q. Yu, *J. Am. Chem. Soc.* **2006**, 128, 12634-12635



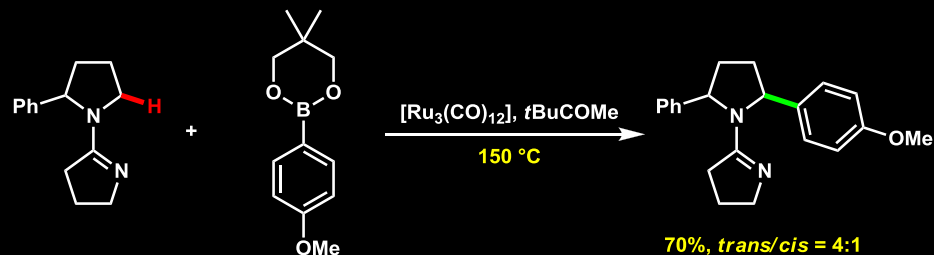
J. -Q. Yu, *J. Am. Chem. Soc.* **2007**, 129, 3510-3511



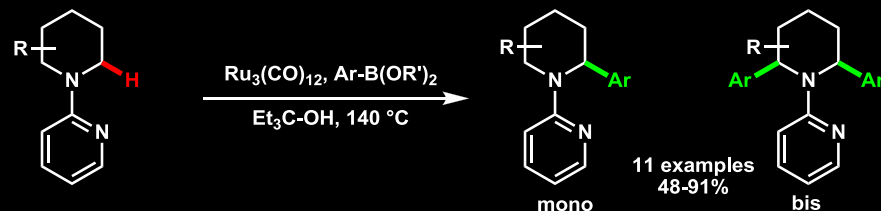
J. -Q. Yu, *J. Am. Chem. Soc.* **2008**, 130, 7190-7191



J. -Q. Yu, *ACIE*, **2008**, 47, 4882-4886



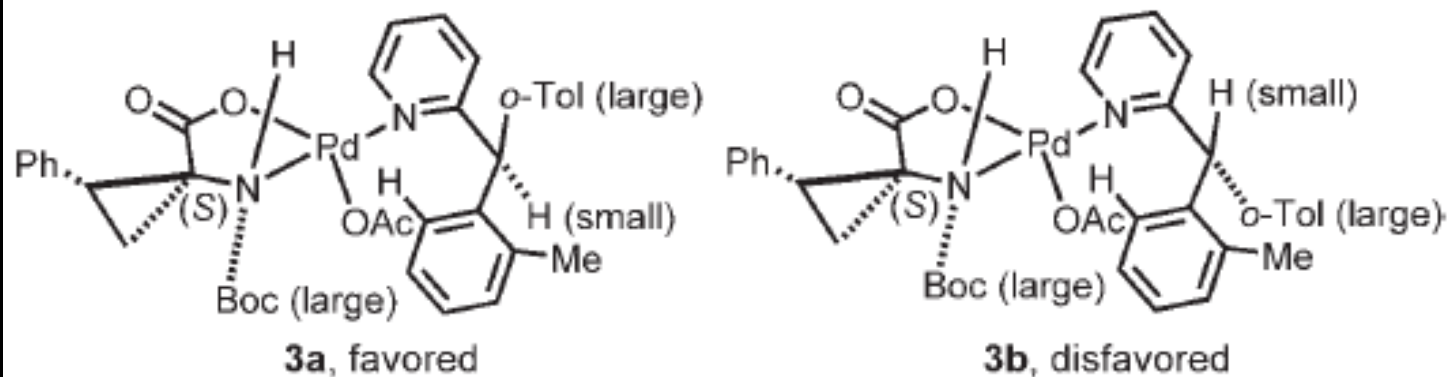
D. Sames, *J. Am. Chem. Soc.* **2006**, 128, 14220-14221



B. U. W. Maes, *Chem. -Eur. J.*, **2010**, 16, 13063

Heteroatom-directed C-H arylation

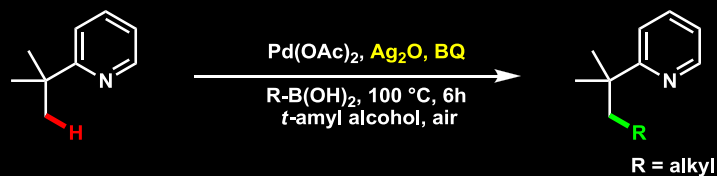
Directed C(sp³)-H arylation with arylboronic reagents



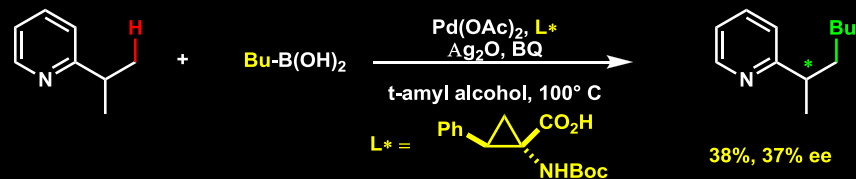
Scheme 3. Key intermediates in the mechanism for the enantioselective C-H activation. Boc = *tert*-butoxycarbonyl, *o*-Tol = *ortho*-tolyl.

Heteroatom-directed C-H arylation

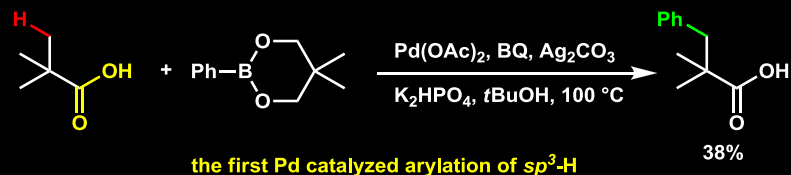
Directed C(sp³)-H arylation with arylboronic reagents



J. -Q. Yu, *J. Am. Chem. Soc.* **2006**, *128*, 12634-12635

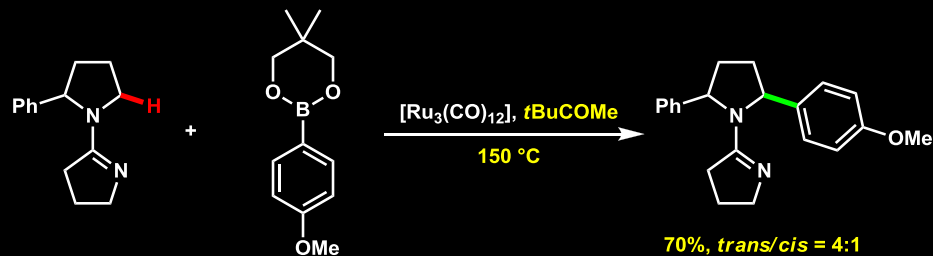


J. -Q. Yu, *ACIE*, **2008**, *47*, 4882-4886

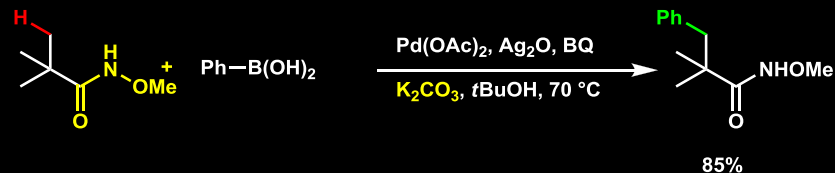


the first Pd catalyzed arylation of sp³-H

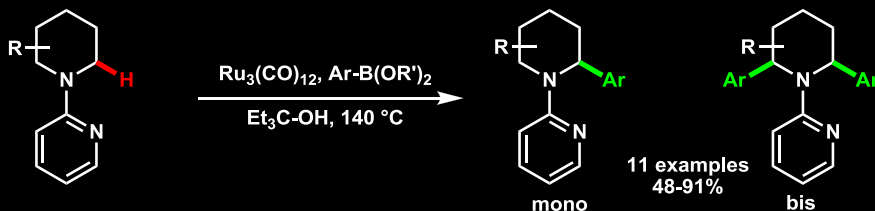
J. -Q. Yu, *J. Am. Chem. Soc.* **2007**, *129*, 3510-3511



D. Sames, *J. Am. Chem. Soc.* **2006**, *128*, 14220-14221



J. -Q. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 7190-7191

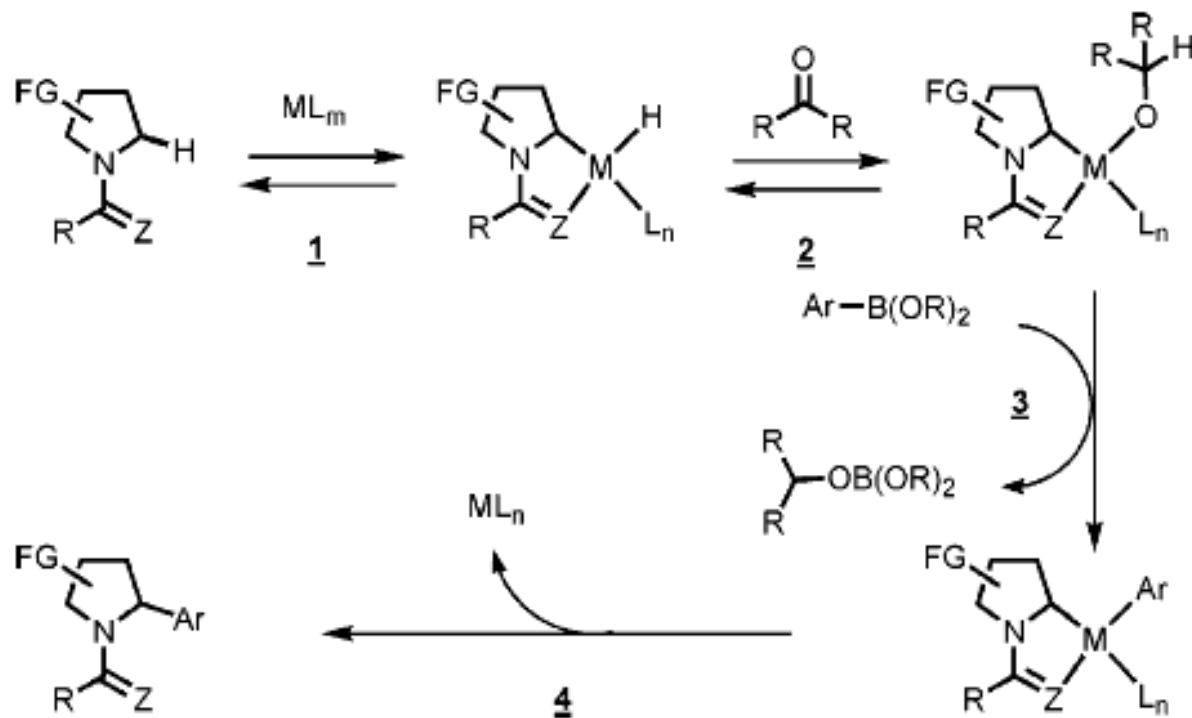


B. U. W. Maes, *Chem. -Eur. J.*, **2010**, *16*, 13063

Heteroatom-directed C-H arylation

Directed C(sp³)-H arylation with arylboronic reagents

Scheme 1. A Mechanistic Guide for the New sp³ C-H Bond Arylation^a

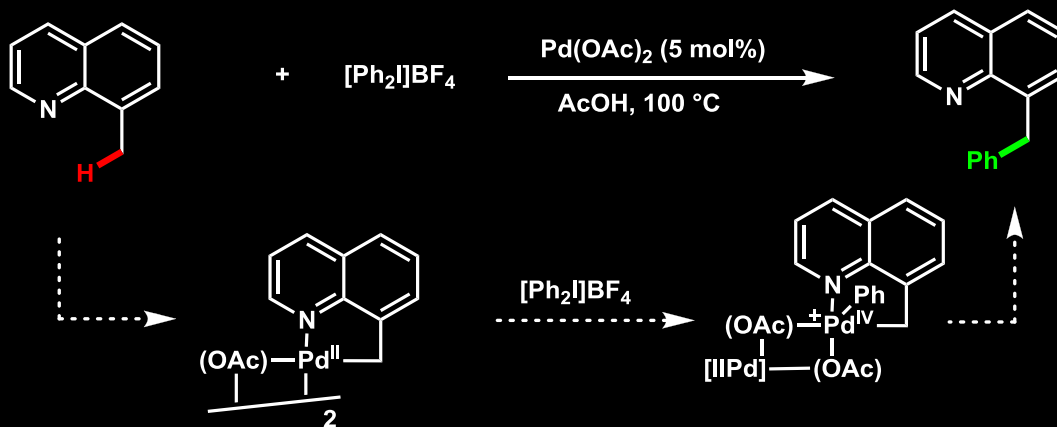


^a The four key steps: (1) metal insertion (directed); (2) ketone insertion; (3) transmetalation; (4) C-C bond formation.



Heteroatom-directed C-H arylation

Directed C(sp³)-H arylation with diaryliodonium reagents and aryl halides

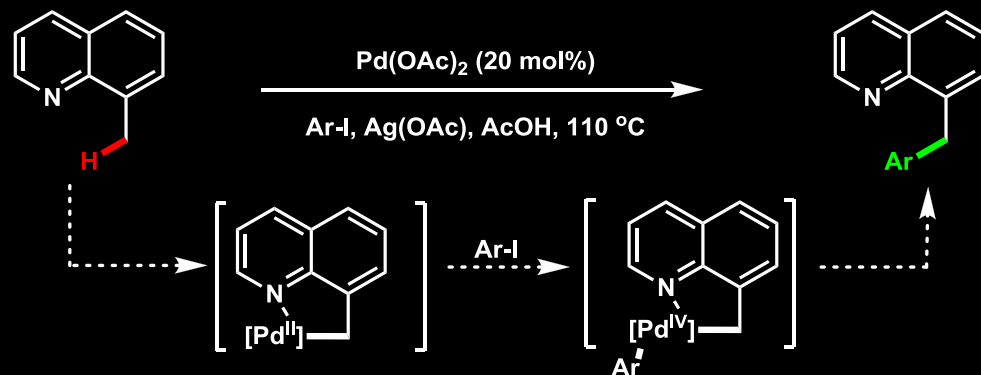


M. S. Sanford, *J. Am. Chem. Soc.* **2005**, 127, 7330-7331.
M.S. Sanford, *J. Am. Chem. Soc.* **2009**, 131, 11234

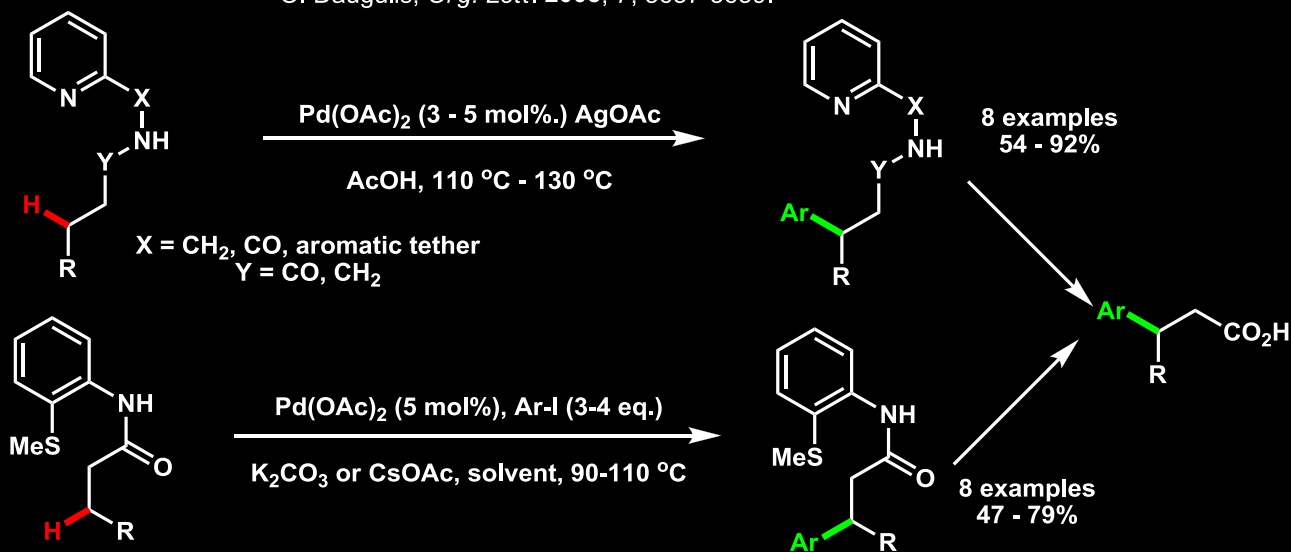


Heteroatom-directed C-H arylation

Directed C(sp³)-H arylation with diaryliodonium reagents and aryl halides



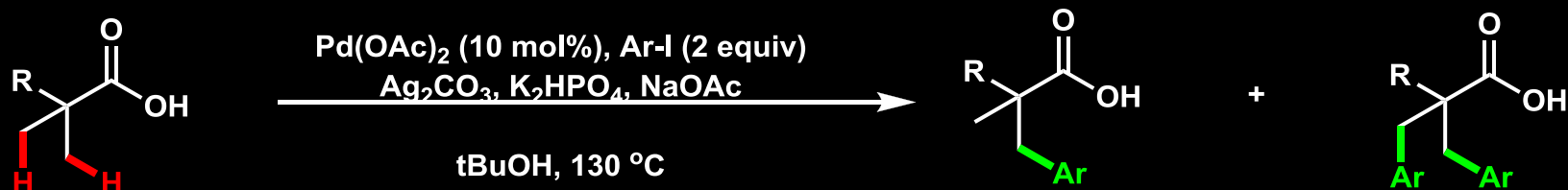
O. Daugulis, *Org. Lett.* **2005**, 7, 3657-3659.



O. Daugulis, *J. Am. Chem. Soc.* **2005**, 127, 13154-13155

Heteroatom-directed C-H arylation

Directed C(sp³)-H arylation with diaryliodonium reagents and aryl halides

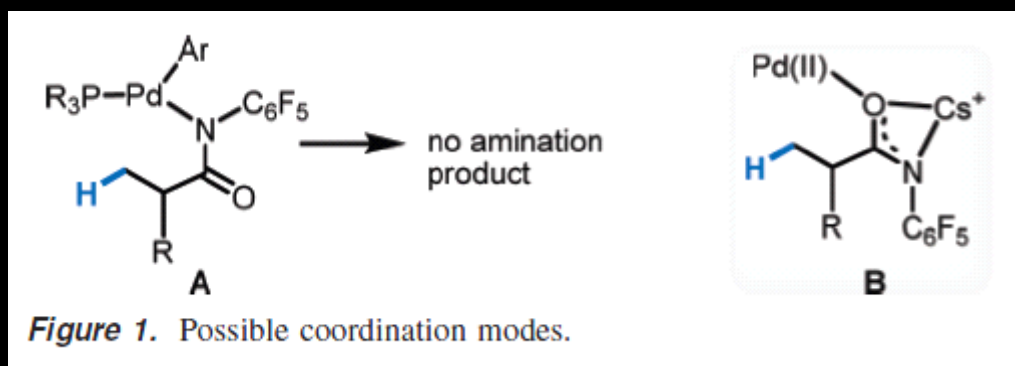


J. -Q. Yu, *J. Am. Chem. Soc.* **2007**, 129, 3510.

8 examples
mono/bis 5:2-5:1

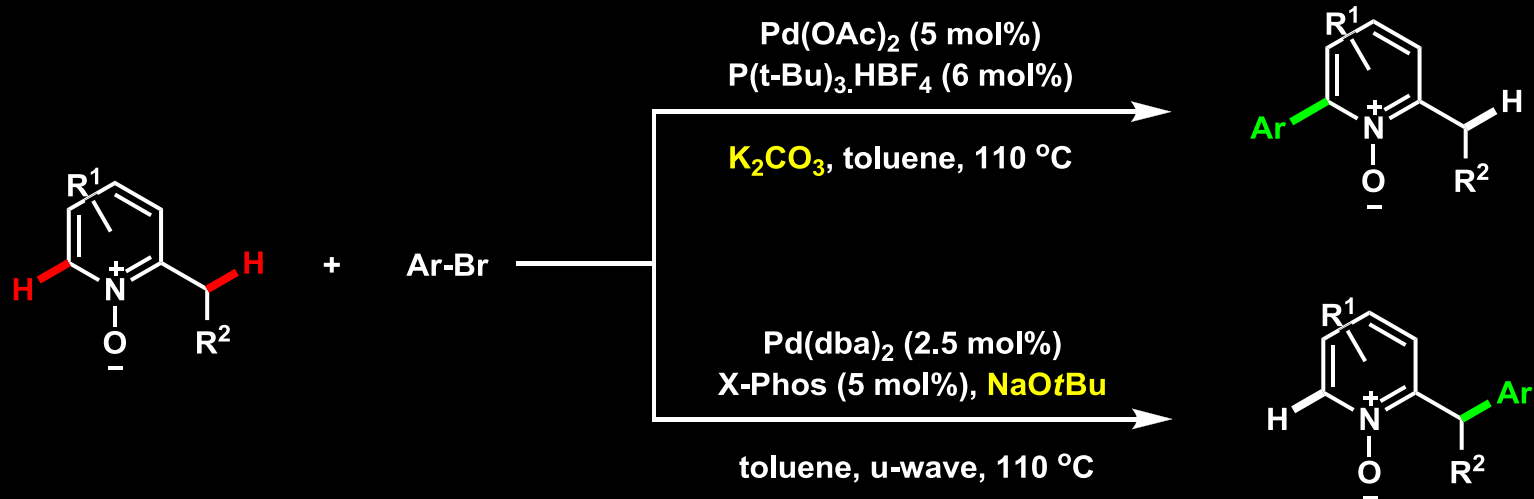


J. -Q. Yu, *J. Am. Chem. Soc.* **2009**, 131, 9886-9887.

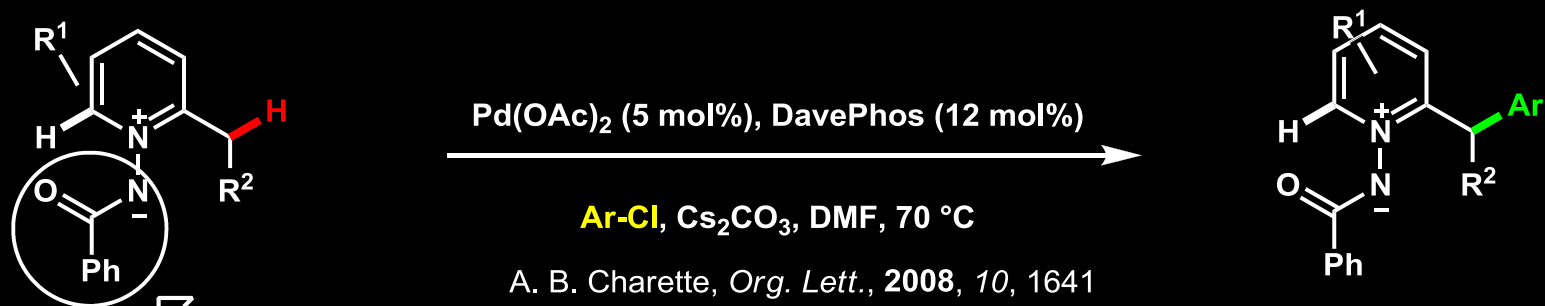


Heteroatom-directed C-H arylation

Directed C(sp³)-H arylation with diaryliodonium reagents and aryl halides



K. Fagnou, *J. Am. Chem. Soc.*, **2008**, *130*, 3266



A. B. Charette, *Org. Lett.*, **2008**, *10*, 1641

strong lewis base = direct group

Content

Part I Introduction

Part II Heteroatom-directed C-H arylation

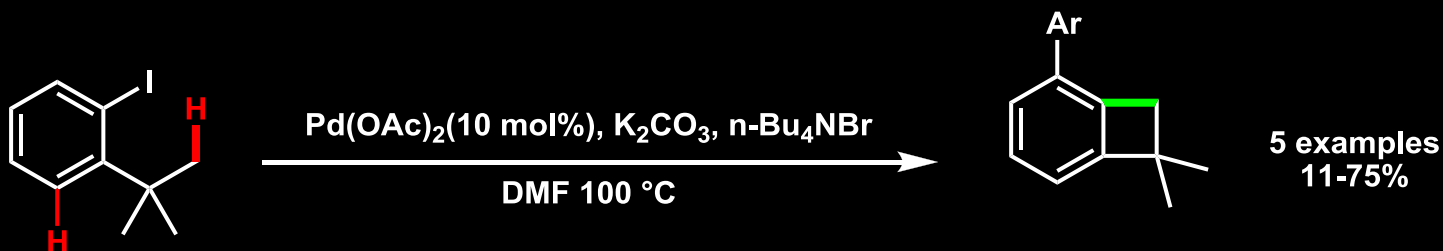
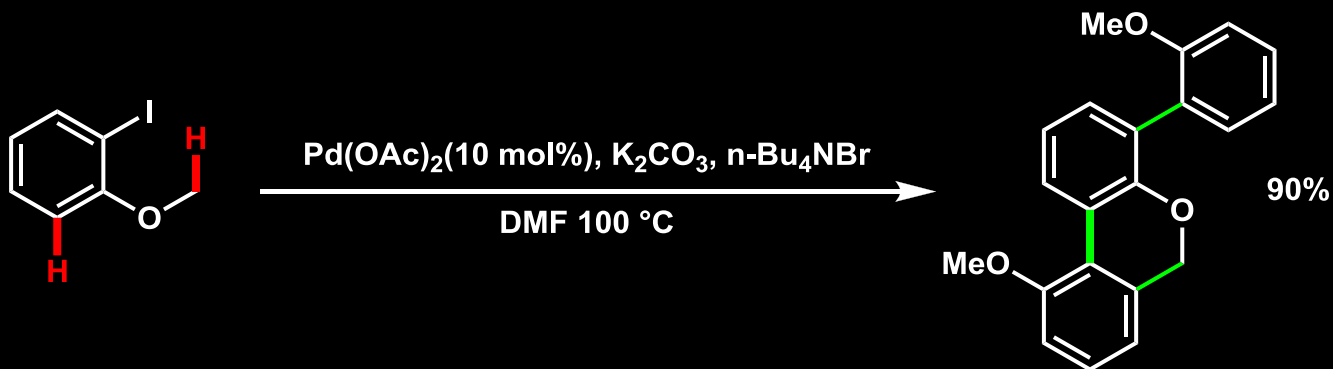
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Part V Summary

Oxidative addition/metalation-induced C(sp³)-H arylation

Oxidative addition-induced intramolecular arylation

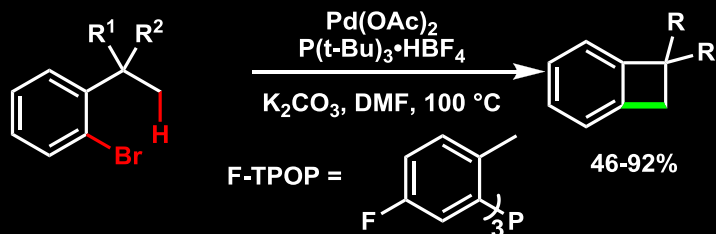
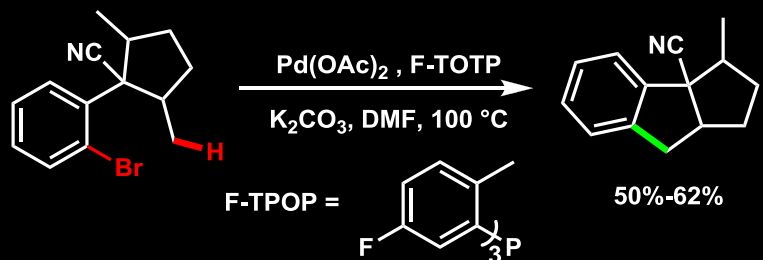


G. Dyker, *ACIE*, **1992**, 31, 1023

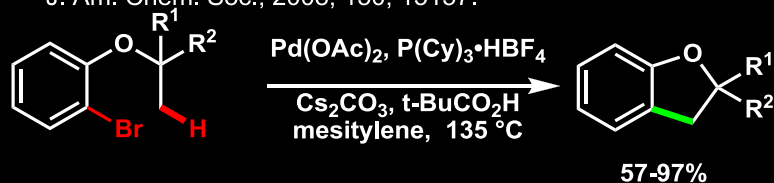
G. Dyker, *ACIE*, **1994**, 33, 103

Oxidative addition/metalation-induced C(sp³)-H arylation

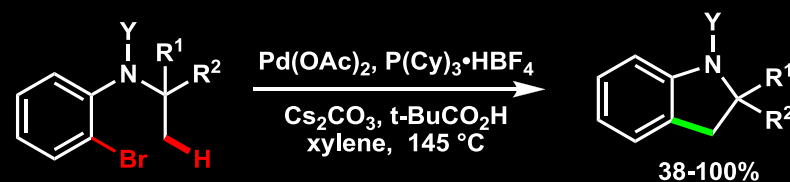
Oxidative addition-induced intramolecular arylation



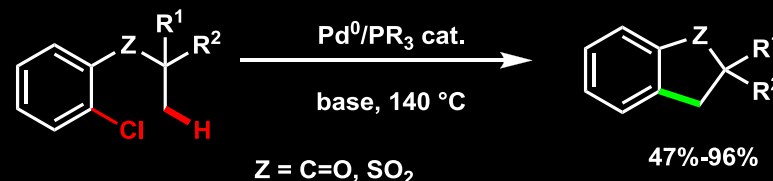
O. Baudoin, *ACIE*, **2003**, 42, 5736; *Chem. -Eur. J.*, 2007, 13, 792;
J. Am. Chem. Soc., 2008, 130, 15157.



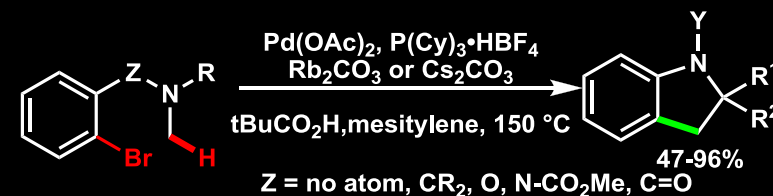
K. Fangou, *J. Am. Chem. Soc.*, **2007**, 129, 14570



H. Ohno, *Org. Lett.*, **2008**, 10, 1759.



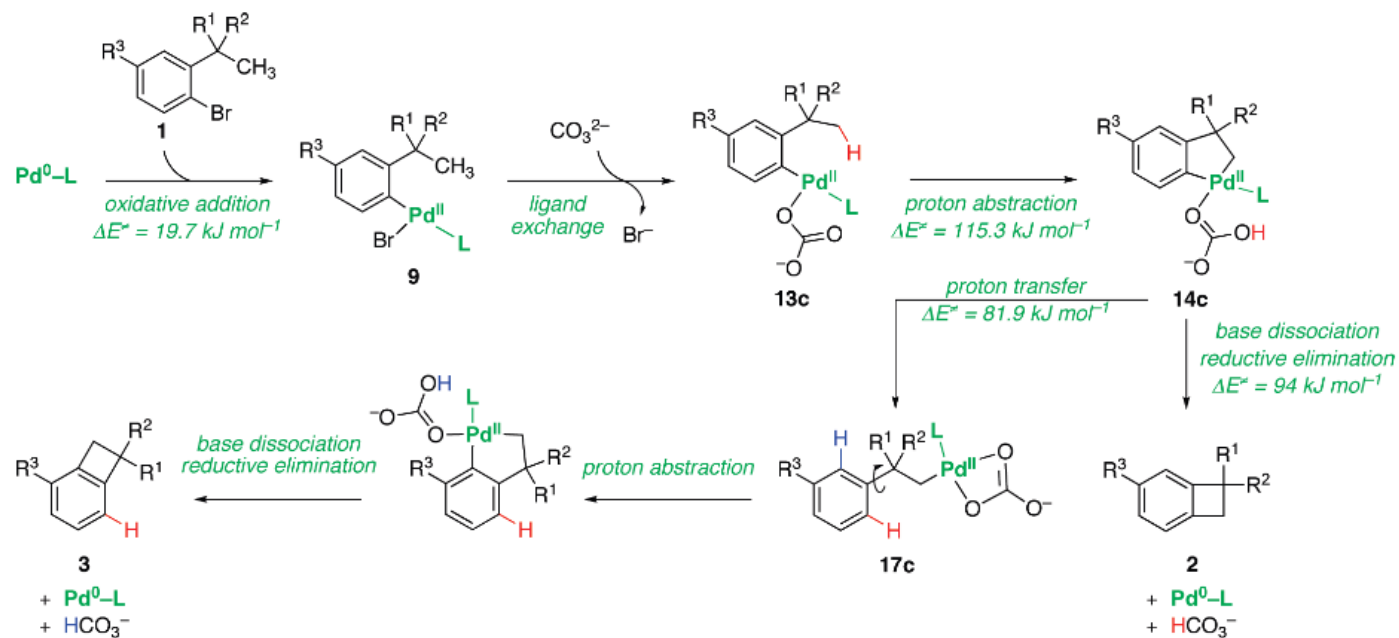
K. Fangou, *J. Am. Chem. Soc.*, **2010**, 132, 10692.



K. Fangou, *J. Am. Chem. Soc.*, **2010**, 132, 10706.

Oxidative addition/metalation-induced C(sp³)-H arylation

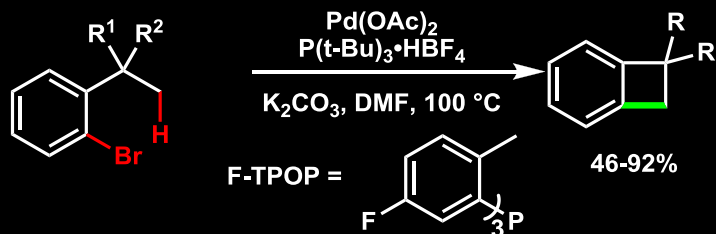
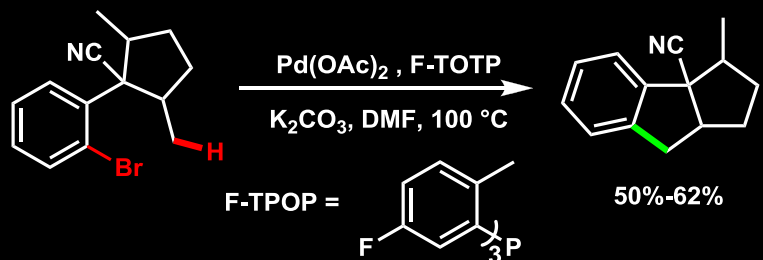
Oxidative addition-induced intramolecular arylation



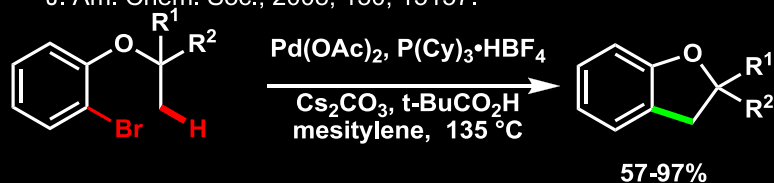
Olivier Baudoin

Oxidative addition/metalation-induced C(sp³)-H arylation

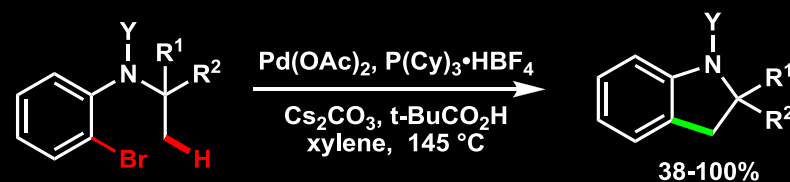
Oxidative addition-induced intramolecular arylation



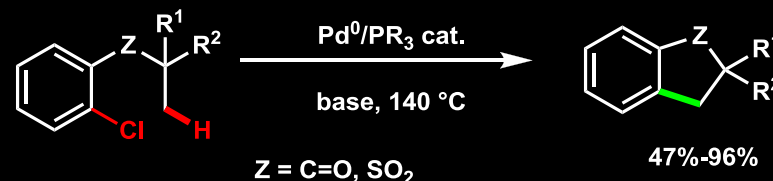
O. Baudoin, *ACIE*, **2003**, 42, 5736; *Chem. -Eur. J.*, **2007**, 13, 792;
J. Am. Chem. Soc., **2008**, 130, 15157.



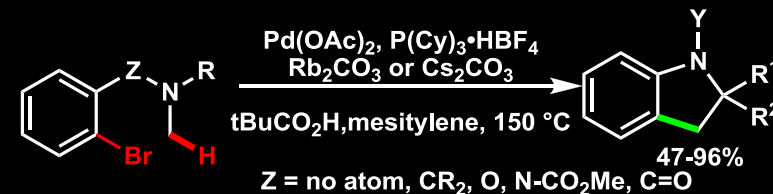
K. Fangou, *J. Am. Chem. Soc.*, **2007**, 129, 14570



H. Ohno, *Org. Lett.*, **2008**, 10, 1759.



K. Fangou, *J. Am. Chem. Soc.*, **2010**, 132, 10692.

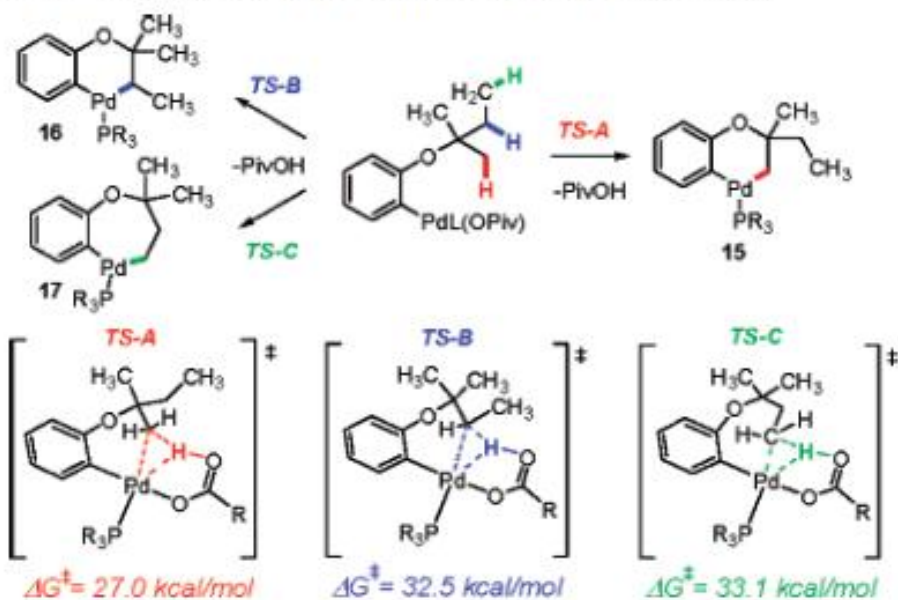


K. Fangou, *J. Am. Chem. Soc.*, **2010**, 132, 10706.

Oxidative addition/metalation-induced C(sp³)-H arylation

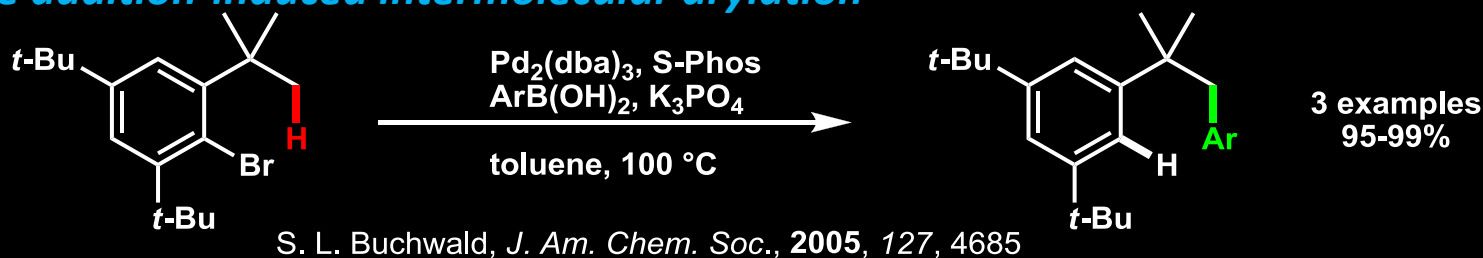
Oxidative addition-induced intramolecular arylation

Scheme 2. Mechanistic Rationale for Site Selectivity

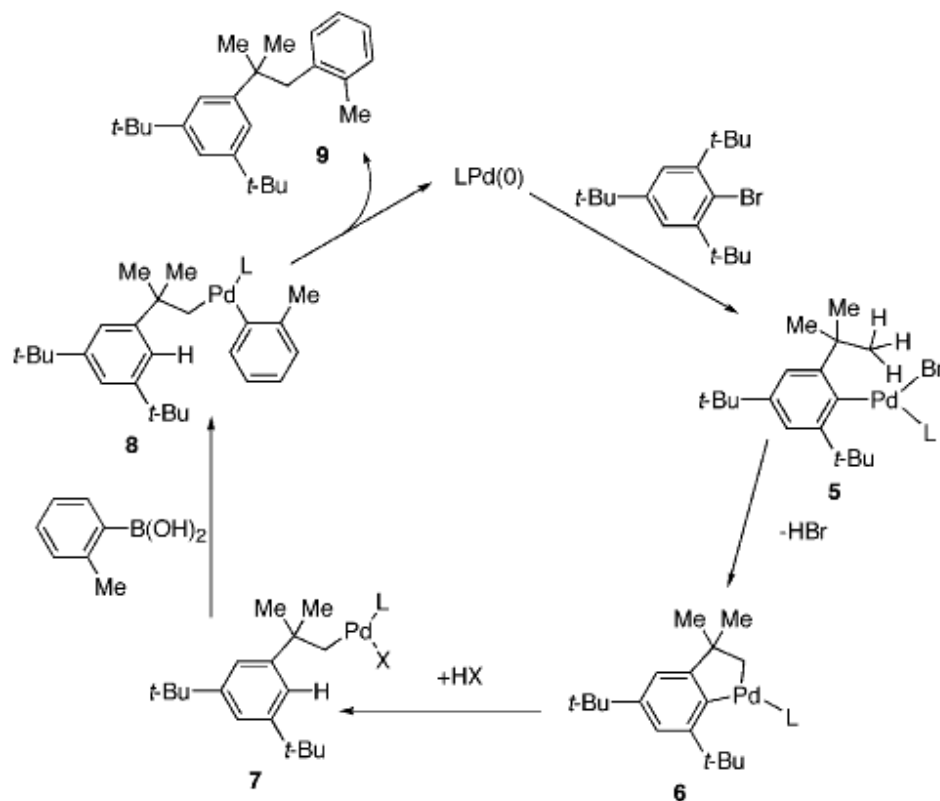


Oxidative addition/metalation-induced C(sp³)-H arylation

Oxidative addition-induced intermolecular arylation

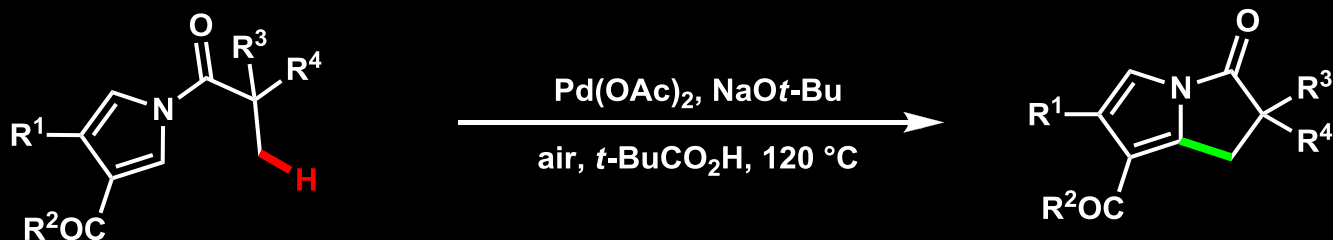


Scheme 2. Suggested Mechanism of the Tandem C–H Functionalization Suzuki–Miyaura Coupling

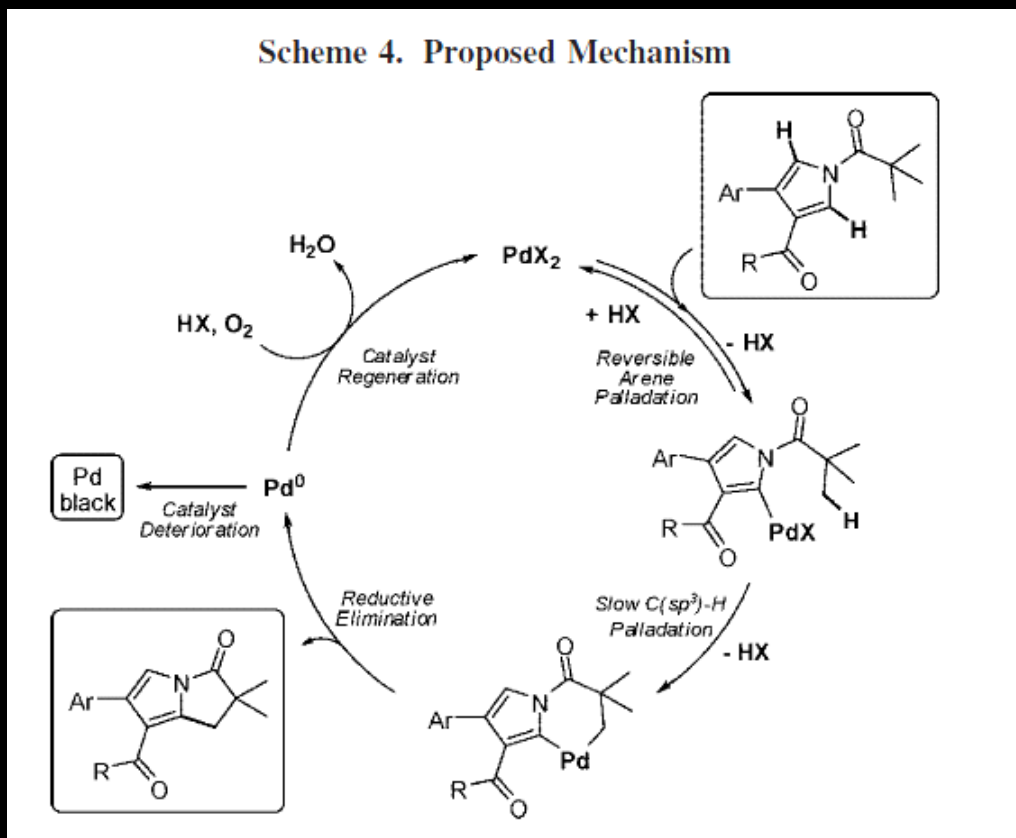


Oxidative addition/metalation-induced C(sp³)-H arylation

Metalation-induced intramolecular arylation



Scheme 4. Proposed Mechanism



Content

Part I Introduction

Part II Heteroatom-directed C-H arylation

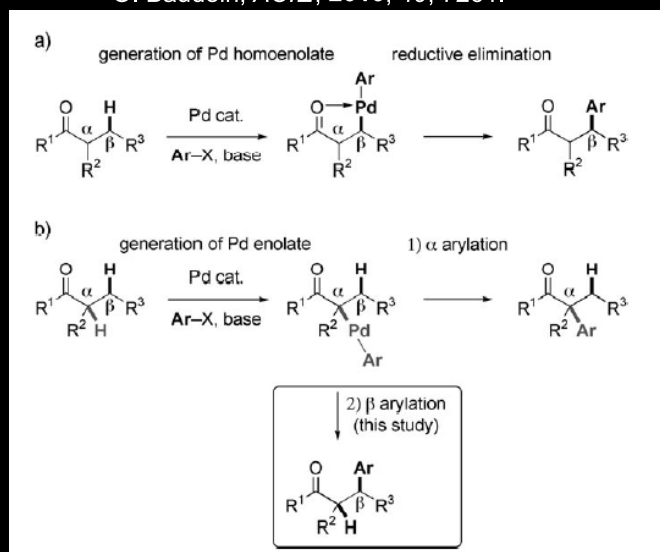
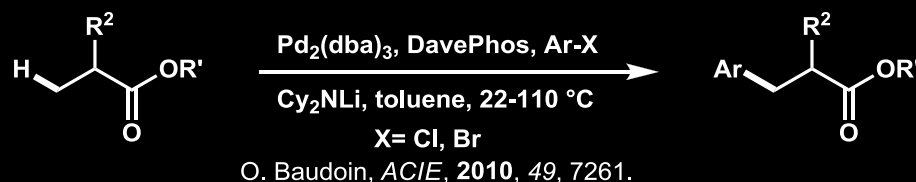
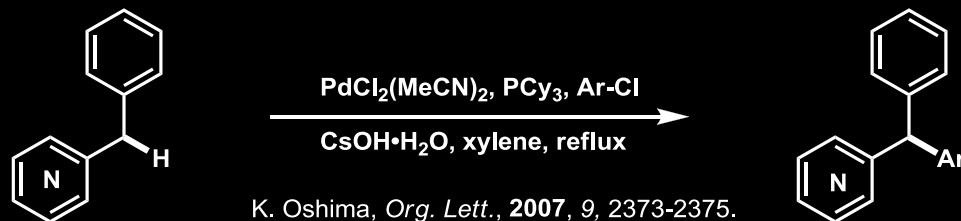
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Non-directed intermolecular C(sp³)-H arylation

Metalation-induced intramolecular arylation



Non-directed intermolecular C(sp³)-H arylation

Metalation-induced intramolecular arylation

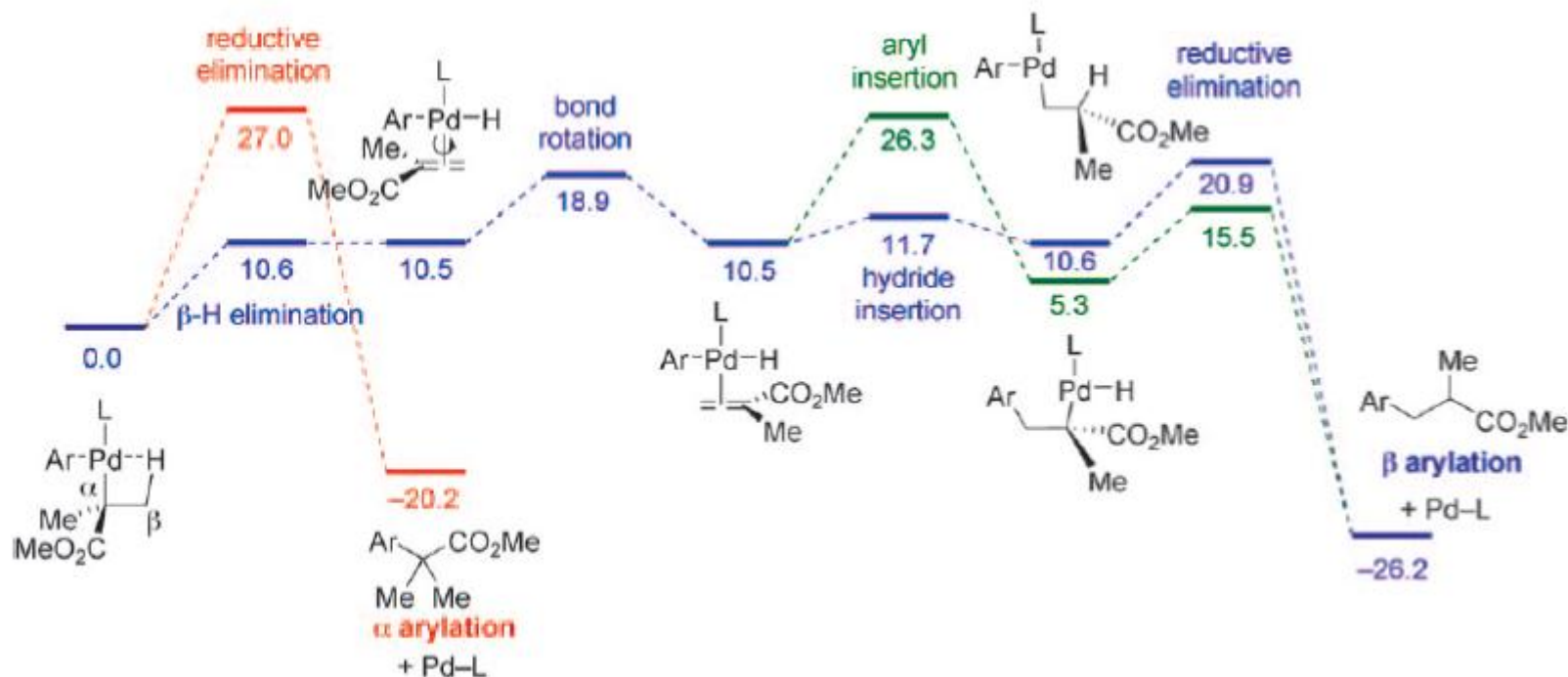


Figure 1. Gibbs free energy (kcal mol⁻¹) diagram for the α - and β -arylation pathways (L = PCy₃, Ar = 2-fluorophenyl).

Summary



Two element for the C-H activation: 1) direct group
2) acidic of C-H bond



Sophicated Substrate Design



Quick Access to Useful Scaffold



Asymmetric version C-H direction

Thank You for Your Attention