

Bidentate Directing Groups

Reporter: Weiyu Yin

Supervisor: Prof. Yong Huang

2014-3-3

Contents:

1. Introduction

2. Pd catalyst

3. Cu catalyst

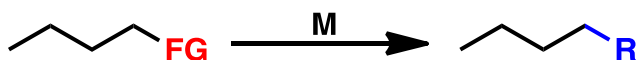
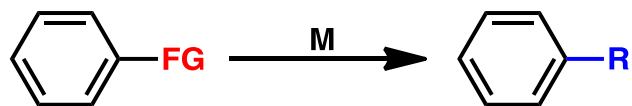
4. Ru, Ni catalyst

5. Summary

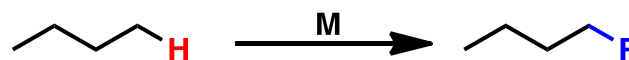
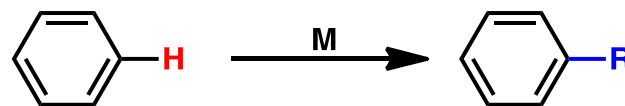
6. Acknowledgement

Introduction

Traditional approach:



CH activation approach:



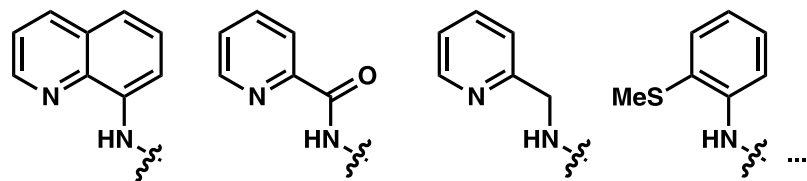
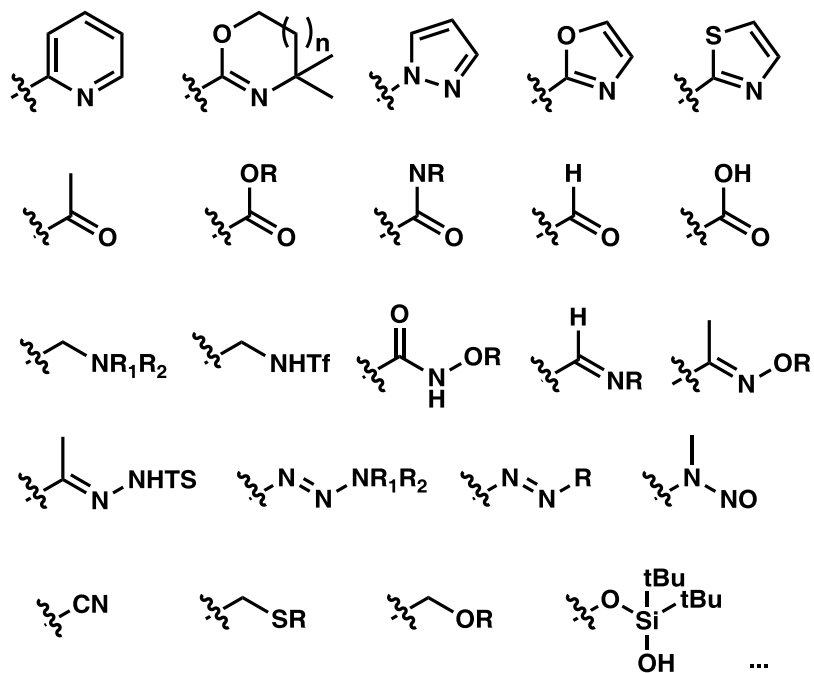
Challenges:

- ✓ *Reactivity: C-H bond is not a traditionally reactive bond (i.e. $pK_a > 30-35$)*
- ✓ *Selectivity is a large issue due to the ubiquitous presence of C-H bonds in all organic molecules*

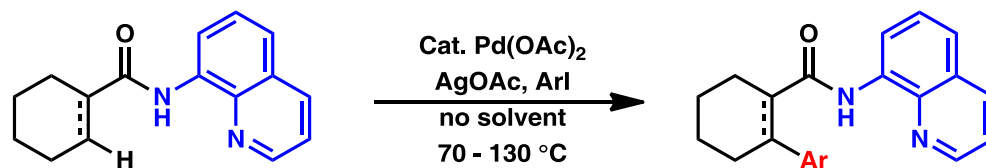
Directing group:

- ✓ *Direct the transition metal into **close proximity** to the C-H bond to be activated*
- ✓ *Higher effective concentration of the catalyst at the site of interest*
- ✓ *High levels of regioselectivity and increased reactivity*

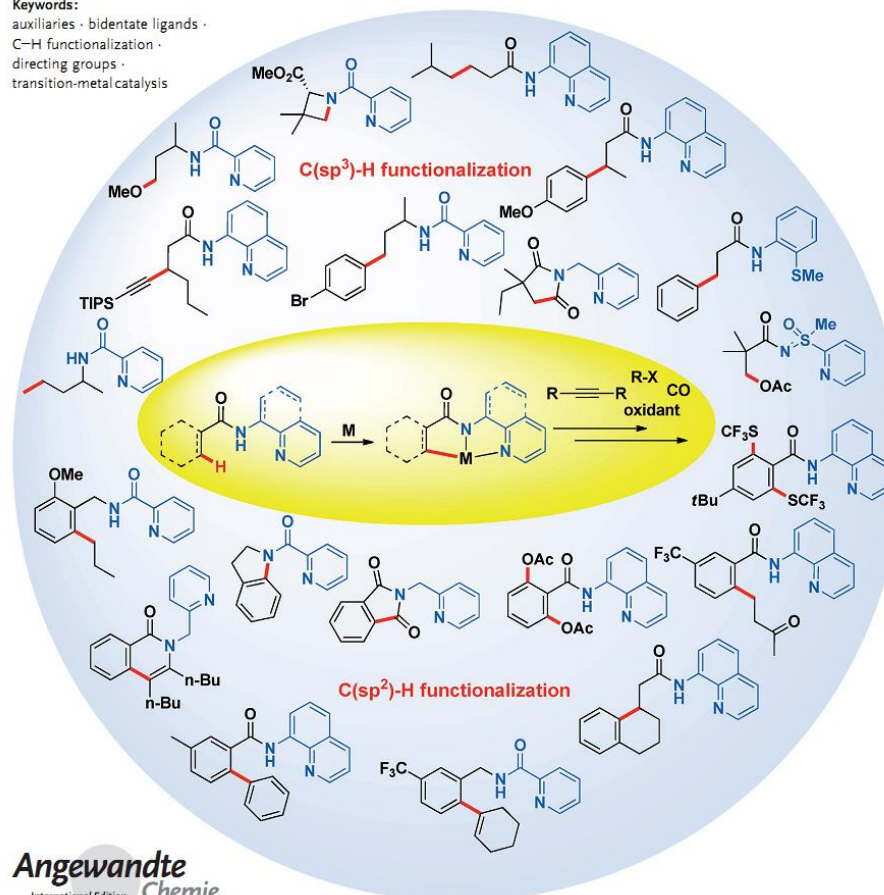
Directing group



Sp³ C-H activation



Keywords:
auxiliaries · bidentate ligands ·
C-H functionalization ·
directing groups ·
transition-metal catalysis



Contents:

1. Introduction

2. Pd catalyst

3. Cu catalyst

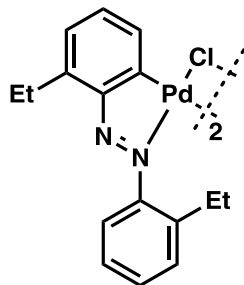
4. Ru, Ni catalyst

5. Acknowledgement

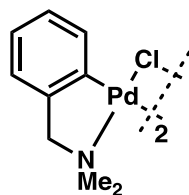
Pd catalysis



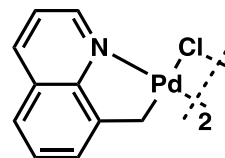
Some pioneering examples of Pd palladacycles from CH activation



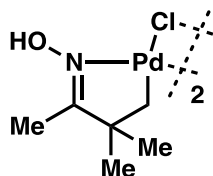
Cope, 1965



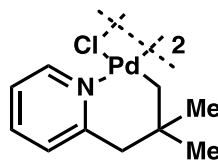
Cope, 1968



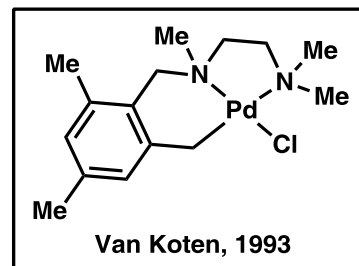
Hartwell, 1970



Shaw, 1965



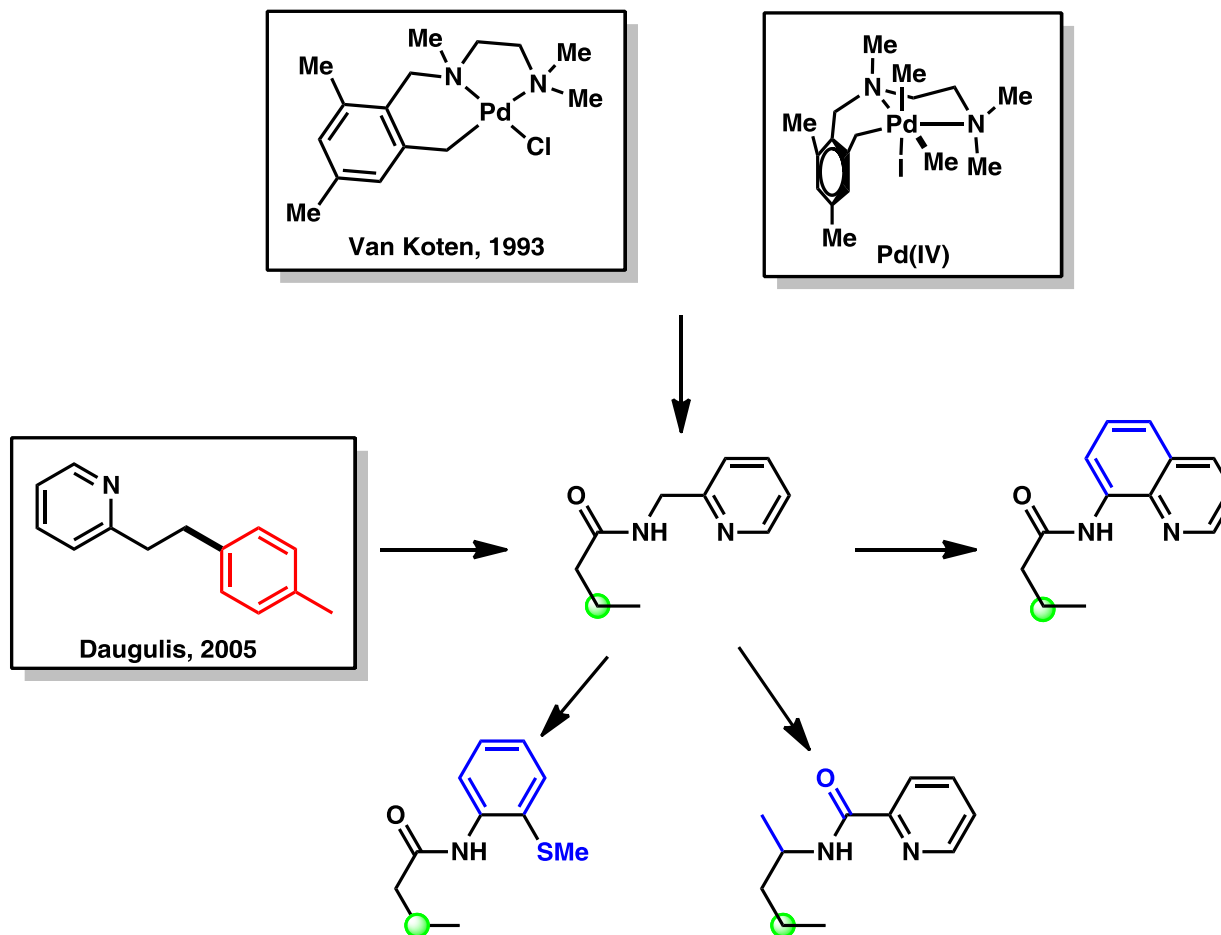
Hiraki, 1983



Van Koten, 1993

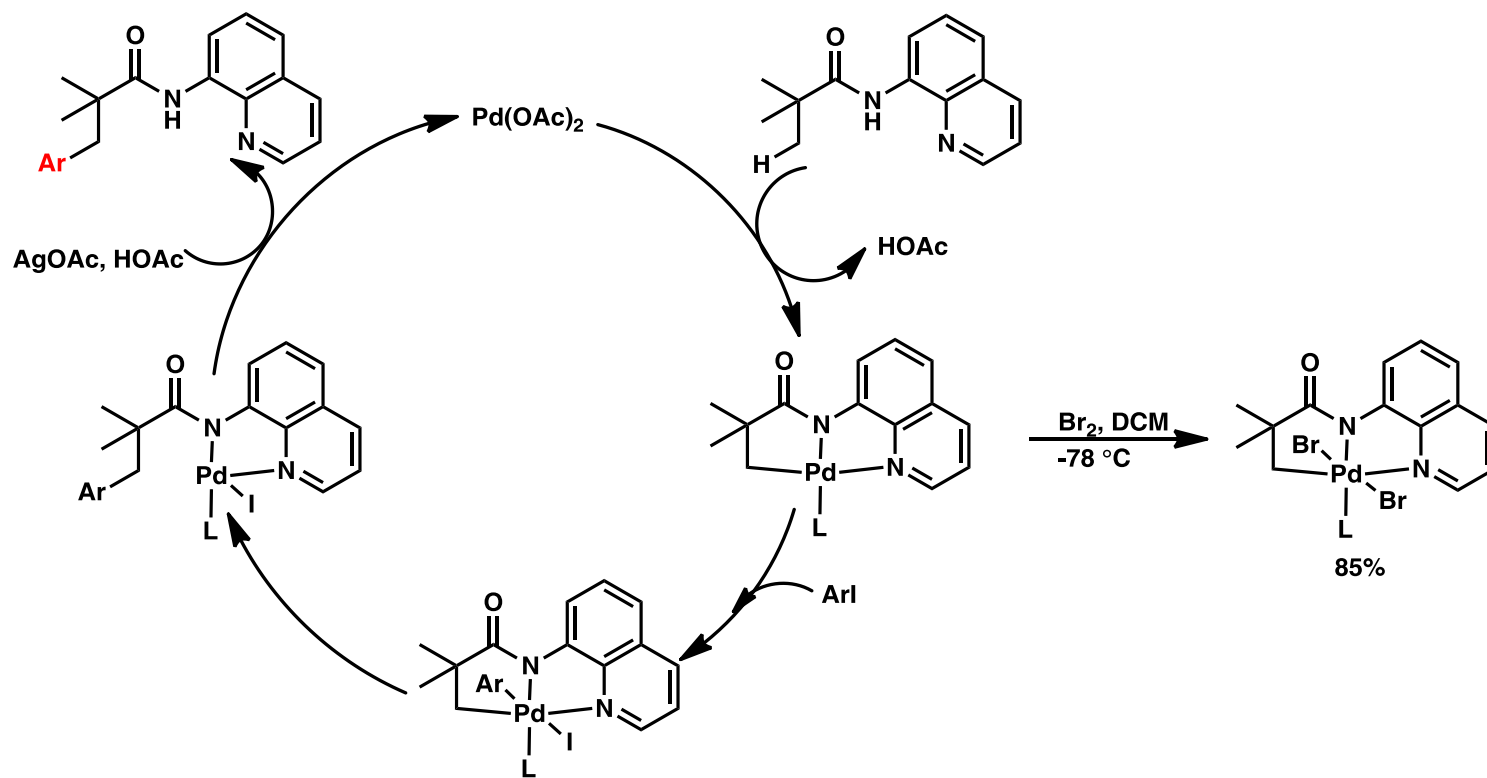
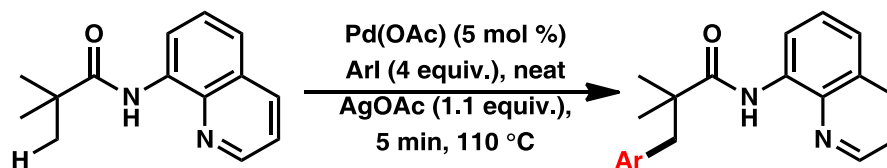
- [1] Cope, *J. Am. Chem. Soc.* **1965**, 87, 3272
- [2] Cope, *J. Am. Chem. Soc.* **1968**, 90, 909
- [3] Hartwell, *J. Chem. Soc. Chem. Commun.* **1970**, 912
- [4] Shaw, *J. Chem. Soc. Chem. Commun.* **1978**, 1061
- [5] Hiraki, *J. Chem. Soc. Dalton Trans.* **1983**, 897
- [6] Van Koten, *Organometallics* **1993**, 12, 1831

Development of Daugulis's directing group

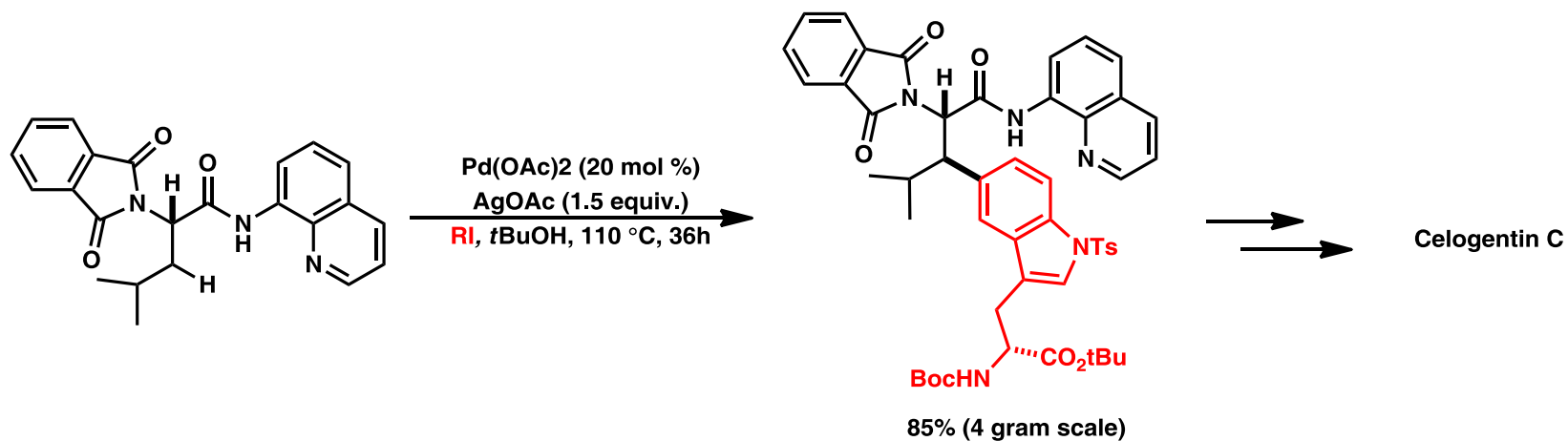
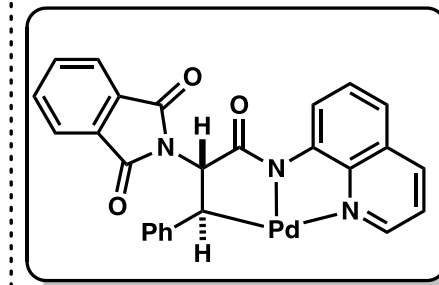
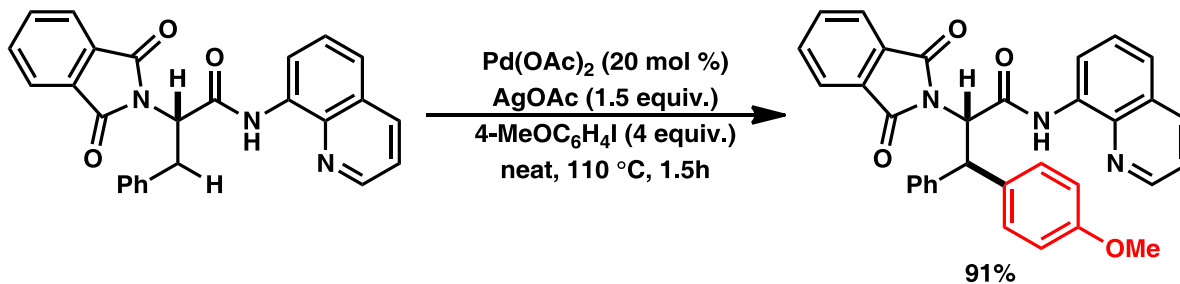


- [1] Van Koten, *Organometallics* **1993**, 12, 1831
[2] Daugulis, *J. Am. Chem. Soc.* **2005**, 127, 13154

Mechanism



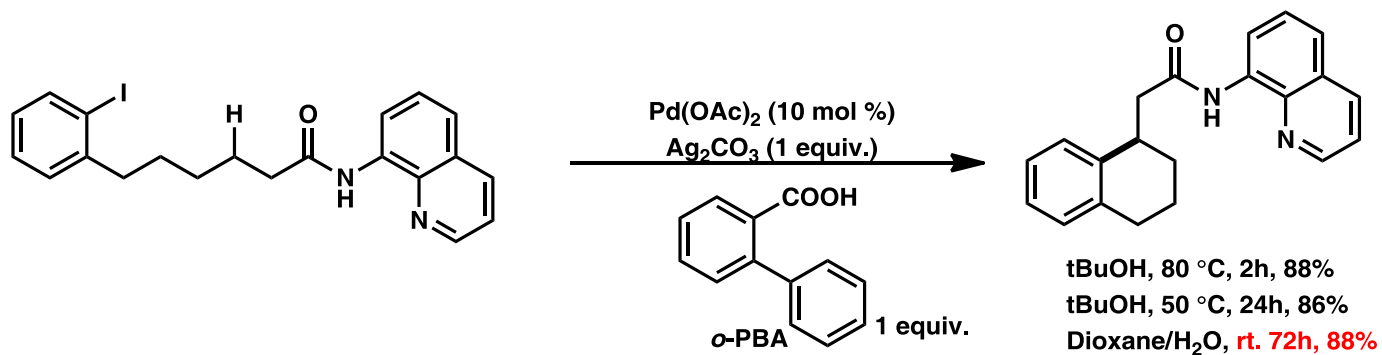
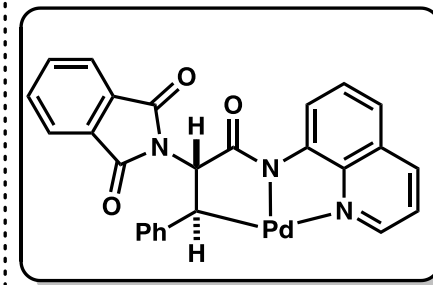
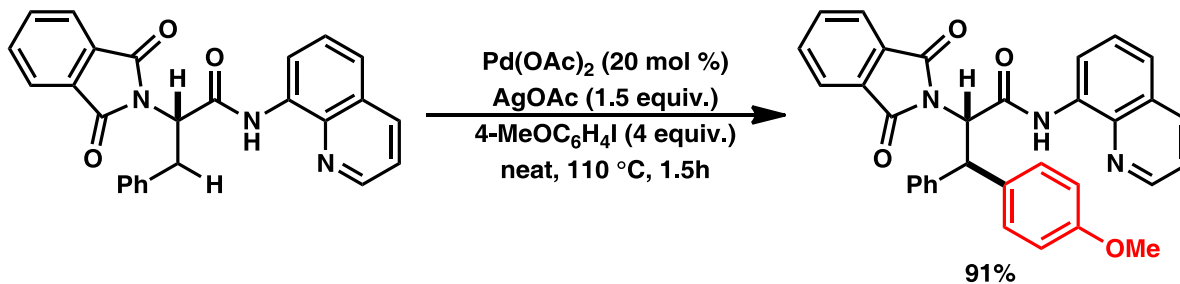
Arylation



[1] Corey, *Org. Lett.* **2006**, 8, 3391

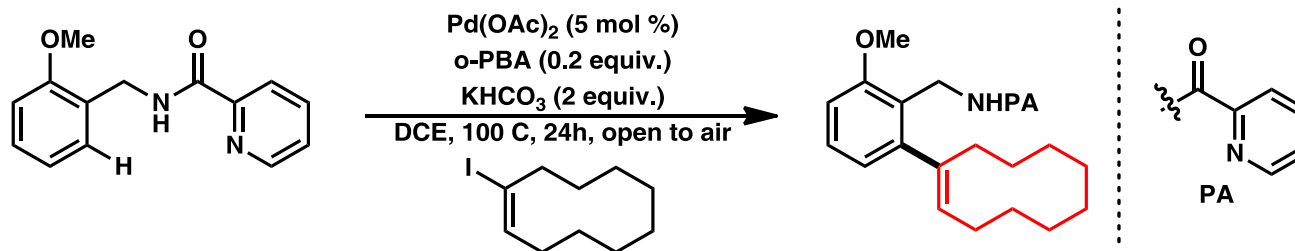
[2] Chen, *Angew. Chem. Int. Ed.* **2010**, 49, 958

Arylation

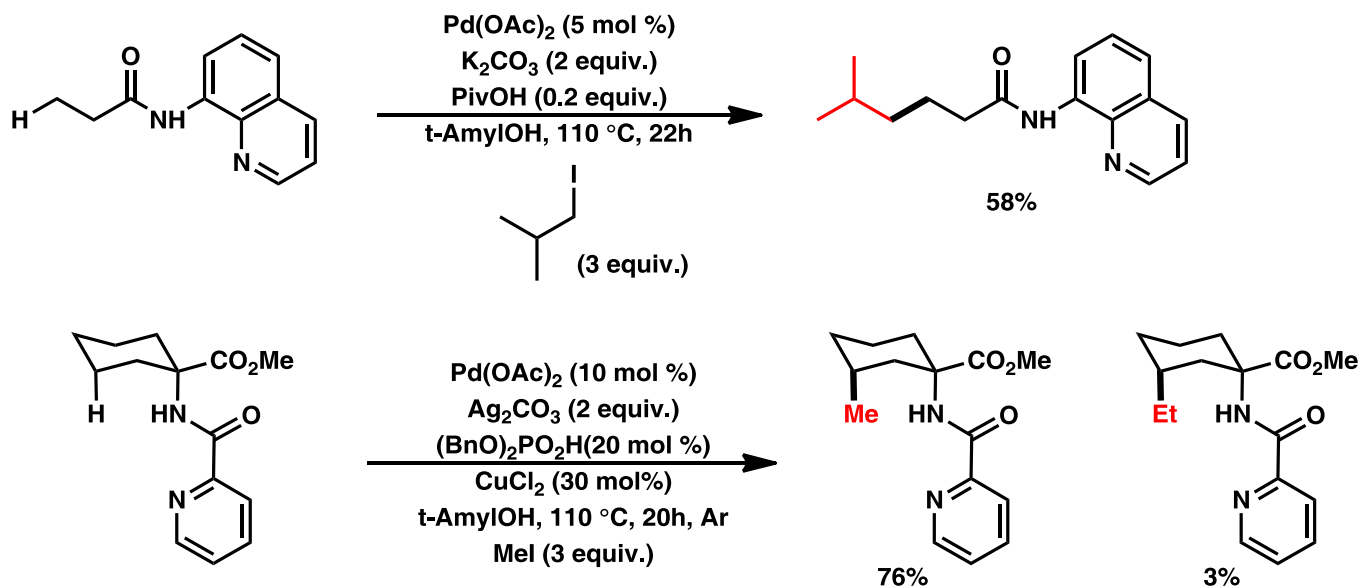


- [1] Corey, *Org. Lett.* **2006**, 8, 3391
[2] Chen, *Org. Lett.* 2010, 12, 3414

Alkenylation



Alkylation

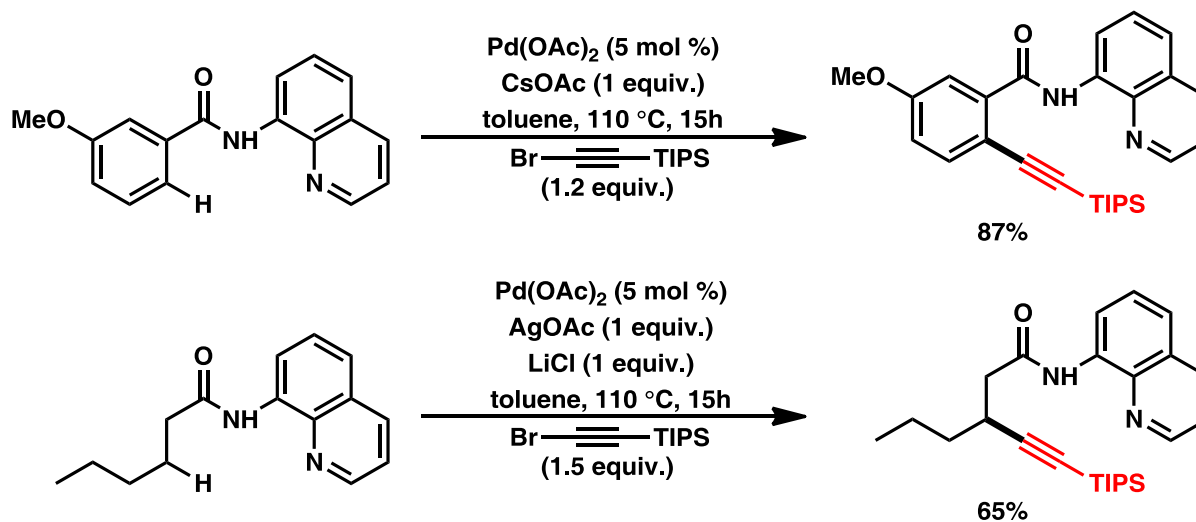


[1] Chen, *Org. Lett.* **2012**, *14*, 2948

[2] Daugulis, *J. Am. Chem. Soc.* **2010**, *132*, 3965

[3] Chen, *J. Am. Chem. Soc.* **2013**, *135*, 2124.

Alkynylation

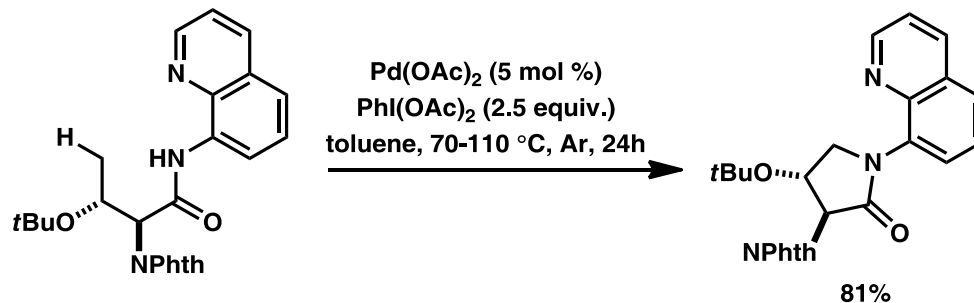
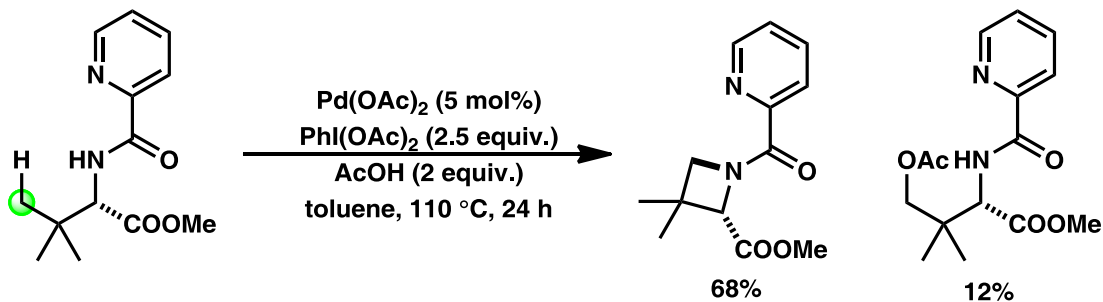
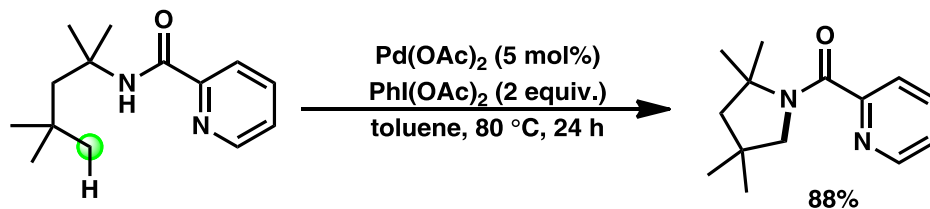


[1] Chatani, *Org. Lett.* **2012**, *14*, 354

[2] Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 12984.



Formation of C-N bonds



[1] Daugulis, *J. Am. Chem. Soc.* **2012**, 134, 7

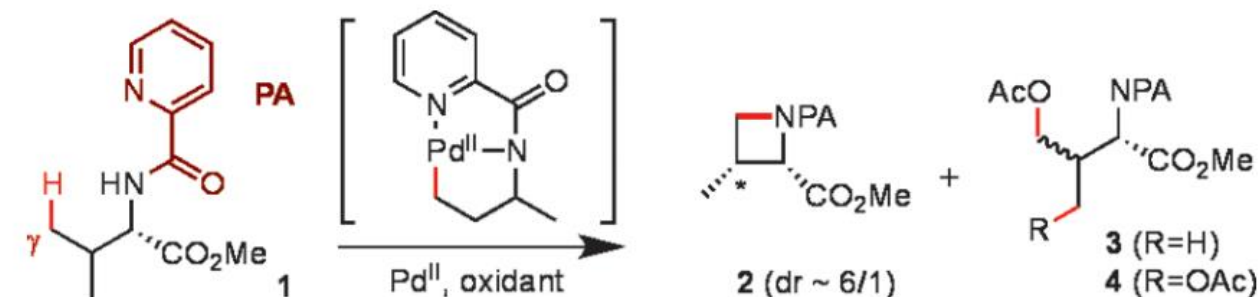
[2] Chen, *J. Am. Chem. Soc.* **2012**, 134, 3

[3] Chen, *Angew. Chem. Int. Ed.* **2013**, 52, 11124

Formation of C-N bonds- Bystanding oxidant

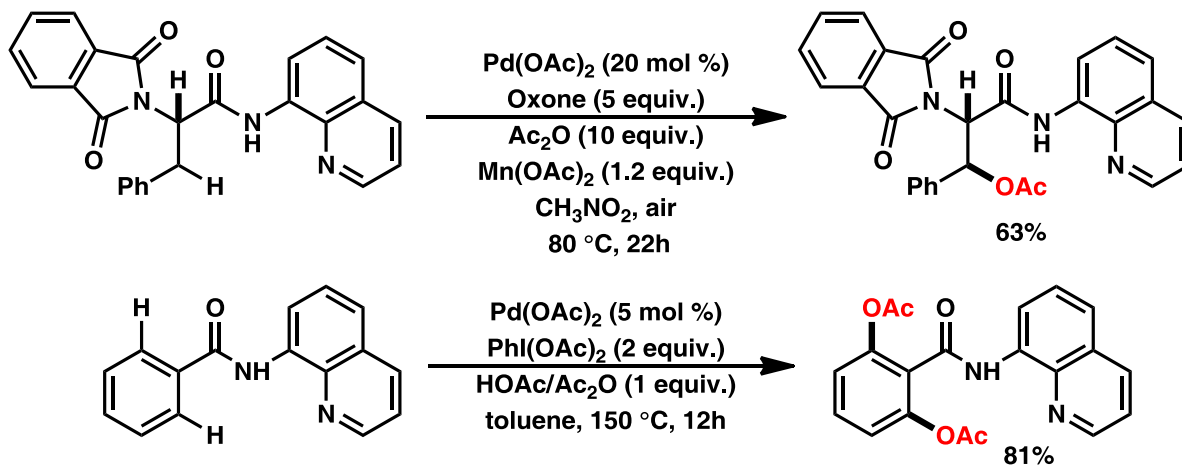


Table 1. Pd-Catalyzed Intramolecular Amination of γ -C(sp³)-H Bonds^a



entry	catalysis (mol%)	additive (equiv)	solvent /atmosphere ^b	temp (°C)	yield (%) ^c 2 + 3/4	
1	Pd(OAc) ₂ (10)	AgOAc (2)	Toluene/Air	110	<2%	<2%
2	Pd(OAc) ₂ (10)	BQ (2)	Toluene/Air	110	<2%	<2%
3	Pd(OAc) ₂ (10)	Ce(SO ₄) ₂ (2)	Toluene/Air	110	<2%	<2%
4	Pd(OAc) ₂ (10)	K ₂ S ₂ O ₈ (2)	Toluene/Air	110	<2%	<2%
5	Pd(OAc) ₂ (10)	NIS (2)	Toluene/Air	110	<2%	<2%
6	Pd(OAc) ₂ (10)	F ⁺ (2) ^d	Toluene/Air	110	<2%	<2%
7	Pd(OAc) ₂ (10)	Cu(OAc) ₂ (2)	Toluene/Air	110	<2%	<2%
8	Pd(OAc) ₂ (10)	PhI(OCOCF ₃) ₂ (2)	Toluene/Air	110	10	<2%
9	Pd(OAc) ₂ (10)	PhI(OPiv) ₂ (2)	Toluene/Ar	110	56	2/5
10	Pd(OAc) ₂ (10)	PhI(OAc) ₂ (2)	Toluene/Air	110	71	8/7

Formation of C-O bond



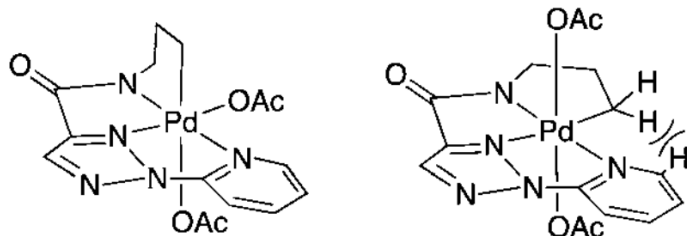
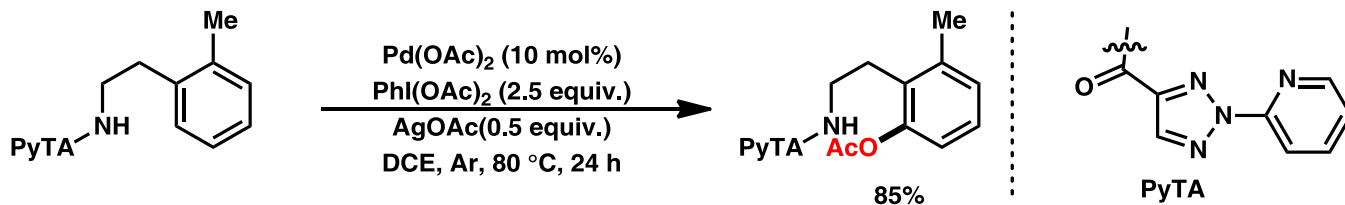
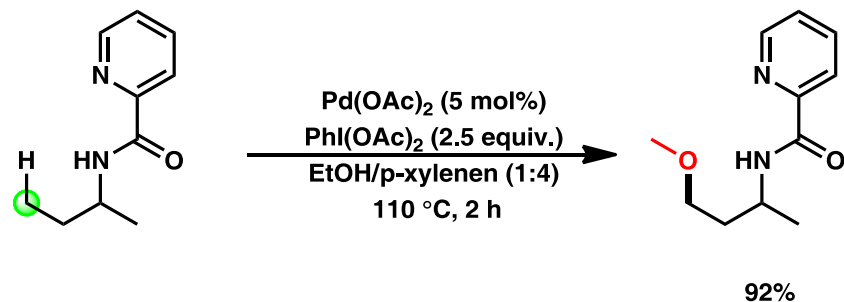
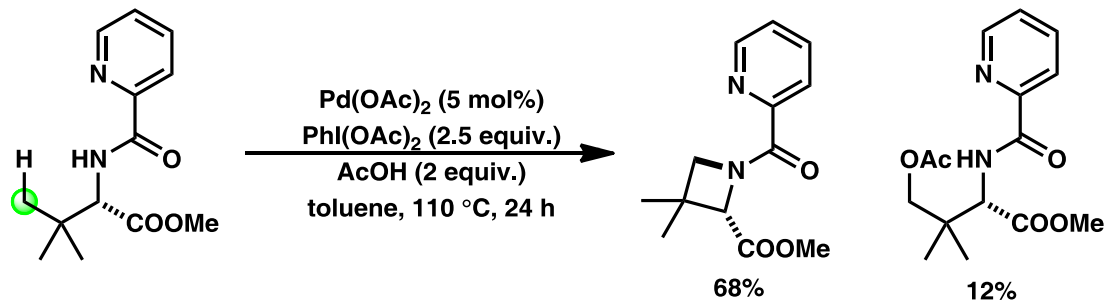
entry	pyridine	product	time (h)	isolated yield (%)
1	 (1a)	 (2b)	6	77
2	 (1b)	n.r. ^b	6	-

[1] Corey, *Org. Lett.* **2006**, *8*, 3391

[2] Liang, *Org. Lett.* **2009**, *11*, 5726

[3] Sahoo, *Org. Lett.* **2012**, *14*, 3724

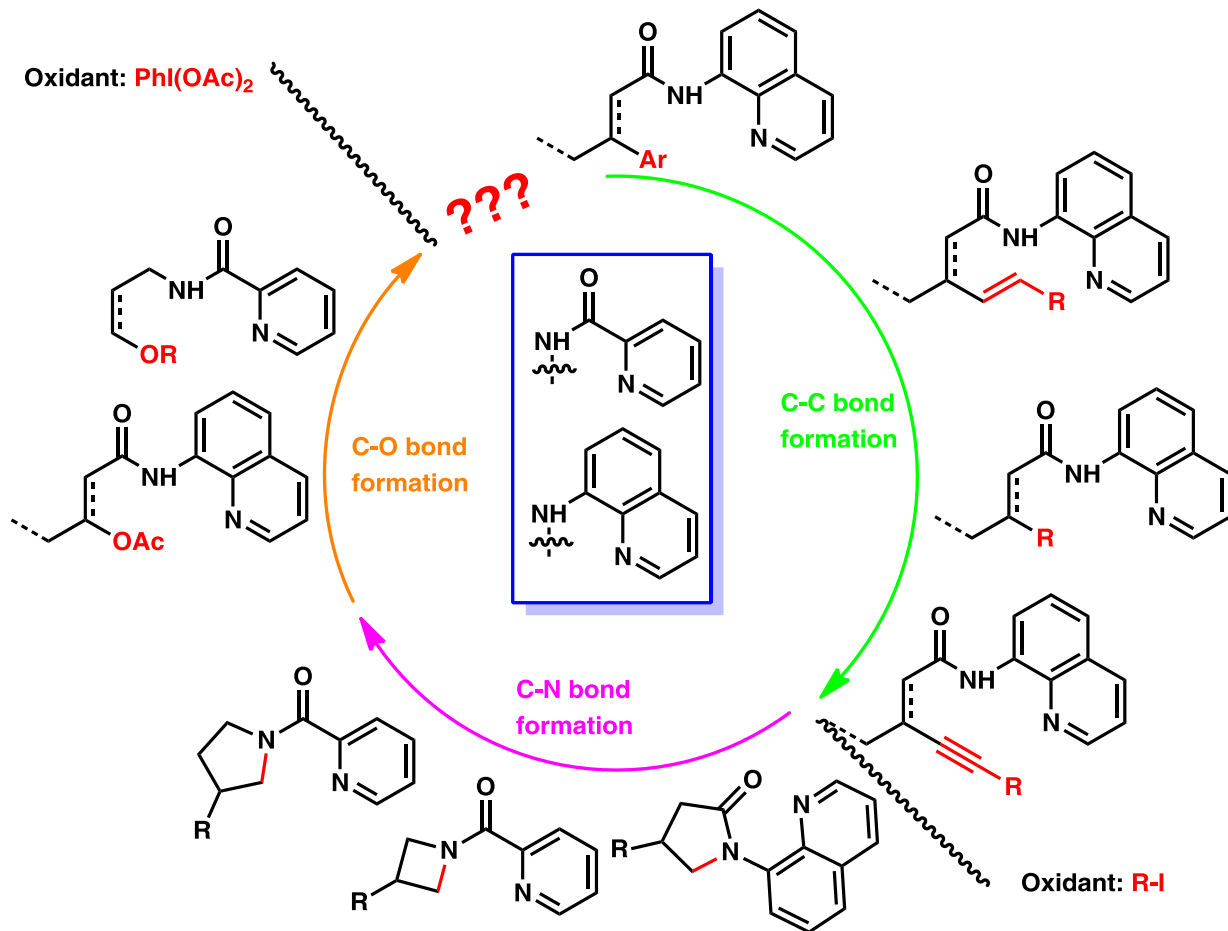
Formation of C-O bond



[1] Chen, *J. Am. Chem. Soc.* **2012**, *134*, 7313

[2] Shi, *Chem. Sci.* **2013**, *4*, 3712

Summary



Contents:

1. Introduction

2. Pd catalyst

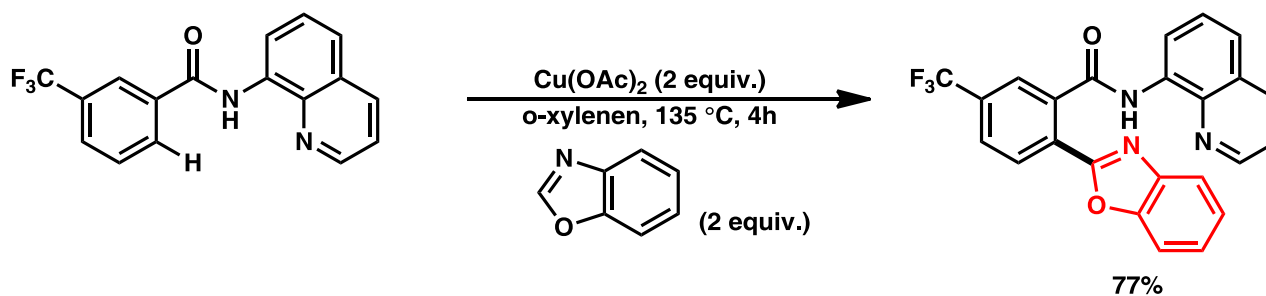
3. Cu catalyst

4. Ru, Ni catalyst

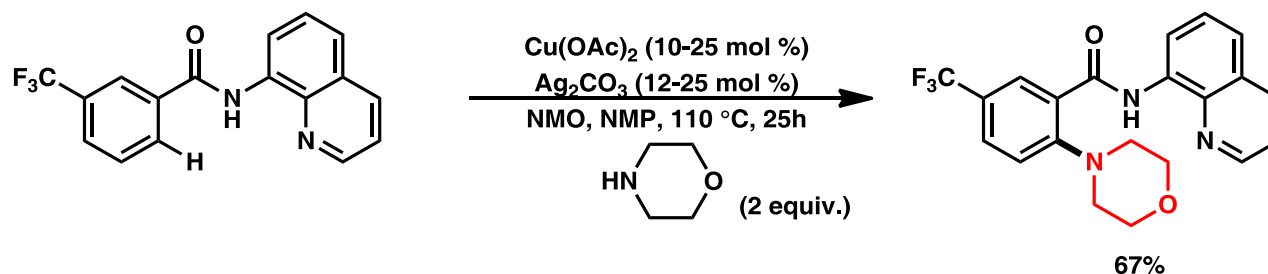
5. Acknowledgement



Arylation: C-C formation



C-N formation

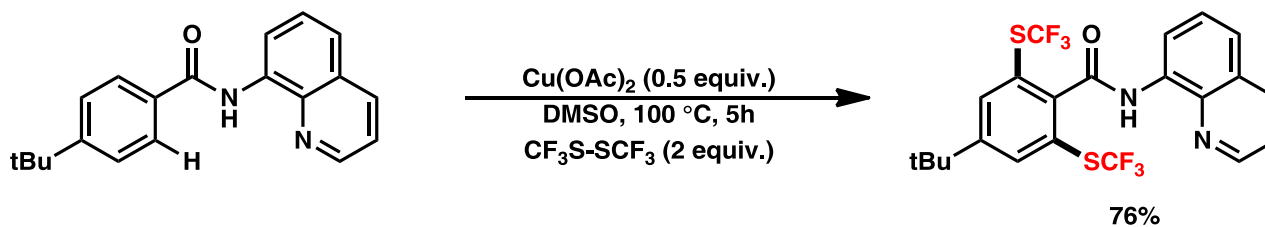


[1] Miura, *Angew. Chem. Int. Ed.* **2013**, 52, 4457

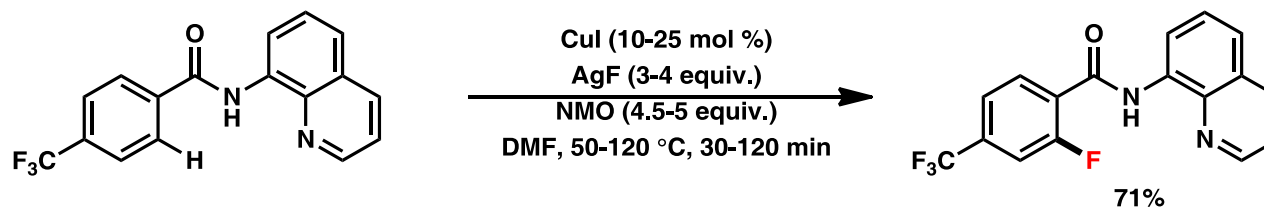
[2] Daugulis, *Angew. Chem. Int. Ed.* **2013**, 52, 6043



C-S bond formation



C-F bond formation



[1] Daugulis, *J. Am. Chem. Soc.* **2012**, *134*, 18237

[2] Daugulis, *J. Am. Chem. Soc.* **2013**, *135*, 9342

Contents:

1. Introduction

2. Pd catalyst

3. Cu catalyst

4. Ru, Ni catalyst

5. Acknowledgement

Ru and Ni catalyst

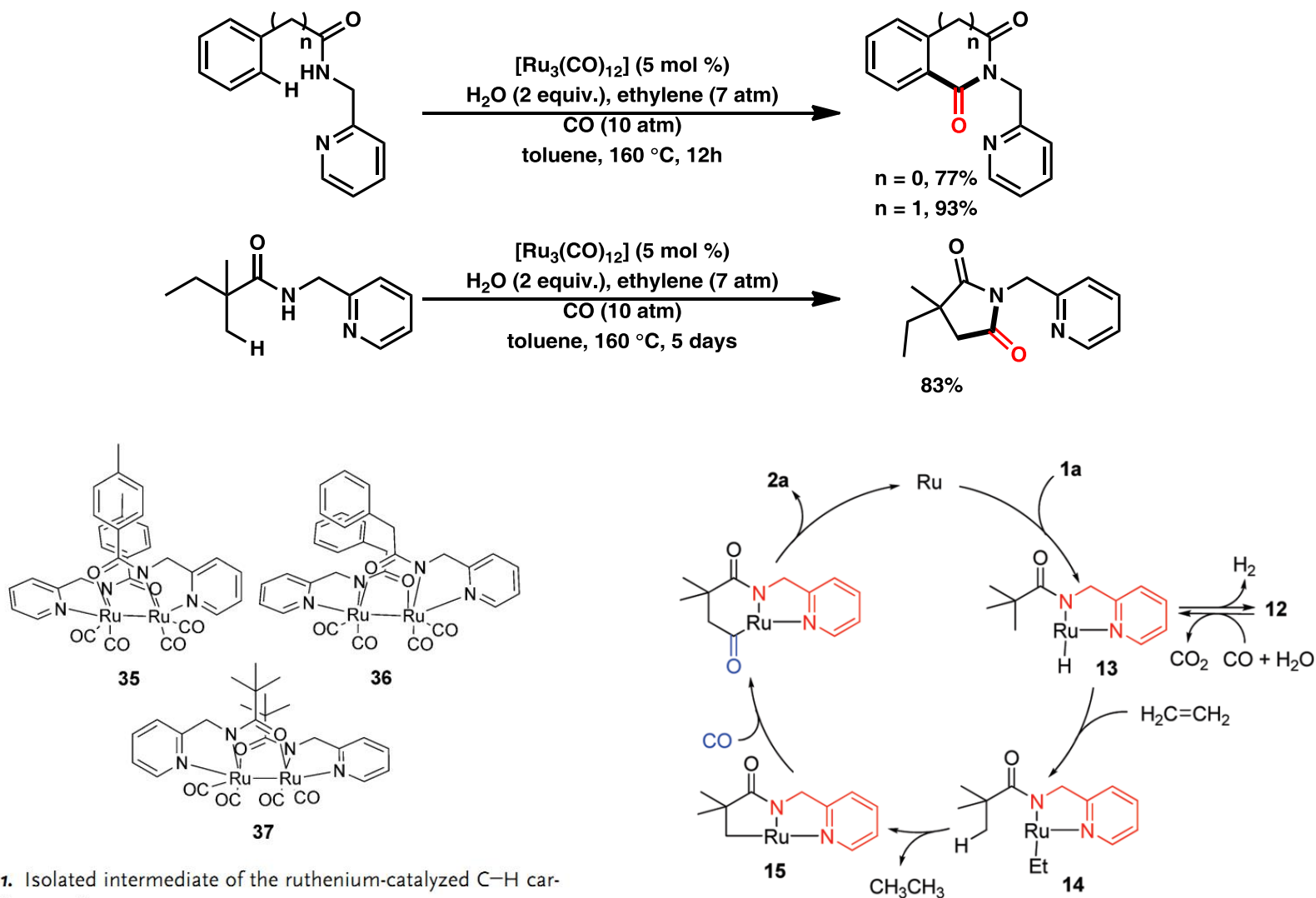
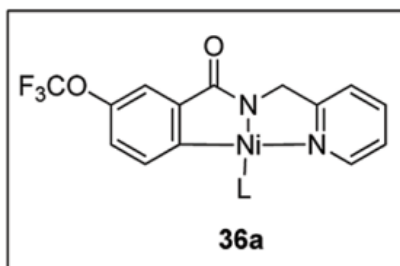
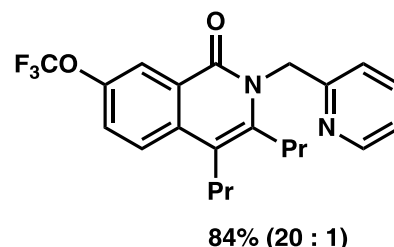
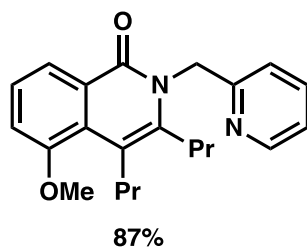
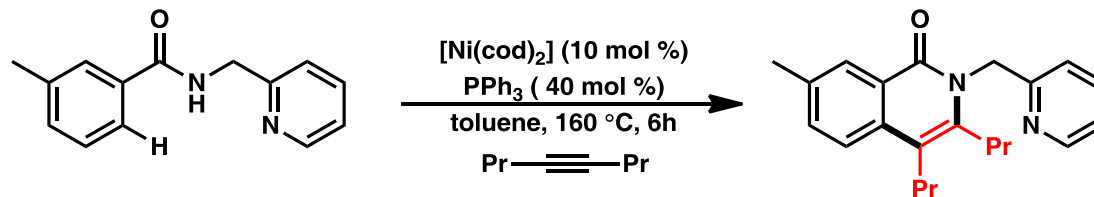


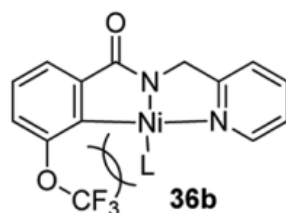
Figure 1. Isolated intermediate of the ruthenium-catalyzed C–H carbonylation reaction.

- [1] Chatani, *J. Am. Chem. Soc.* **2009**, *131*, 6898
[2] Chatani, *J. Am. Chem. Soc.* **2011**, *133*, 8070

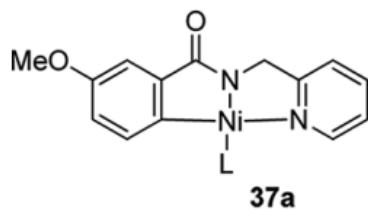
Ru and Ni catalyst



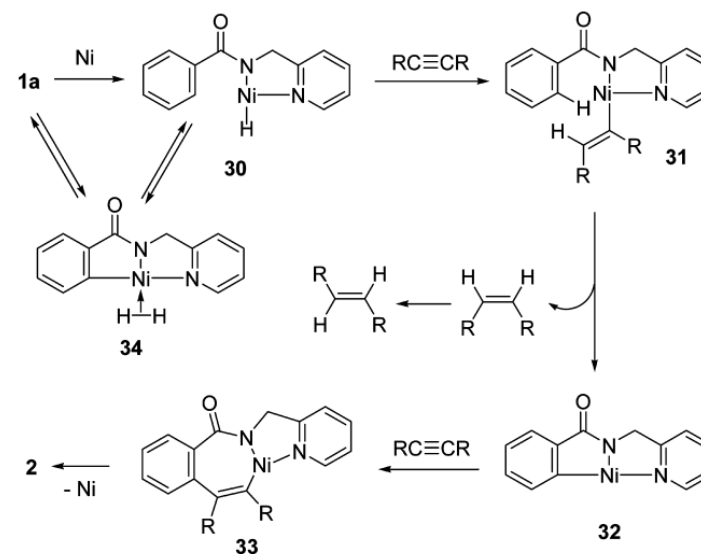
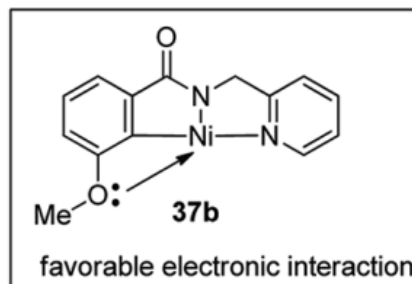
vs



unfavorable steric interaction



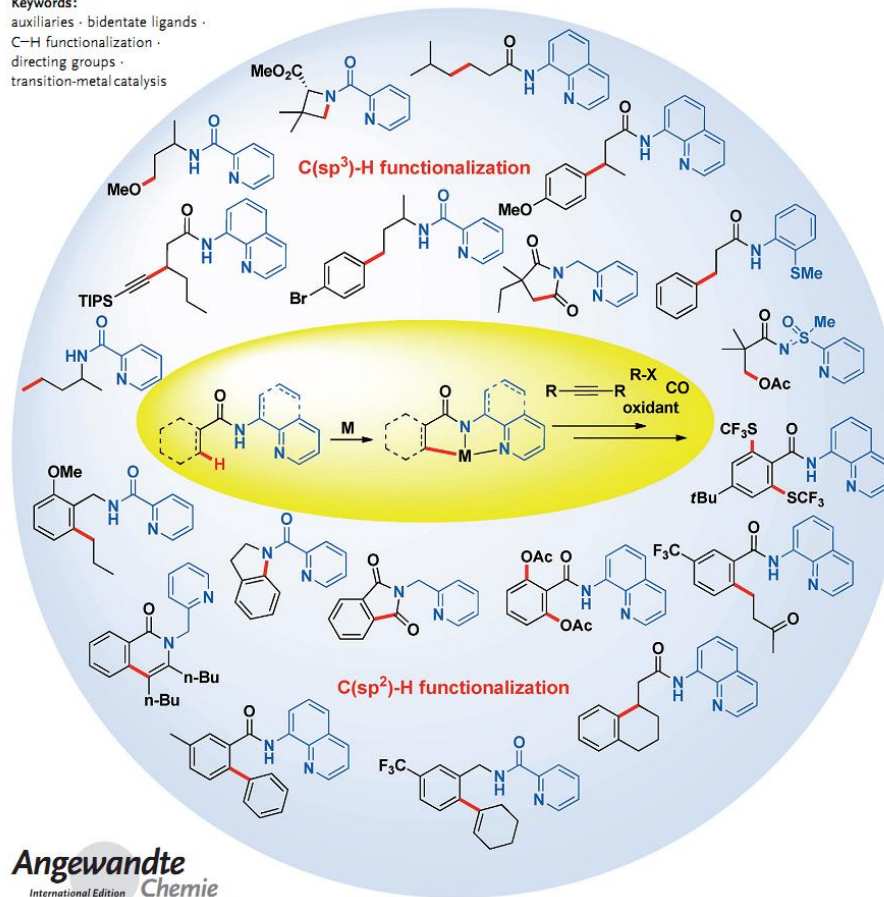
vs



Summary

Keywords:

auxiliaries · bidentate ligands ·
C-H functionalization ·
directing groups ·
transition-metal catalysis



- Character: chelating ability, rigid backbone, relatively acidic N-H bond
- Application in the sp³ C-H activation (amino acid)
- Pd/Cu catalyst (high valent Pd/Cu chemistry, narrow reaction type)
- Opportunity: Ru, Ni, Fe...

- Thank you!

