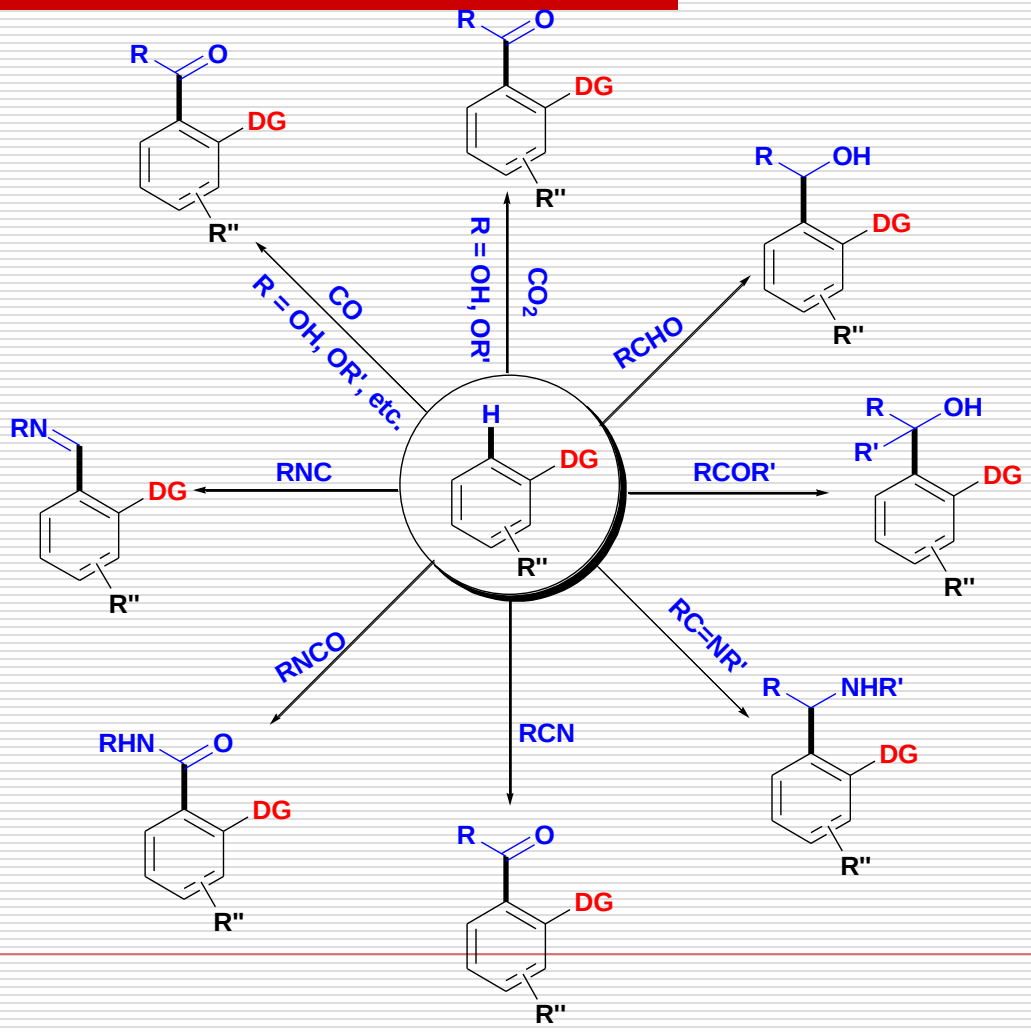
Transition-Metal-Catalyzed Additions of C-H bond to C-X (X = N, O) Multiple Bonds *via* C-H Bond Activation

Dong group, Literature report

Guobing Yan

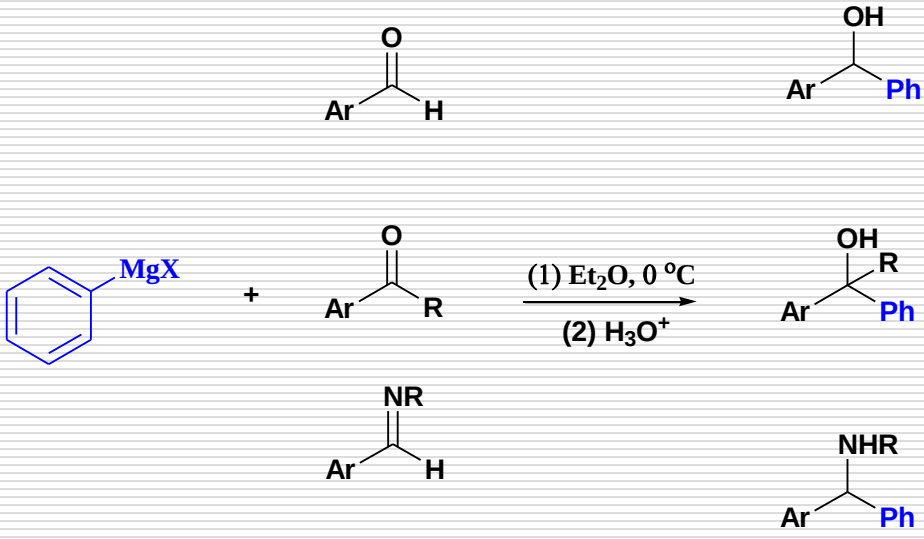
5/15/2013

Contents


R
O
DG
R''
R = OH, OR', etc.
CO
R = OH, OR'
CO2
RCHO
R
OH
DG
R''
RN
DG
R''
RNC
H
DG
R''
RCOR'
R
OH
R'
DG
R''
RNCO
RC=NR'
RHN
O
DG
R''
RCN
R
O
DG
R''
R
NHR'
DG
R''

1 Background

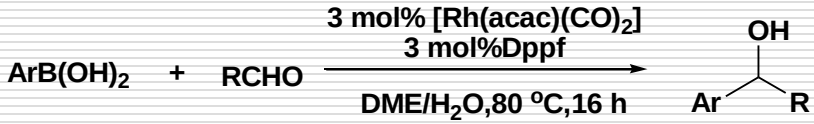
1. Nucleophilic addition of organometallic reagents to carbonyl compounds and their derivatives



Drawbacks: **(1) strict anhydrous conditions**
(2) imperfect functional group tolerance
(3) prefunctionalization of nucleophilic coupling partners
(4) unwanted formation of stoichiometric salt waste

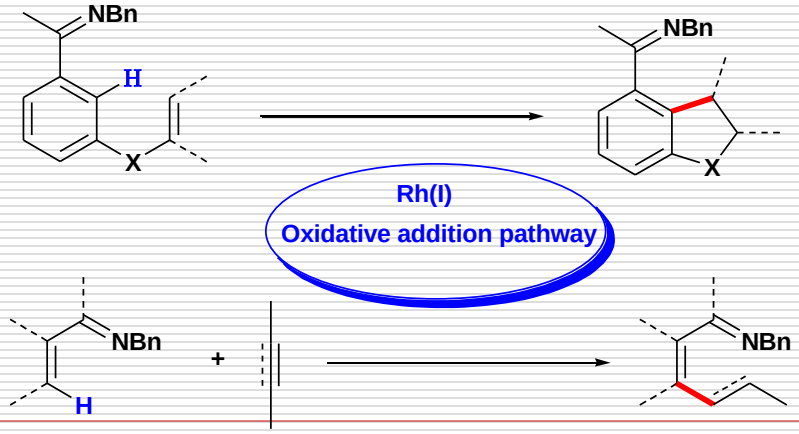
1 Background

2.Rhodium-catalyzed 1,2-addition reactions of organoboronic acids to aldehydes



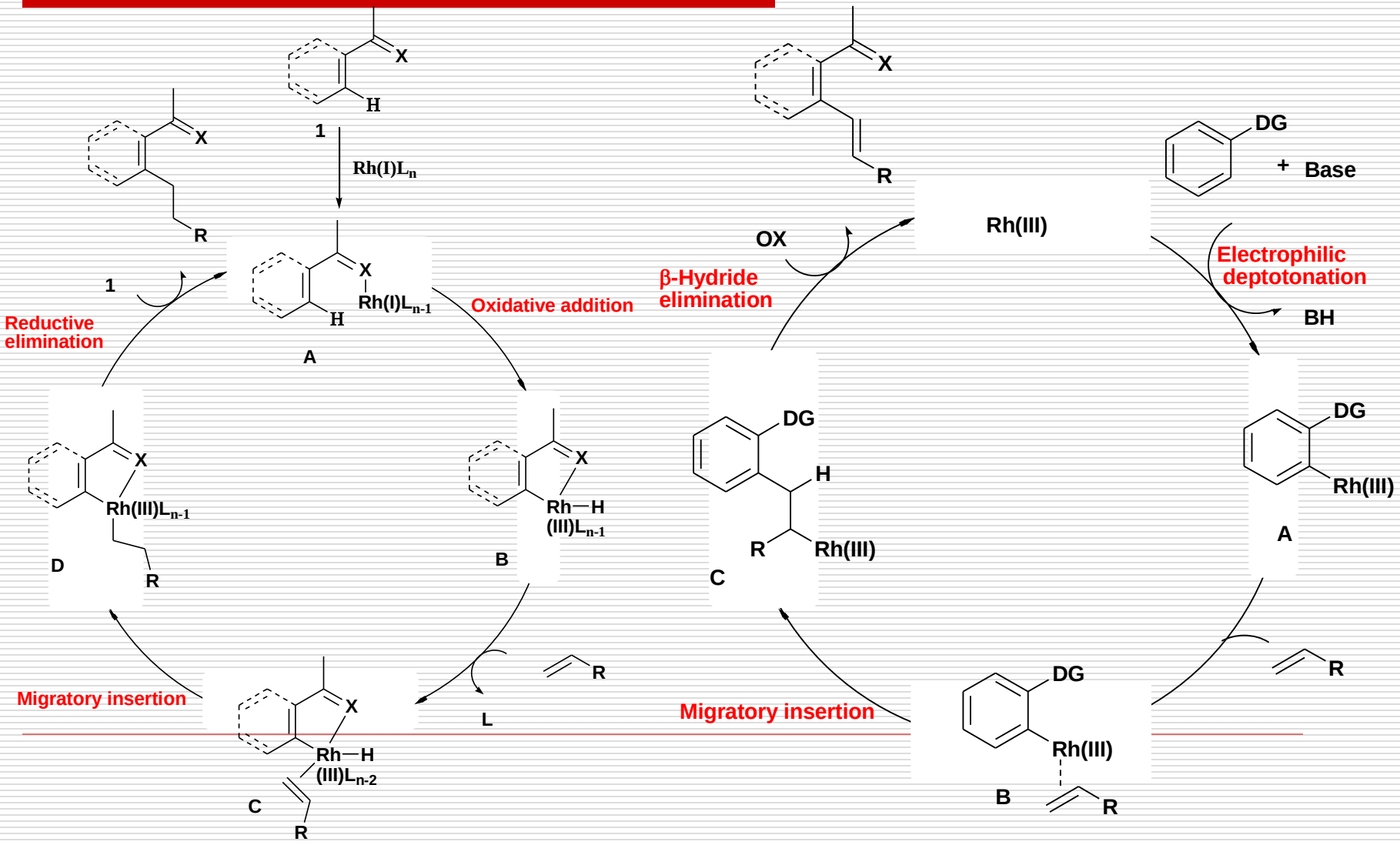
M. Sakai, M. Ueda, N. Miyaura, *Angew. Chem., Int. Ed.* 1998, **37**, 3279-3281.

3.Transition metal-catalyzed addition reactions of C-H bond to alkene and alkyne

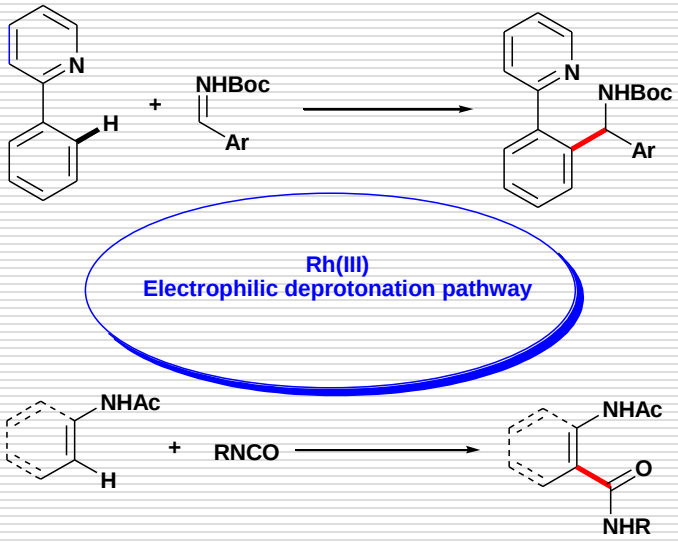


D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* 2012, **45**, 814-825

1 Background

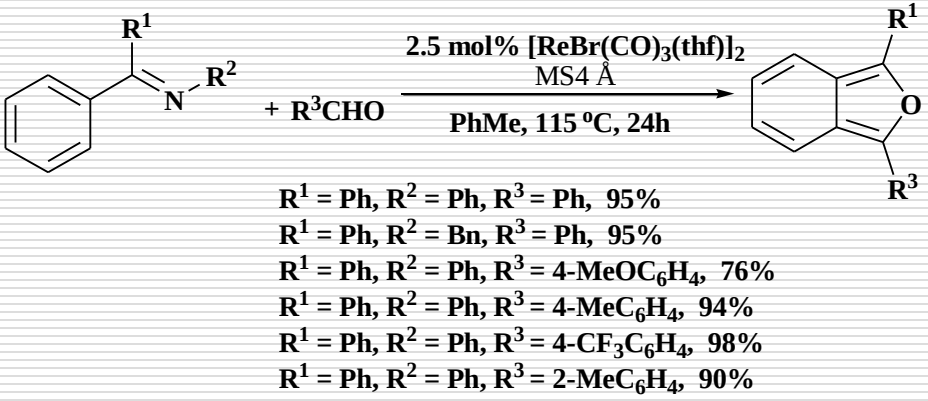


1 Background

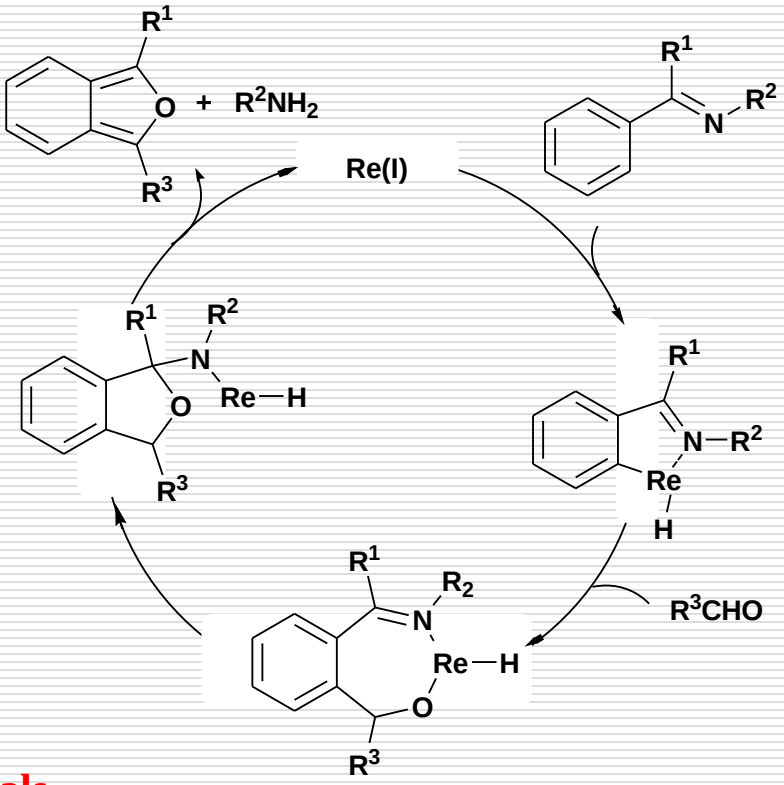


D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* 2012, **45**, 814-825

2 Addition of C-H bonds to aldehydes



R^1 = Ph, R^2 = Ph, R^3 = Ph, 95%
R^1 = Ph, R^2 = Bn, R^3 = Ph, 95%
R^1 = Ph, R^2 = Ph, R^3 = 4-$MeOC_6H_4$, 76%
R^1 = Ph, R^2 = Ph, R^3 = 4-MeC_6H_4, 94%
R^1 = Ph, R^2 = Ph, R^3 = 4-$CF_3C_6H_4$, 98%
R^1 = Ph, R^2 = Ph, R^3 = 2-MeC_6H_4, 90%

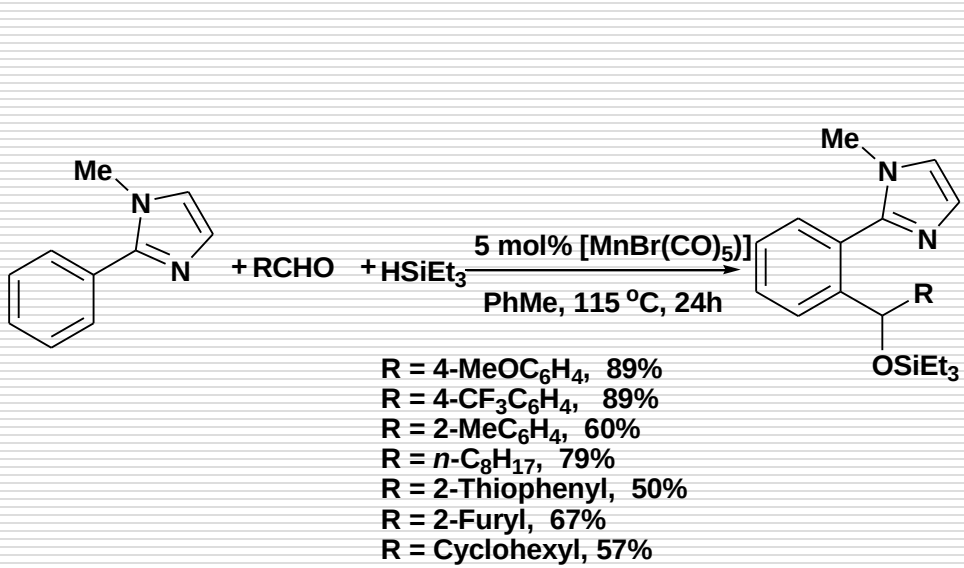


Rhenium has some properties of early and late transition metals

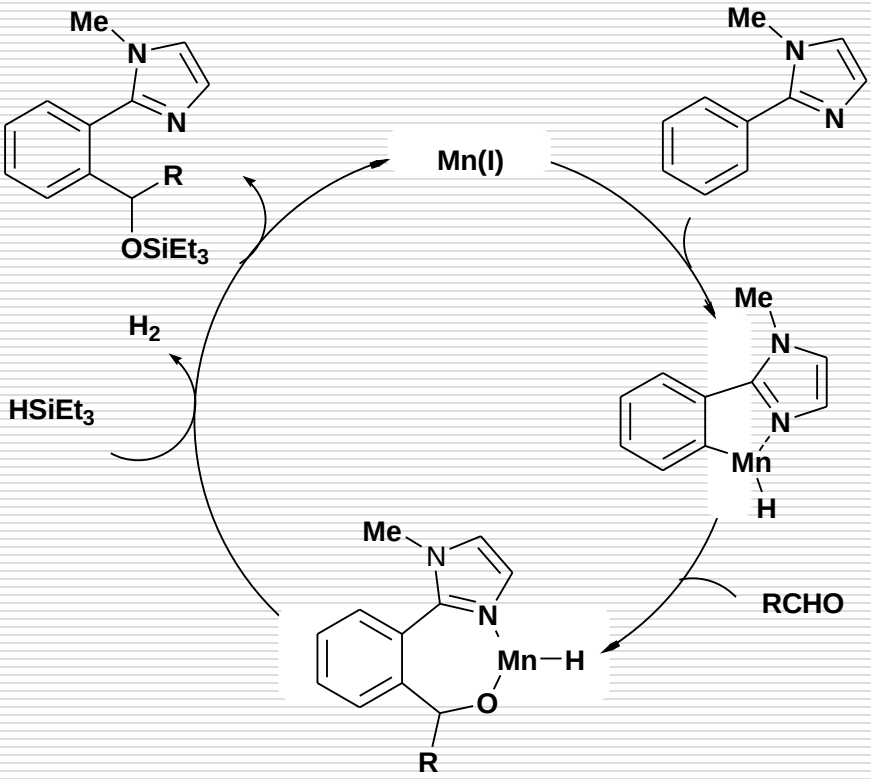
Notes: (1) carbon-rhenium bonds show nucleophilicity of early transition metals
(2) the rhenium complex can also take place reductive elimination of late transition metals

Y. Kuninobu, Y. Nishina, C. Nakagawa, K. Takai, *J. Am. Chem. Soc.* 2006, **128**, 12376-12377.

2 Addition of C-H bonds to aldehydes



R = 4-$MeOC_6H_4$, 89%
R = 4-$CF_3C_6H_4$, 89%
R = 2-MeC_6H_4, 60%
R = *n*-C_8H_{17}, 79%
R = 2-Thiophenyl, 50%
R = 2-Furyl, 67%
R = Cyclohexyl, 57%

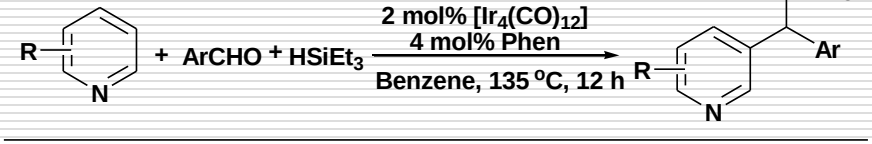


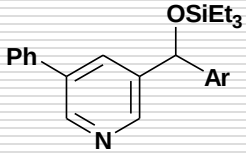
Notes: (1) polarity of the manganese–carbon bond

(2) asymmetric transformation using an aromatic compound with a chiral substituent

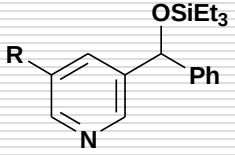
Y. Kuninobu, Y. Nishina, T. Takeuchi, K. Takai, *Angew. Chem. Int. Ed.* 2007, **46**, 6518-6520.

2 Addition of C-H bonds to aldehydes

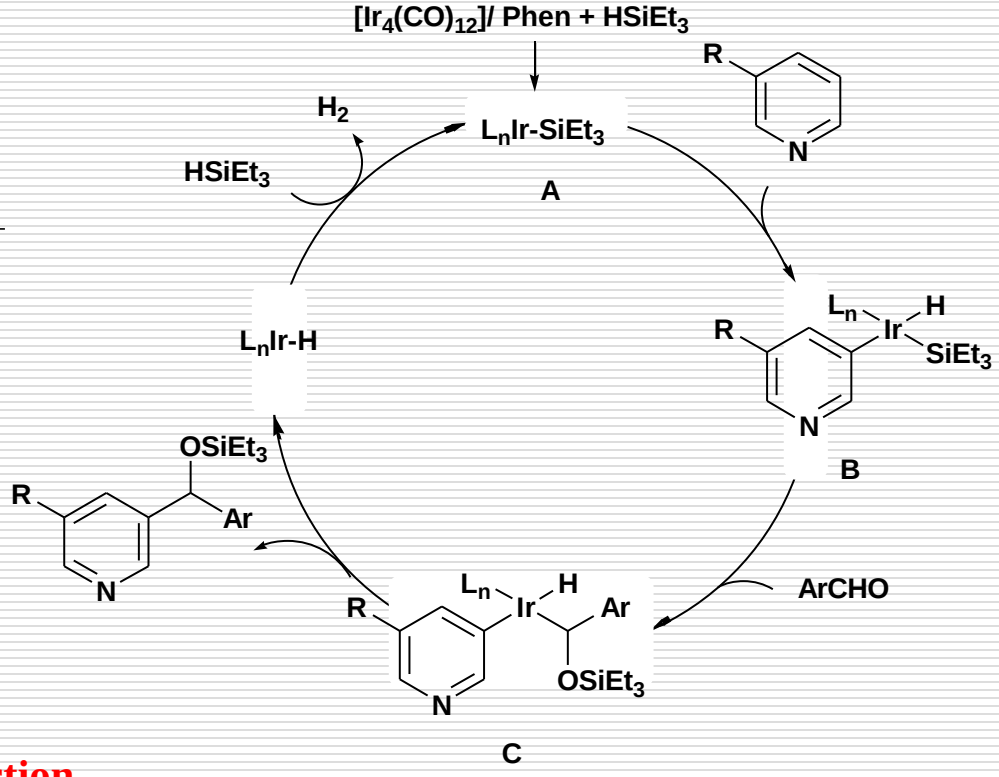




Ar = C_6H_5, 73%
Ar = 2-MeC_6H_4, 78%
Ar = 4-$MeOC_6H_4$, 57%
Ar = 4-FC_6H_4, 74%
Ar = 4-ClC_6H_4, 62%
Ar = 2-Naphthyl, 72%
Ar = 2-Benzofuryl, 55%



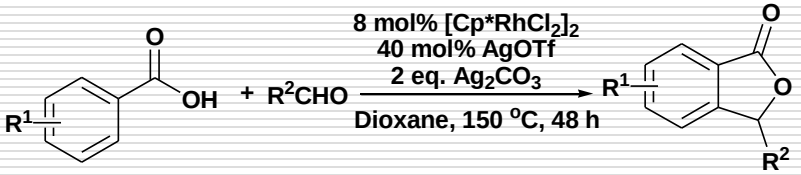
R = 4-FC_6H_4, 68%
R = 4-$MeOC_6H_4$, 66%
R = Me, 61%
R = Bn, 66%
R = OMe, 53%
R = OBn, 55%

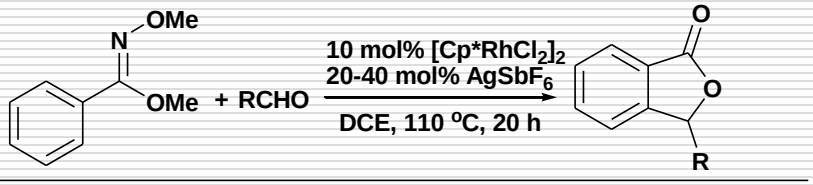


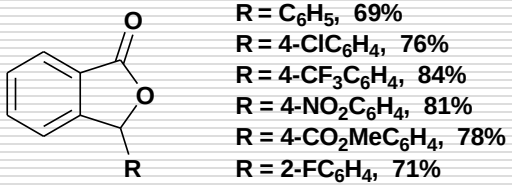
Notes: (1) trialkylsilane was essential for the reaction
(2) a silyl iridium complex might be the active catalytic intermediate
(3) unusual meta selectivity
(4) without directing group

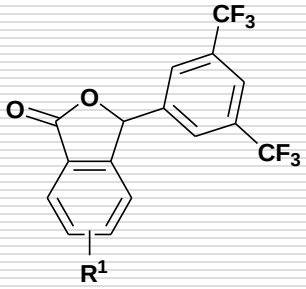
B.-J. Li, Z.-J. Shi, *Chem. Sci.* 2011, **2**, 488-493.

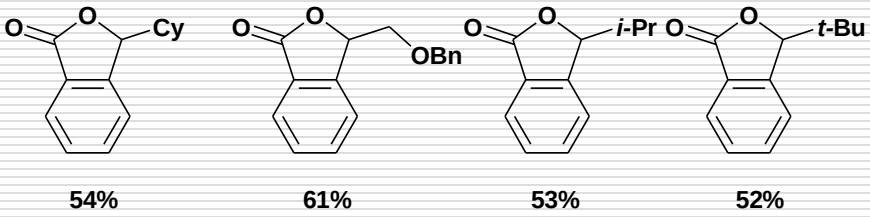
2 Addition of C-H bonds to aldehydes

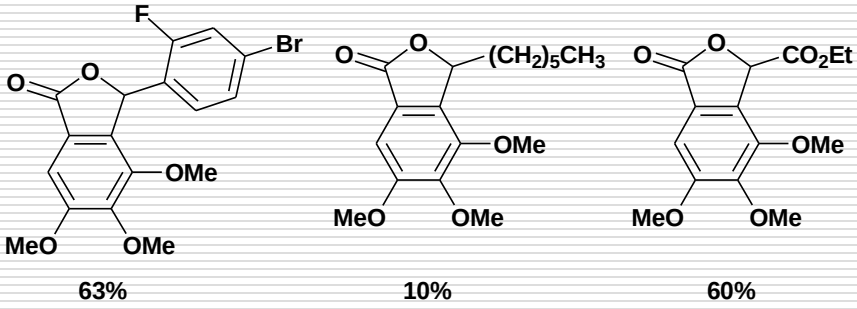










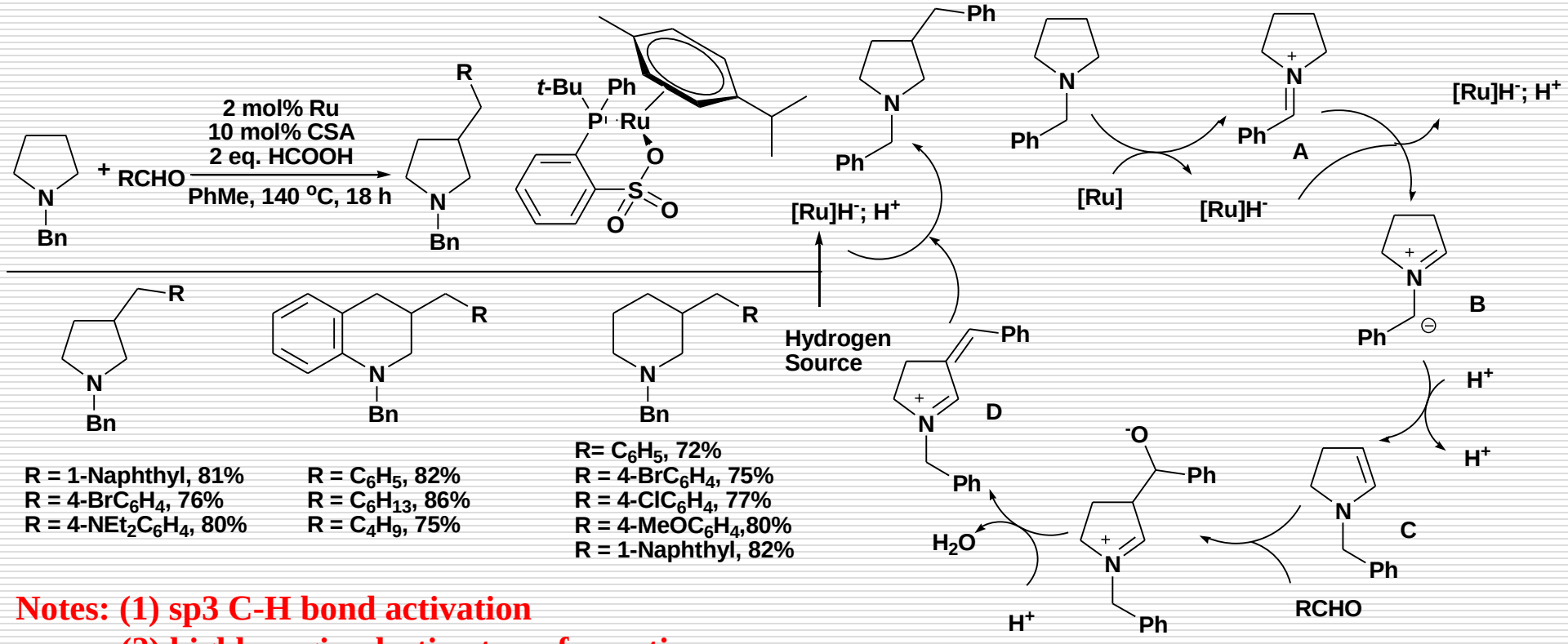


Notes：Synthesize biologically important phthalides in a single step.

Y. Lian, R. G. Bergman, J. A. Ellman, *Chem. Sci.* 2012, **3**, 3088-3092.

X. Shi, C.-J. Li, *Adv. Synth. Catal.* 2012, **354**, 2933-2938.

2 Addition of C-H bonds to aldehydes



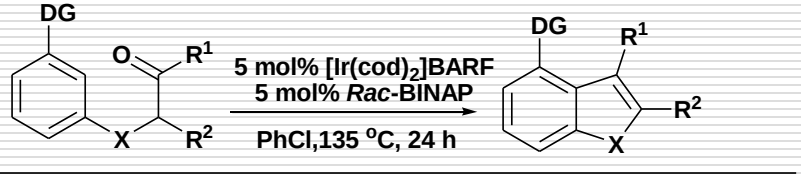
Notes: (1) sp3 C-H bond activation

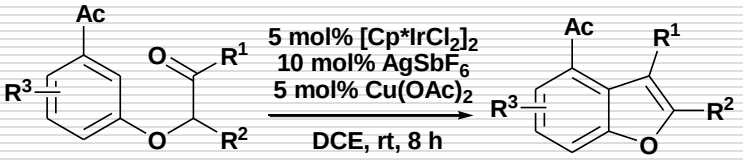
(2) highly regioselective transformation

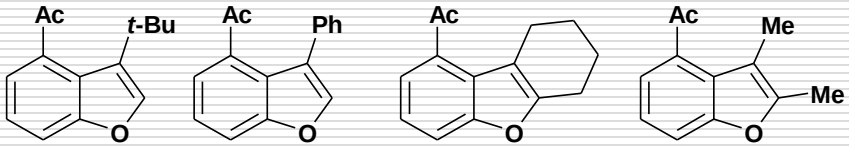
(3) camphor sulfonic acid was essential for the reaction

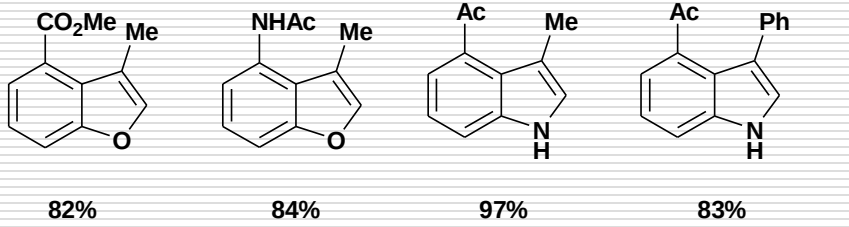
B. Sundararaju, M. Achard, G. V. M. Sharma, C. Bruneau, *J. Am. Chem. Soc.* 2011, **133**, 10340-10343.

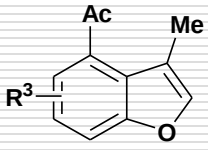
3 Addition of C-H bonds to ketones



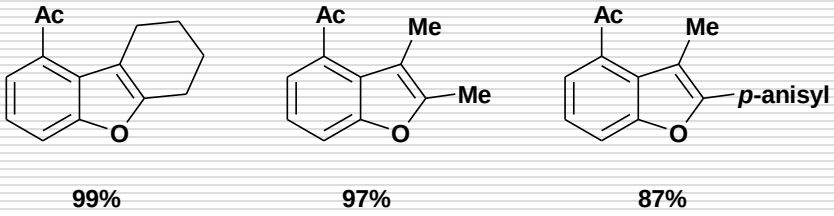








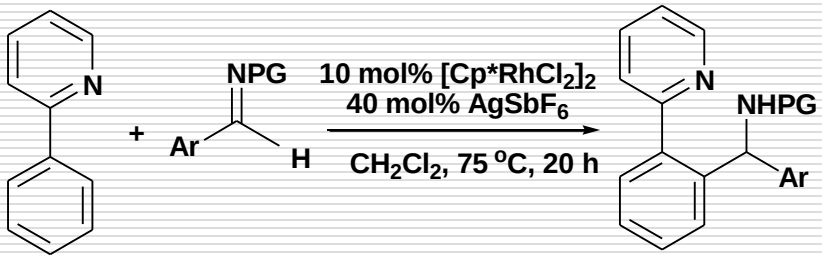
R^3 = 5-OMe, 91%
R^3 = 6-OMe, 99%
R^3 = 7-OMe, 91%
R^3 = 5-Cl, 87%
R^3 = 6-Cl, 89%
R^3 = 7-Cl, 89%
R^3 = 6-F, 77%



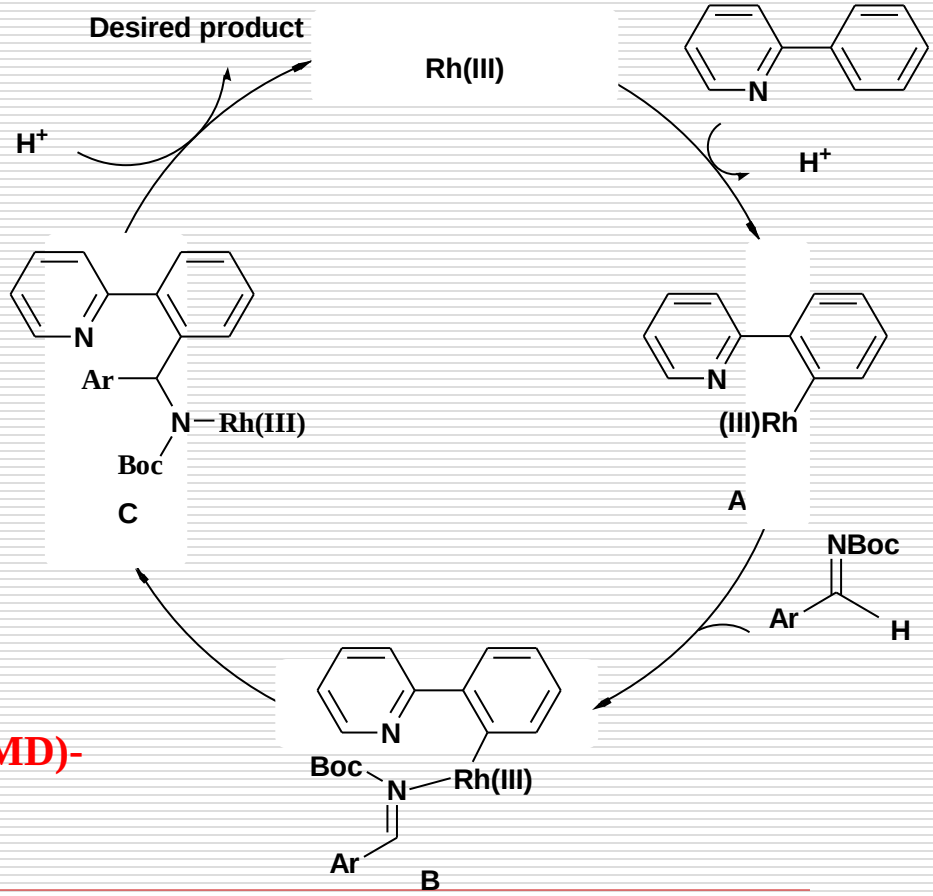
Notes: （1）Ketones are less reactive than aldehydes in this tpye addition reactions
（2）directed C-H bond cleavage or electrophilic metalation

K. Tsuchikama, Y. Hashimoto, K. Endo, T. Shibata, *Adv. Synth. Catal.* 2009, **351**, 2850-2854.
T. Shibata, Y. Hashimoto, M. Otsuka, K. Tsuchikama, K. Endo, *Synlett* 2011, **14**, 2075-2079.

4 Addition of C-H bonds to imines



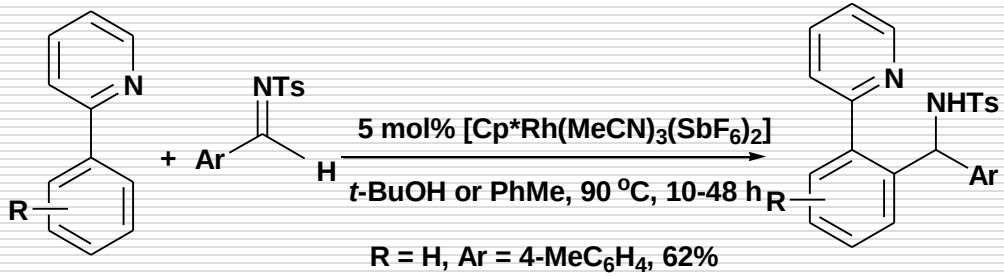
Ar = C_6H_5, PG = Boc, 82%
Ar = 4-ClC_6H_4, PG = Boc, 77%
Ar = 4-$NO_2C_6H_4$, PG = Boc, 77%
Ar = 4-CNC_6H_4, PG = Boc, 50%
Ar = 4-$CF_3C_6H_4$, PG = Boc, 95%
Ar = 2-MeC_6H_4, PG = Boc, 92%
Ar = C_6H_5, PG = Ts, 40%
Ar = C_6H_5, PG = Ns, 51%



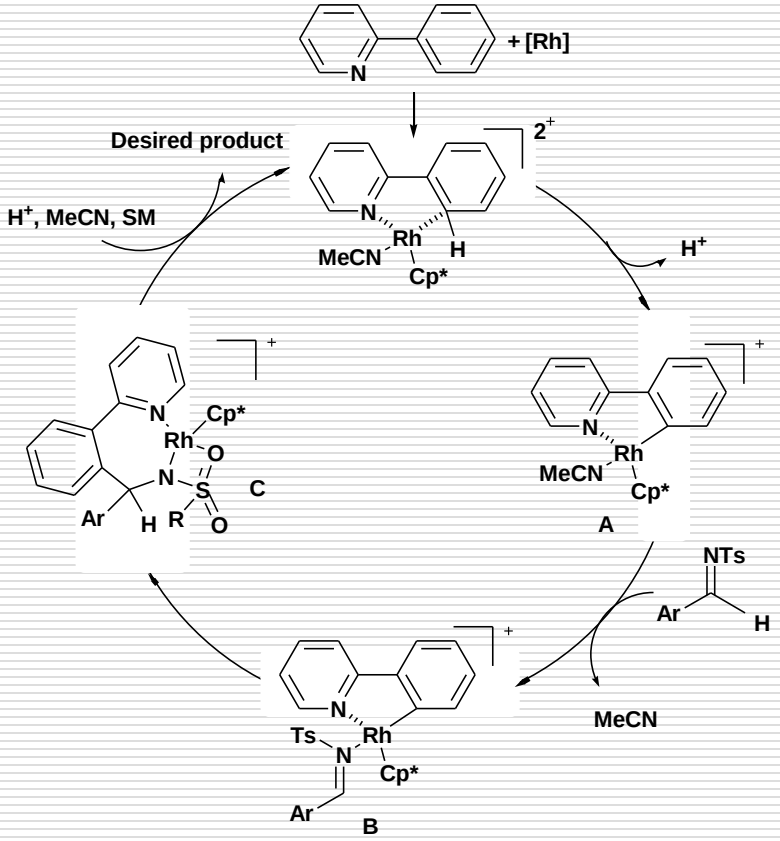
Notes: （1）**electrophilic deprotonation**
（2）**concerted metalation-deprotonation (CMD)-**

A. S. Tsai, M. E. Tauchert, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* 2011, **133**, 1248-1250.

4 Addition of C-H bonds to imines



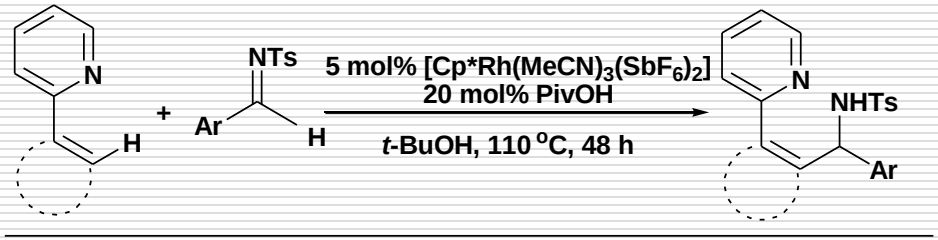
R = H, Ar = 4-MeC_6H_4, 62%
R = H, Ar = 4-BrC_6H_4, 76%
R = H, Ar = 4-ClC_6H_4, 83%
R = H, Ar = 4-FC_6H_4, 83%
R = H, Ar = 3-FC_6H_4, 82%
R = H, Ar = 2-Thiophenyl, 82%
R = 4-OMe, Ar = C_6H_5, 81%
R = 4-OH, Ar = C_6H_5, 86%
R = 4-Cl, Ar = C_6H_5, 73%
R = 4-Br, Ar = C_6H_5, 74%
R = 4-$OCONMe_2$, Ar = C_6H_5, 70%
R = 4-CO_2Me, Ar = C_6H_5, 78%

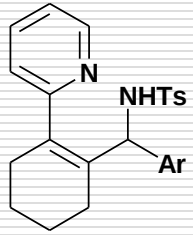


Notes: mild conditions and without any additives

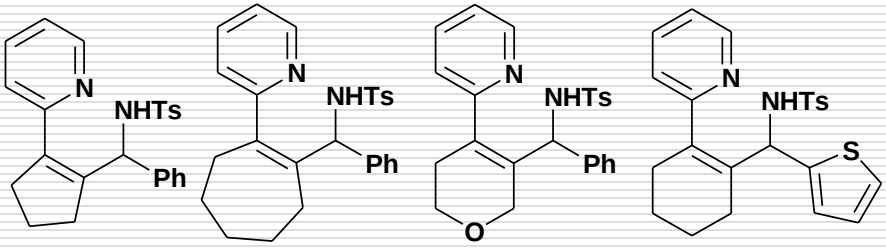
Y. Li, B.-J. Li, W.-H. Wang, W.-P. Huang, X.-S. Zhang, K. Chen, Z.-J. Shi, *Angew. Chem. Int. Ed.* 2011, **50**, 2115-2119.

4 Addition of C-H bonds to imines





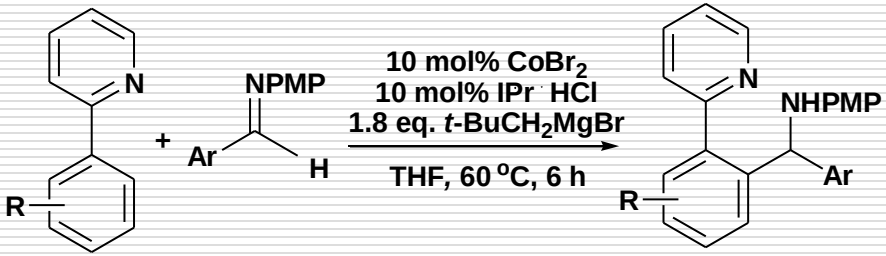
Ar = C_6H_5, 69%
Ar = 4-$CF_3C_6H_4$, 69%
Ar = 4-FC_6H_4, 71%
Ar = 3-FC_6H_4, 66%
Ar = 2-FC_6H_4, 58%
Ar = 3-MeC_6H_4, 63%
Ar = 2-MeC_6H_4, 33%



The first example of direct alkenyl C-H addition to imines and aldehydes.

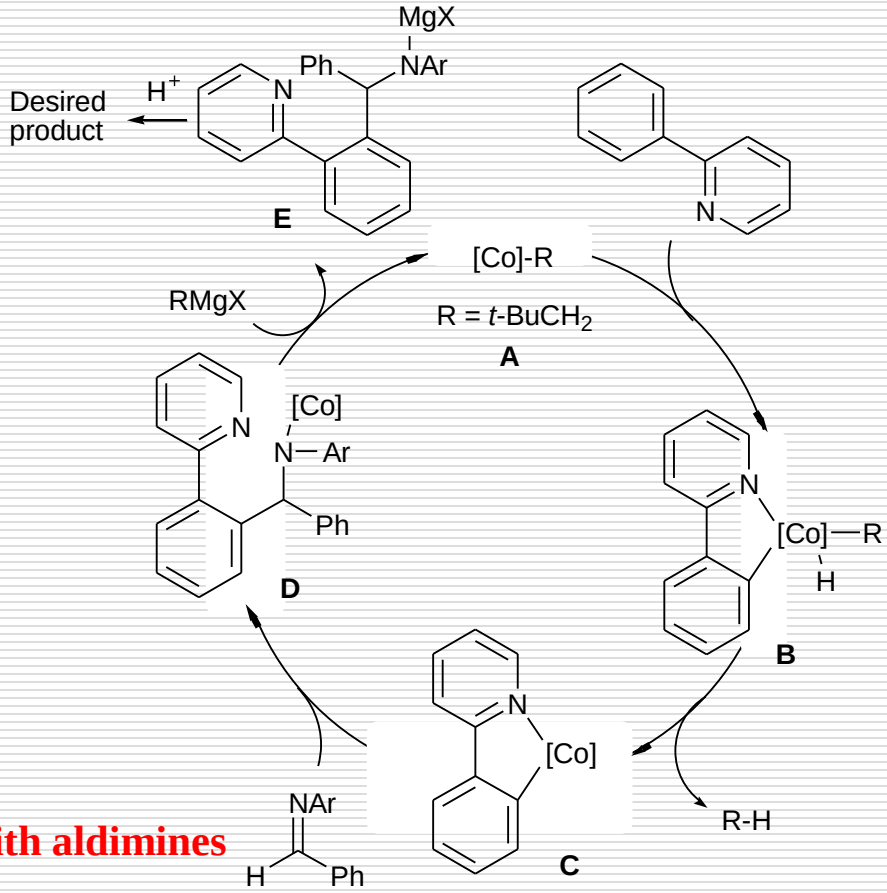
Y. Li, X.-S. Zhang, Q.-L. Zhu, Z.-J. Shi, *Org. Lett.*, 2012, **14**, 4498-4501.

4 Addition of C-H bonds to imines



R = H, Ar = 4-MeC_6H_4,85%
R = H, Ar = 4-$MeOC_6H_4$, 78%
R = H, Ar = 4-ClC_6H_4, 83%
R = H, Ar = 4-FC_6H_4, 26%
R = H, Ar = 3-MeC_6H_4, 77%
R = H, Ar = 2-MeC_6H_4, 77%
R = H, Ar = 2-$MeOC_6H_4$, 53%

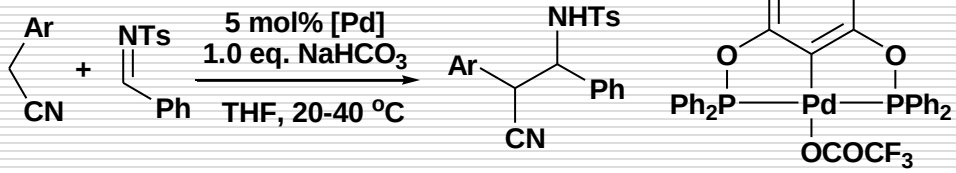
R = H, Ar = 2-$C_6H_5C_6H_4$,41%
R = H, Ar = C_6H_5, 81%
R = 4-OMe, Ar = C_6H_5, 76%
R = 4-F, Ar = C_6H_5, 64%
R = 4-NMe_2, Ar = C_6H_5, 28%
R = 5-Me, Ar = C_6H_5, 47%
R = 6-OMe, Ar = C_6H_5, 70%



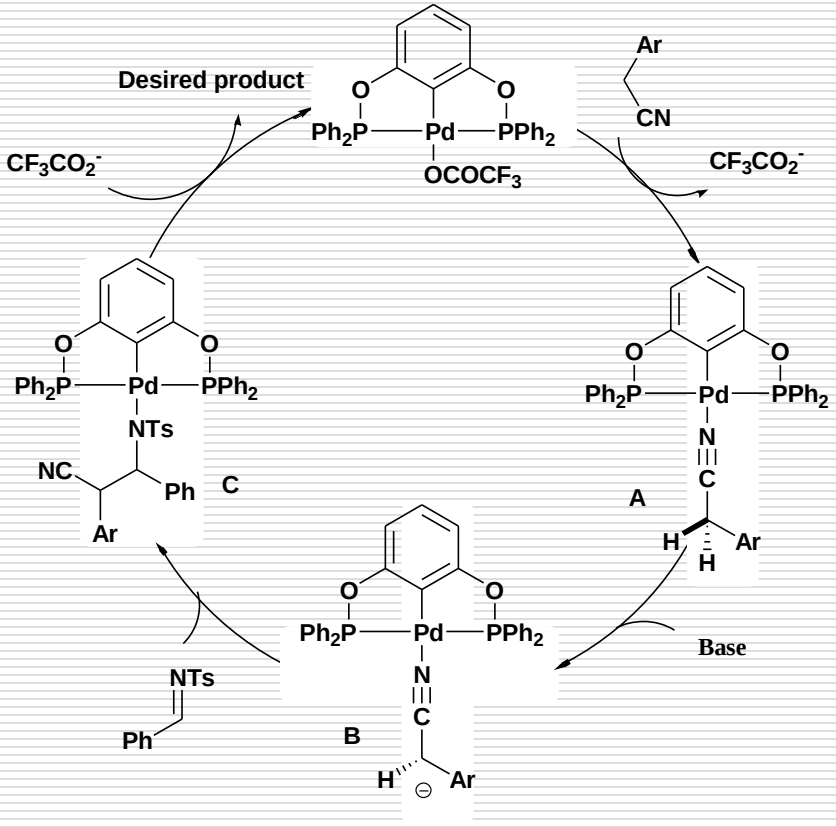
This mechanism is different from that of the rhodium(III)-catalyzed reaction of 2-arylpyridines with aldimines

K. Gao, N. Yoshikai, *Chem. Commun.* 2012, **48**, 4305-4307.

4 Addition of C-H bonds to imines



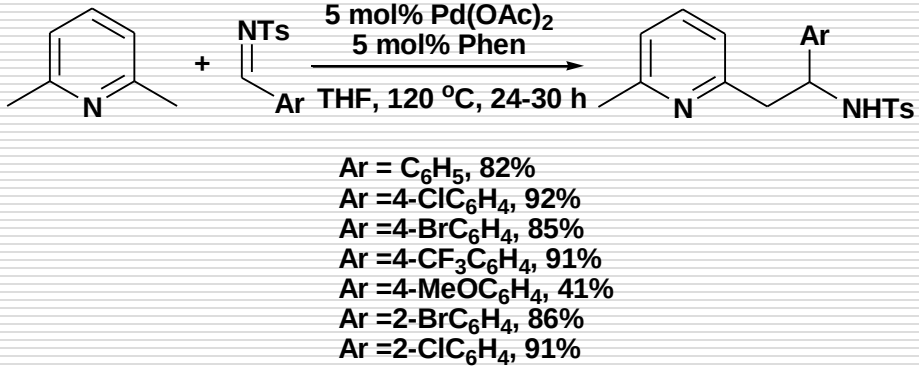
Ar = C_6H_5, 99%, dr = 2:1
Ar =2-FC_6H_4, 95%, dr = 4.6:1
Ar =2-ClC_6H_4, 99%, dr = 8.4:1
Ar =2-BrC_6H_4, 83%, dr = 10:1
Ar =2-IC_6H_4, 99%, dr = 10:1
Ar =2-MeC_6H_4, 92%, dr = 4:1
Ar =2-$CF_3C_6H_4$, 84%, dr = 4:1
Ar =2-$MeOC_6H_4$, 91%, dr = 5.6:1

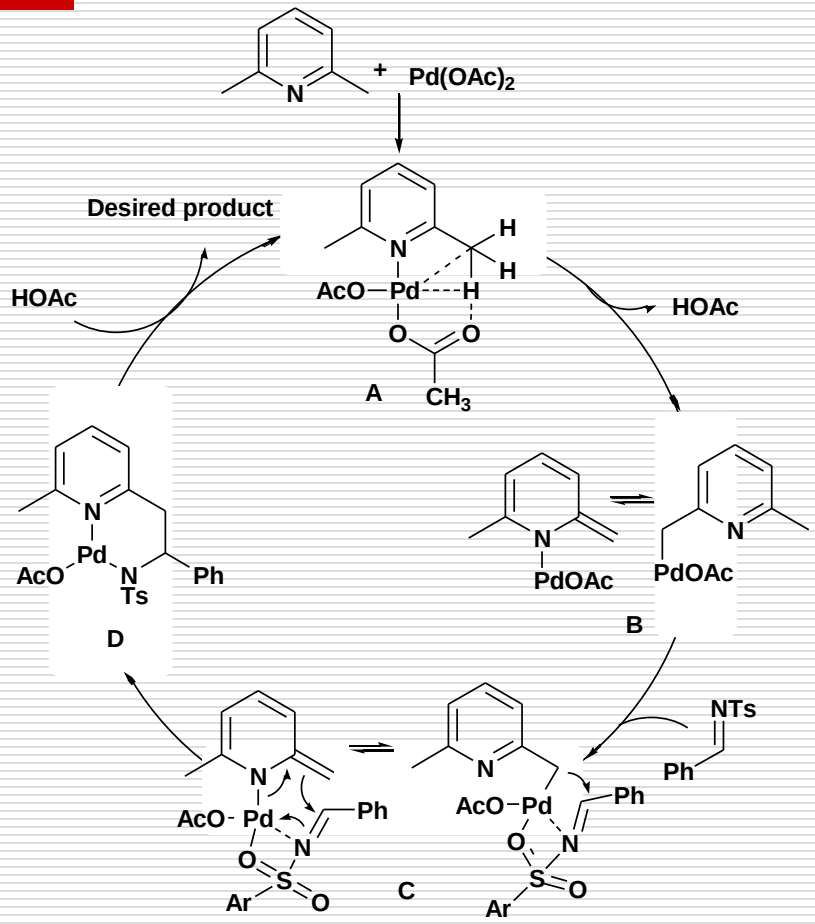


Notes: （1）**mild conditions**
（2）**high regioselectivity**
（3）**new palladium-pincer complex**

J. Aydin, C. S. Conrad, K. J. Szabó, *Org. Lett.*, 2008, **10**, 5175-5178.

4 Addition of C-H bonds to imines



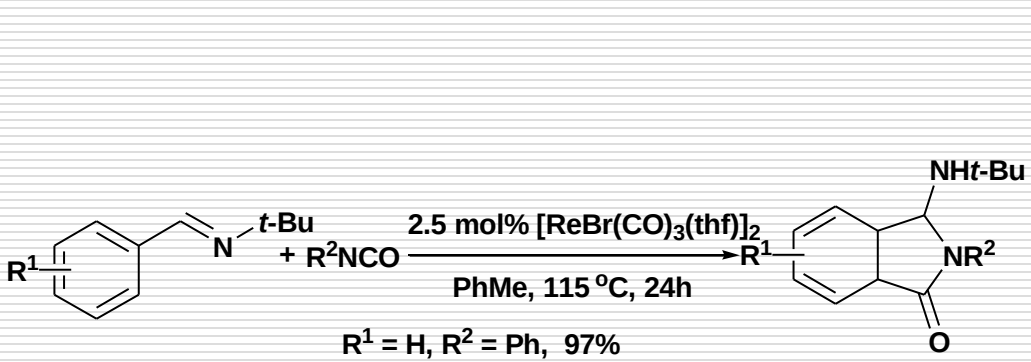


Notes: （1）**mild conditions**

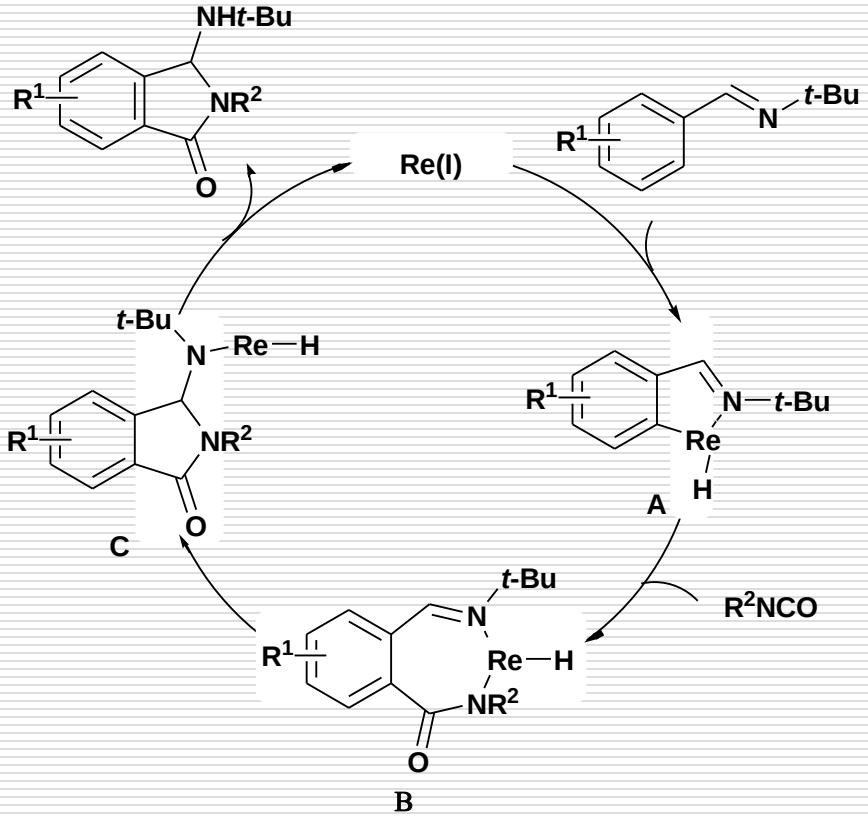
(2) **sp3 C-H bond activation**

B. Qian, S. Guo, J. Shao, Q. Zhu, L. Yang, C. Xia, H. Huang, *J. Am. Chem. Soc.* 2010, **132**, 3650-3651.

5 Addition of C-H bonds to isocyanates



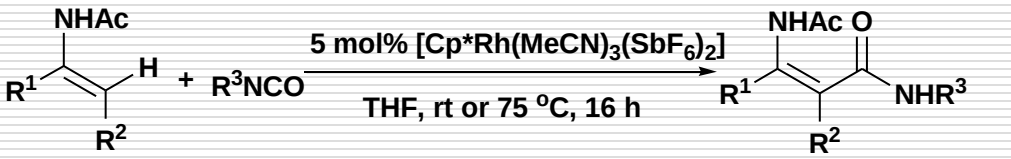
R^1 = H, R^2 = Ph, 97%
R^1 = H, R^2 = 4-$MeOC_6H_4$, 81%
R^1 = H, R^2 = 4-$CF_3C_6H_4$, 94%
R^1 = 4-OMe, R^2 = Ph, 80%
R^1 = 4-Me, R^2 = Ph, 92%
R^1 = 4-CF_3, R^2 = Ph, 87%

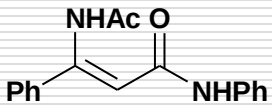


Notes: mild conditions and without any additives

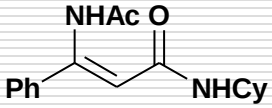
Y. Kuninobu, Y. Tokunaga, A. Kawata, K. Takai, *J. Am. Chem. Soc.* 2006, **128**, 202-209.

5 Addition of C-H bonds to isocyanates

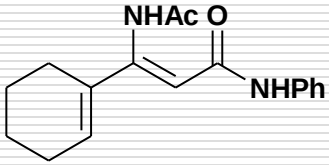




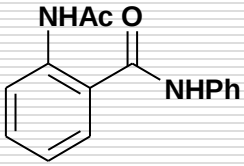
96%



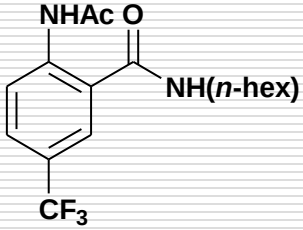
84%



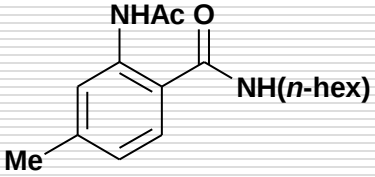
80%



60%



44%



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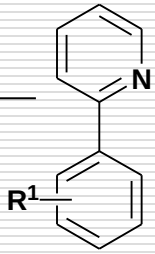
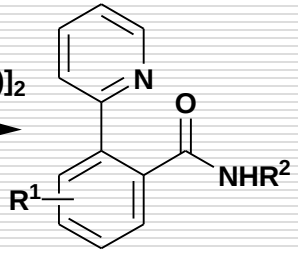


+ R^2NCO

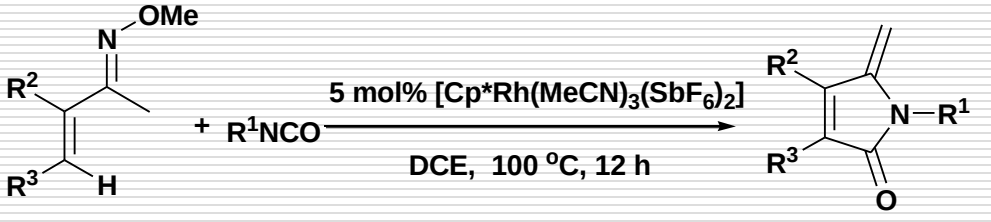
5 mol% $[RuCl_2(p\text{-cymene})]_2$
30 mol% NaOAc
o-xylene, 80 °C, 24 h

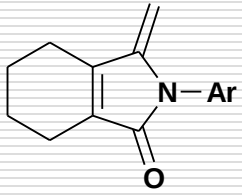


R^1 = H, R^2 = Ph, 90%
R^1 = 4-Me, R^2 = Ph, 81%
R^1 = 4-OMe, R^2 = Ph, 79%
R^1 = 4-Br, R^2 = Ph, 83%
R^1 = 4-CN , R^2 = Ph, 63%
R^1 = 4-CHO, R^2 = Ph, 61%
R^1 = H, R^2 = 4-MeC_6H_4, 86%
R^1 = H, R^2 = 4-ClC_6H_4, 81%

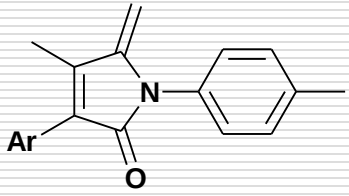
K. D. Hesp, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* 2011, **133**, 11430-11433.
K. Muralirajan, K. Parthasarathy, C.-H. Cheng, *Org. Lett.*, 2012, **14**, 4262-4265

5 Addition of C-H bonds to isocyanates

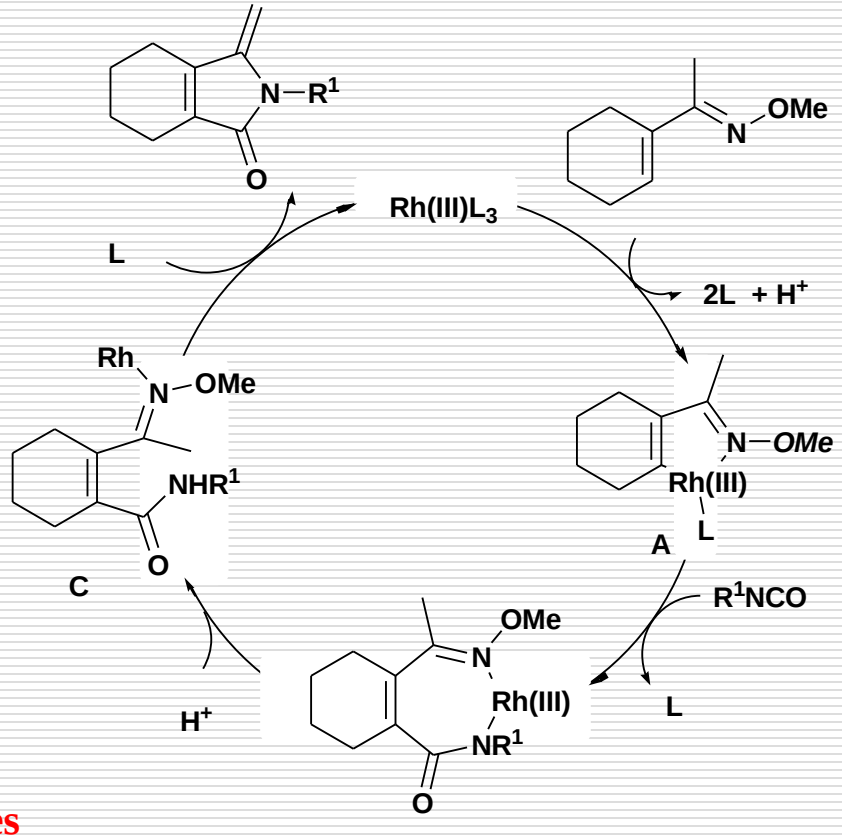




Ar =4-MeC_6H_4, 86%
Ar =4-$MeOC_6H_4$, 82%
Ar =4-$NO_2C_6H_4$, 84%
Ar =4-$CF_3C_6H_4$, 87%
Ar =4-$CO_2EtC_6H_4$, 82%
Ar =4-BrC_6H_4, 92%
Ar =4-ClC_6H_4, 93%
Ar =4-FC_6H_4, 80%



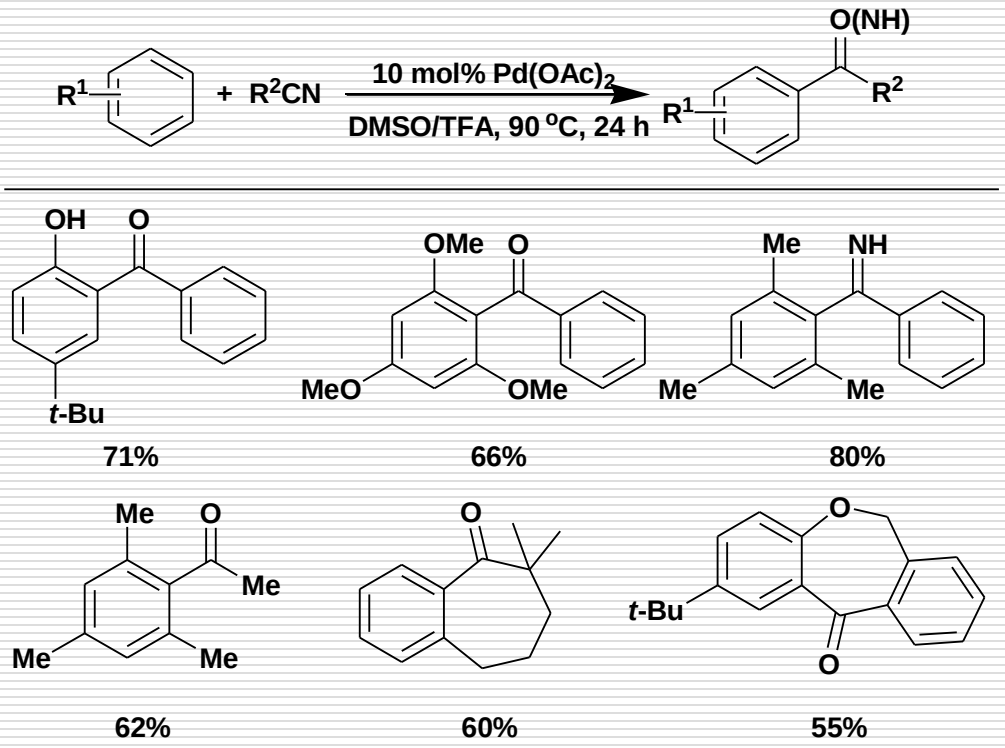
Ar = C_6H_5, 65%
Ar =4-MeC_6H_4, 60%
Ar =4-$MeOC_6H_4$, 57%
Ar =4-FC_6H_4, 64%
Ar =2-Naphthyl, 55%

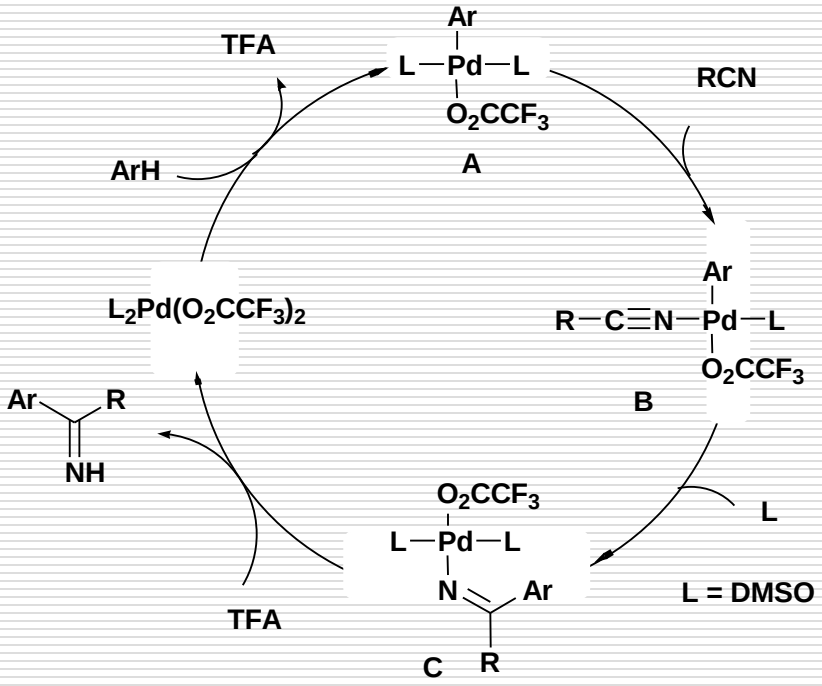


Notes: (1) mild conditions and without any additives
(2) high regioselectivity and excellent functional group tolerance

W. Hou, B. Zhou, Y. Yang, H. Feng, Y. Li, *Org. Lett.*, 2013, **15**, 1814-1817

6 Addition of C-H bonds to nitriles

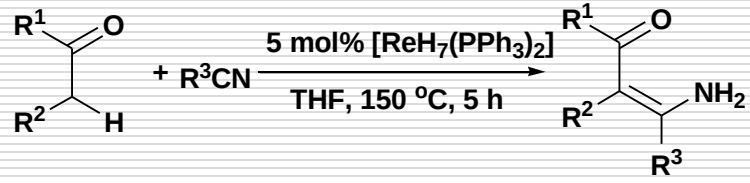


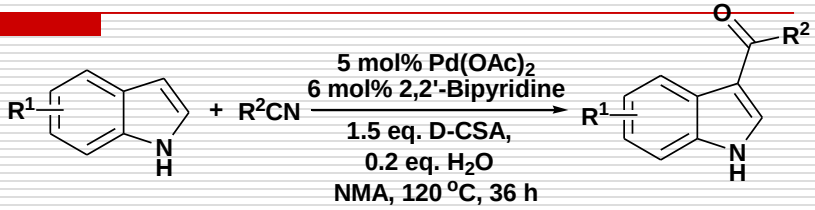


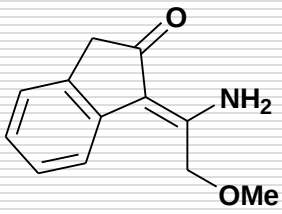
Notes: the reaction can even be improved dramatically by adding only a catalytic amount of DMSO

C. Zhou, R. C. Larock, *J. Am. Chem. Soc.* 2004, **126**, 2302-2303

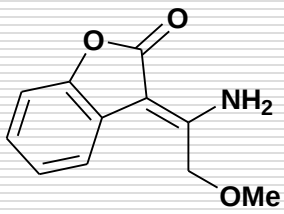
6 Addition of C-H bonds to nitriles



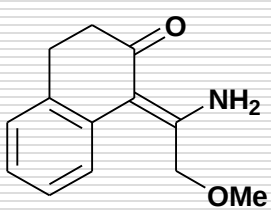




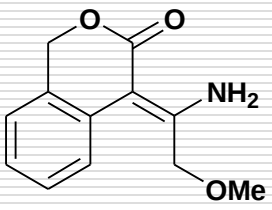
97%



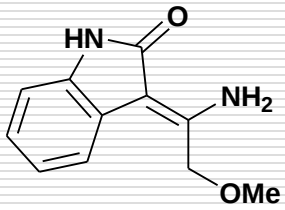
92%



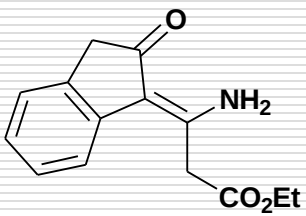
76%



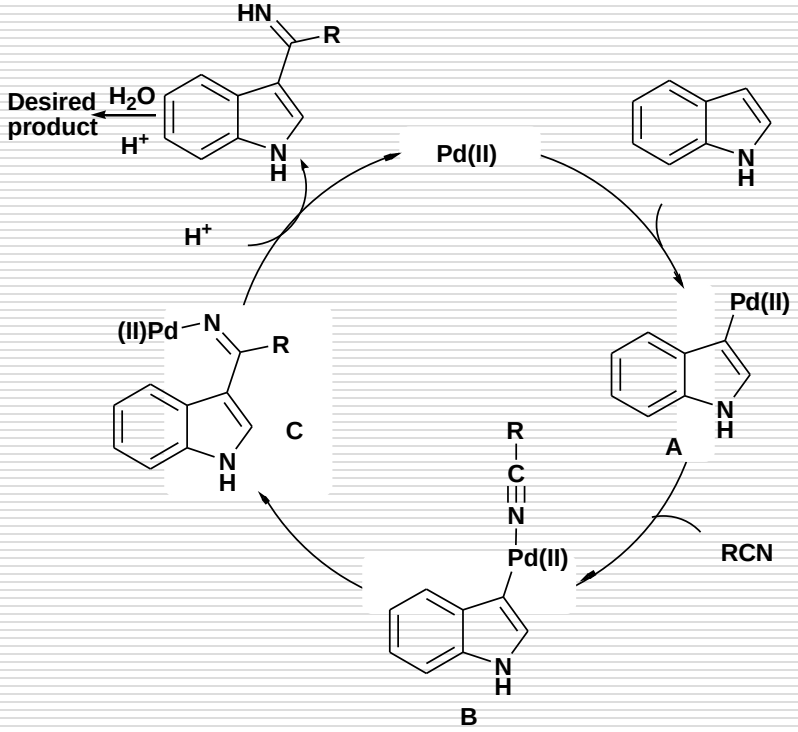
88%



76%



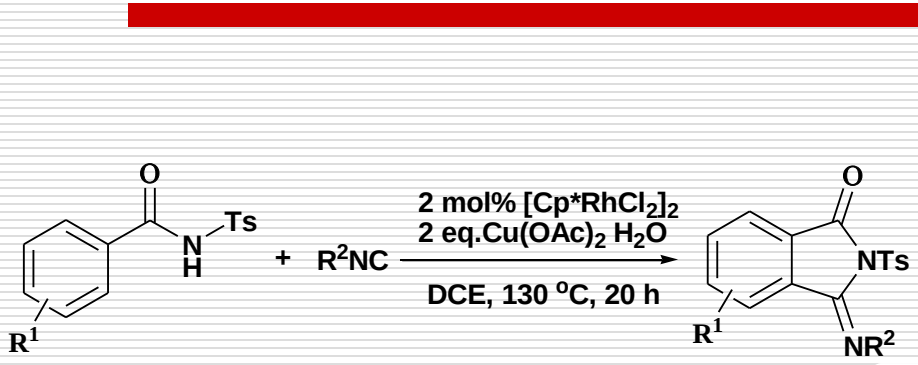
59%



H. Takaya, M. Ito, S.-I. Murahashi, *J. Am. Chem. Soc.* 2009, **131**, 10824-10825.

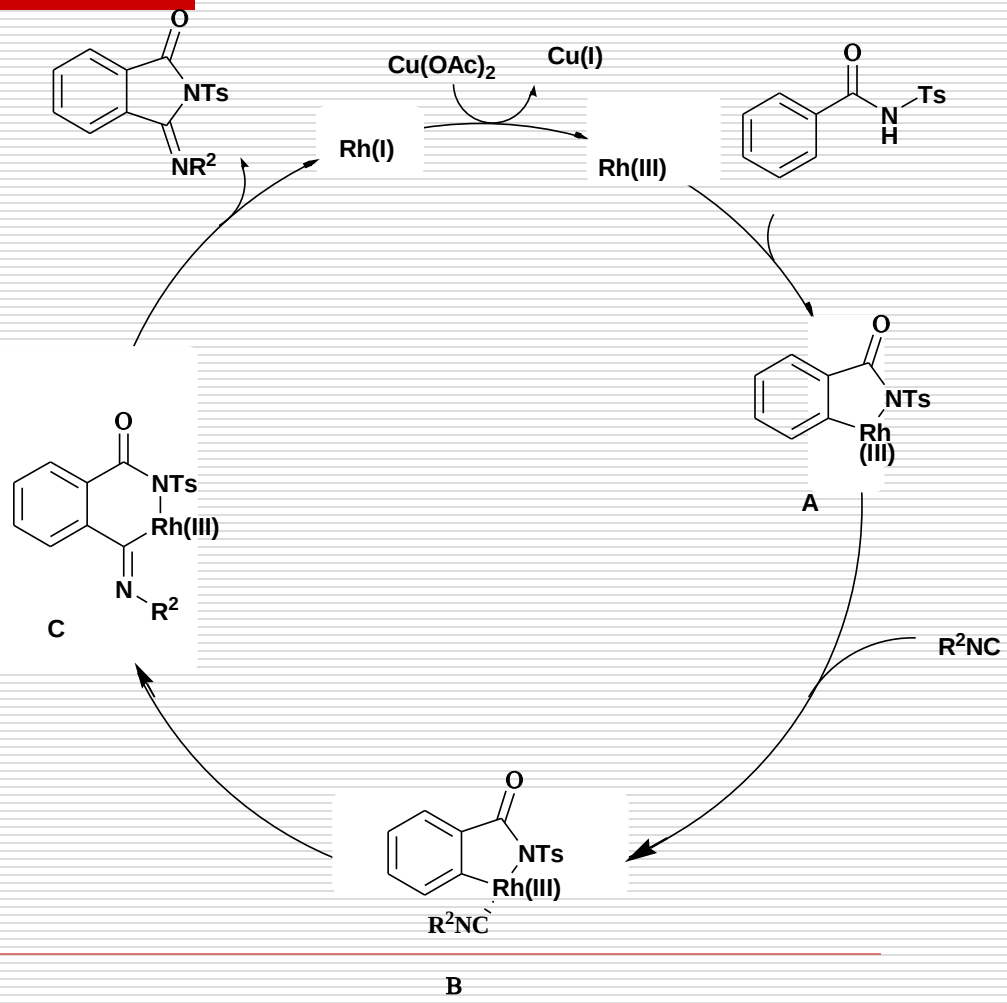
T.-S. Jiang, G.-W. Wang, *Org. Lett.*, 2013, **15**, 788-791

7 Addition of C-H bonds to isocyanides



R^1 = H, Me, OMe, F, CF_3
R^2 = Alkyl, Aryl

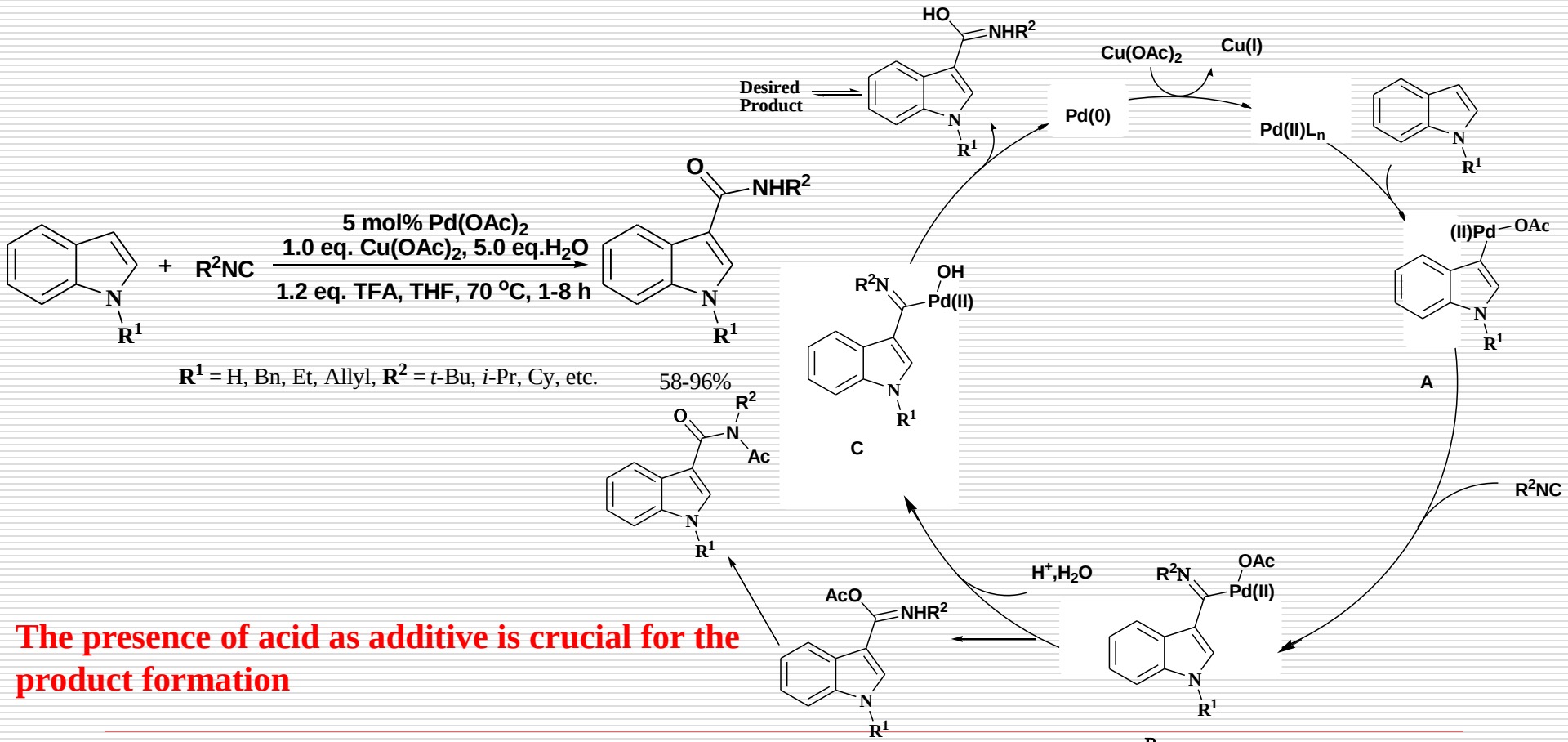
40-81%



Notes: N-H and C-H activation

C. Zhu, W. Xie and J. Falck, *Chem.–Eur. J.*, 2011, **17**, 12591

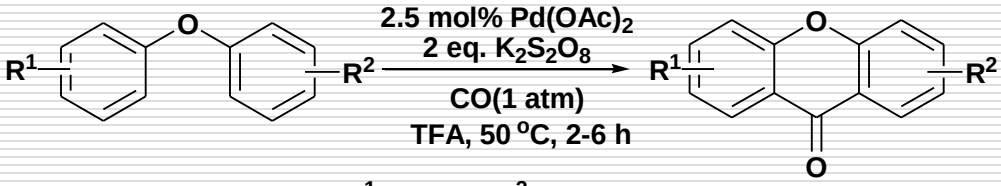
7 Addition of C-H bonds to isocyanides



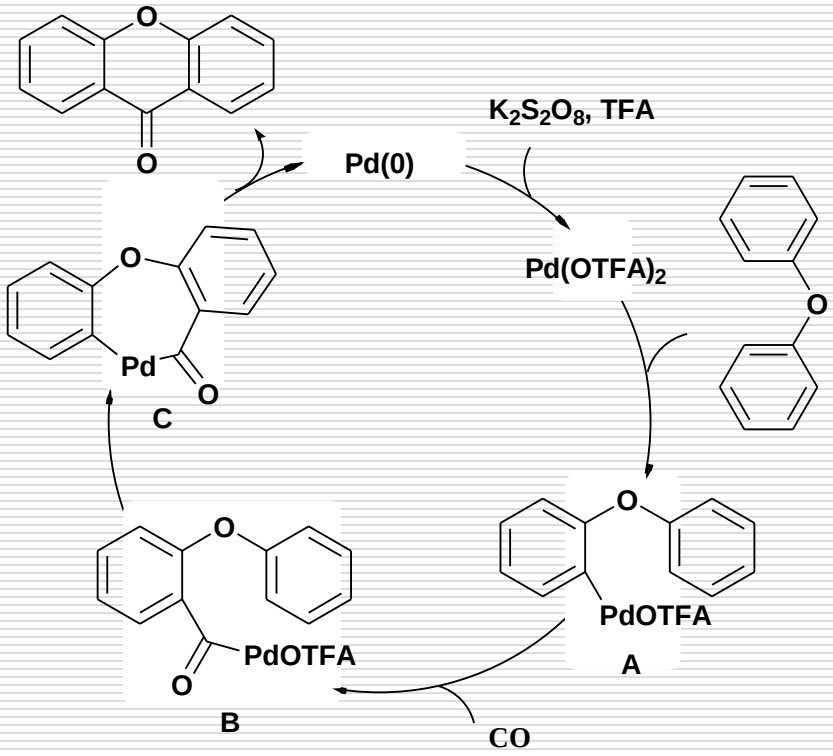
The presence of acid as additive is crucial for the product formation

J. Peng, L. Liu, Z. Hu, J. Huang and Q. Zhu, *Chem. Commun*., 2012, **48**, 3772

8 Addition of C-H bonds to carbon monoxide



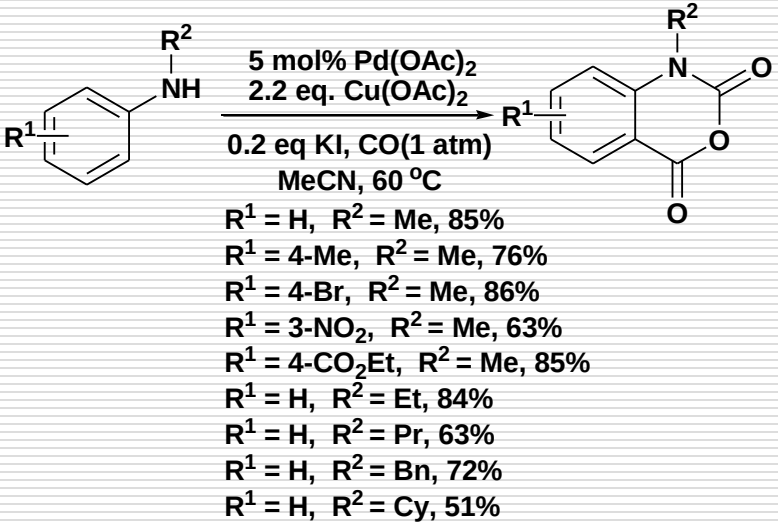
R^1 = 4-Me, R^2 = 4-Me, 96%
R^1 = 4-Me, R^2 = 4-*t*-Bu, 82%
R^1 = 4-Me, R^2 = 4-CF_3, 56%
R^1 = 4-Me, R^2 = 4-CO_2Et, 51%
R^1 = 4-Me, R^2 = 4-Br, 70%
R^1 = 4-Me, R^2 = 4-COMe, 58%



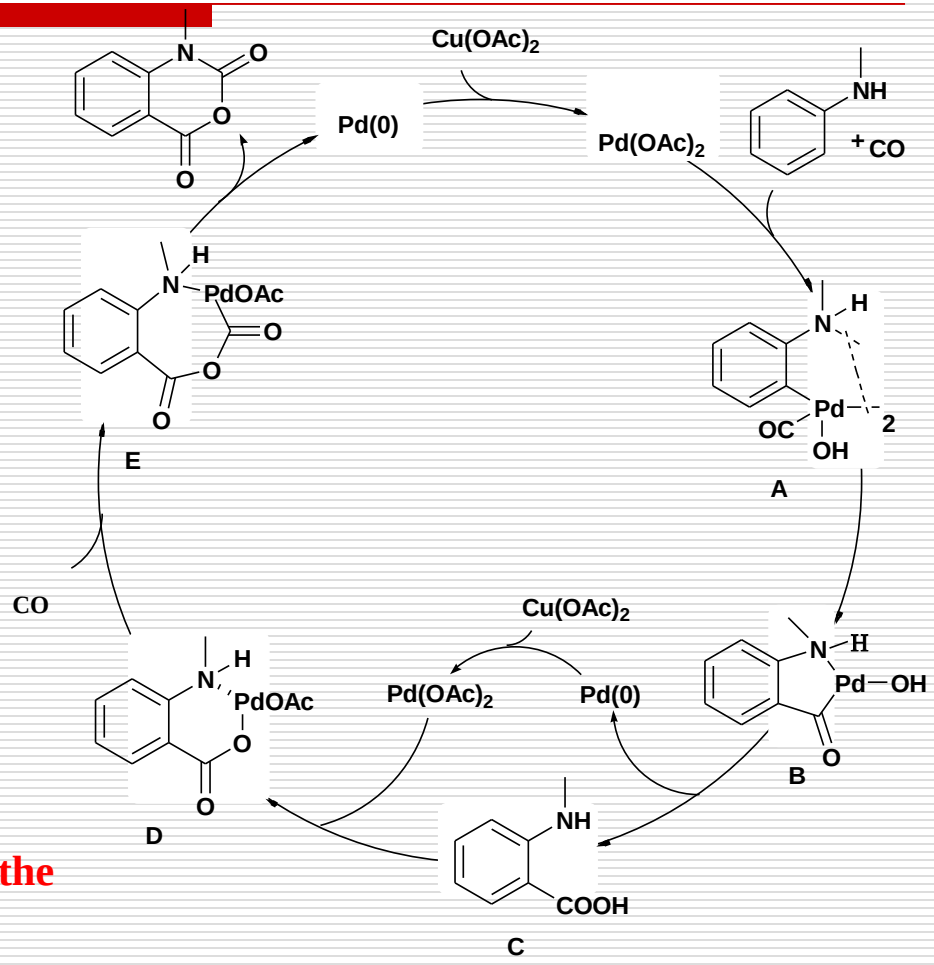
Notes: (1)double C-H functionalization
(2) a simple catalytic system

H. Zhang, R. Shi, P. Gan, C. Liu, A. Ding, Q. Wang, A. Lei, *Angew. Chem. Int. Ed.* 2012, **51**, 5204-5207.

8 Addition of C-H bonds to carbon monoxide



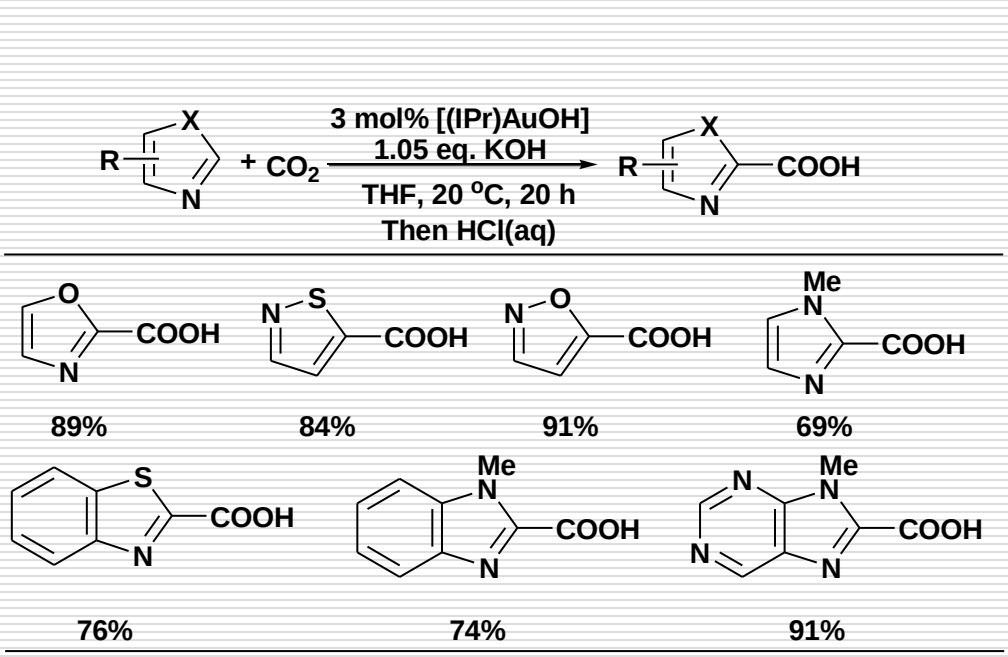
R^1 = H, R^2 = Me, 85%
R^1 = 4-Me, R^2 = Me, 76%
R^1 = 4-Br, R^2 = Me, 86%
R^1 = 3-NO_2, R^2 = Me, 63%
R^1 = 4-CO_2Et, R^2 = Me, 85%
R^1 = H, R^2 = Et, 84%
R^1 = H, R^2 = Pr, 63%
R^1 = H, R^2 = Bn, 72%
R^1 = H, R^2 = Cy, 51%

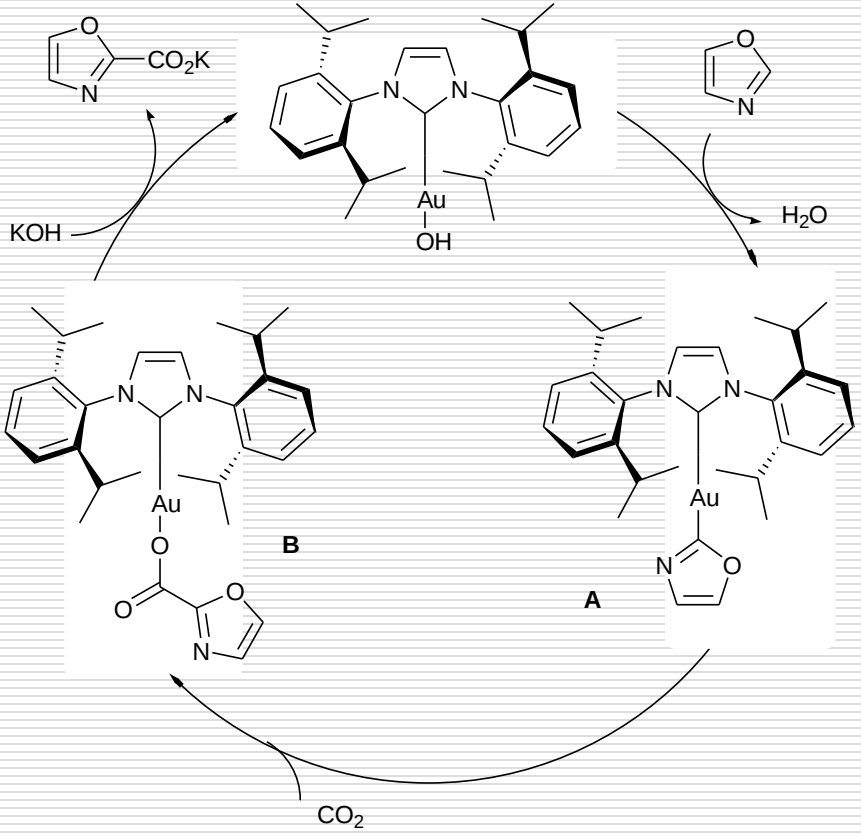


Iodide compounds have been shown to improve the efficiency of Pd-catalyzed carbonylations

Z.-H. Guan, M. Chen, Z.-H. Ren, *J. Am. Chem. Soc.* 2012, **134**, 17490-17493.

9 Addition of C-H bonds to carbon dioxide

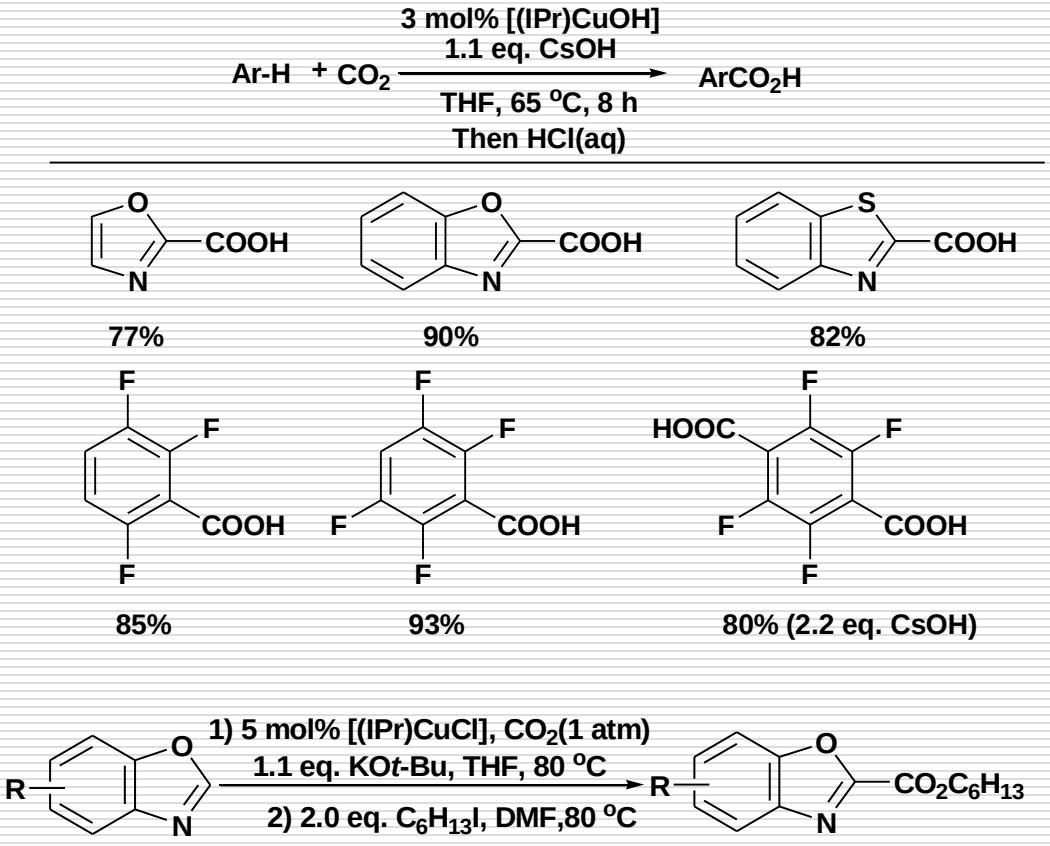




The carboxylation of carbo- and heterocycles with high regioselectivity at the most acidic C-H bond position

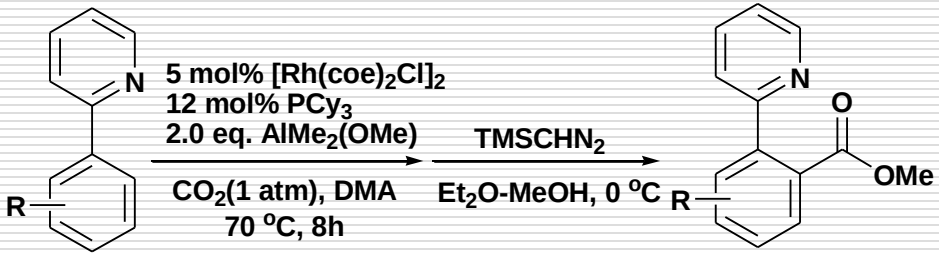
I. I. F. Boogaerts, S. P. Nolan, *J. Am. Chem. Soc.* 2010, **132**, 8858-8859.

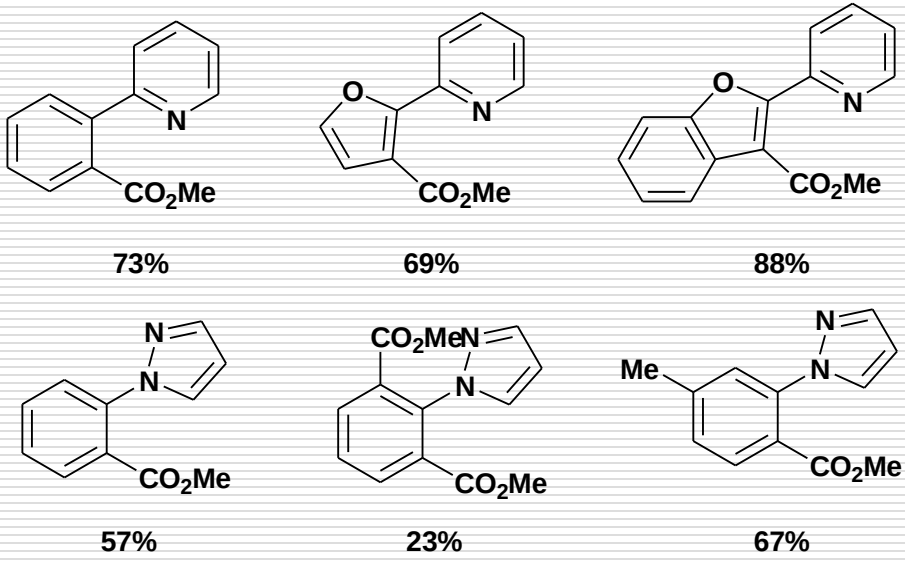
9 Addition of C-H bonds to carbon dioxide

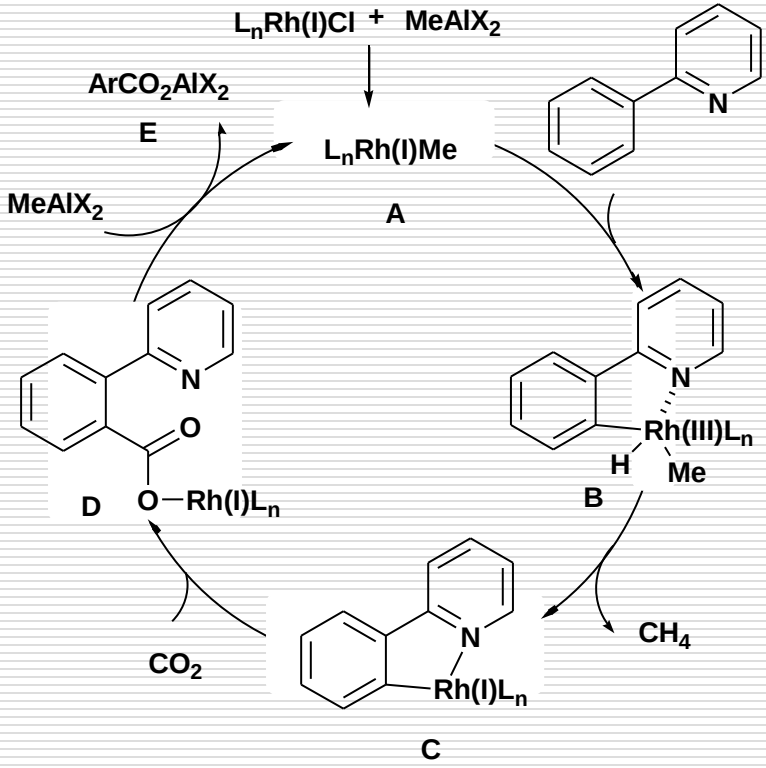


G. C. Fortman, M. R. L. Furst, C. S. J. Cazin, S. P. Nolan, *Angew. Chem. Int. Ed.* 2010, **49**, 8674-8677.
L. Zhang, J. Cheng, T. Ohishi, Z. Hou, *Angew. Chem. Int. Ed.* 2010, **49**, 8670-8673.

9 Addition of C-H bonds to carbon dioxide







H. Mizuno, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* 2011, **133**, 1251-1253

10 Conclusions and outlook

(1) Noble metals: rhodium, ruthenium, rhenium, iridium and palladium.

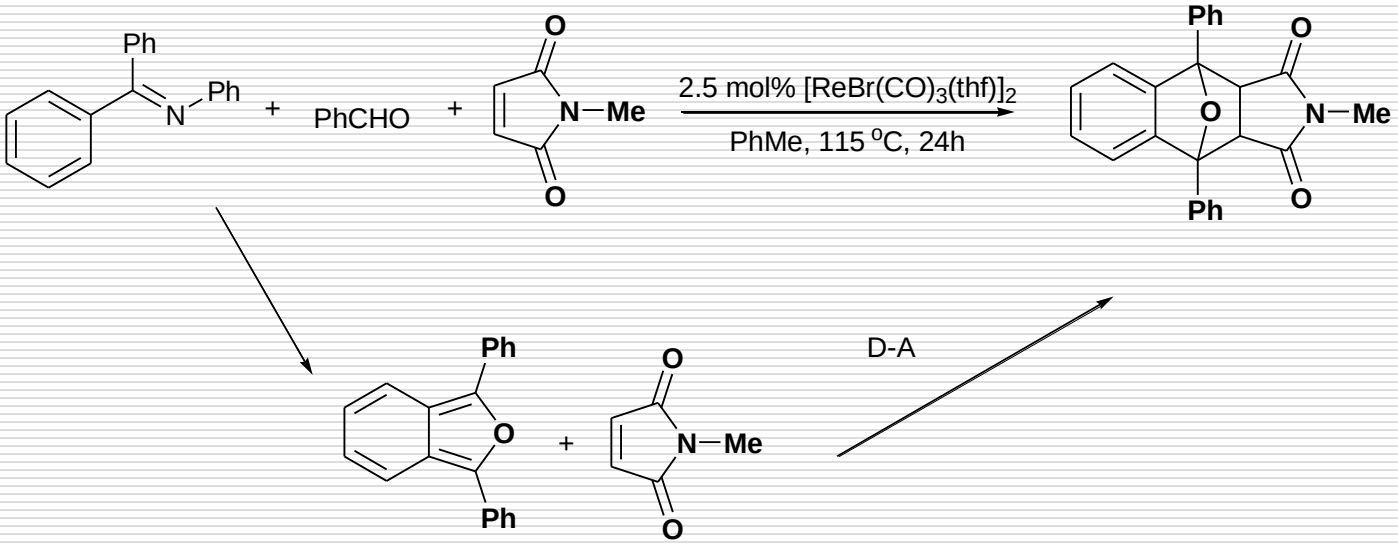
(2) Most subsrtates with directing group.

(3) Reactions with chiral ligands could realize the asymmetric catalysis.

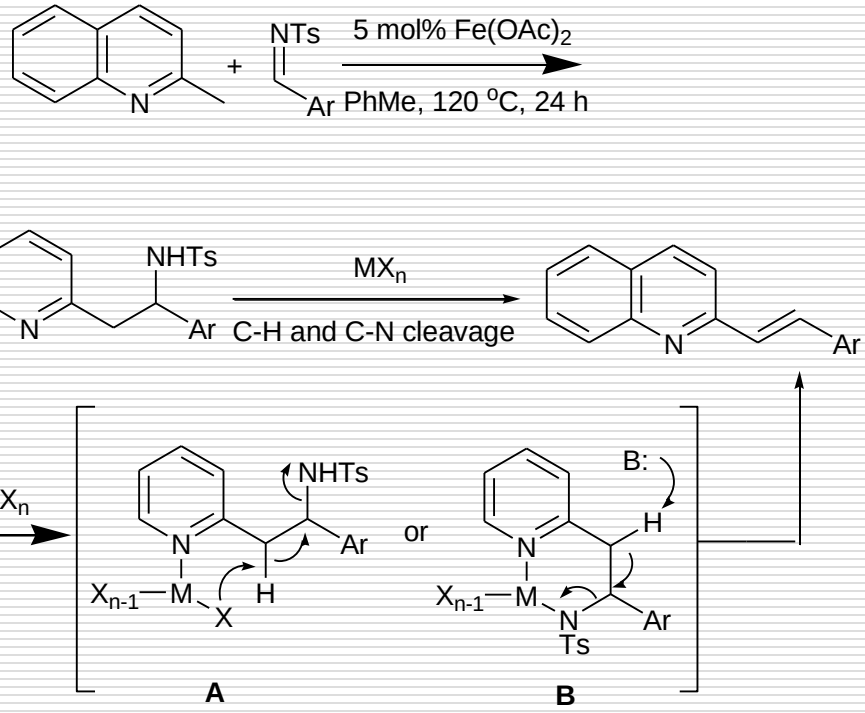
Thank you for your attention

Answers of questions

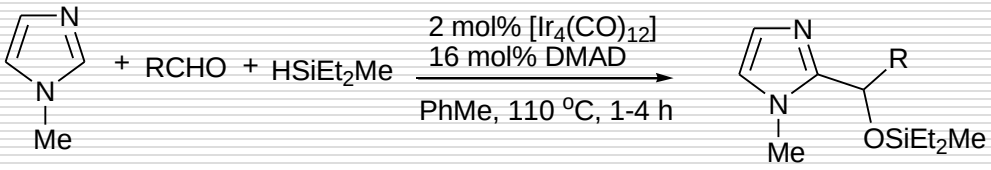
(1)

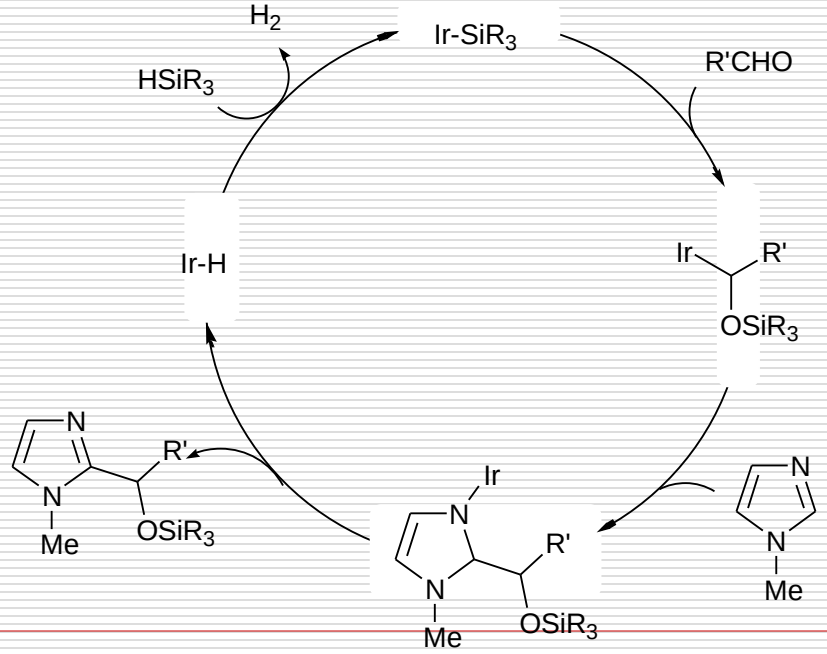


(2)


NTs
Ar
5 mol% Fe(OAc)2
PhMe, 120 °C, 24 h
N
NHTs
Ar
MXn
C-H and C-N cleavage
N
Ar
MXn
NHTs
N
Ar
Xn-1—M
X
H
A
or
B:
H
N
Xn-1—M
N
Ts
Ar
B

(3)


N
N
Me
+ RCHO + HSiEt2Me
2 mol% [Ir4(CO)12]
16 mol% DMAD
PhMe, 110 °C, 1-4 h
N
N
Me
R
OSiEt2Me


H2
HSiR3
Ir-SiR3
R'CHO
Ir-H
Ir
R'
OSiR3
N
N
Me
R'
OSiR3
Ir
N
N
Me
R'
OSiR3
N
N
Me