

Palladium/Norbornene Cooperative Catalysis

Fenggang Sun

14.04.2022

Outline

1. Introduction

2. Pd(0)-Initiated Catalytic Reactions

3. Pd(II)-Initiated Catalytic Reactions

4. Summary

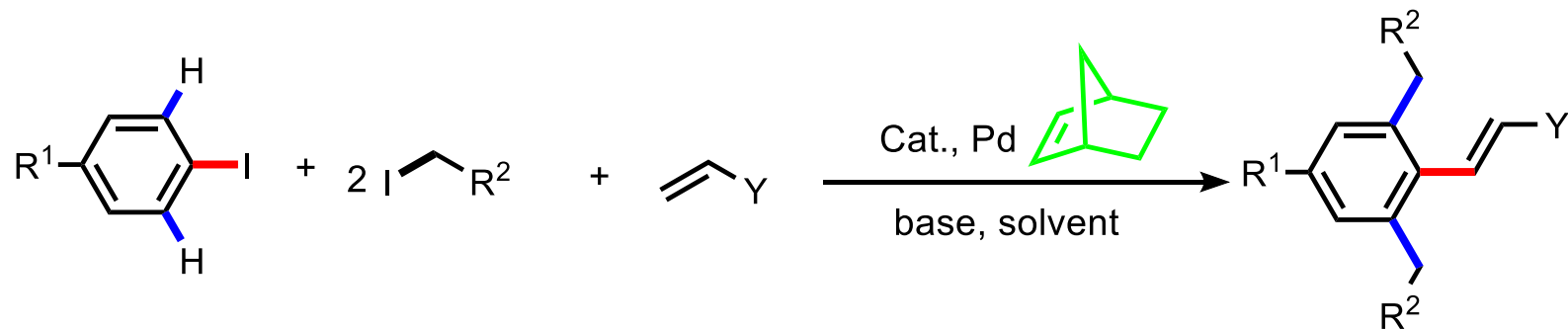
Introduction



Marta Catellani

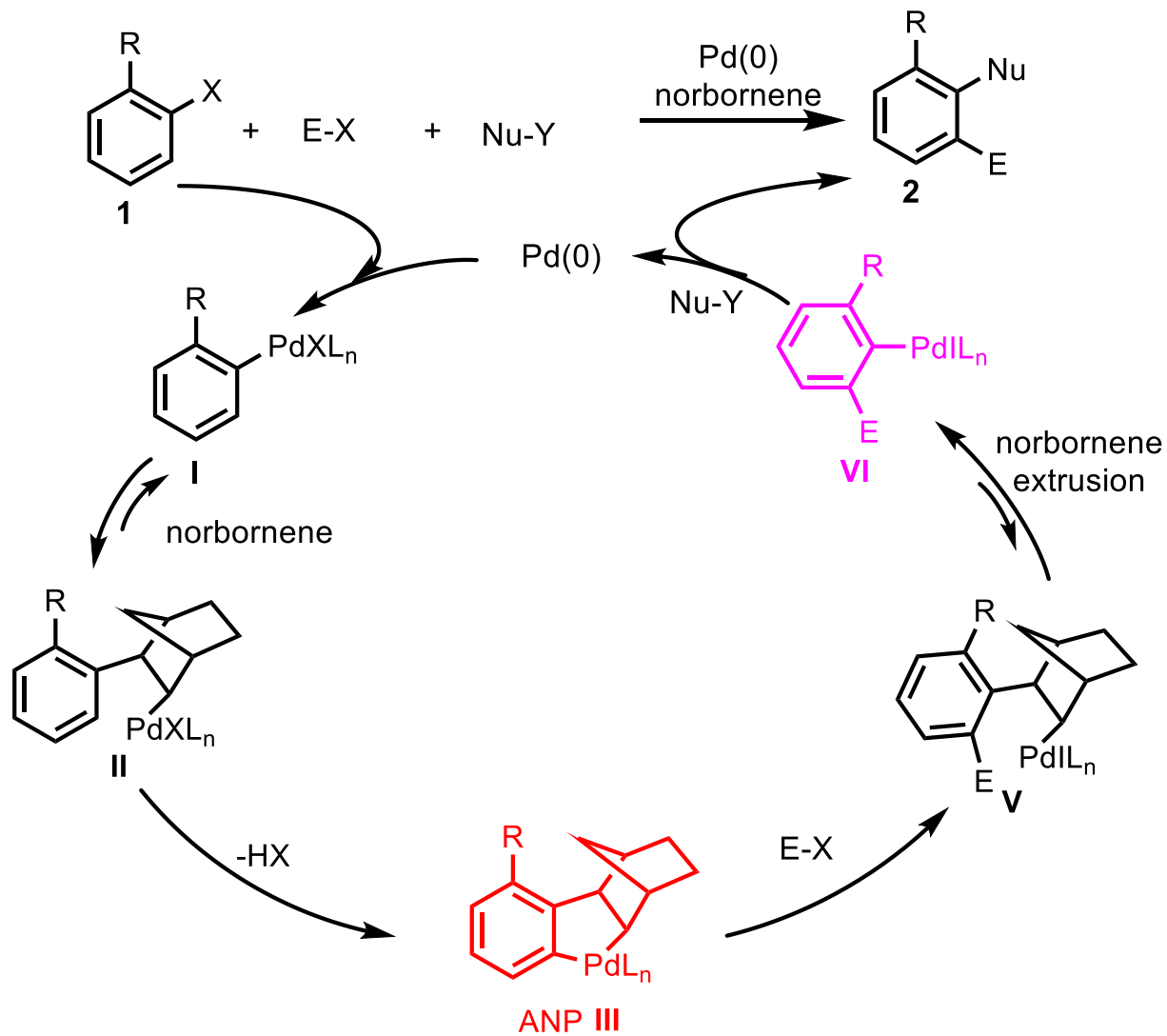
Ph.D. in chemistry from the University of Parma
postdoctoral education at the University of Chicago
Professor, University of Parma, Italy

Catellani reaction



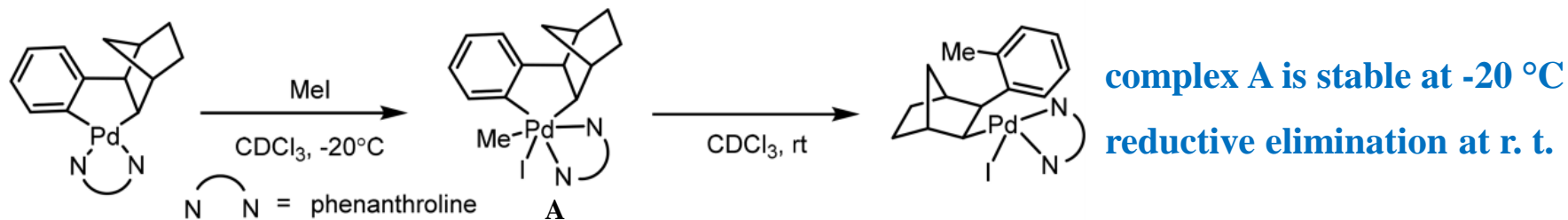
Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem. Int. Ed.* **1997**, 36, 119.

Proposed Mechanism:



Proposed Mechanism

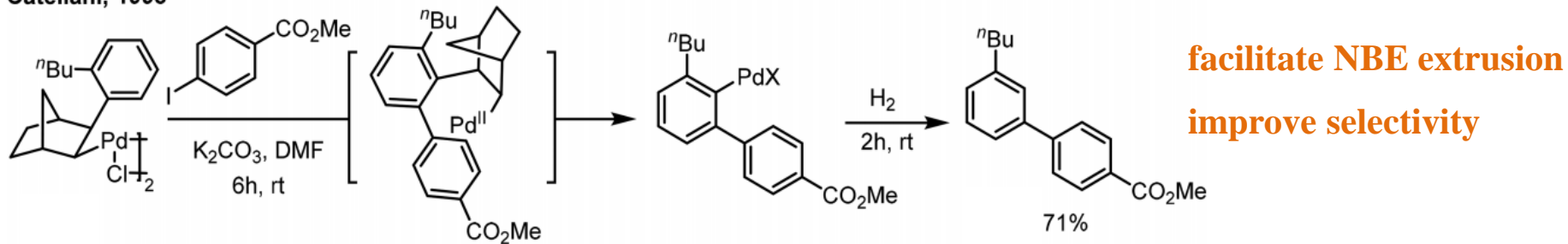
Catellani, 1988



J. Organomet. Chem. **1988**, 346, C27-C30.

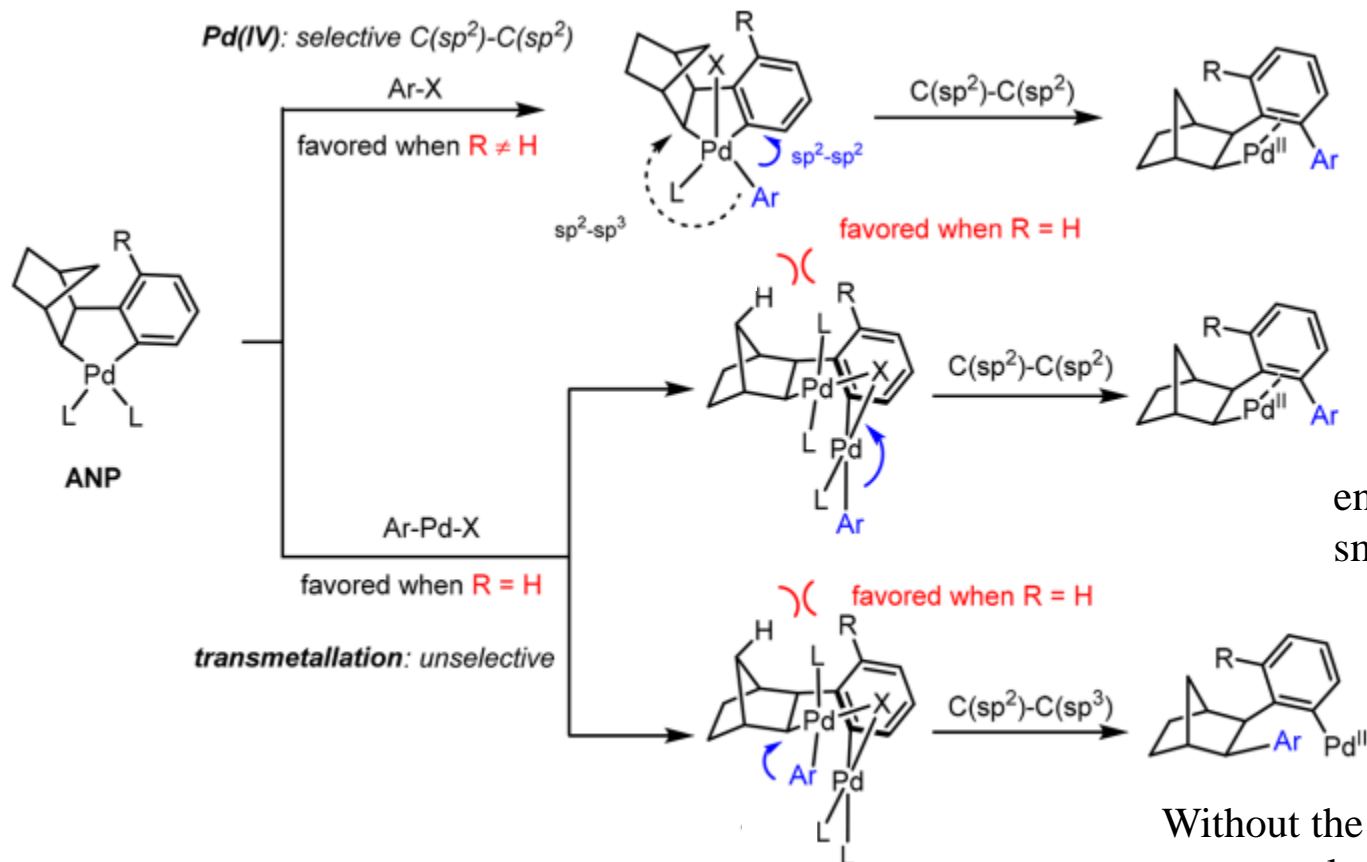
Ortho Effect

Catellani, 1998



New J. Chem. **1998**, 22, 759-761.

Origin of the Ortho Effect



J. Am. Chem. Soc. **2011**, *133*, 8574-8585.

the Pd(IV) pathway becomes the preferred pathway when an ortho substituent is present in the aryl moiety of ANP by 1-7 kcal/mol.

energy difference is small (1.5-2.0 kcal/mol)

Without the ortho substituent, the transmetalation pathway is favored over the Pd(IV) pathway by 8-10 kcal/mol for different substrates

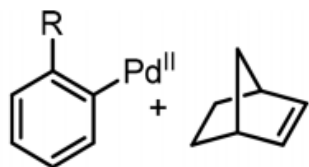
NBE Extrusion



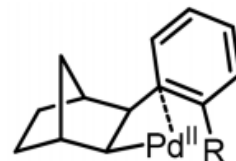
strain energy = 21.6 kcal/mol



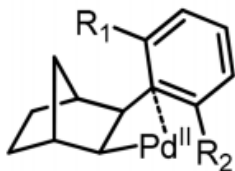
strain energy = 32.4 kcal/mol



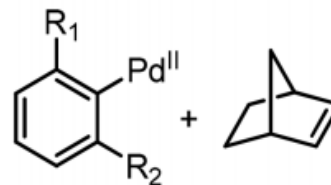
favor insertion



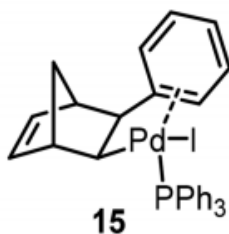
ligands and additives could also have an influence on the equilibrium



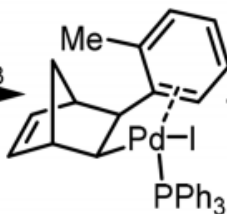
favor de-insertion



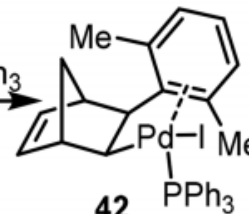
Cheng, 1994



1. NaOH, PPh₃
2. MeI



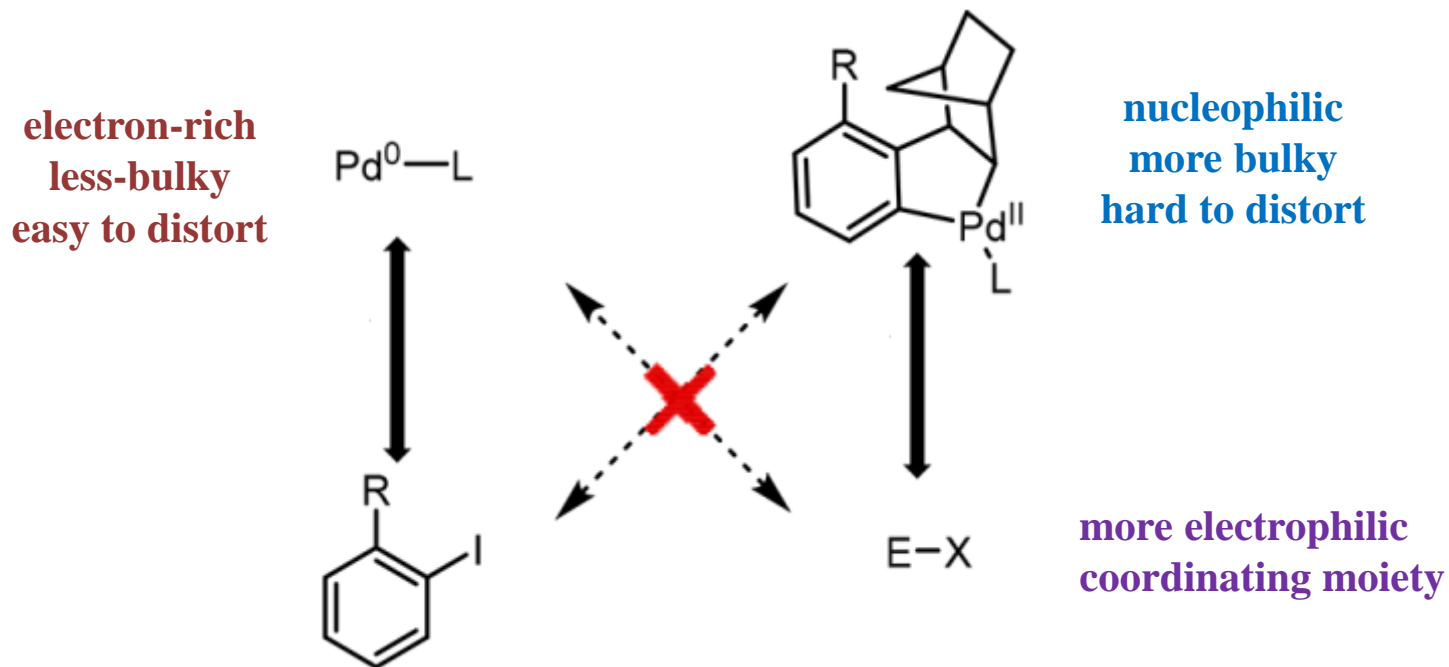
1. NaOH, PPh₃
2. MeI



**migratory insertion
less reversible!**

Organometallics **1994**, 13, 18-20.

Selectivity Issue for Oxidative Addition of Pd(0) versus ANP



- electrophile selectively oxidizes the ANP intermediate than the Pd(0) catalyst
- aryl halide substrate selectively reacts with the Pd(0) instead of ANP

Outline

1. Introduction

2. Pd(0)-Initiated Catalytic Reactions

3. Pd(II)-Initiated Catalytic Reactions

4. Summary

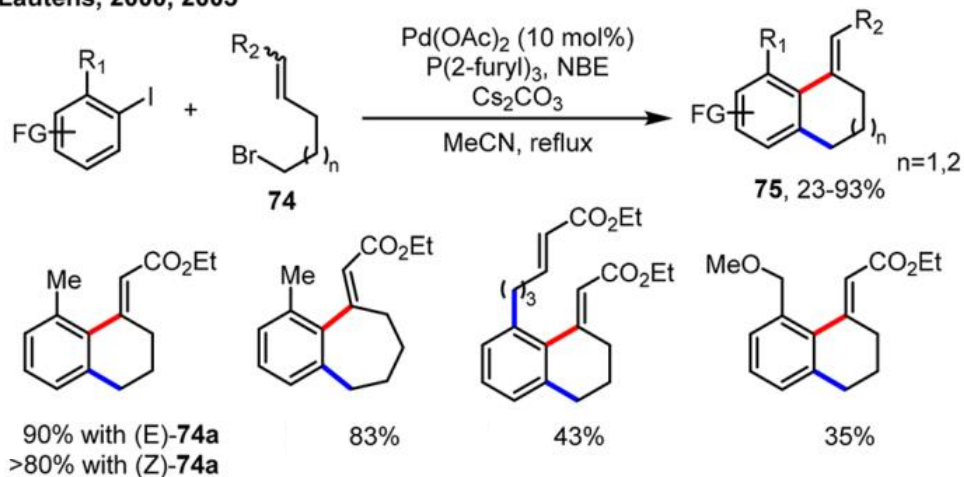
Pd(0)-Initiated Catalytic Reactions

***ipso* functionalizations** : Heck, Suzuki, Sonogashira, C–N coupling, C–H activation, carbene coupling, borylation...

***ortho* functionalizations** {
alkylation/arylation
amination
acylation/alkoxycarbonylation
thiolation

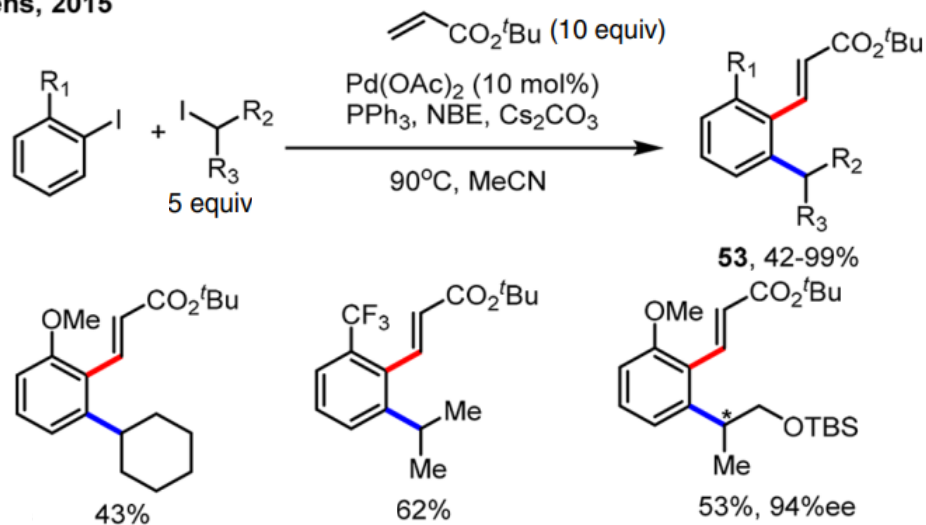
ortho-alkylation of Aryl Iodides

Lautens, 2000, 2005



Angew. Chem., Int. Ed. **2000**, *39*, 1045-1046.

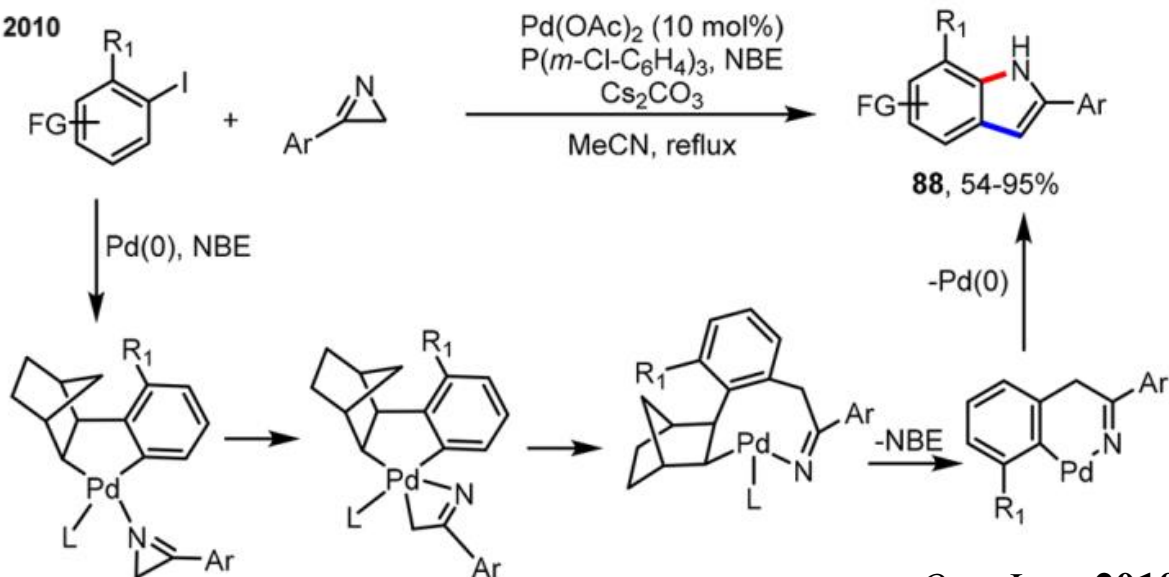
Lautens, 2015



Synthesis **2015**, *47*, 2446-2456.

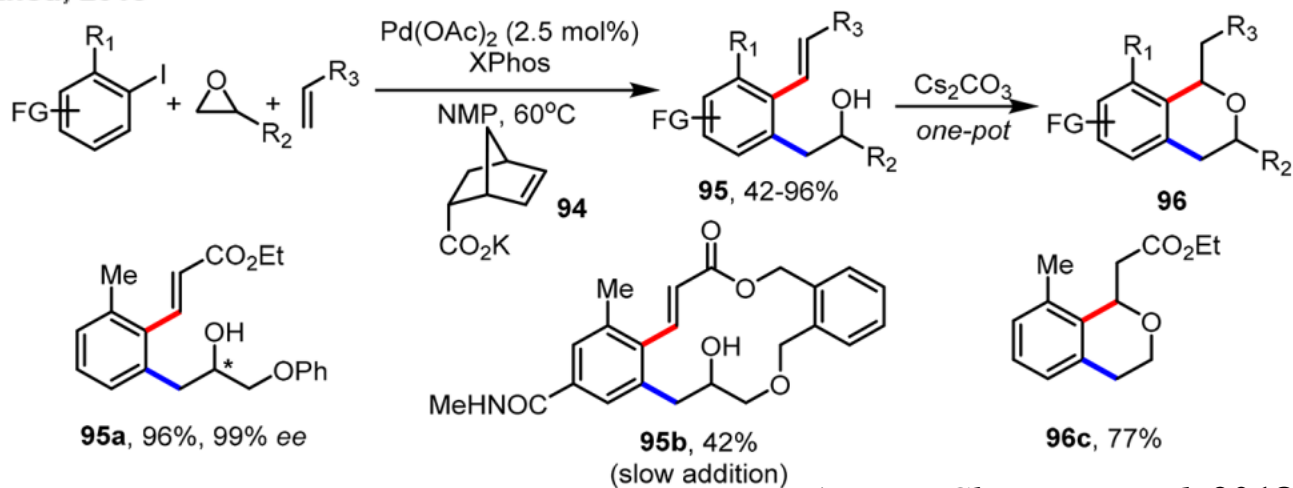
ortho-alkylation of Aryl Iodides

Lautens, 2010



Org. Lett. **2010**, *12*, 3312-3315.

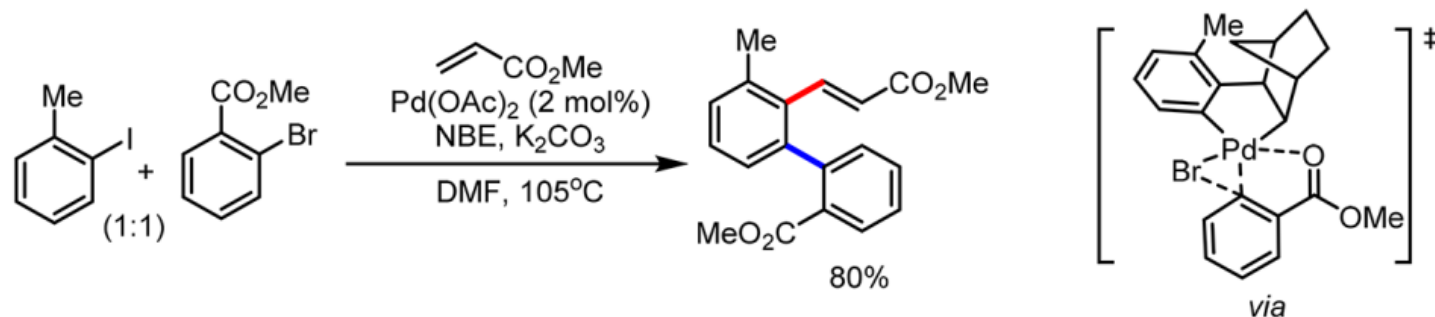
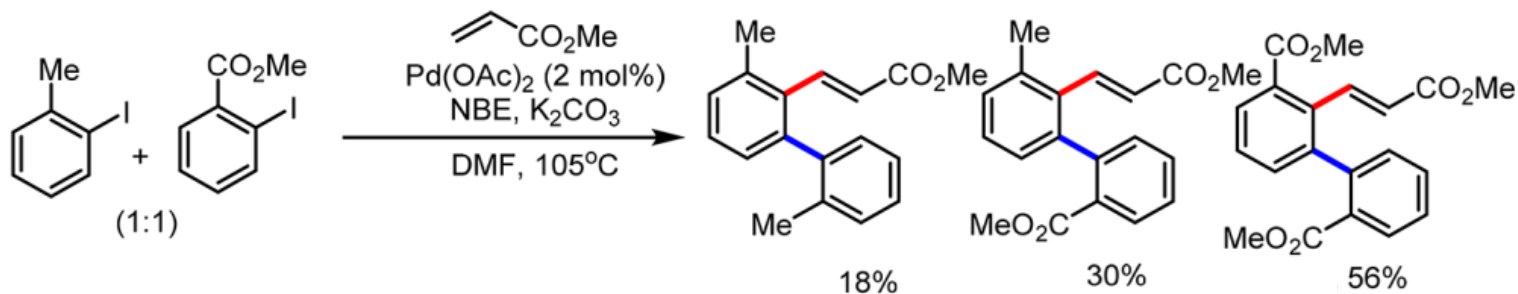
Zhou, 2018



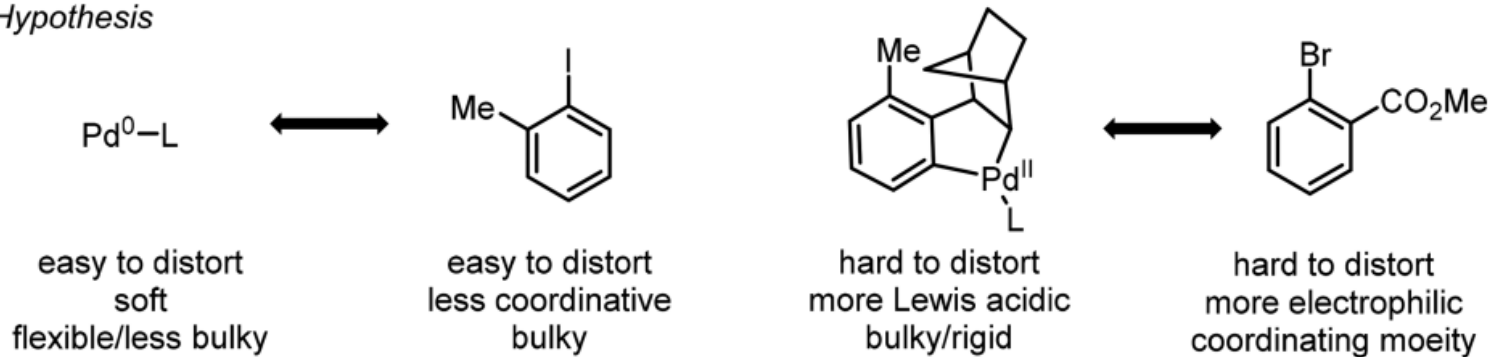
Angew. Chem., Int. Ed. **2018**, *57*, 3444-3448.

ortho-Arylation of Aryl Iodides

Catellani, 2004



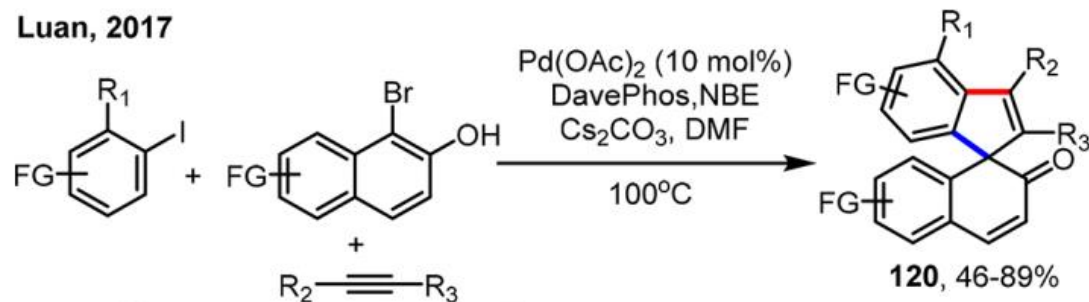
Hypothesis



J. Am. Chem. Soc. **2004**, *126*, 78-79.

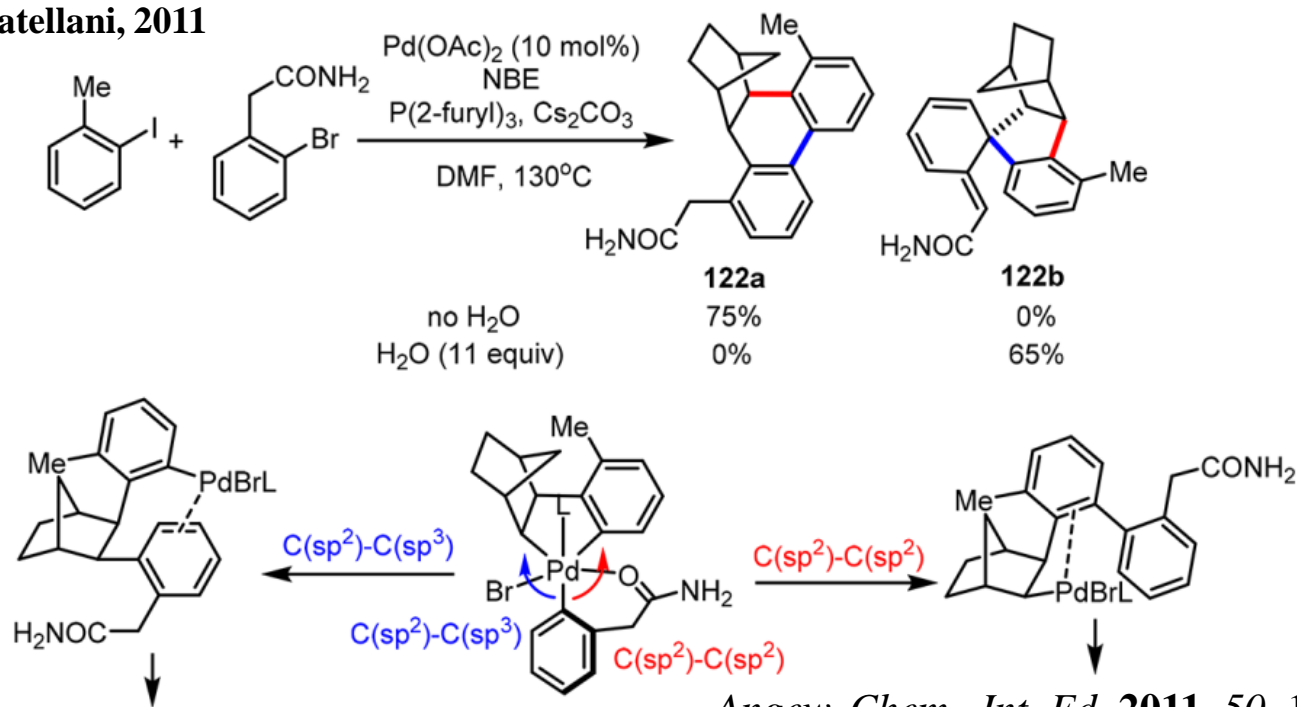
ortho-Arylation of Aryl Iodides

Luan, 2017



Angew. Chem., Int. Ed. **2017**, *56*, 2767-2771.

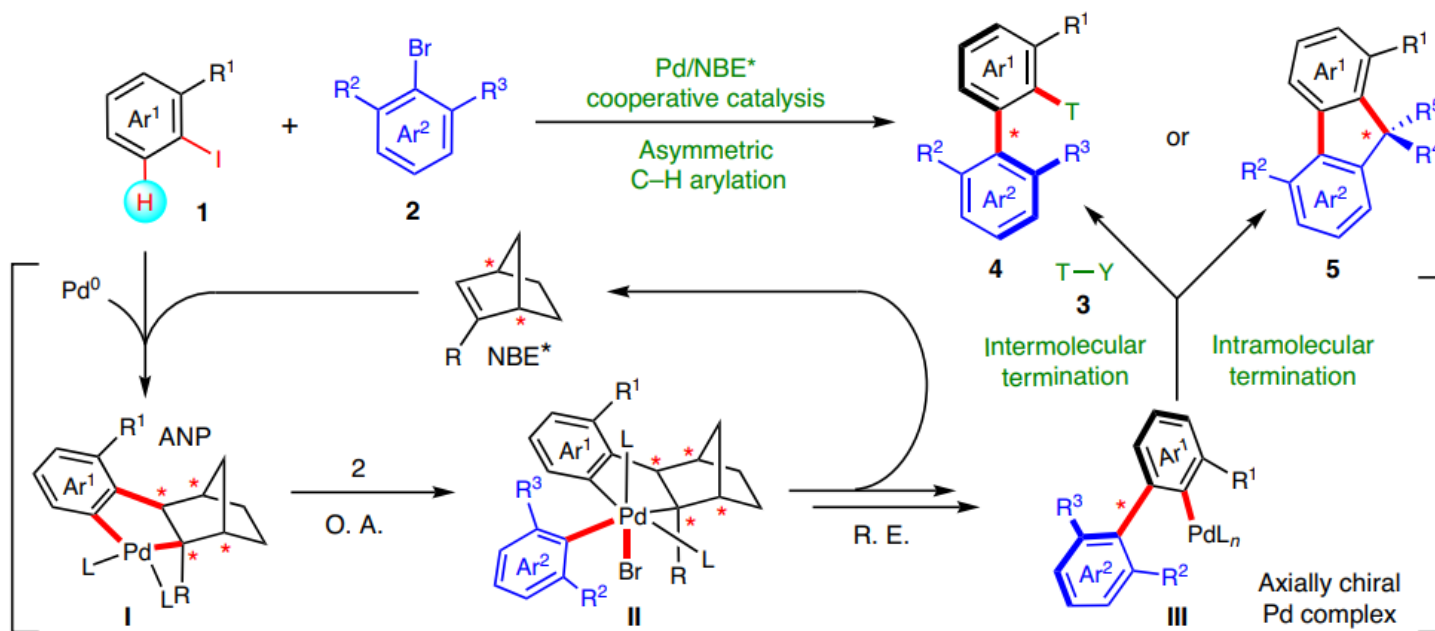
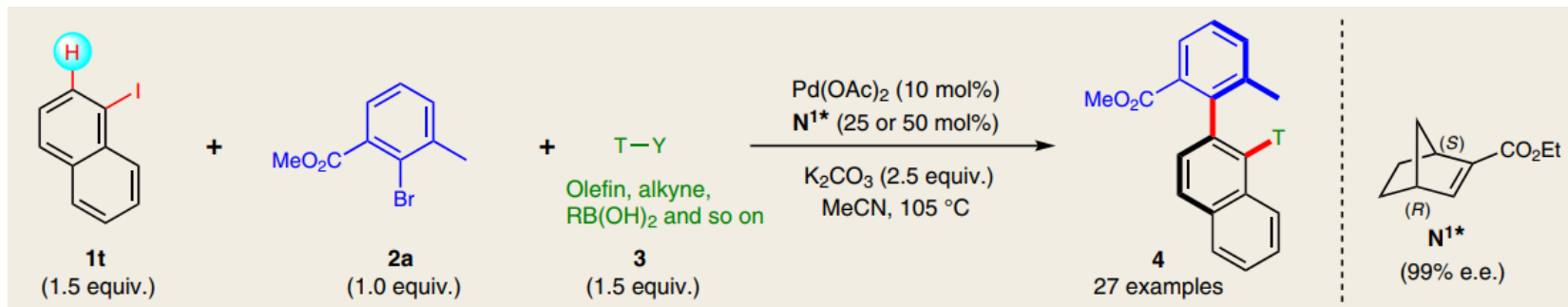
Catellani, 2011



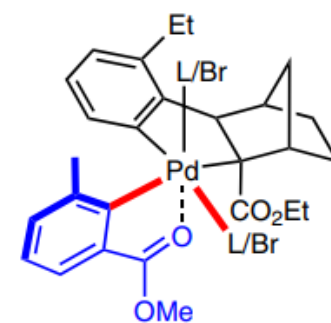
Angew. Chem., Int. Ed. **2011**, *50*, 12253-12256.

ortho-arylation of Aryl Iodides

Zhou, 2020



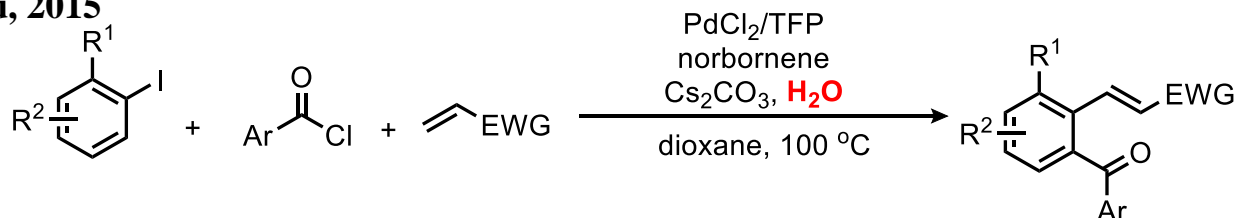
stereinduction models



Nat. Catal. **2020**, *3*, 727-733.

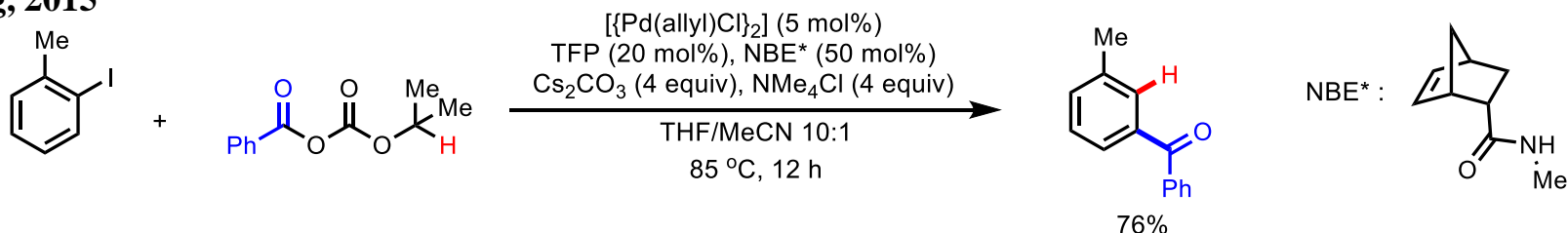
ortho-acylation/alkoxycarbonylation of Aryl Iodides

Gu, 2015



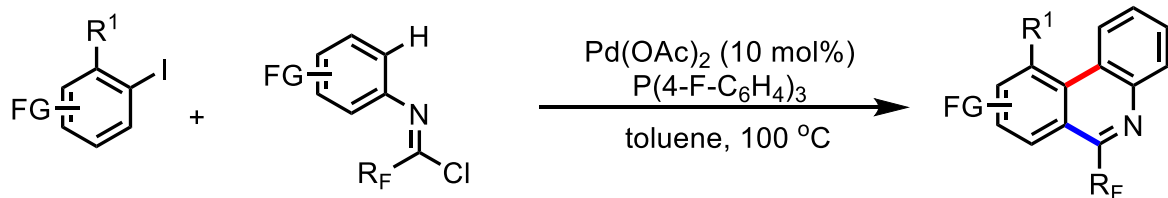
Angew. Chem., Int. Ed. **2015**, *54*, 12669-12672.

Dong, 2015



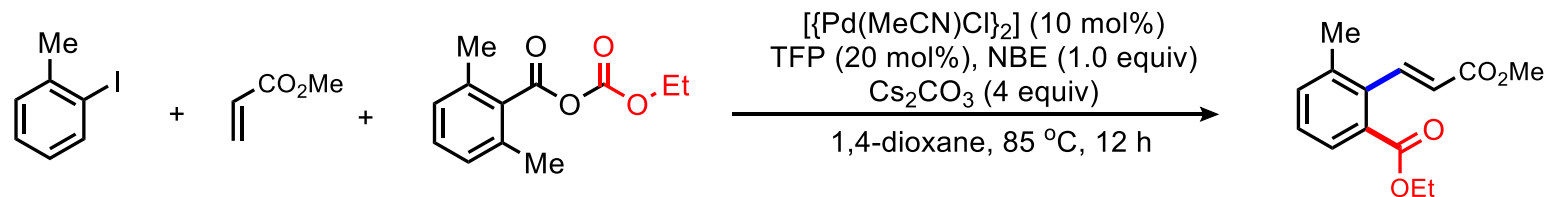
Angew. Chem., Int. Ed. **2015**, *54*, 12664-12668.

Zhu, 2018



Org. Lett. **2018**, *20*, 6640-6645.

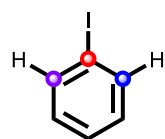
Dong, 2015



Chem **2016**, *1*, 581-591.

ortho-acylation/alkoxycarbonylation of Aryl Iodides

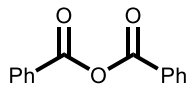
Luan, 2020



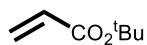
(1.0 equiv)



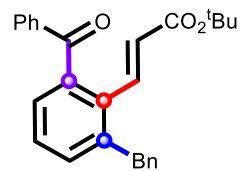
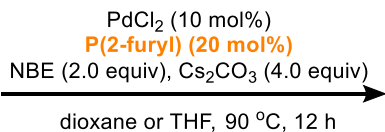
(1.5 equiv)



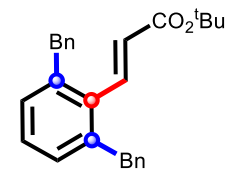
(1.5 equiv)



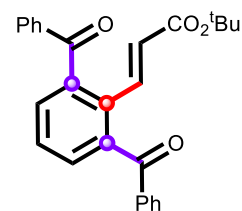
(1.2 equiv)



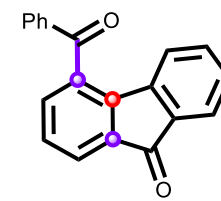
62%



10%

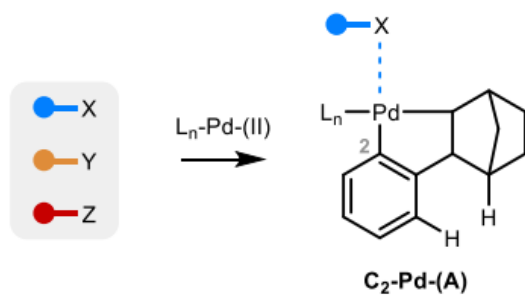


5%

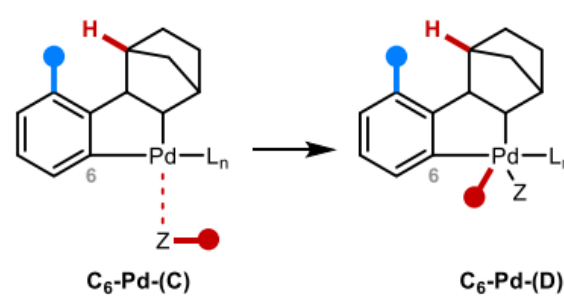
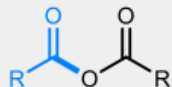


16%

Mechanistic Framework



X = most Lewis basic partner
large geometric distortion for OA



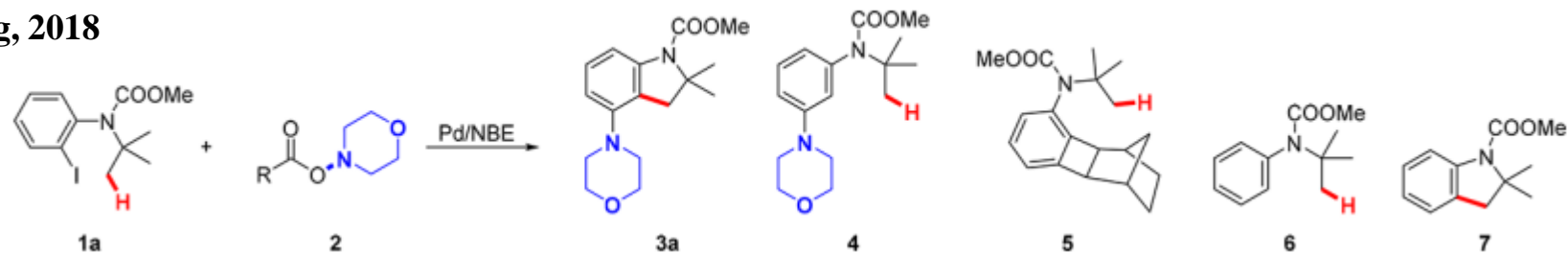
Z = association less important
small geometric distortion for OA

alkyl-Br

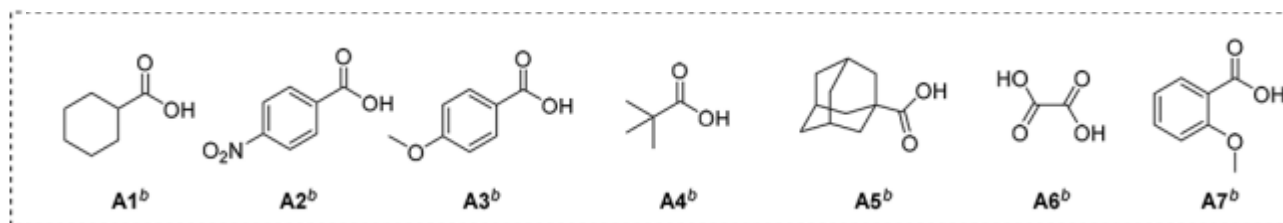
Chem 2020, 6, 2097–2109.

ortho-Amination of Aryl Iodides

Liang, 2018



catalyst	amination reagent	carboxylic acid ^b	GC yield of 6 , 7 , 5 , 4 , 3a					yield ^c (3a)
			6	7	5	4	3a	
Pd(OAc) ₂ /PPh ₃	2a	A1	8	0	16	41	17	15
Pd(OAc) ₂ /PPh ₃	2a	A2	5	0	2	39	30	28
Pd(OAc) ₂ /PPh ₃	2a	A3	8	0	18	46	16	14
Pd(OAc)₂/PPh₃	2a	A4	2	1	3	9	80	74
Pd(OAc) ₂ /PPh ₃	2a	A5	5	0	3	34	26	23
Pd(OAc) ₂ /PPh ₃	2a	A6	4	0	3	39	28	25
Pd(OAc) ₂ /PPh ₃	2a	A7	8	0	20	50	11	9
Pd(OAc) ₂ /PCy ₃	2a	A4	18	43	4	2	32	26
Pd(OAc) ₂ /P ^t Bu ₃ -HBF ₄	2a	A4	4	0	25	33	4	<5

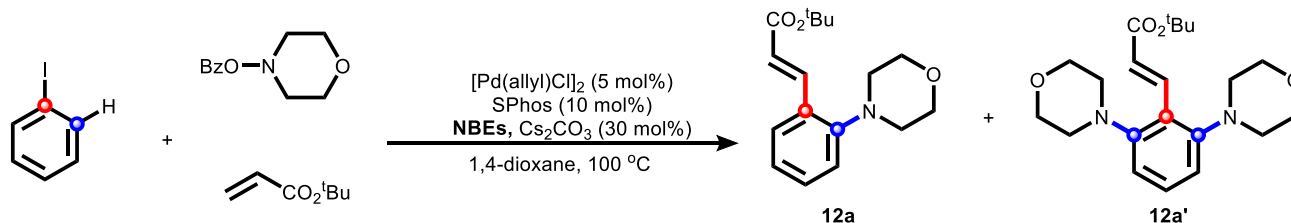


concerted metalation deprotonation (CMD) process

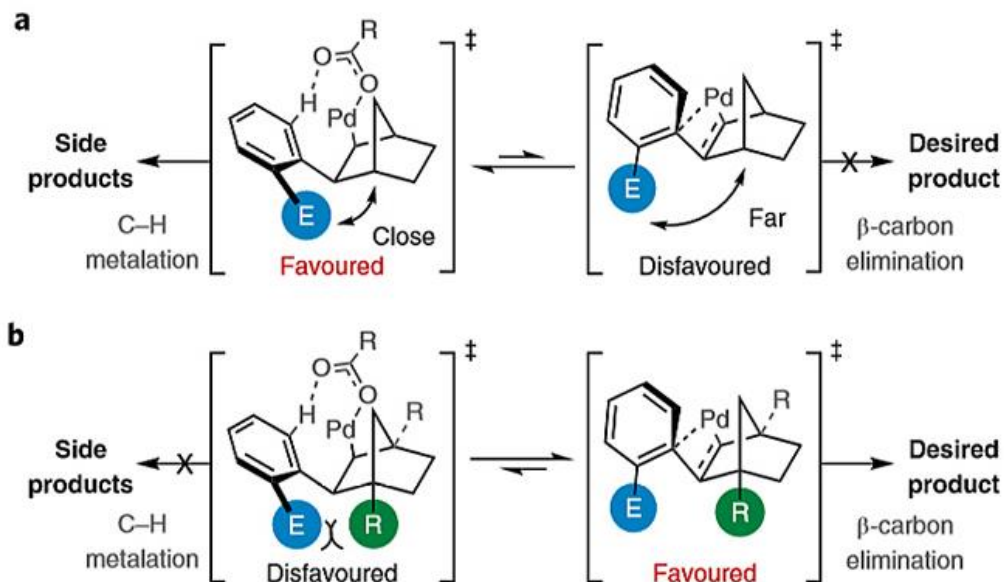
ACS Catal. **2018**, *8*, 11827–11833.

Mono **ortho**-Amination with **ortho** Unsubstituted Aryl Iodides

Dong, 2018



proposed pathways

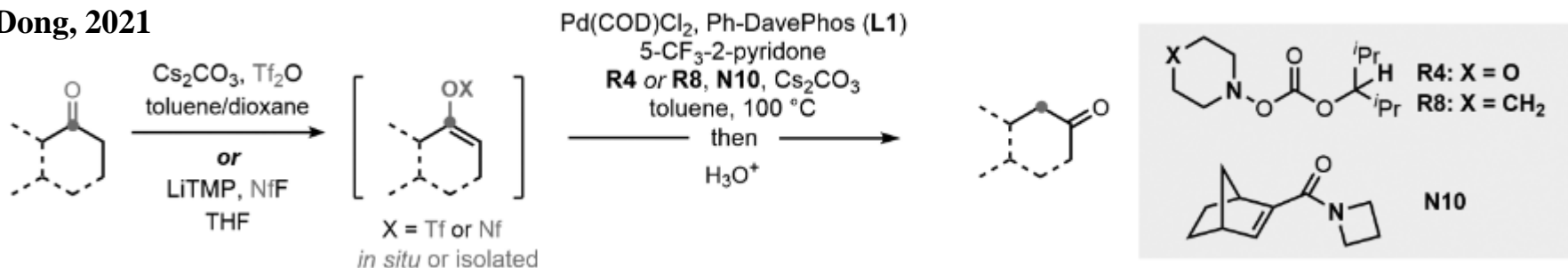


N1	N3	N4
12a, ND	12a, 2%	12a, 36%
12a', 29%	12a', 12%	12a', 6%
N8	N9	N10
12a, 55% ^a	12a, ND	12a, ND
12a', 2%	12a', 30%	12a', 13%
(mono:di > 20:1)		

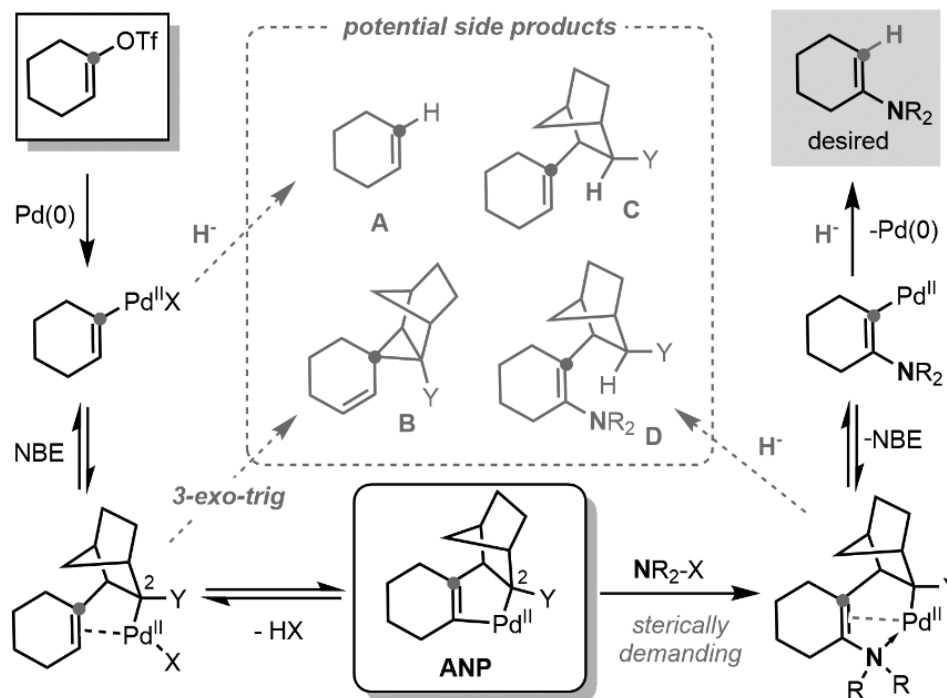
Nat. Chem. 2018, 10, 866-872.

Triflate-mediated α -Amination Promoted Carbonyl 1,2-Transposition

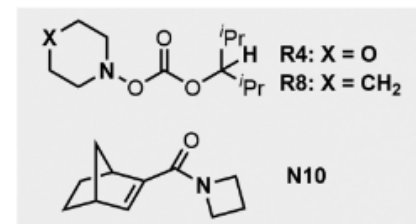
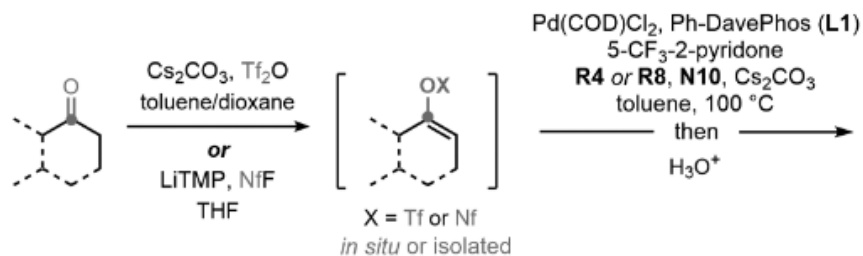
Dong, 2021



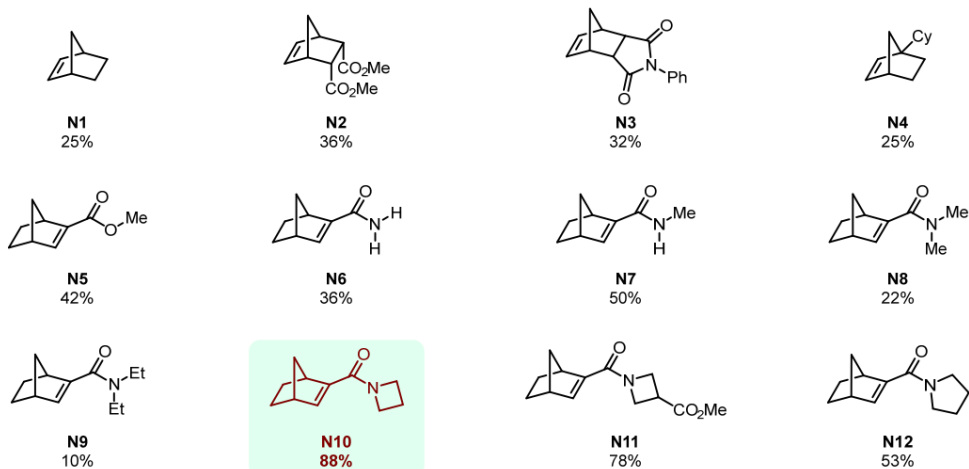
proposed mechanism



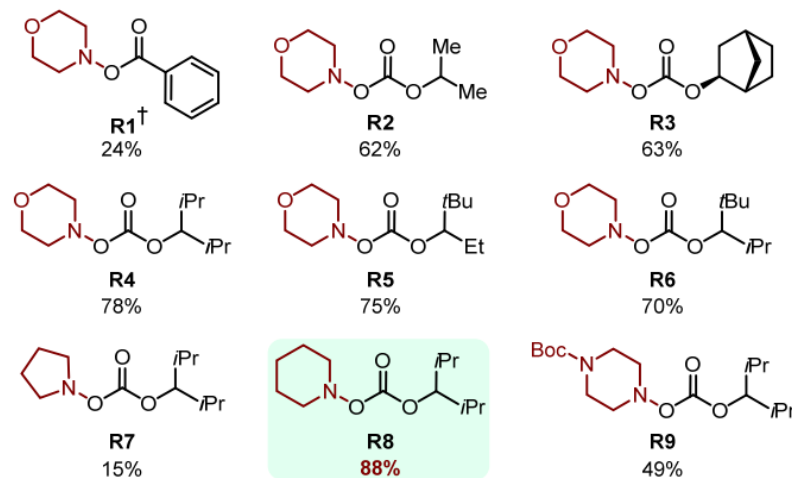
Science **2021**, *374*, 734–740.



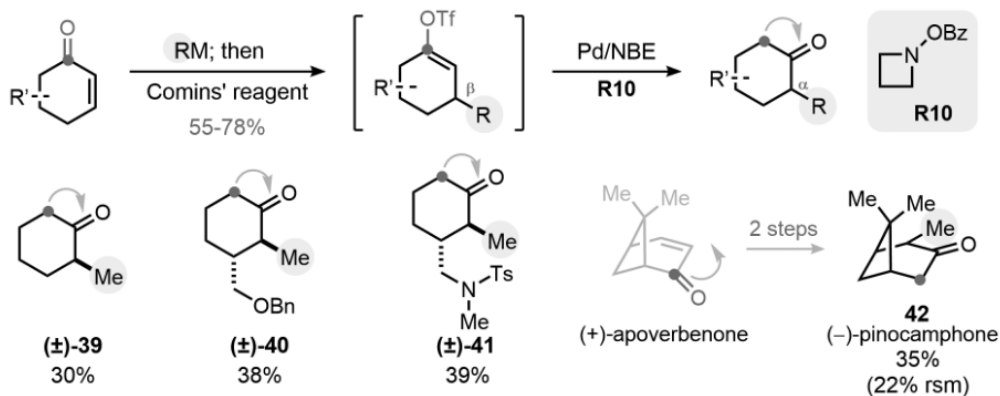
NBE effect



bifunctional reagents

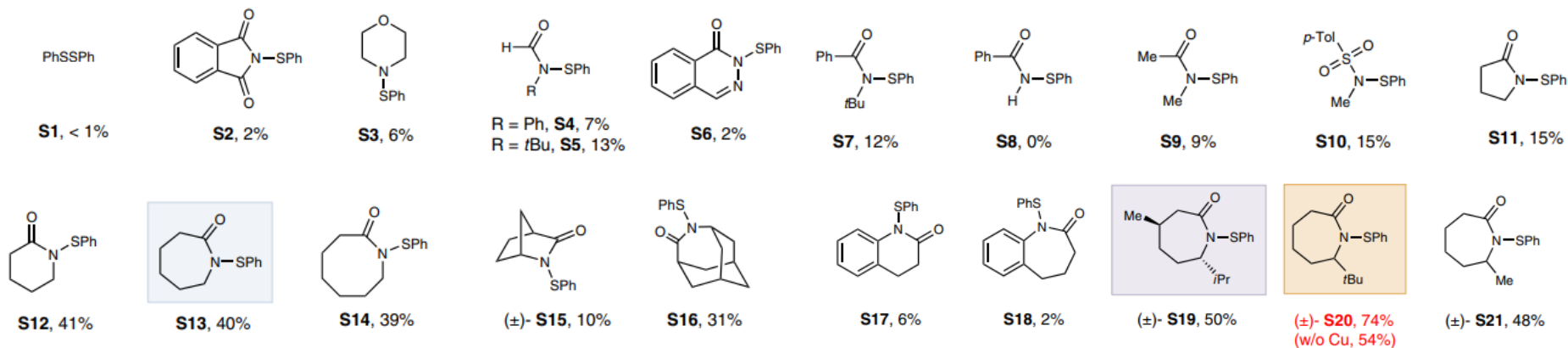
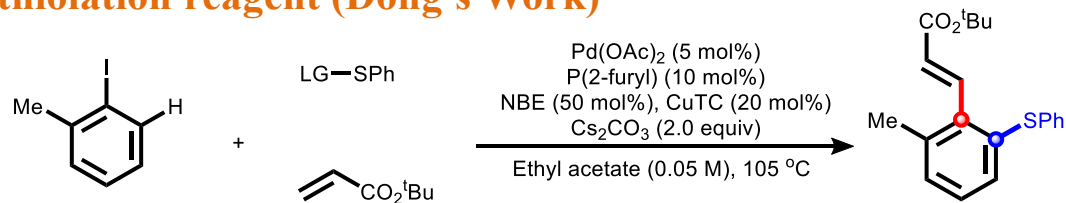


“β-to-α”migration



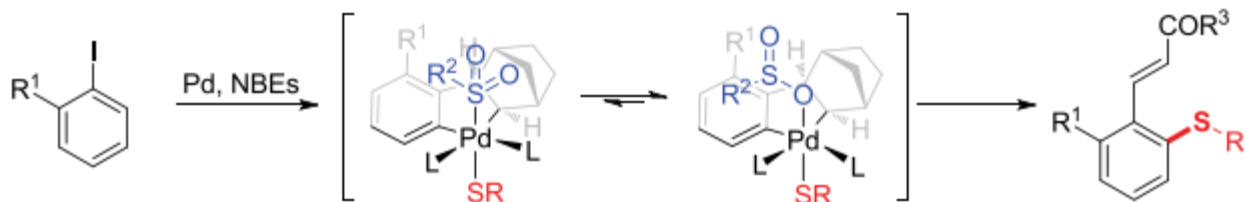
ortho-Thiolation of Aryl Iodides

A. Sulfenamide as thiolation reagent (Dong's Work)



Nat. Comm. **2019**, *10*, 3555.

B. Thiosulfonate as thiolation reagent (Gu's Work)



Org. Lett. **2019**, *21*, 3204–3209.

Outline

1. Introduction

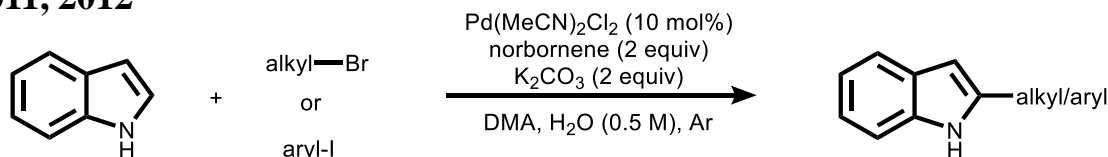
2. Pd(0)-Initiated Catalytic Reactions

3. Pd(II)-Initiated Catalytic Reactions

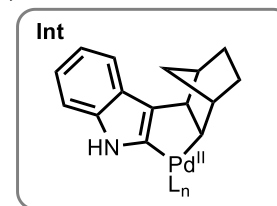
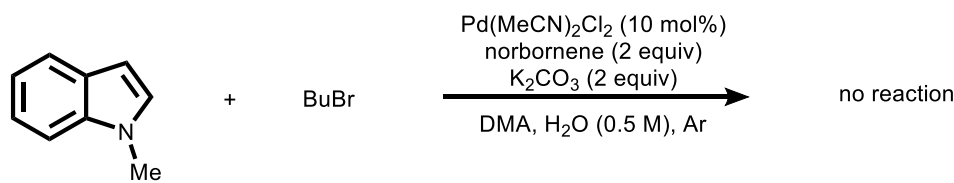
4. Summary

N-H Bond Activation-Initiated 2-Functionalization of Indoles

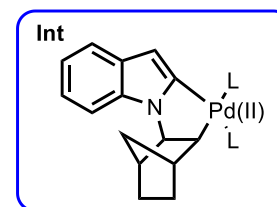
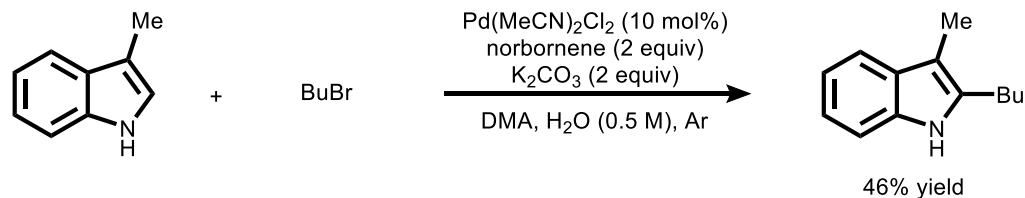
Bach, 2011, 2012



J. Am. Chem. Soc. **2011**, *133*, 12990-12993.



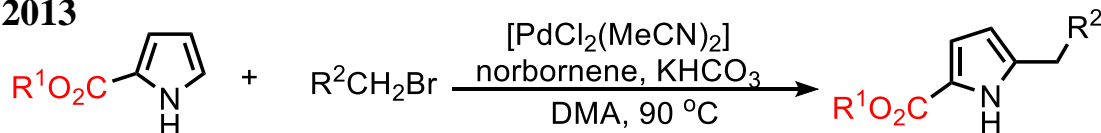
Vs



✓

J. Am. Chem. Soc. **2012**, *134*, 14563-14572.

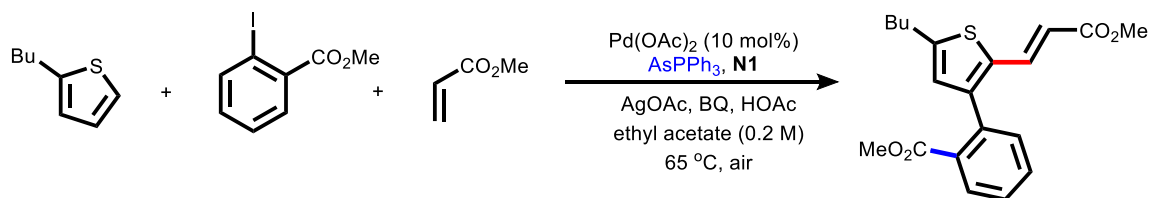
Bach, 2013



Angew. Chem., Int. Ed. **2013**, *52*, 6080-6083.

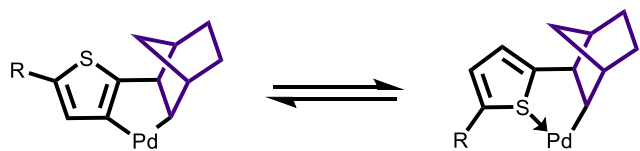
Direct Vicinal Difunctionalization of Thiophenes

Dong, 2019

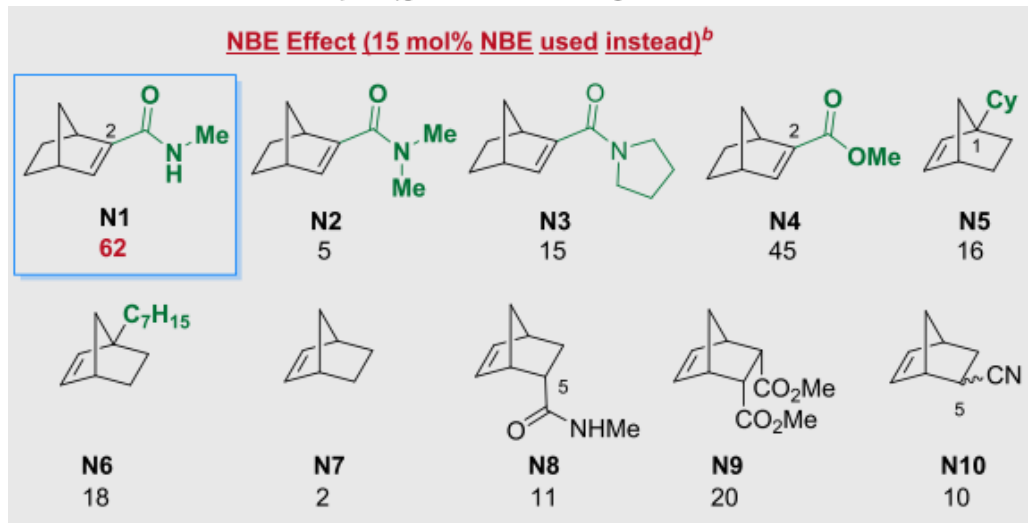


a. lack of an ortho substituent

b. coordinative ability of the sulfur



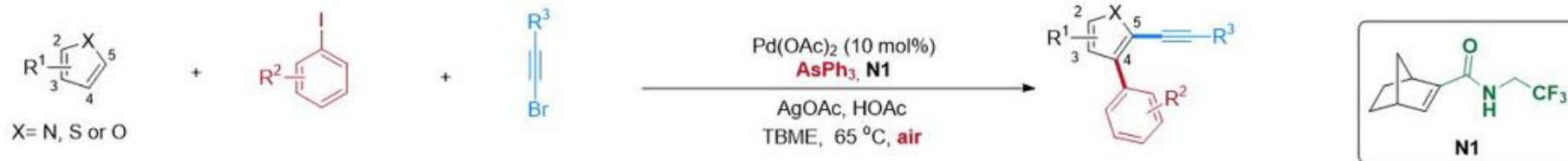
Entry	Change from the "standard condition"	yield of 4a (%) ^a
1	none	82(81)
2	w/o AsPPh ₃	2
3	PPh ₃ instead of AsPPh ₃	1
4	(PhO) ₃ P instead of AsPPh ₃	0



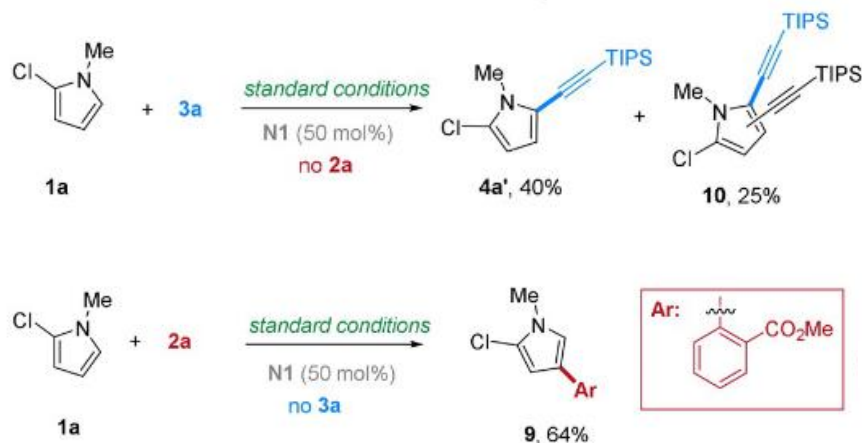
J. Am. Chem. Soc. **2019**, *141*, 18958–18963.

Vicinal Difunctionalization of Heteroarenes with **Dual Electrophiles**

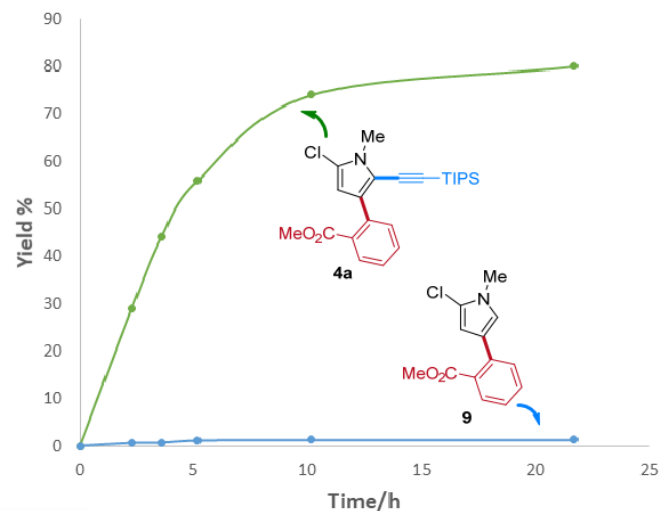
Dong, 2021



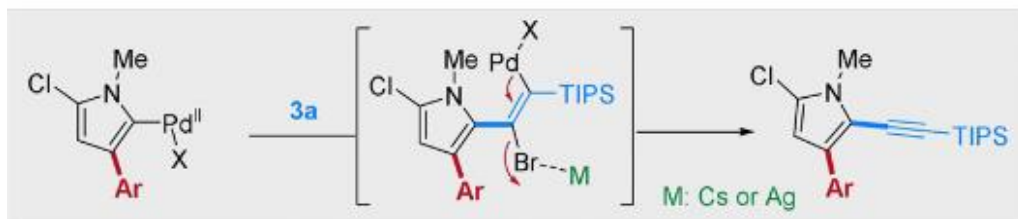
Control experiments



Kinetic profile



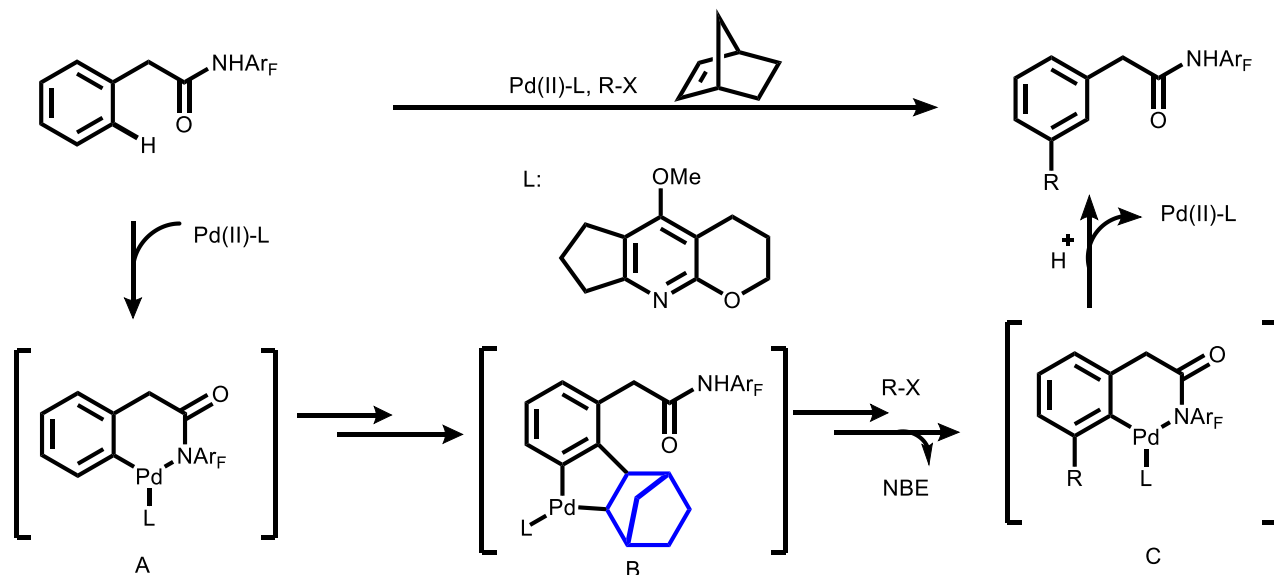
Proposed mechanism



Angew. Chem. Int. Ed. **2021**, *60*, 26184–26191.

C-H Bond Activation-Initiated **Meta** Functionalization of Arenes

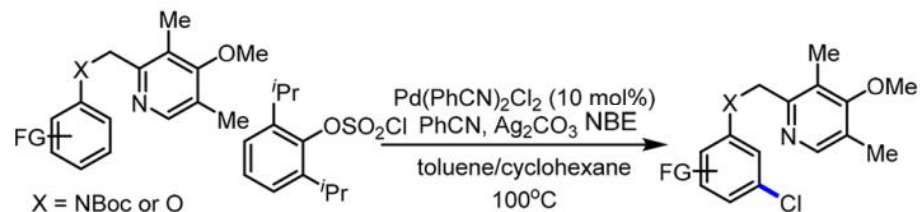
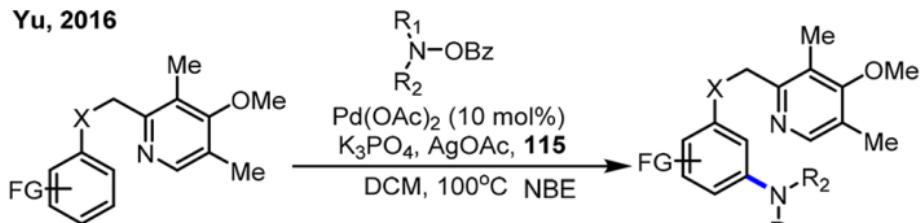
Yu, 2021



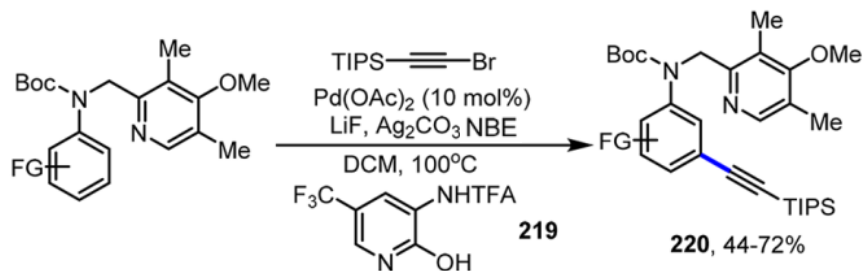
Nature **2015**, 519, 334-338.

Meta-Amination/Alkynylation and Chlorination

Yu, 2016



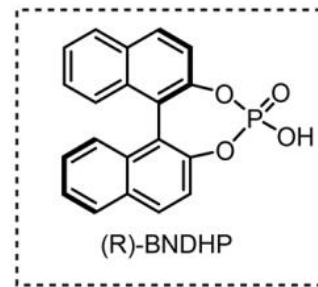
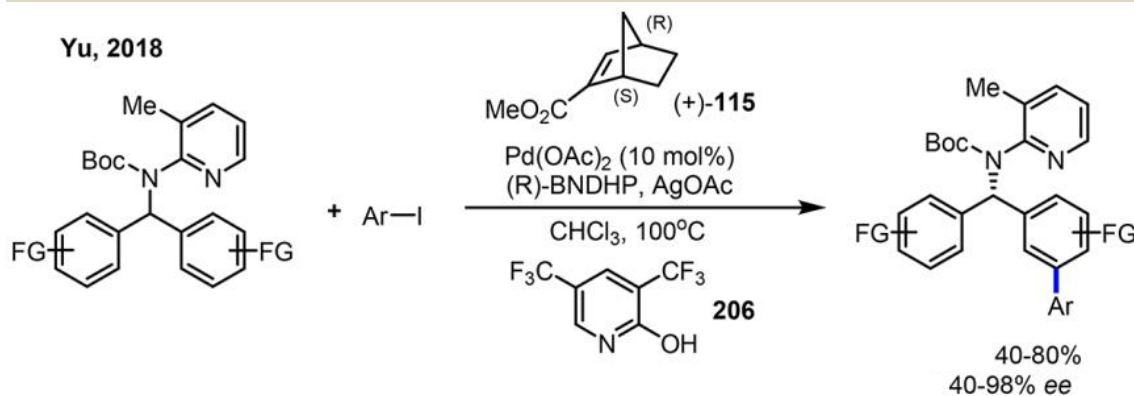
J. Am. Chem. Soc. **2016**, *138*, 14876-14879.



J. Am. Chem. Soc. **2016**, *138*, 14092-14099.

Enantioselective Remote Meta C-H Functionalization

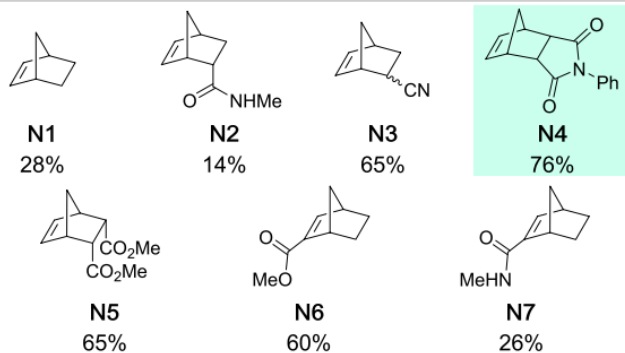
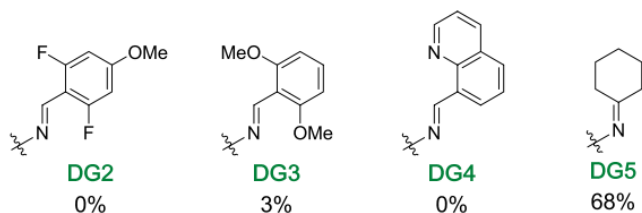
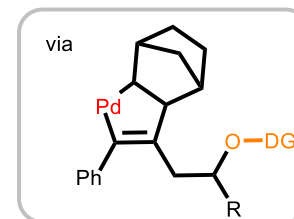
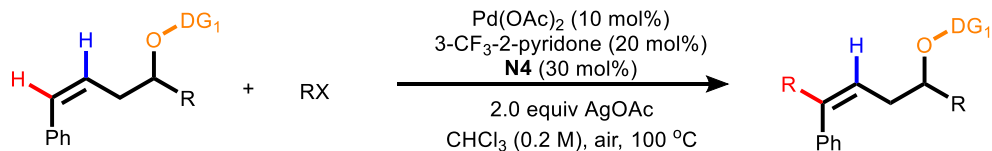
Yu, 2018



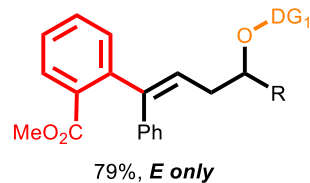
Nature **2018**, *558*, 581-586.

Distal Alkenyl C–H Functionalization

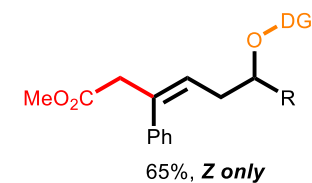
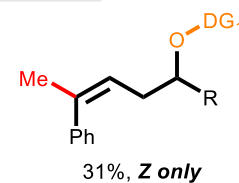
Dong, 2020



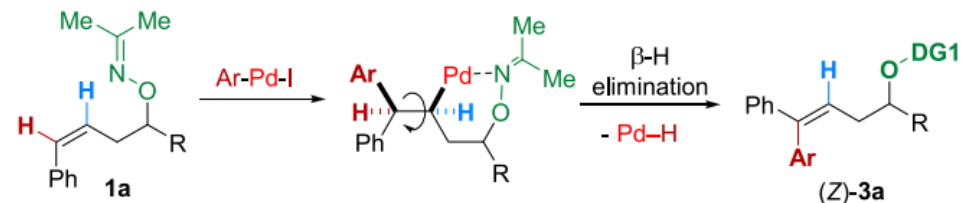
arylation



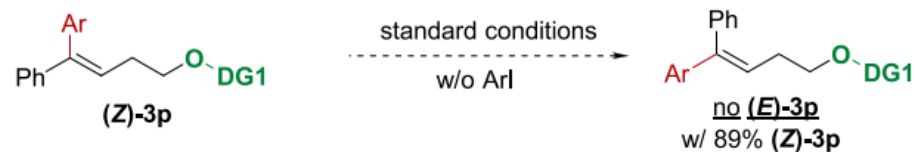
alkylation



a) Heck pathway:



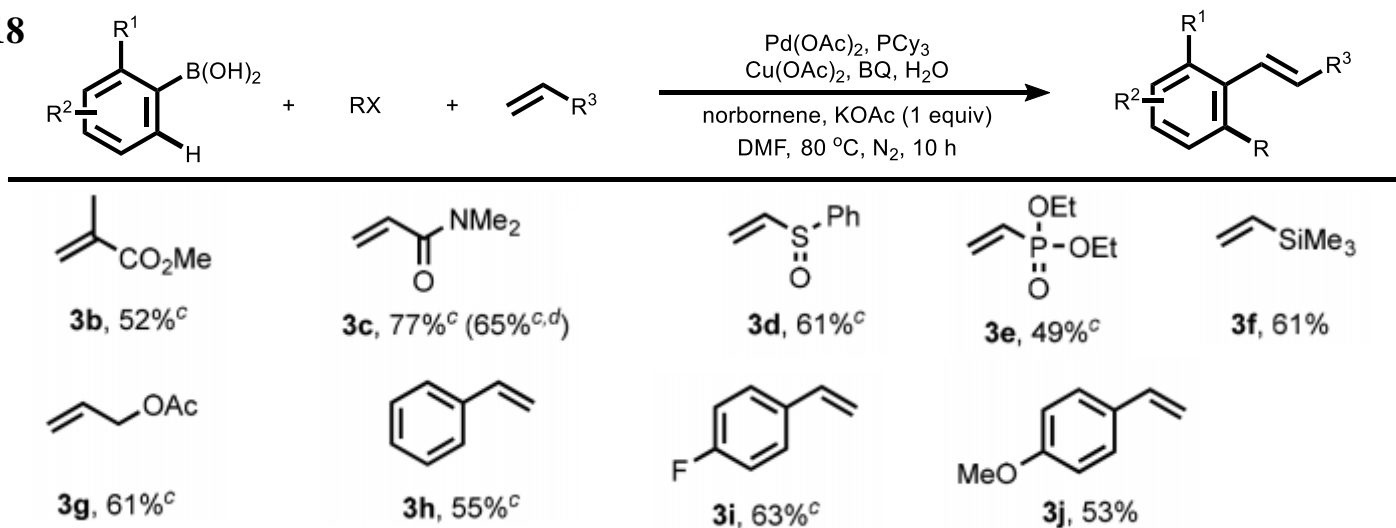
b) control experiments



J. Am. Chem. Soc. 2020, 142, 2715–2720

Transmetalation-Initiated Ortho Functionalization of Arylboron Species.

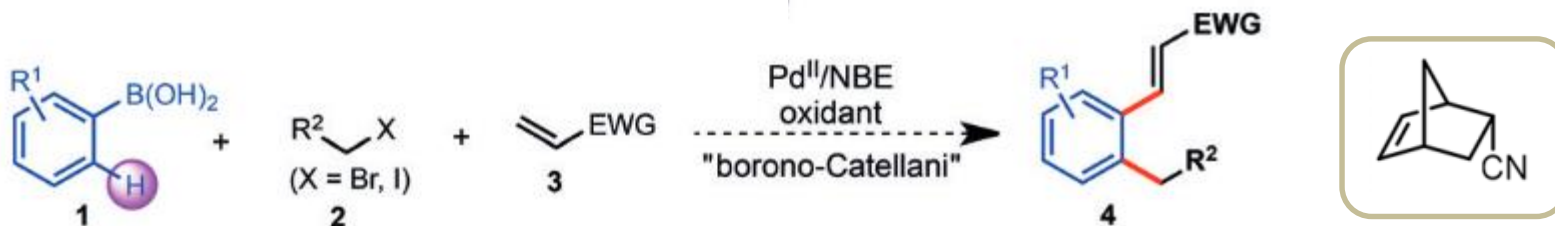
Zhang, 2018



Zhou, 2018

ACS Catal. **2018**, *8*, 3775-3779.

Palladium(II)-Initiated Borono-Catellani Reaction



Angew. Chem., Int. Ed. **2018**, *57*, 7161-7165.

Summary

- **Much development concerning ortho functionalization has been developed over the last ten years.**
 - ✓ Formation of C-C and C-X bonds are possible
 - ✓ Asymmetric catalysis is now possible in many systems
 - **Many areas left to explore**
-

Thanks for your attention !