C-H functionalization
Melanie S. Sanford

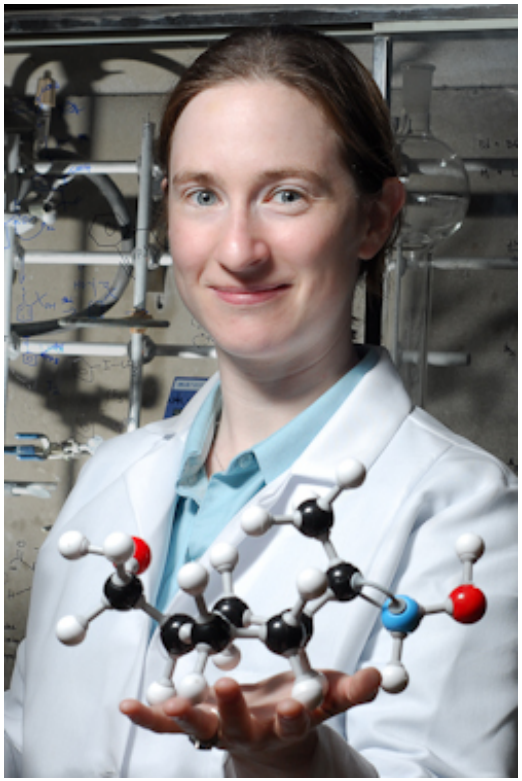
Presenter Tao XU

Presentation Oct. 24th, 2012

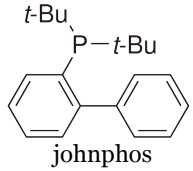
Outline

- Oxidative functionalization of C-H bond
- Synthesis & Reactivity of Pd(IV) and Pt(IV)
- Oxidative functionalization of C-H bond
- C-H functionalization of CH_4 and PhH

Introduction of Melanie S. Sanford

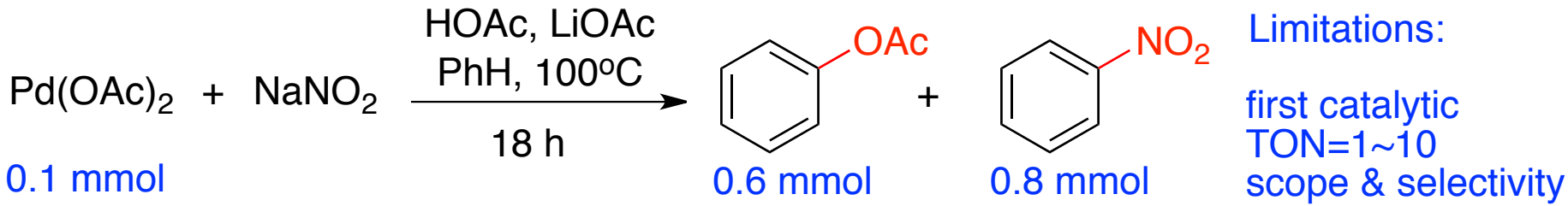


- **Professor of Chemistry** U. of Michigan
- **Postdoc. at Princeton** (supervisor: John T. Groves)
- **Ph.D., Chemistry, Caltech.** (Supervisor: Robert. H. Grubbs)
- **B.S. *cum laude*** with distinction in chemistry at **Yale** (advisor: Robert H. Crabtree)



johnphos

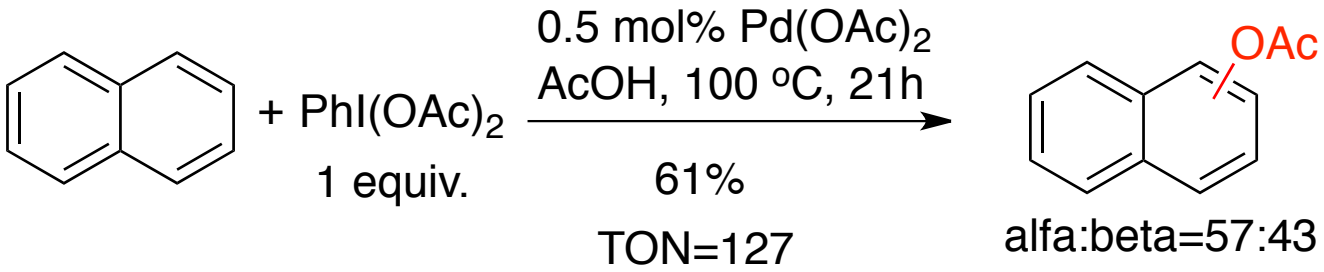
Background of C-H acetoxylation



Limitations:

first catalytic
TON=1~10
scope & selectivity

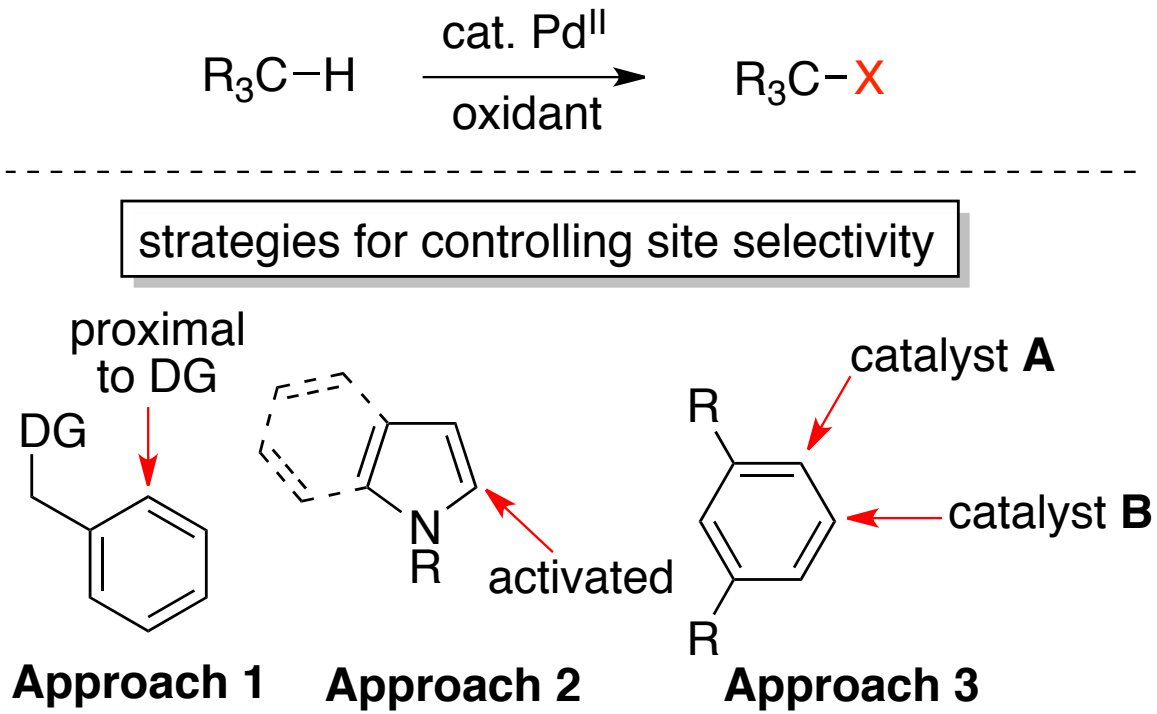
[1] Tissue, T., Downs, W. J.; *J. Chem. Soc. Chem. Commun.* **1969**, 410.
[2] Henry, P. M."Palladium CatalyzedOxidation of Hydrocarbons"; D. Reidel; Dordrecht, Holand, 1980; pp 306-338.



electron poor arenes
poor regioselectivity

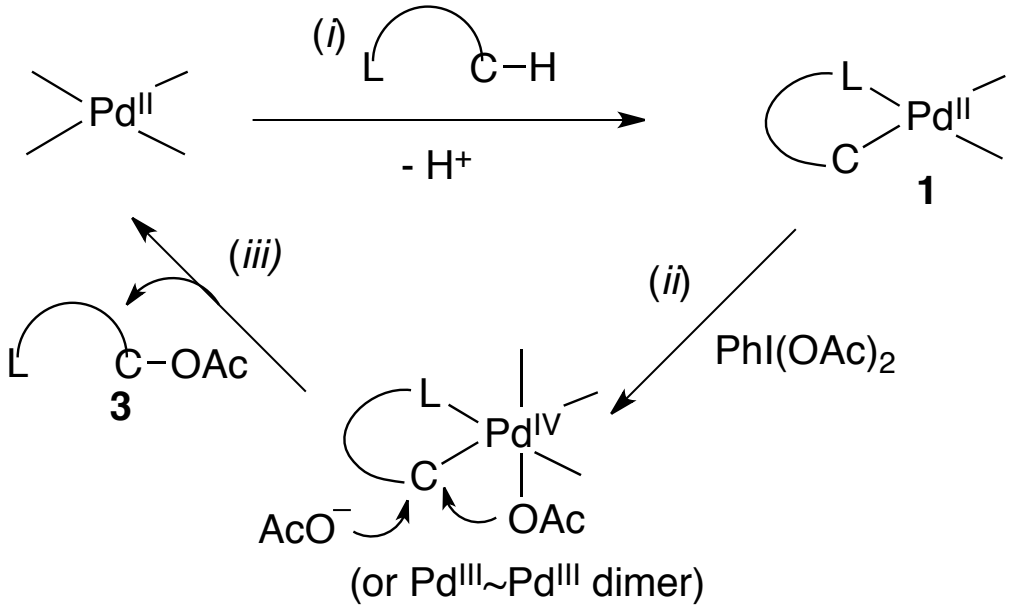
Yoneyama, T.; Crabtree, R. H.; *J. Mol. Catal. A* **1996**, *108*, 35.

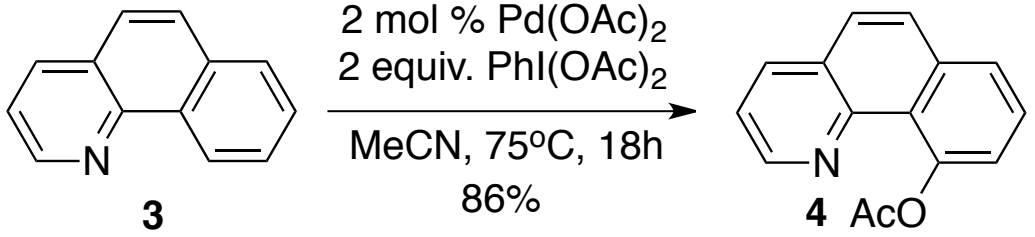
Strategies to control selectivity



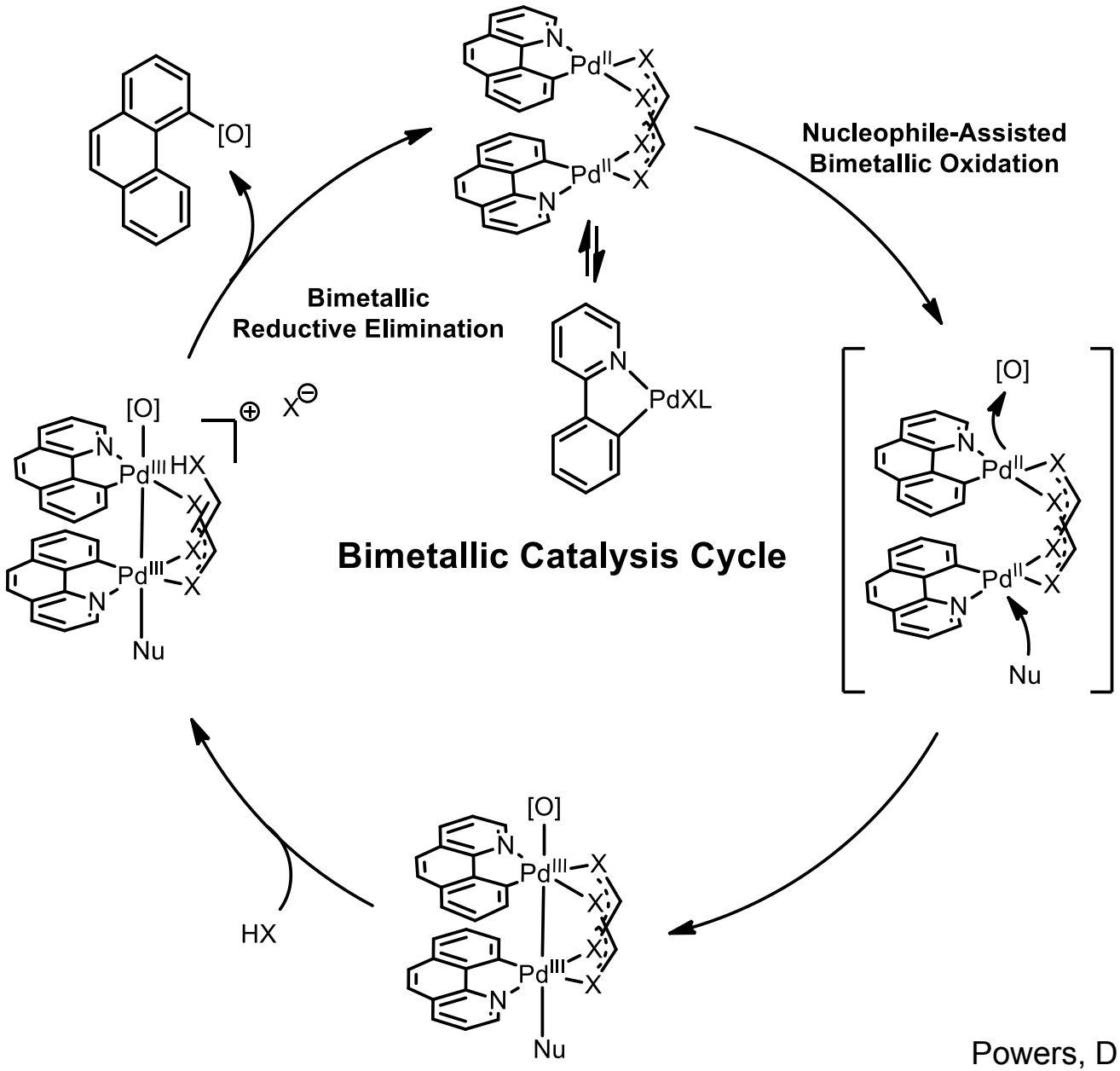
Neufeldt, S. R., Sanford, M. S.; *Acc. Chem. Res.* **2009**, *42*, 1074.

Ligand-directed C-H acetoxylation





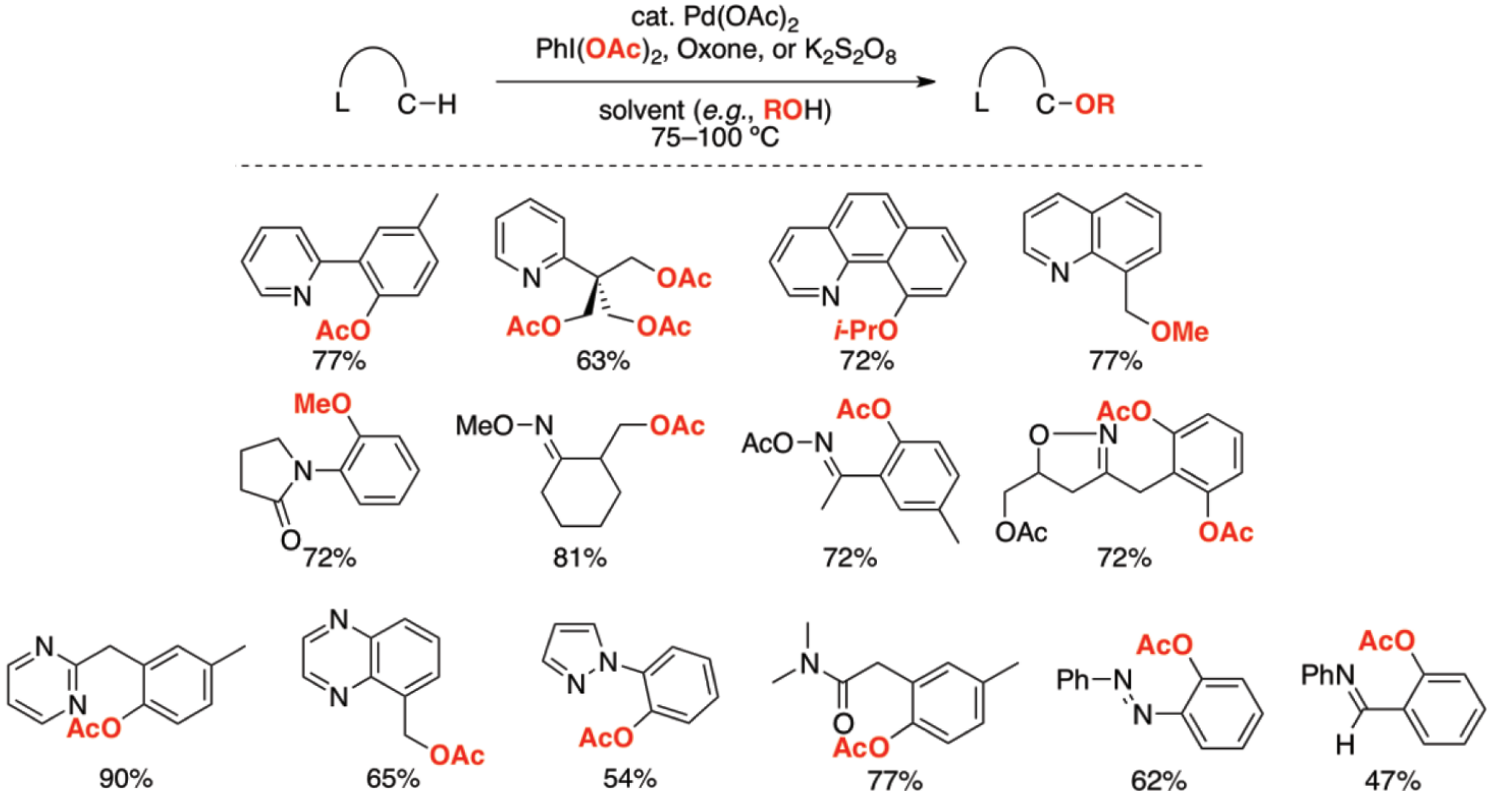
Dick, A. R.; Hull, K. L.; Sanford, M. S.; *J. Am. Chem. Soc.* **2004**, *126*, 2300.



Dr. Ritter

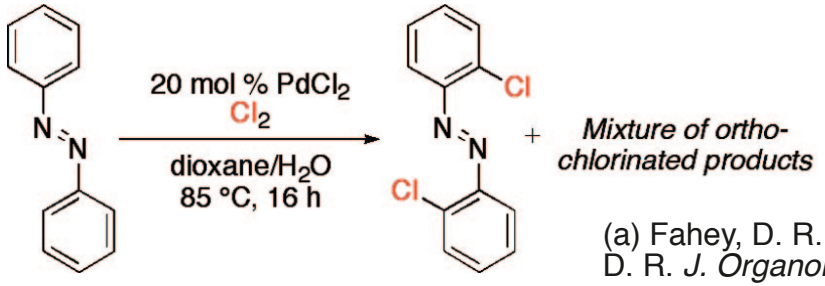
Powers, D.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302

Directing ligand types and substrate scope

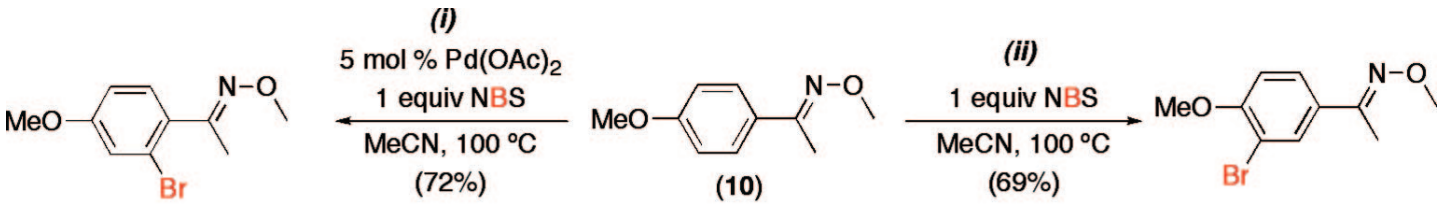


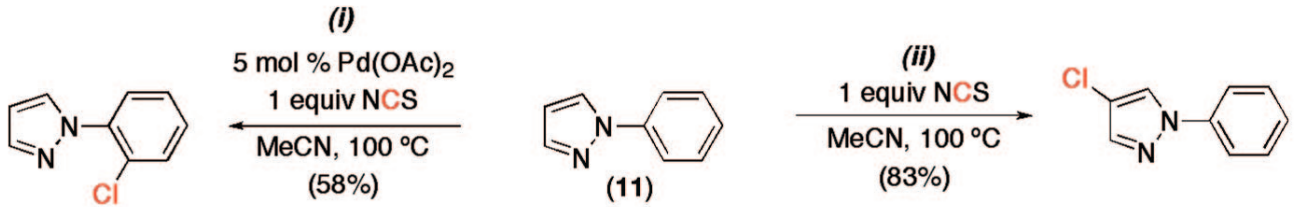
(a) Desai, L. V.; Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2004**, *126*, 9542. (b) Kalyani, D.; Sanford, M. S.; *Org. Lett.* **2005**, *7*, 4149. (c) Desai, L. V.; Malik, H. A.; Sanford, M. S.; *Org. Lett.* **2006**, *8,* 1141. (d) Kalberer, E. W.; Whitfield, S. R.; Sanford, M. S.; *J. Mol. Catal. A* **2006**, *251*, 108. (e) Desai, L. V.; Stowers, K. J.; Sanford, M. S.; *J. Am. Chem. Soc.* **2008**, *130*, 13285. (f) Neufeldt, S. R.; Sanford, M. S. *Org. Lett.* **2010**, *12*, 532.

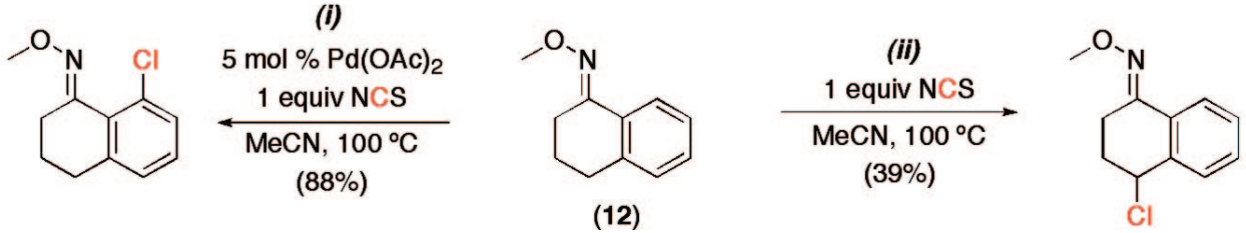
C-H halogenation



(a) Fahey, D. R. *J. Chem. Soc., Chem. Commun.* **1970**, 417. (b) Fahey, D. R. *J. Organomet. Chem.* **1971**, *27*, 283.

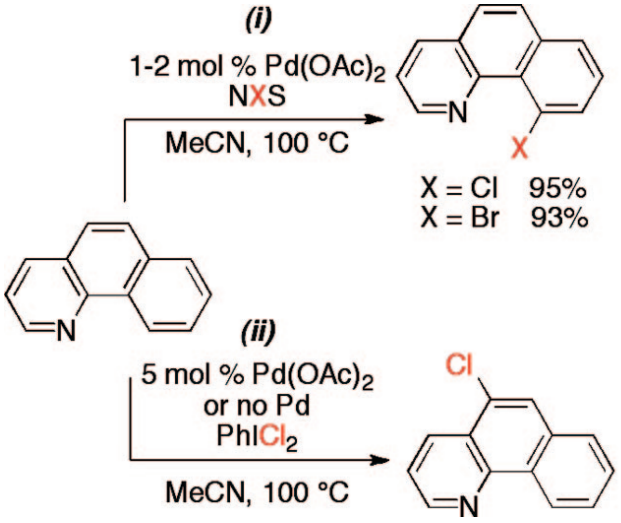




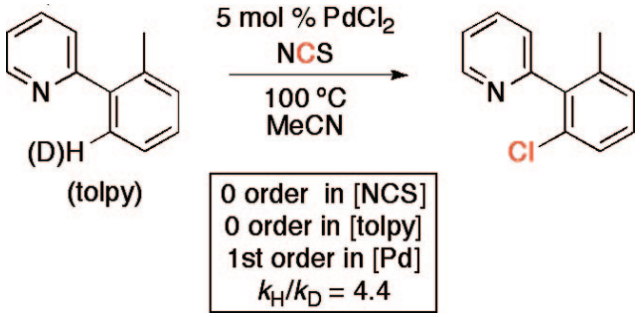


Kalyani, D.; Dick, A. R.; Anani, W. Q.; Sanford, M. S. *Tetrahedron* **2006**, *62*, 11483.

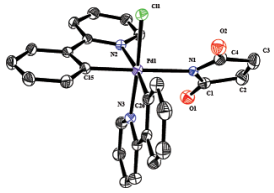
C-H halogenation-NCS vs. PhICl2

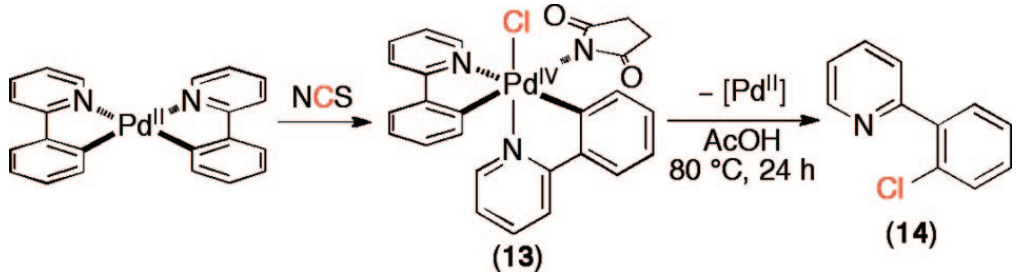


Tetrahedron **2006**, *62*, 11483.



JACS **2007**, *129*, 15142





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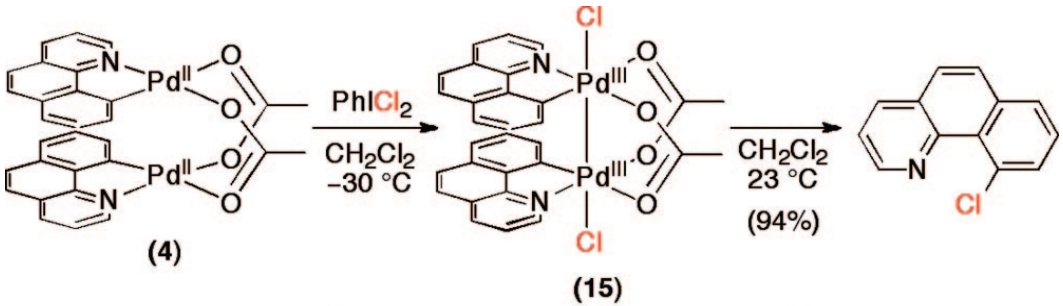
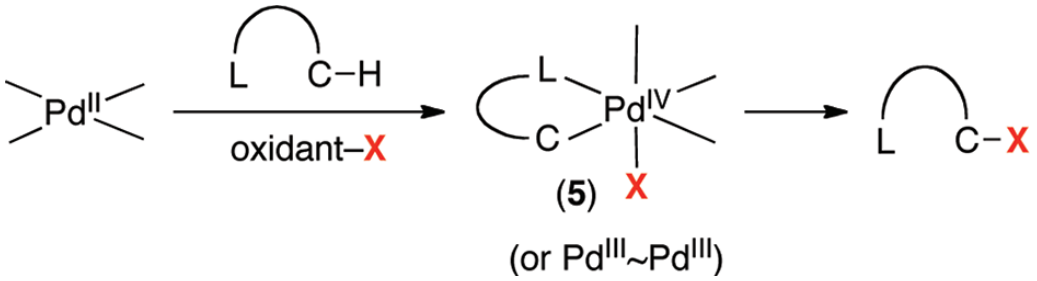
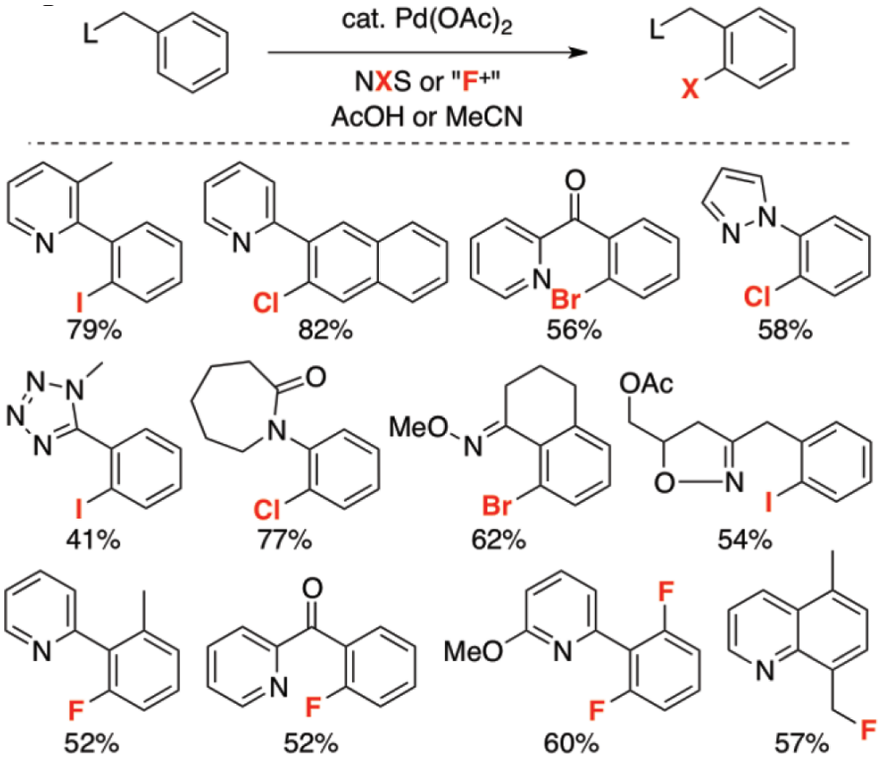


Kinetically competent for Pd(OAc)2 catalyzed C–H chlorination with NCS

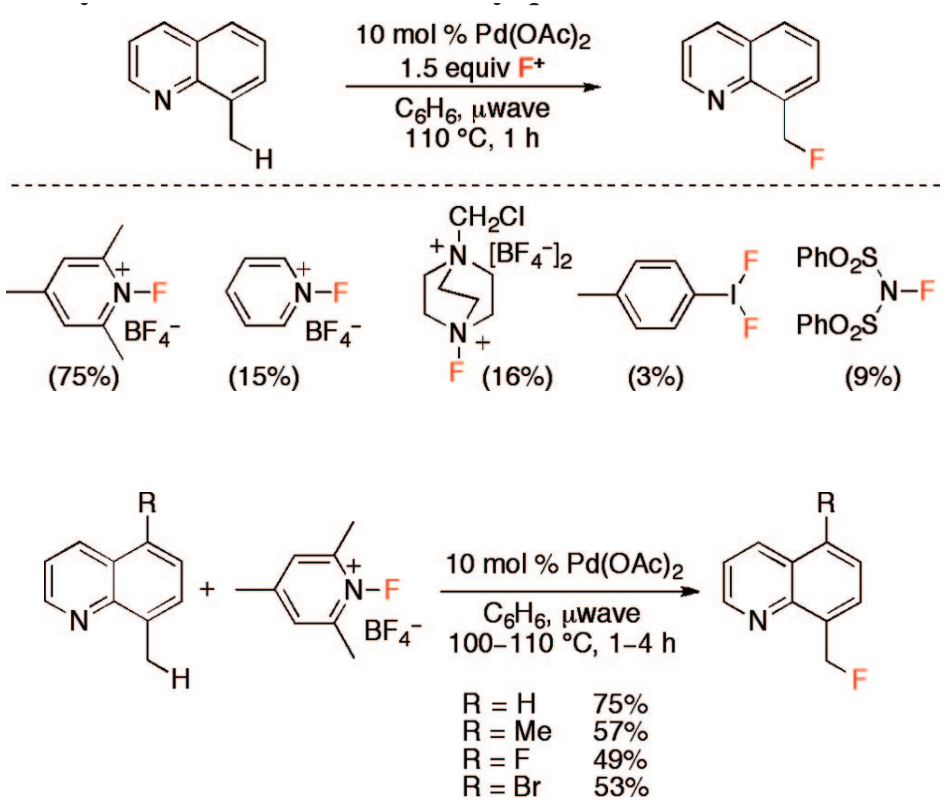
Nat. Chem. **2009**, *1*, 302.

Halogenation of C-H bond



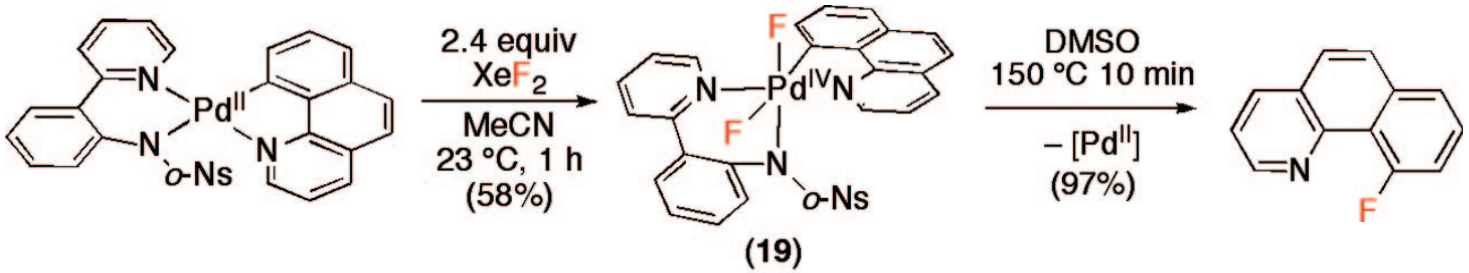


Acc. Chem.Res. **2012**, *45*, 936.

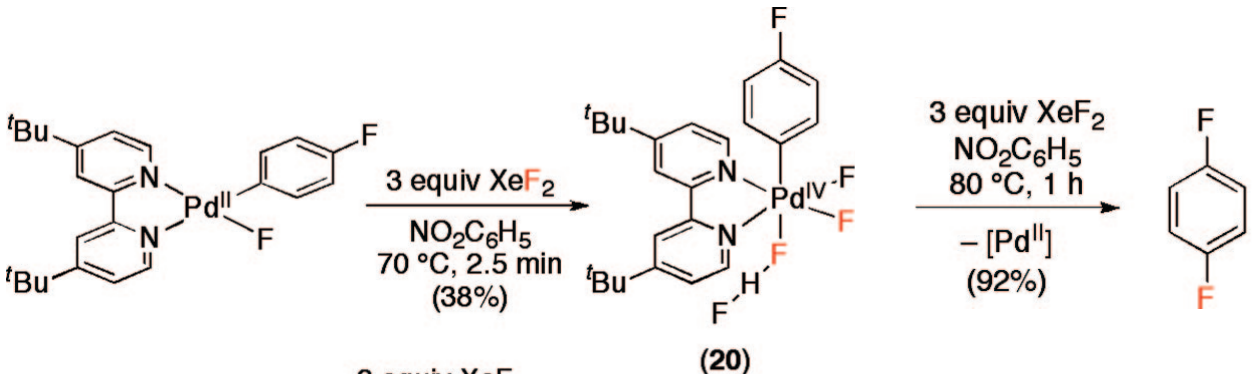


J. Am. Chem. Soc. **2006**, *128*, 7134.

Indirect Mechanistic support

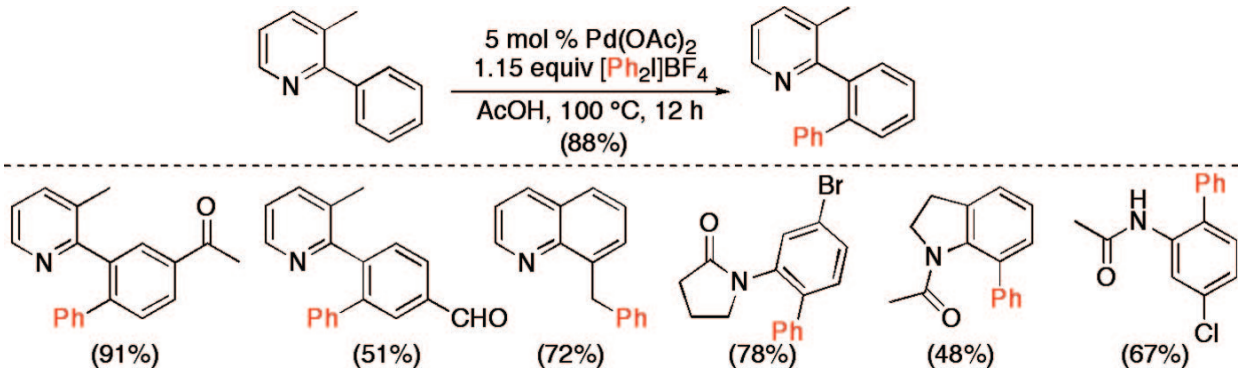


By Ritter group in *JACS* **2008**, *130*, 10060.

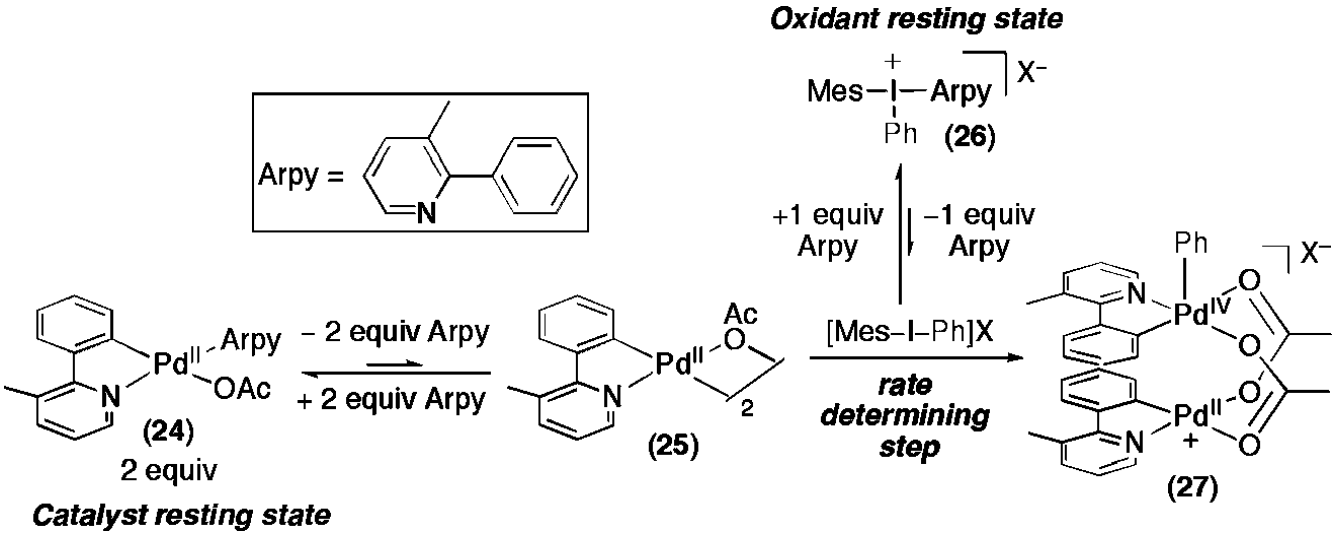


By Sanford in *JACS* **2009**, *131*, 3796.

C-H arylation

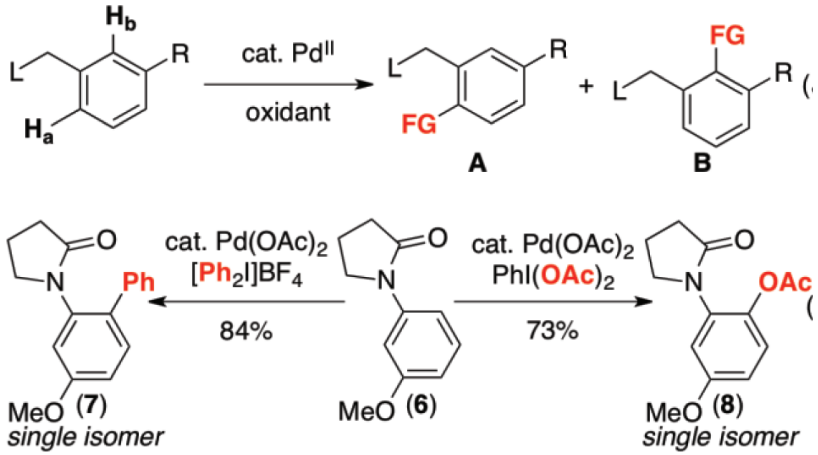


JACS **2005**, *127*, 7330

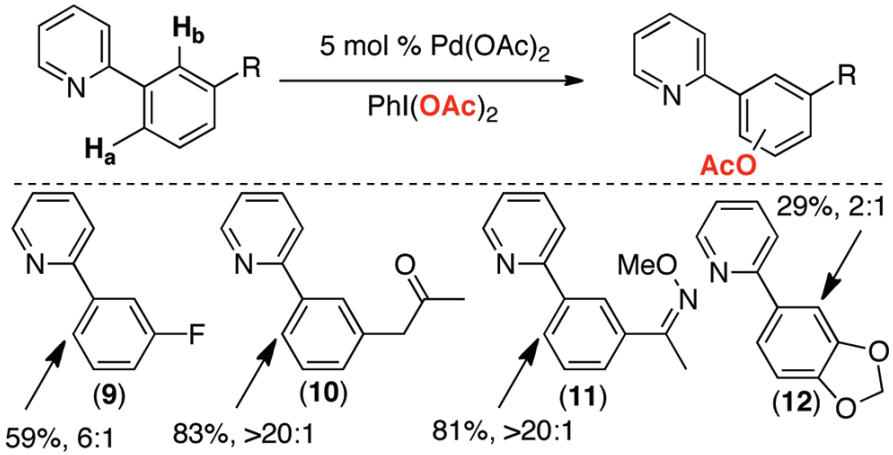


Inorg. Chem. **2007**, *46*, 1924

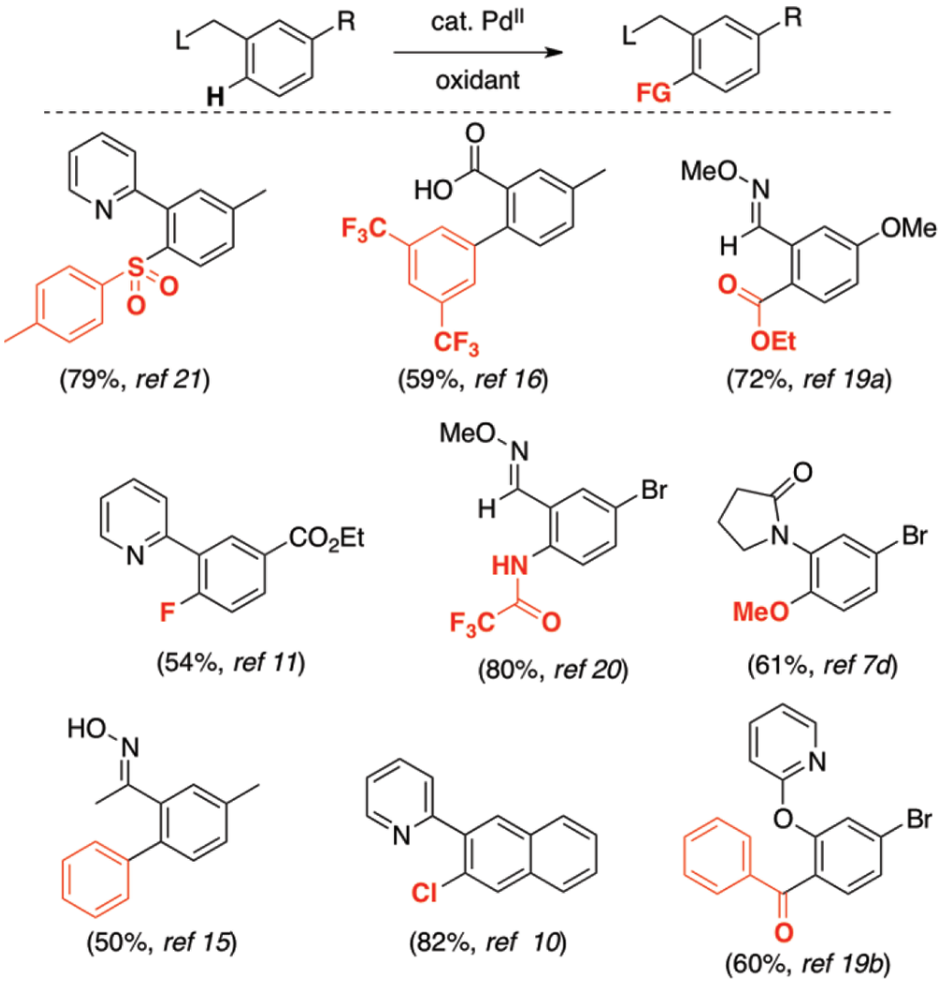
Ligand directing ablities



JACS. **2005**, *127*, 7330.



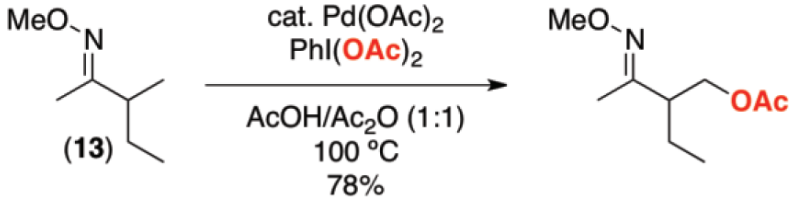
Org.Lett. **2005**, *7*, 4149.



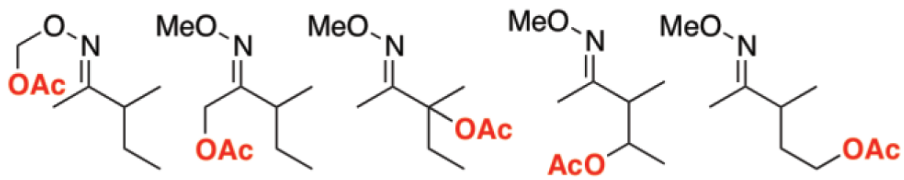
Acc. Chem.Res. **2012**, *45*, 936. and refs cited therein

Trend in aliphatic C-H functionalization

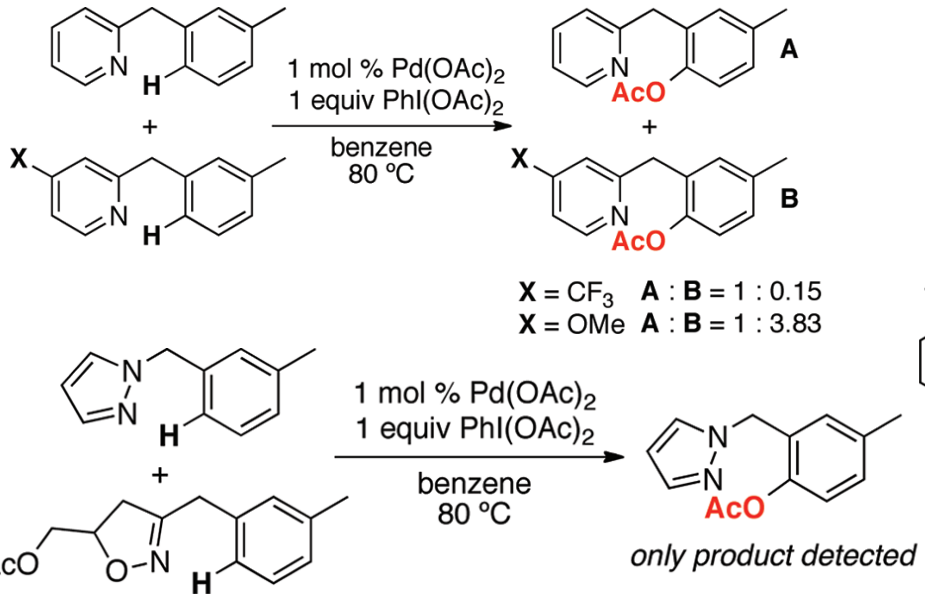
Ligand-directed sp3-C-H functionalization typically proceeds with high selectivity for ***primary over secondary*** C-H bonds. In addition, selectivity is observed for C-H bonds that are β versus R or γ to the directing group (i.e, ***five- membered palladacycles are strongly favored over their four- or six-membered counterparts***)



Not Observed:

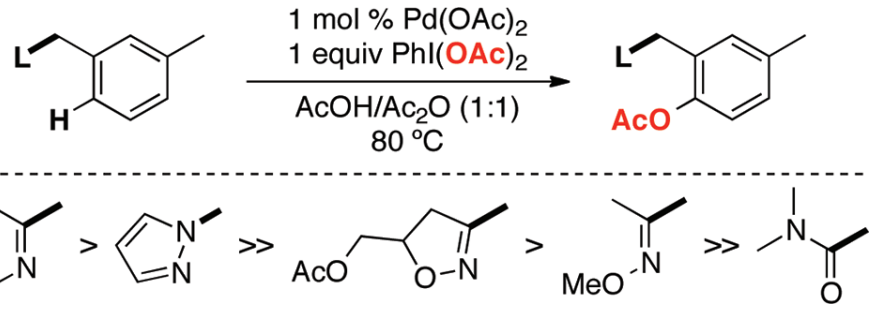


JACS. **2004**, *126*, 9542.

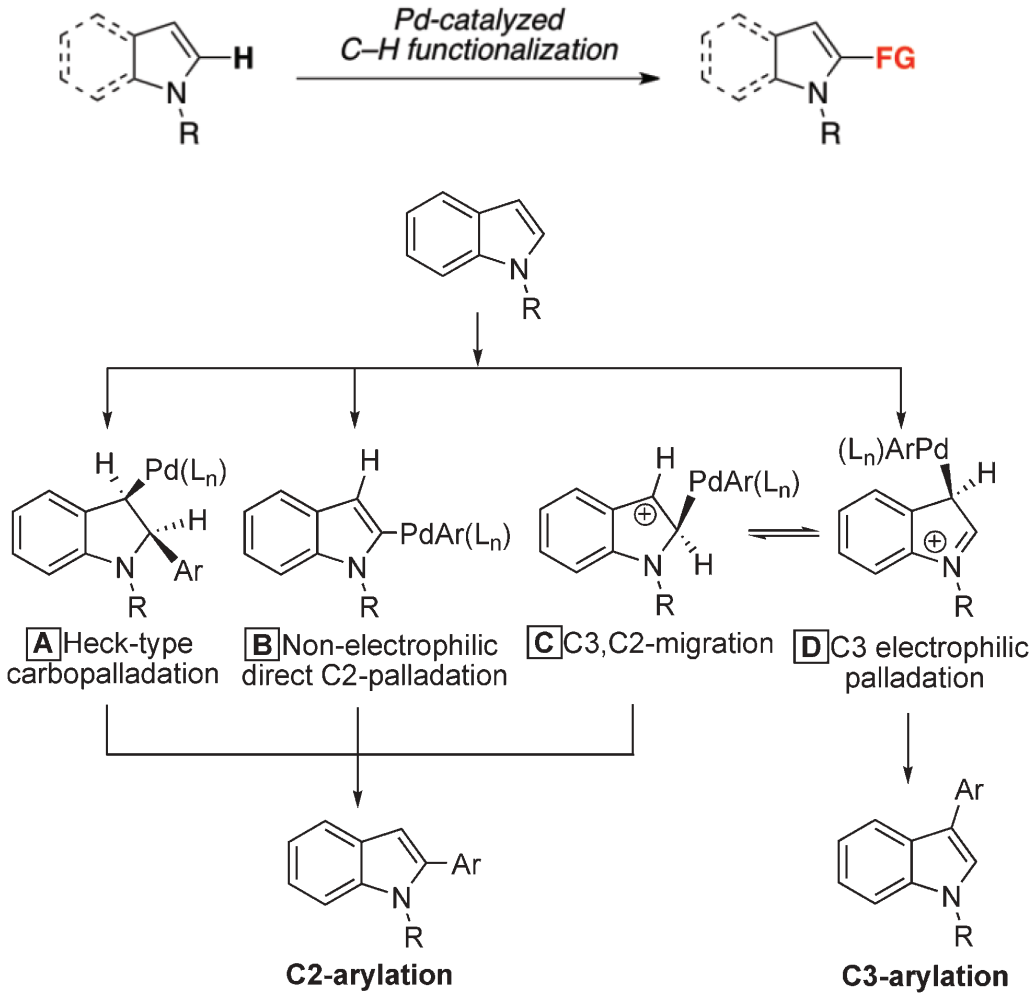


JACS. **2008**, *130*, 13285.

Trend of directing ability

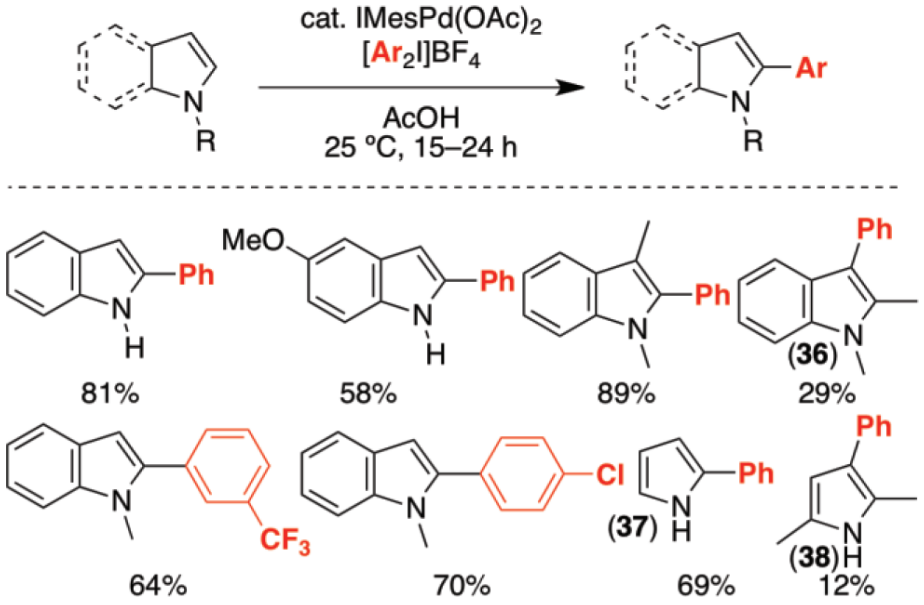


Substrate-based selectivity control

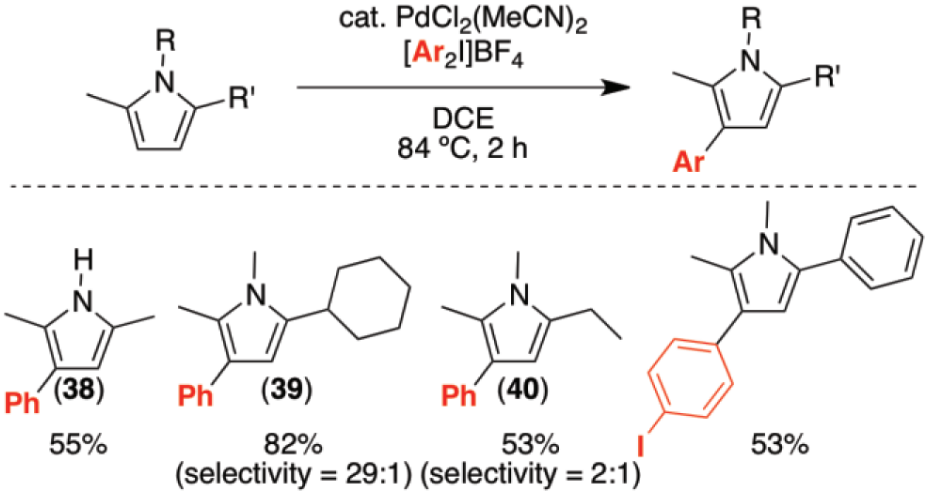


Chem. Soc. Rev., 2007, 36, 1173

Indoles and pyrroles as substrate

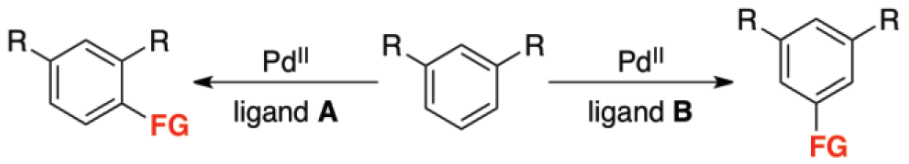


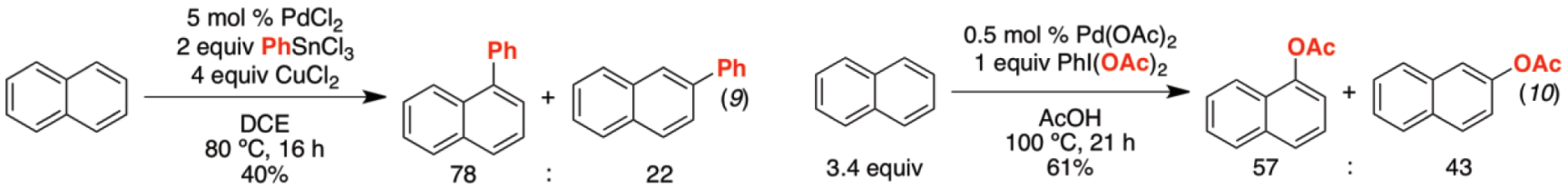
JACS. **2006**, *128*, 4972.

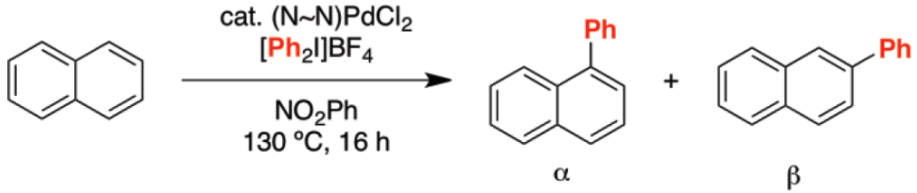


Org. Lett. **2011**, *13*, 288.

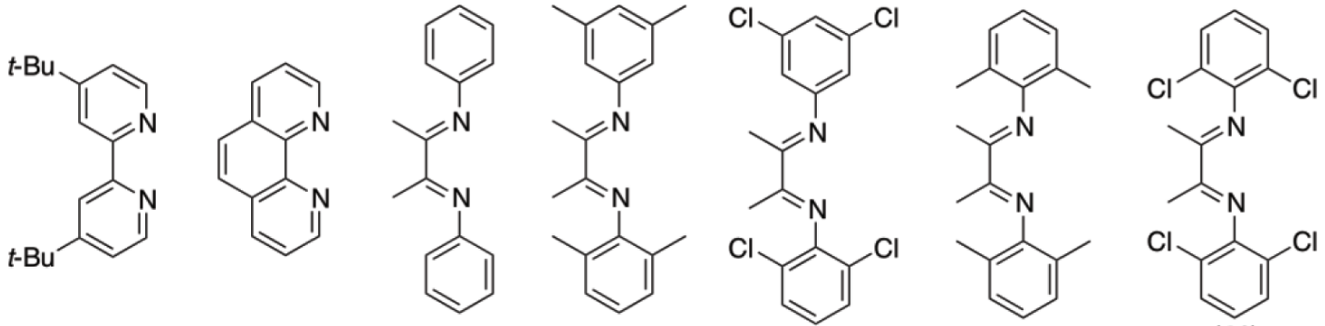
Catalyst-based selectivity controle







N~N Ligand and Product Yield/Selectivity:



22%
α:β = 78:1

12%
α:β = 10:1

54%
α:β = 9:1

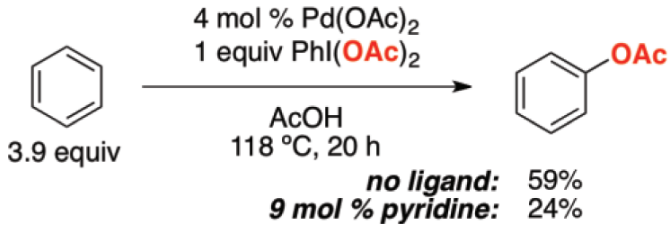
47%
α:β = 9:1

42%
α:β = 22:1

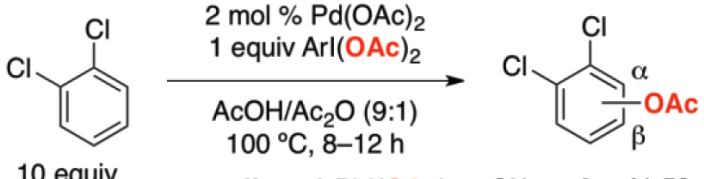
43%
α:β = 27:1

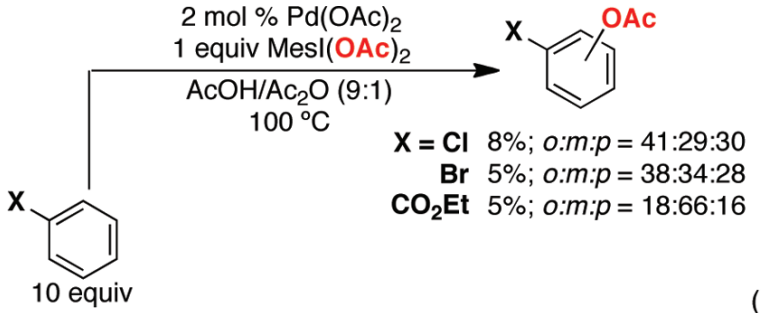
70%
α:β = 71:1

Acetoxylation

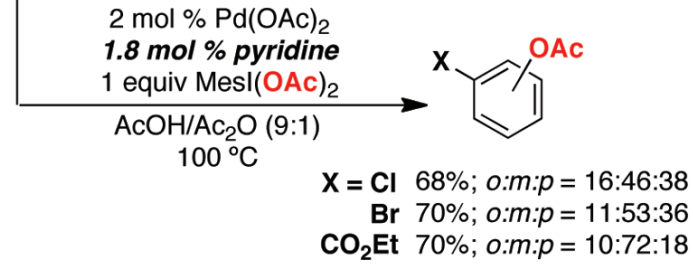


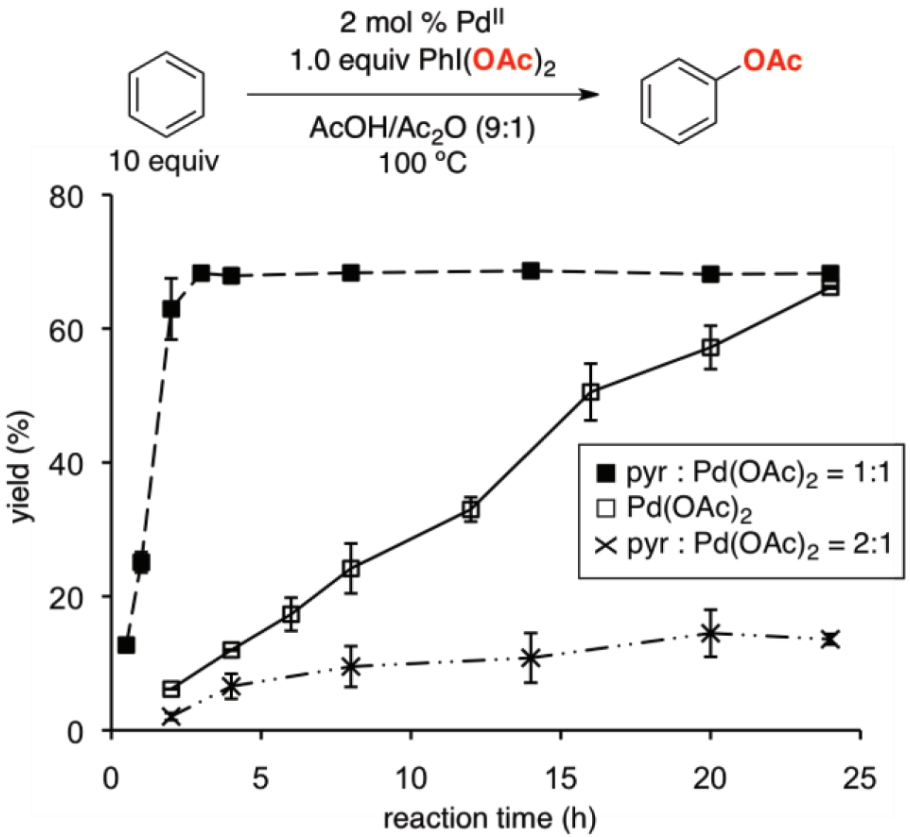
J. Mol. Catal. A **1996**, *108*, 35.





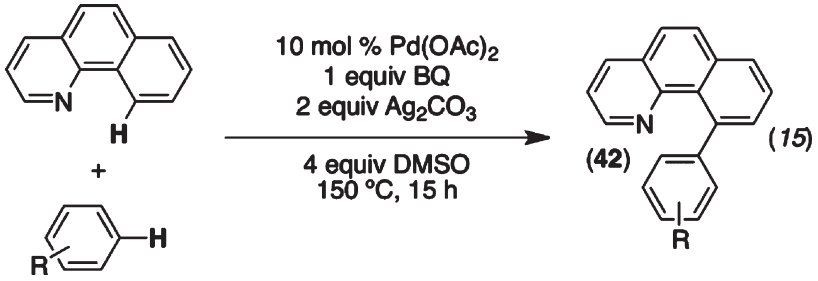
(*14*)



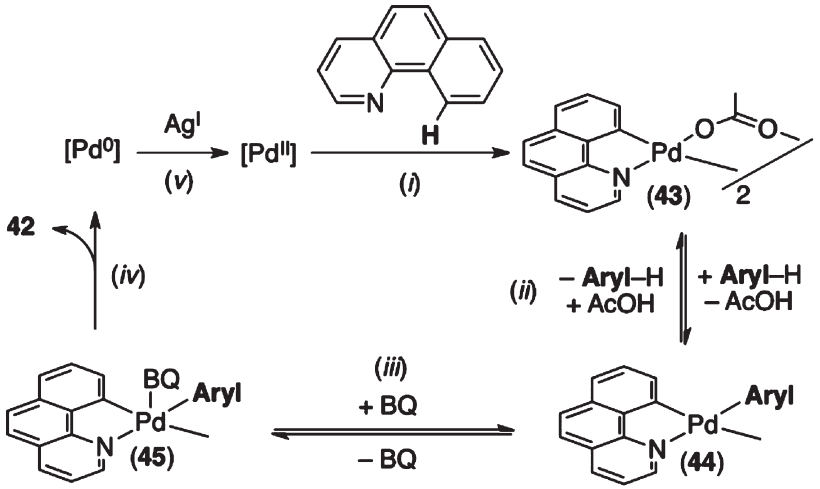


Angew. chem. Int. Ed. **2011**, *50*, 9409.

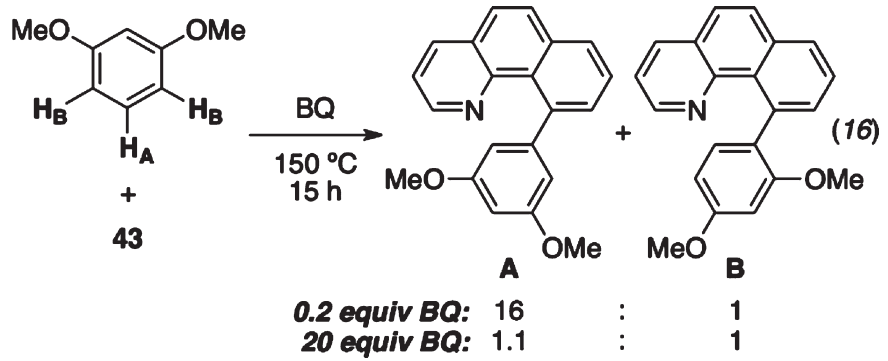
Another set of study

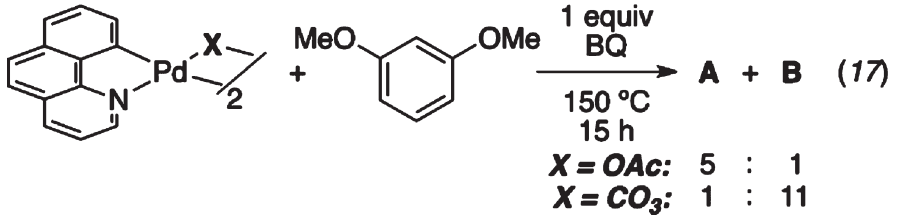


JACS. **2007**, *129*, 11904.



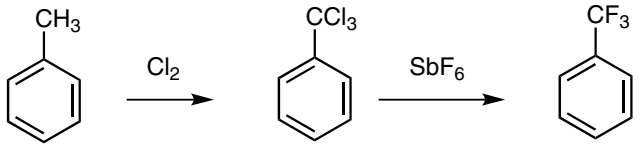
JACS. **2009**, *131*, 9651.



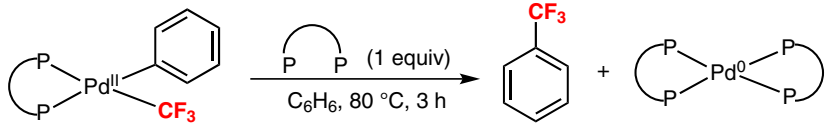


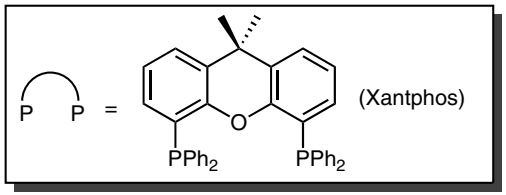
JACS. **2011**, *133*, 4455.

TM-catalyzed arene trofluoromethylation

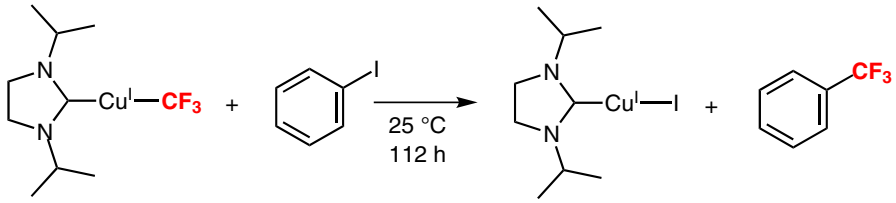


Swarts reaction
Swarts, F. *Bull. Acad. R. Belg.* **1892**, *24*, 309.

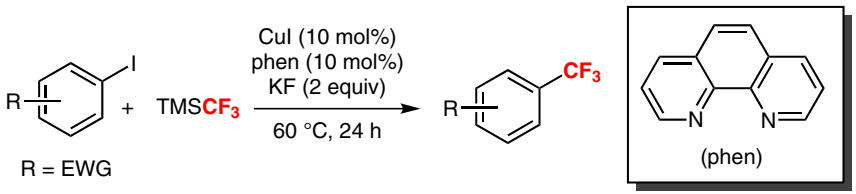




In 2006, first Pd catalyzed CF_3lyation rxn
Grushin etc. JACS **2006**, *128*, 12644.

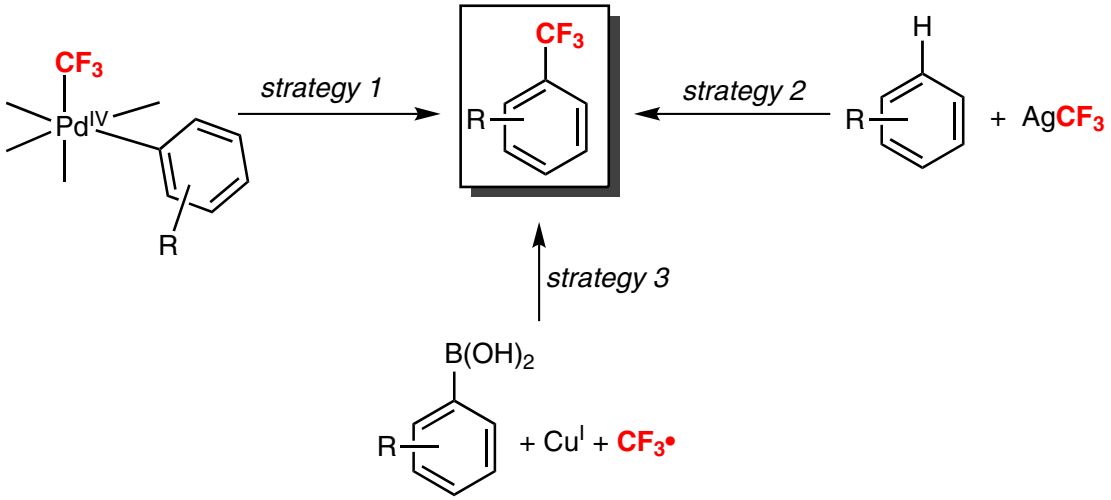


Vicic, D. A. etc. *JACS*, **2008** *130*, 8600.
Organometallics **2008**, 27, 6233.

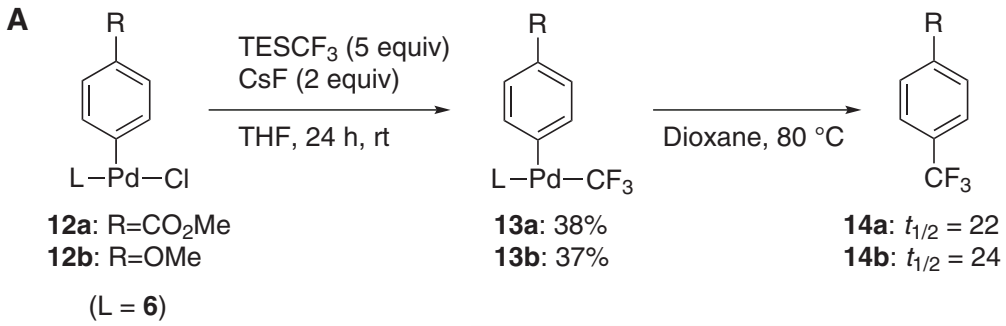


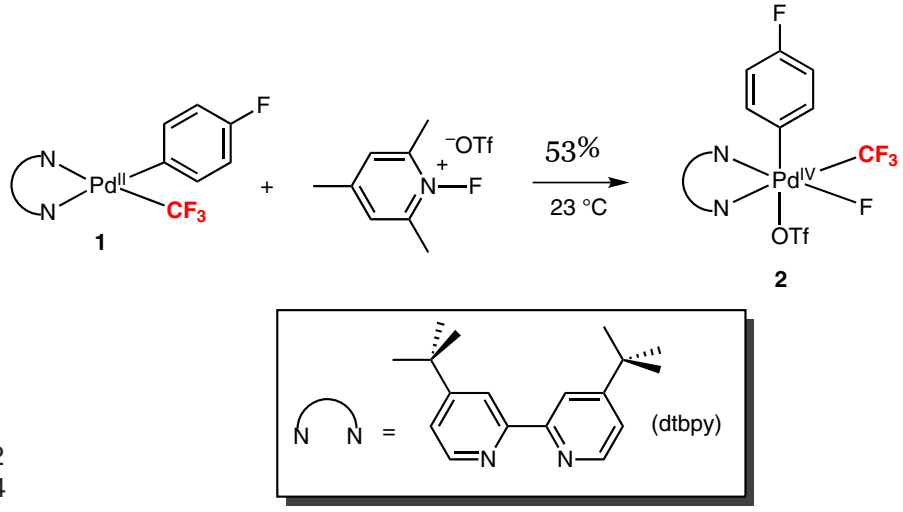
Amii, H. etc. *Chem. Commun.* **2009**, 1909.

Sanford's approach to CF_3lyation

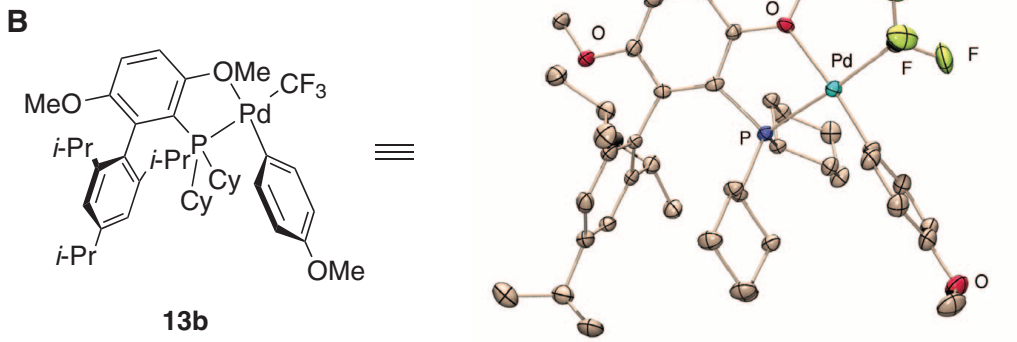


Approach 1 from Pd(IV) center using $PhI(OAc)_2$

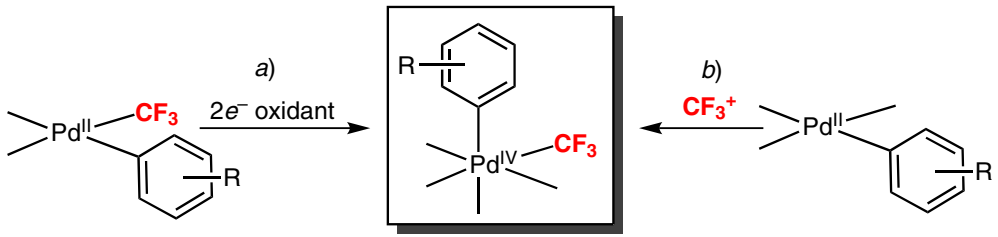


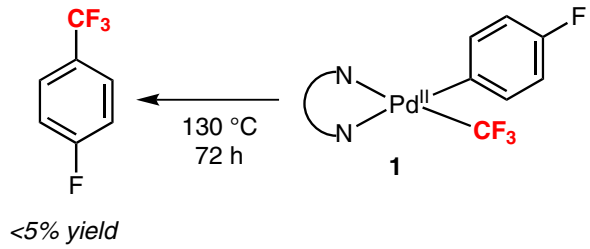


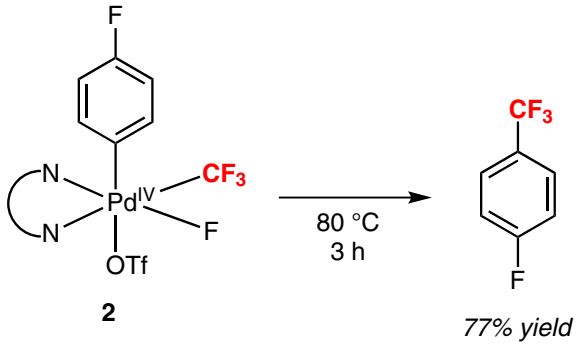
(a) *J. Am. Chem. Soc.* **2010**, *132*, 2878.
(b) *J. Am. Chem. Soc.* **2011**, *133*, 7577.



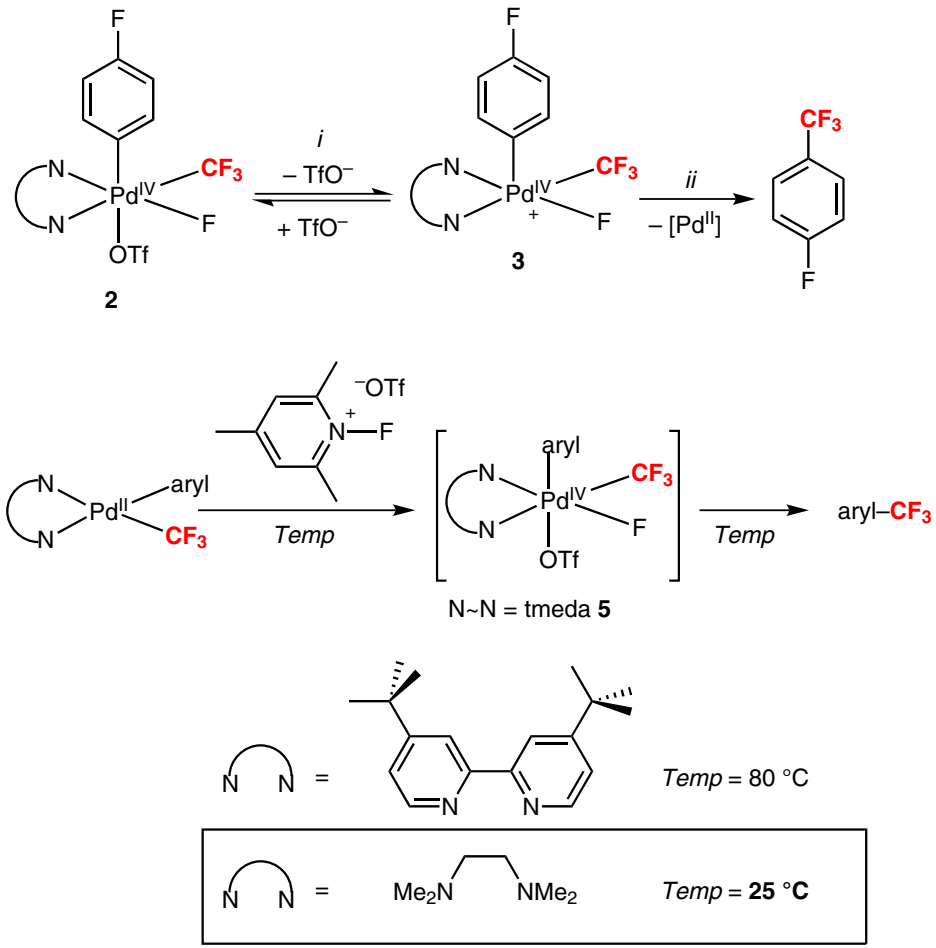
Buchwald *etc* *Science* **328**, 1679 (2010);

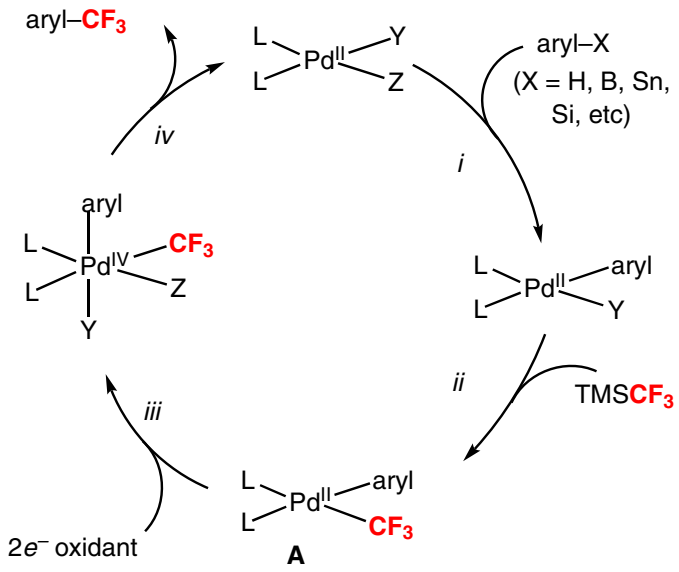






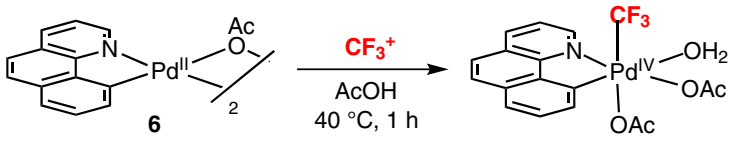
Reaction exploration

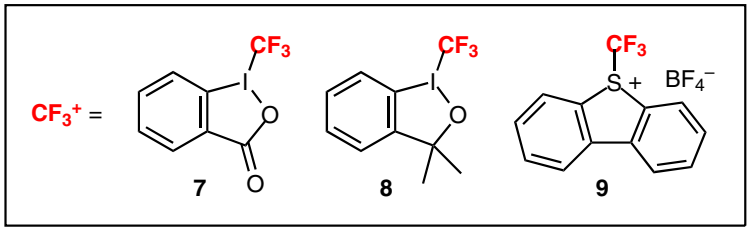


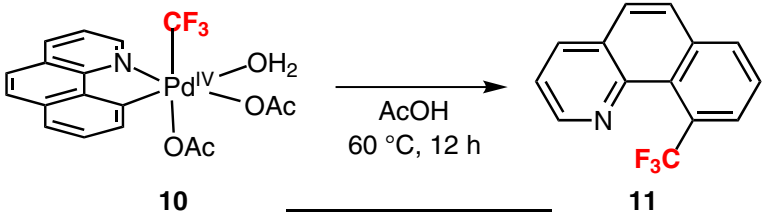


Canty, A. J.; *Organometallics* **1994**, *13*, 2053.

Approach 1 from Pd(IV) center using CF_3^+

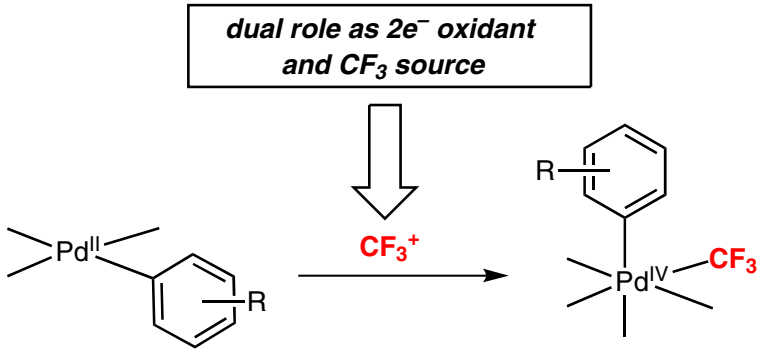


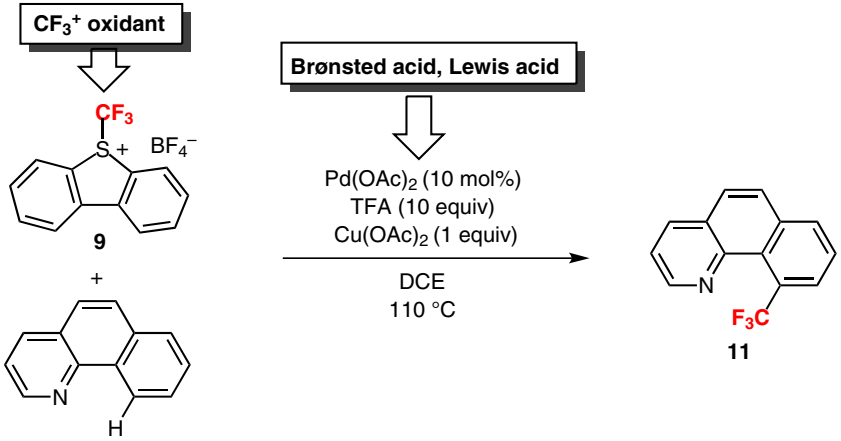




Additive	Yield
none	56%
TFA	73%
$Yb(OTf)_3$	99%

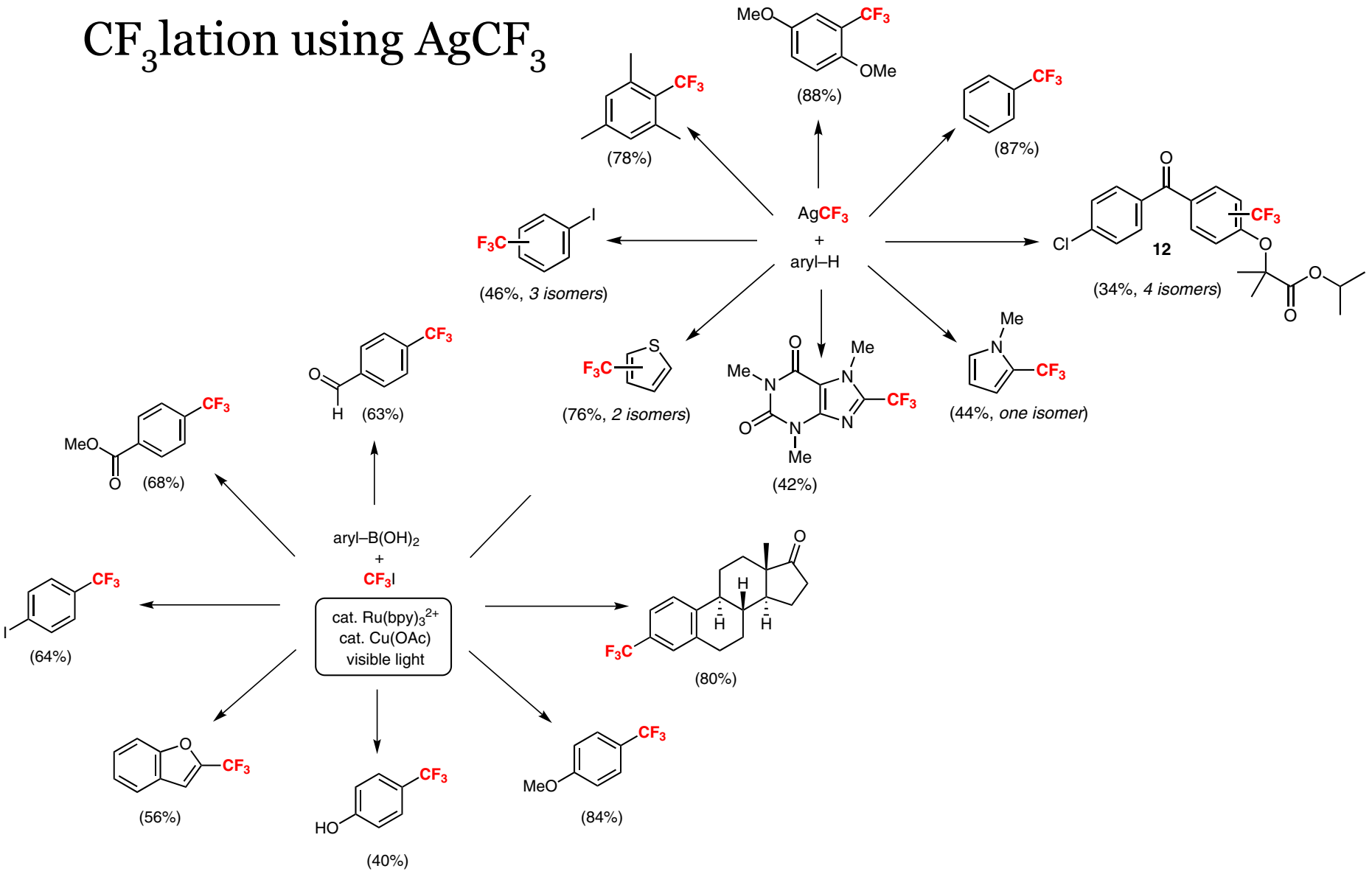
Sanford, M. S. *J. Am. Chem. Soc.* **2010**, *132*, 14682.



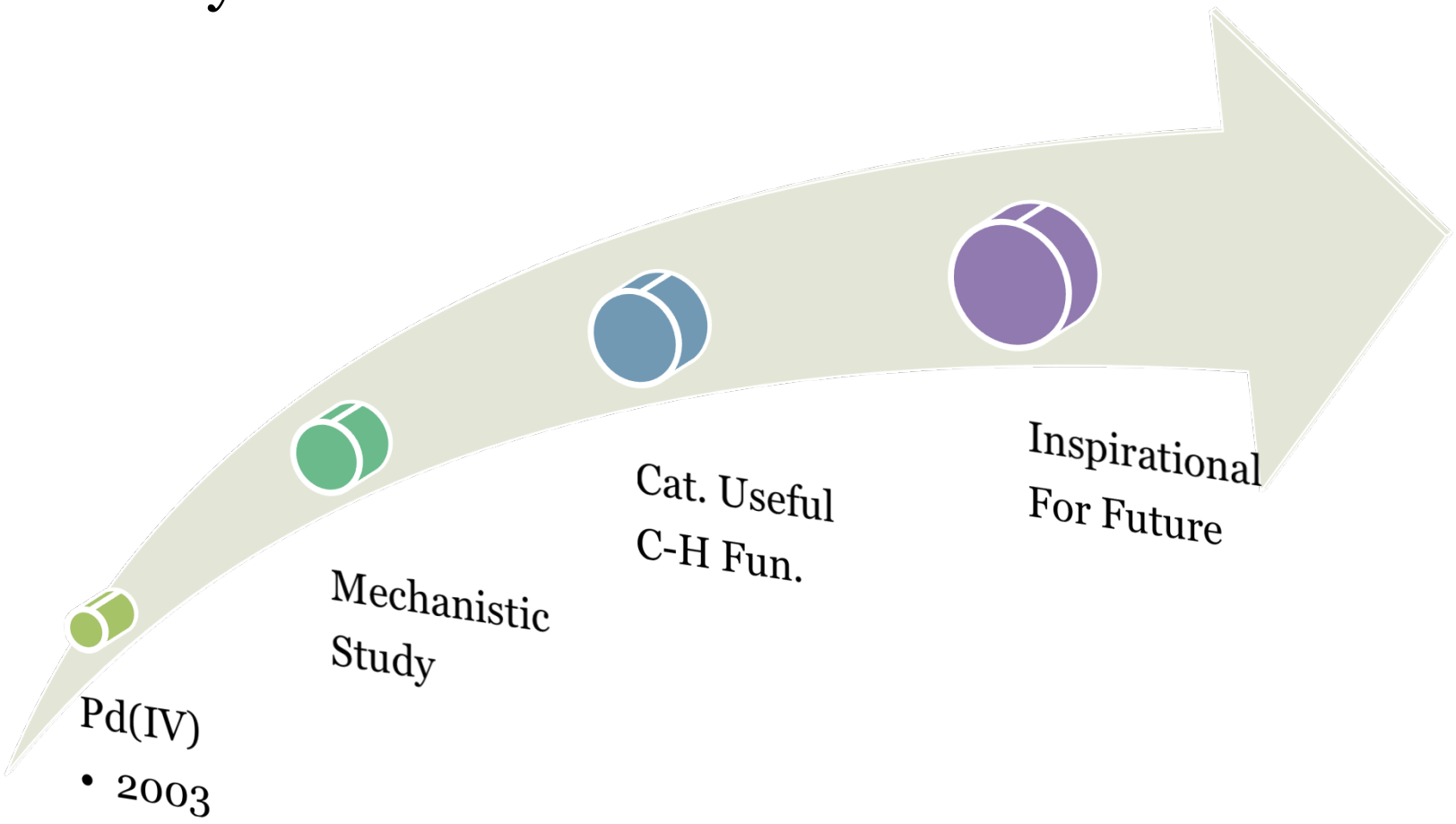


Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 3648.

CF_3lation using $AgCF_3$



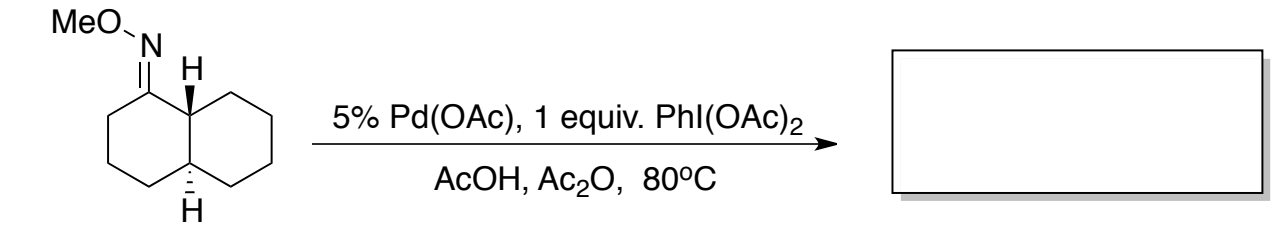
Summary

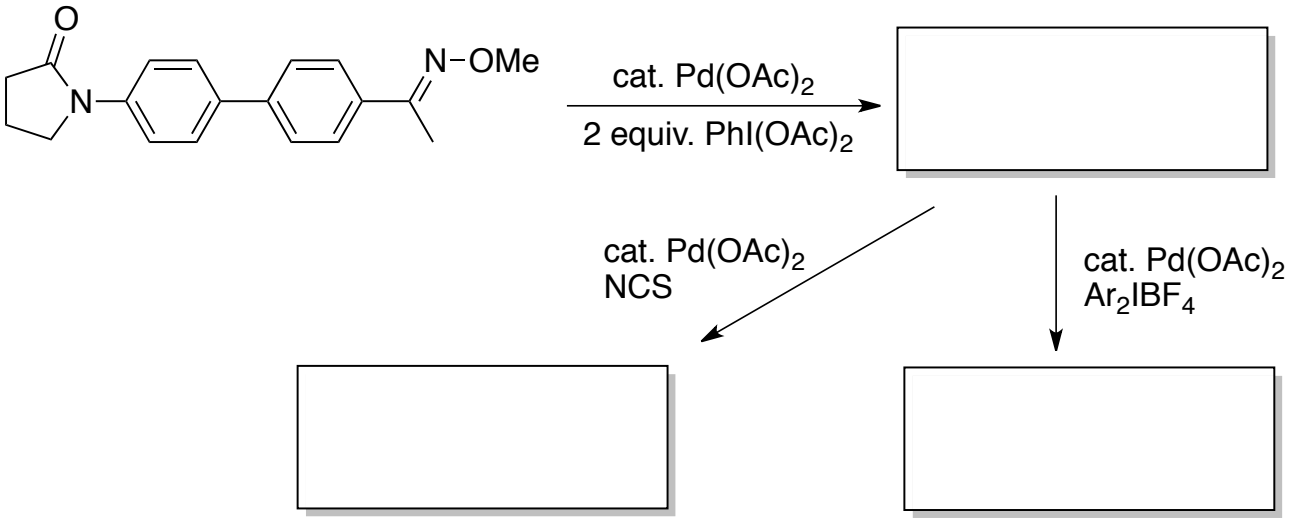

Pd(IV)
• 2003
Mechanistic Study
Cat. Useful C-H Fun.
Inspirational For Future

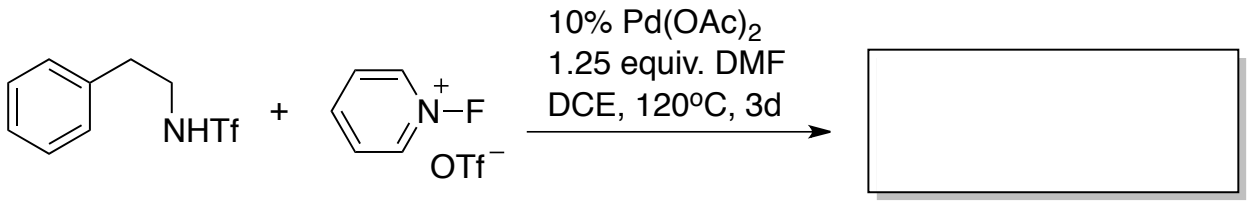
Acknowledgement

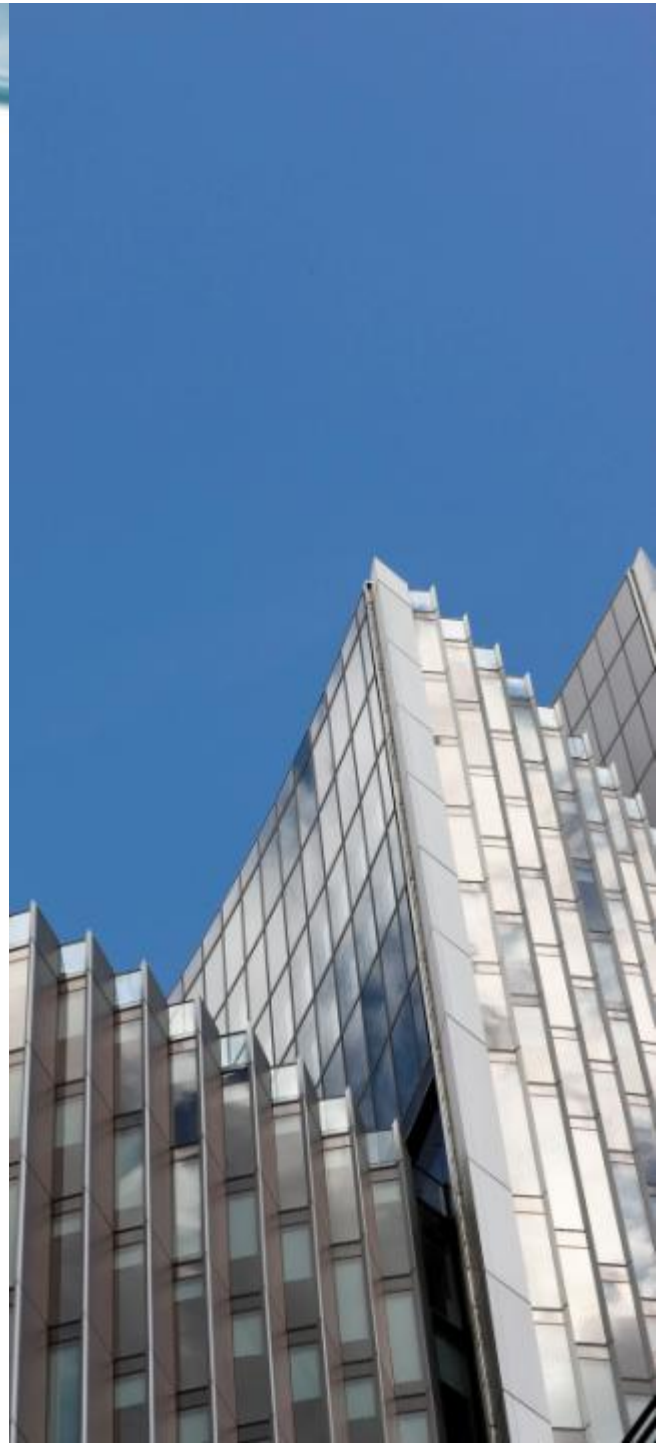
Thank Huang for helpful discussion of Pd(III) chemistry.

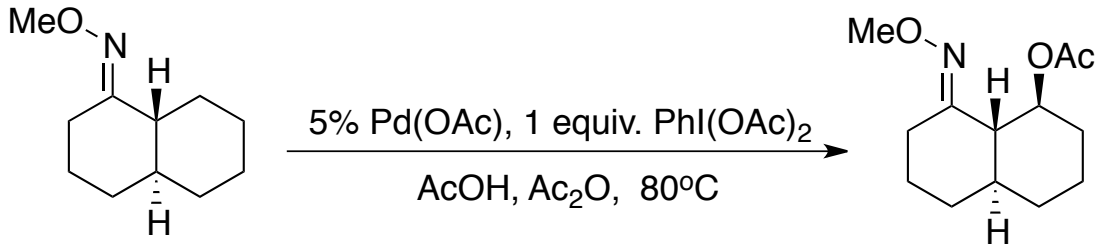
Thank every member of our group.

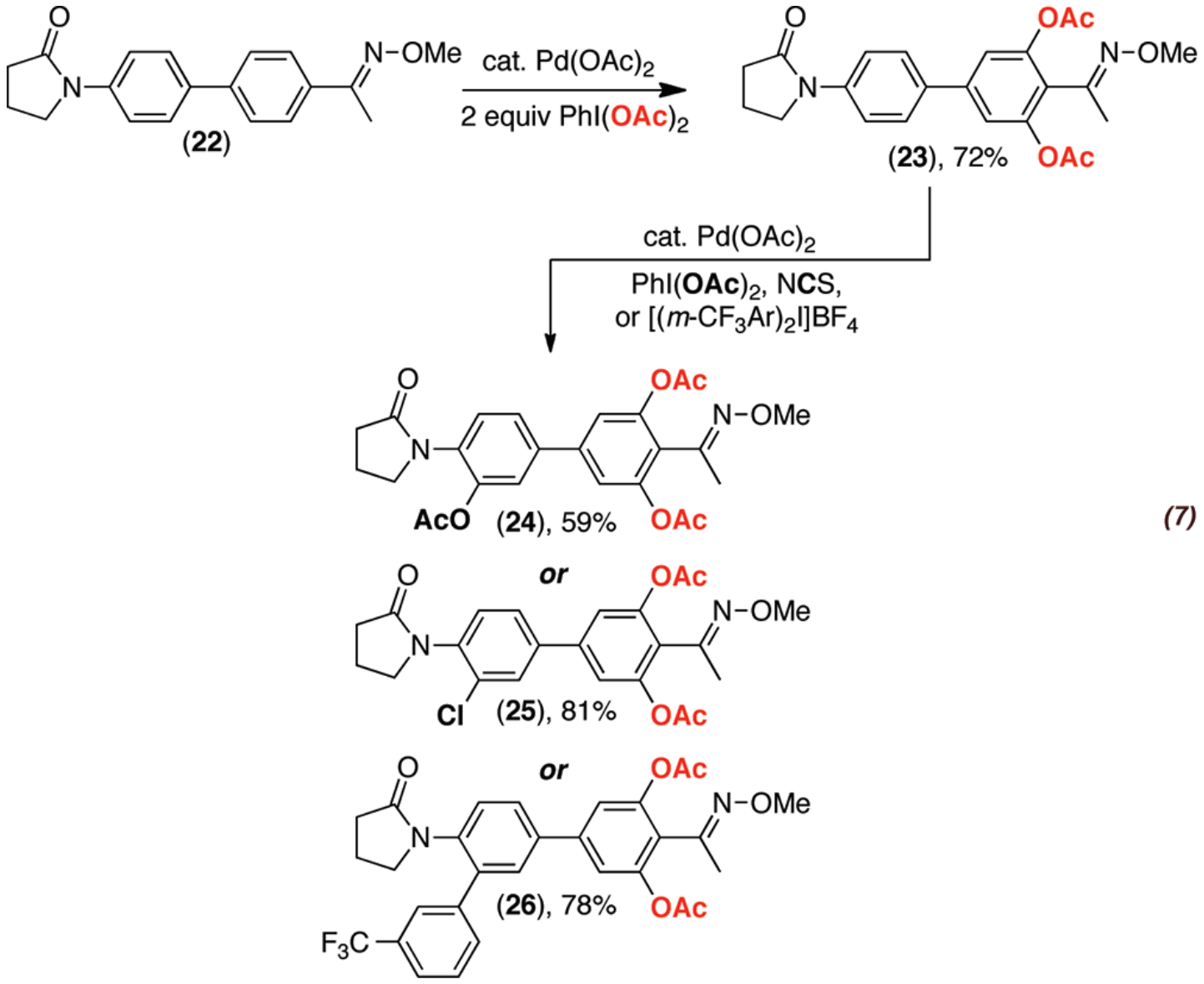

MeO
N
H
H
5% Pd(OAc), 1 equiv. PhI(OAc)2
AcOH, Ac2O, 80°C


O
N
N−OMe
cat. Pd(OAc)2
2 equiv. PhI(OAc)2
cat. Pd(OAc)2
NCS
cat. Pd(OAc)2
Ar2IBF4

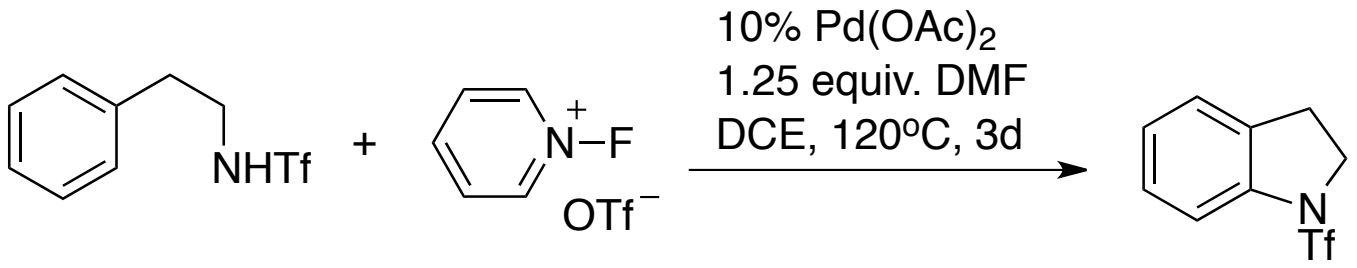

NHTf
+
N−F
OTf−
10% Pd(OAc)2
1.25 equiv. DMF
DCE, 120°C, 3d

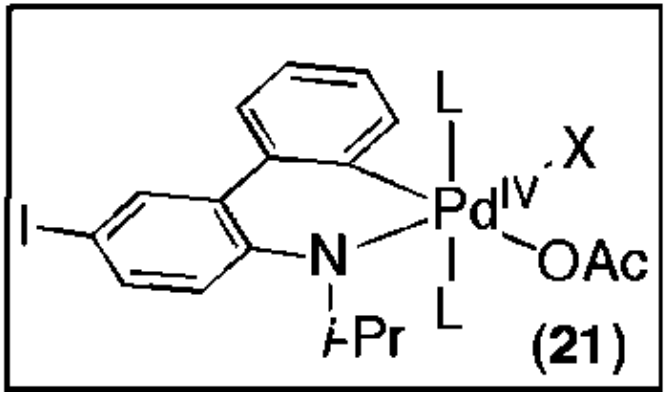



MeO
N
H
H
5% Pd(OAc), 1 equiv. PhI(OAc)2
AcOH, Ac2O, 80oC
MeO
N
H
OAc
H


(22)
cat. Pd(OAc)2
2 equiv PhI(OAc)2
(23), 72%
cat. Pd(OAc)2
PhI(OAc)2, NCS,
or [(m-CF3Ar)2I]BF4
(24), 59%
or
(25), 81%
or
(26), 78%

(7)


NHTf
+
N–F
OTf⁻
10% Pd(OAc)2
1.25 equiv. DMF
DCE, 120ºC, 3d
N
Tf


L
X
Pd^IV
I
N
OAc
i-Pr
L
(21)