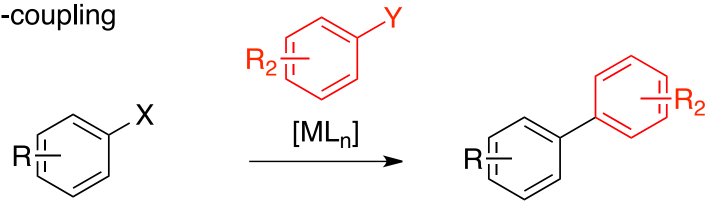
Rhodium-Catalyzed Borylation of Aryl 2-Pyridyl Ethers through Cleavage of the Carbon–Oxygen Bond: Borylative Removal of the Directing Group

J. Am. Chem. Soc., Article ASAP
DOI: 10.1021/ja511622e

James Johnson, Wipf Group Current Literature

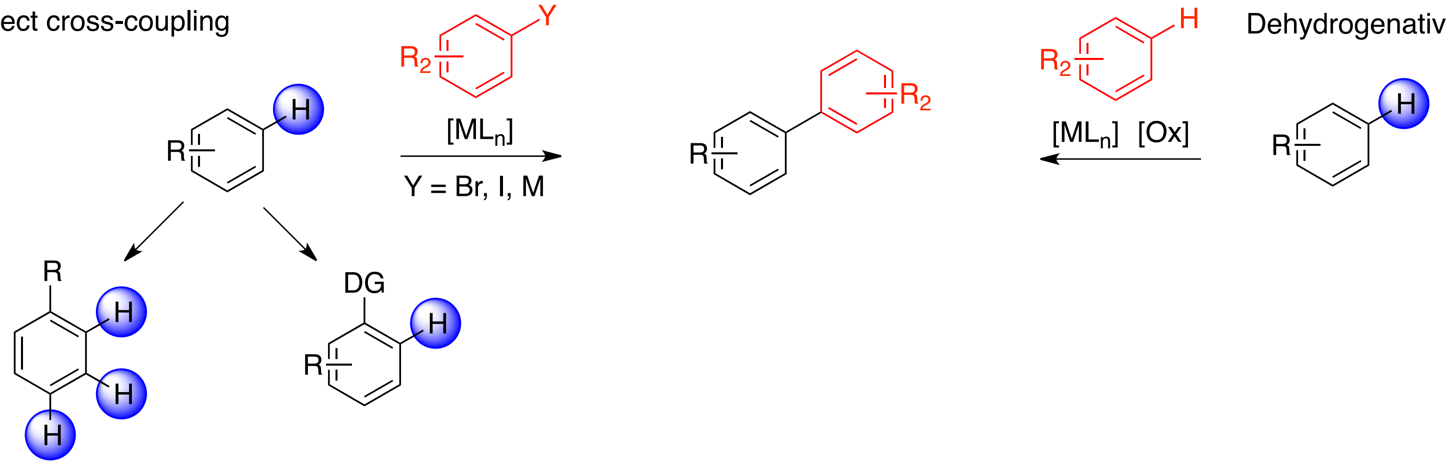
Transition Metal Catalyzed C-H bond transformations

Traditional cross-coupling



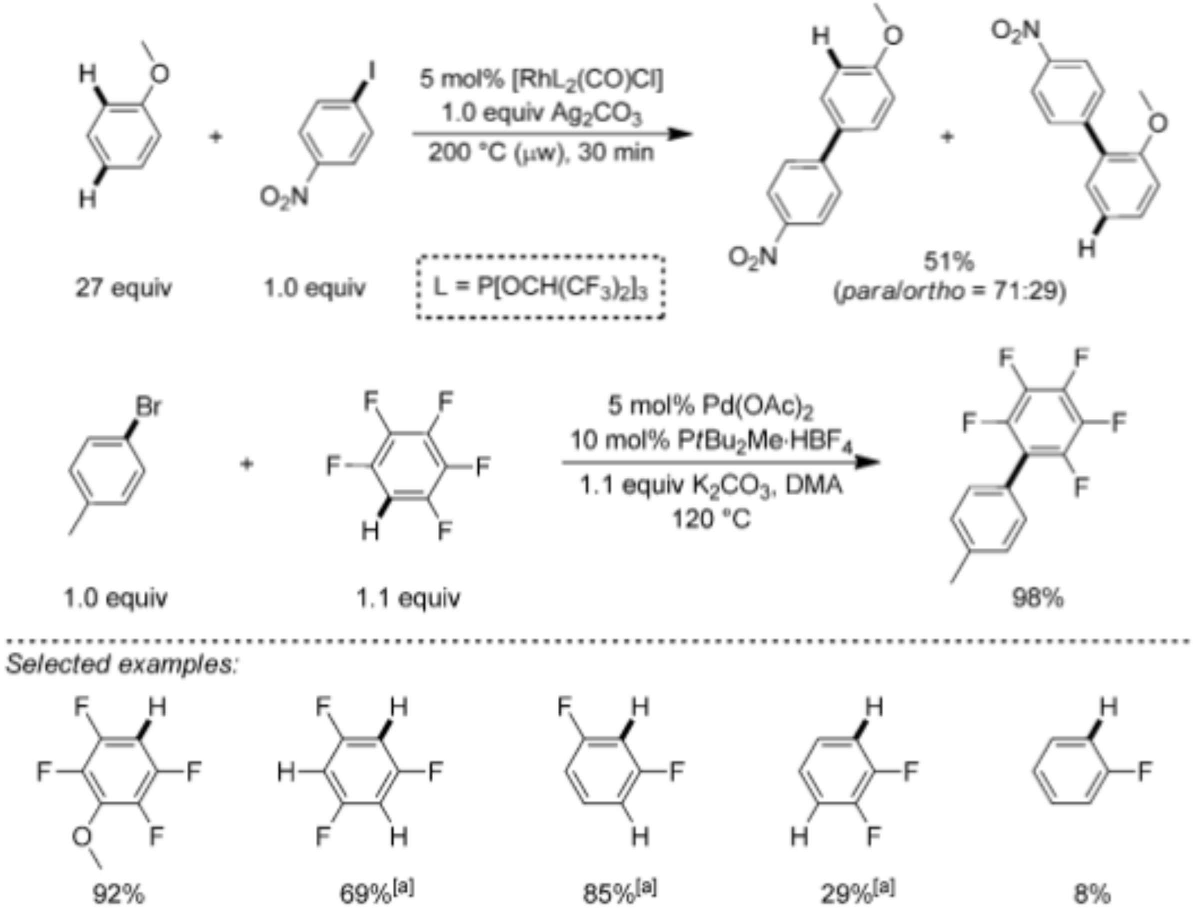
C-H activation
Direct cross-coupling

Dehydrogenative cross-coupling



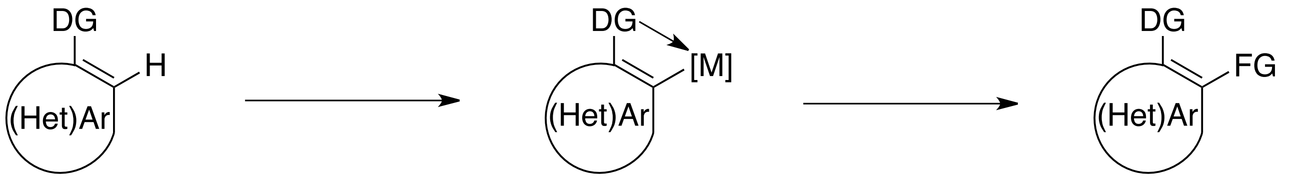
Chem. Soc. Rev., 2011, 40, 5068–5083

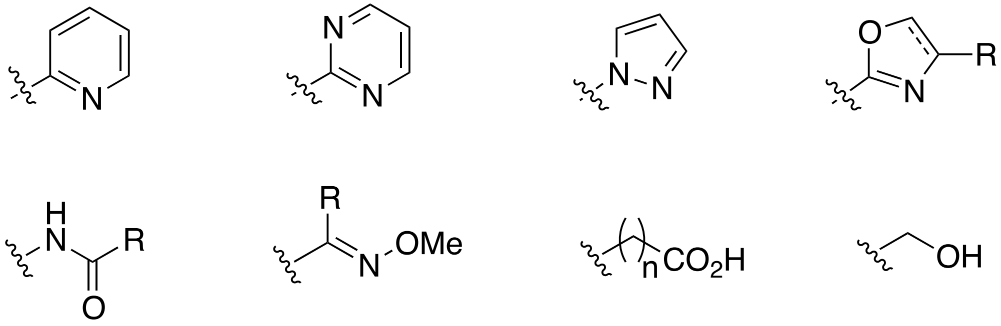
Substrate dependent



Angew. Chem. Int. Ed. 2012, 51, 10236 – 10254

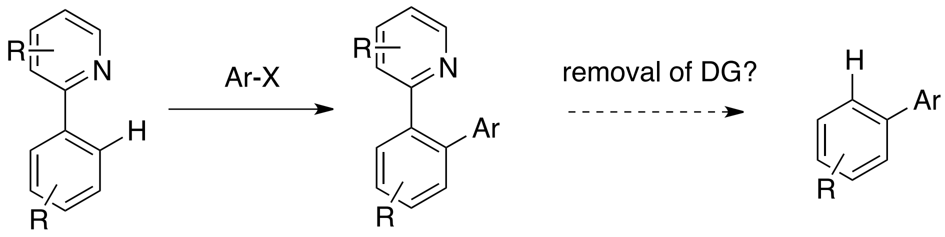
Common directing groups

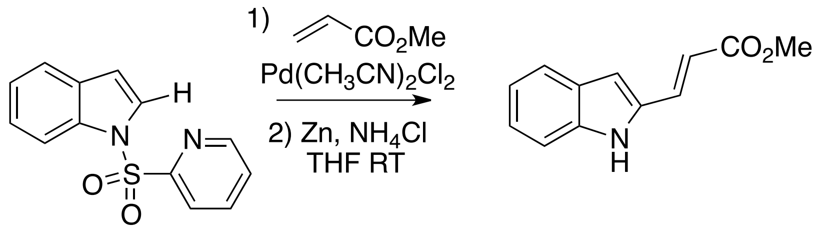


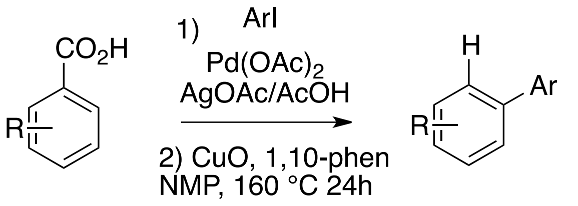


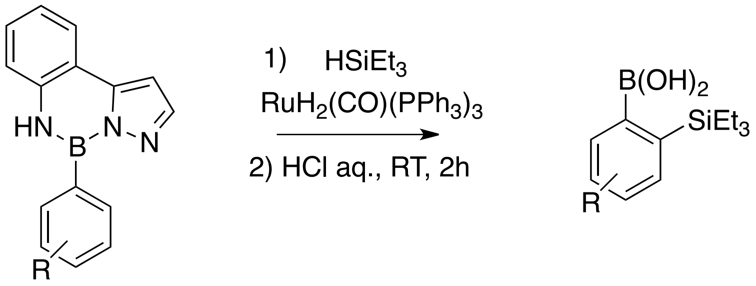
Adv Synth Catal. 2011, 8, 353

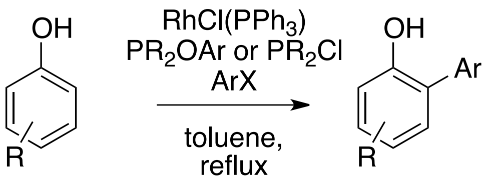
Directing groups in C-H activation





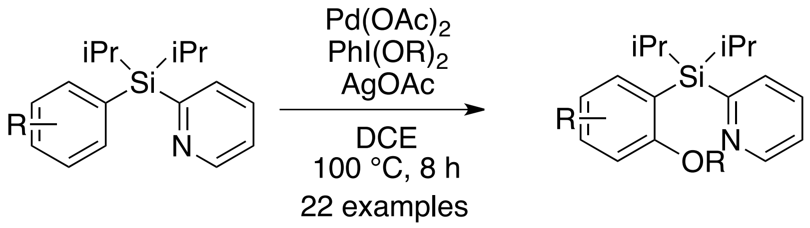


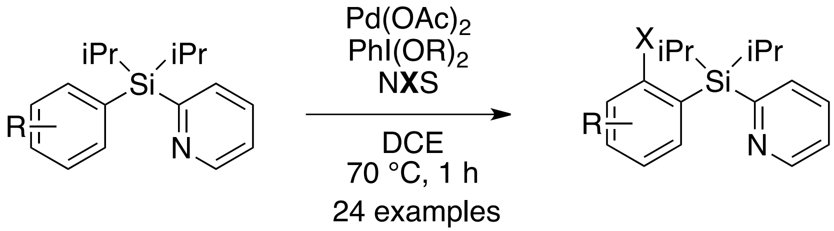


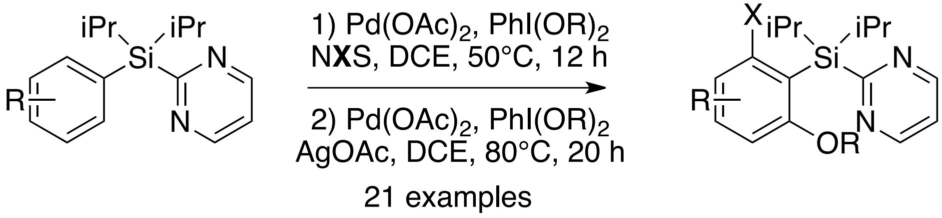


Angew. Chem. Int. Ed. 2011, 50, 2450 – 2494

2-pyridylsilyl directing group

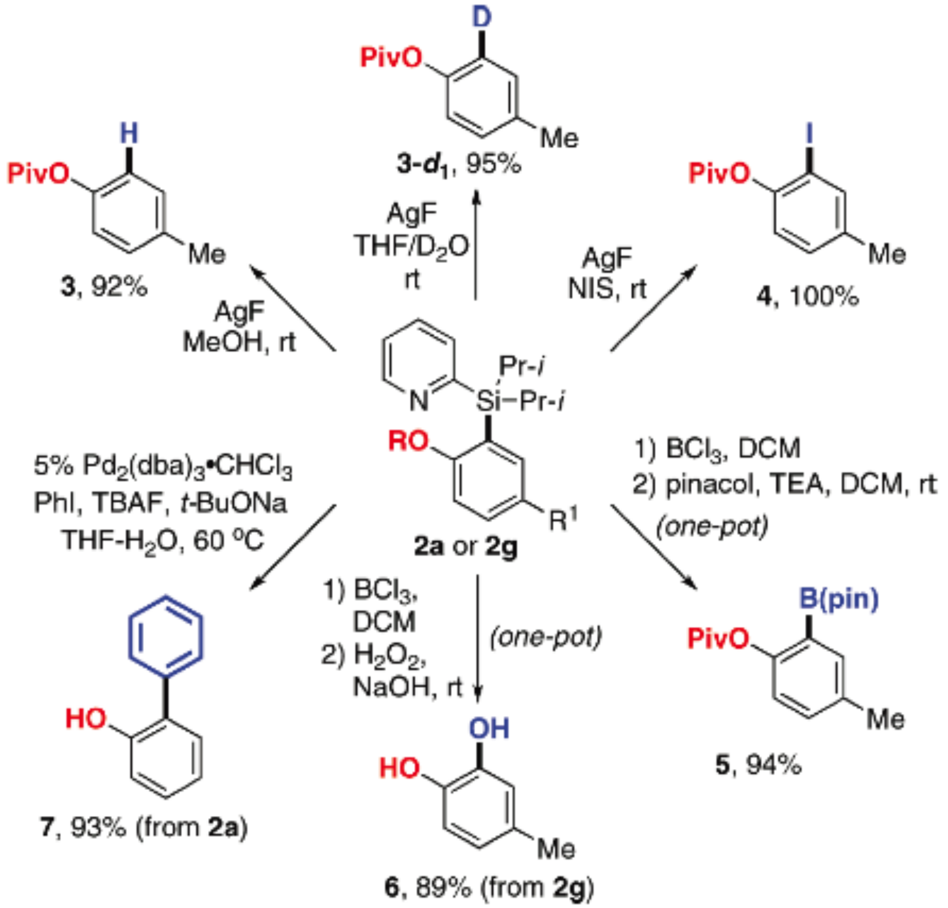






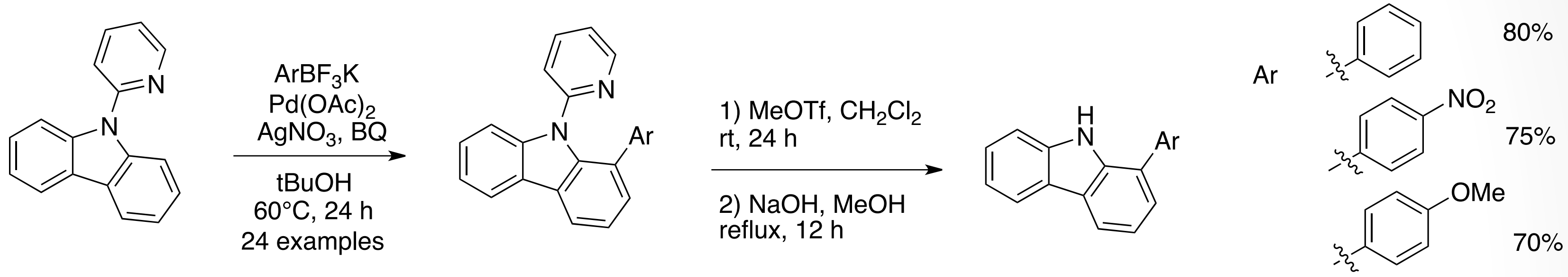
Angew. Chem., Int. Ed. 2011, 50, 2450
Chem. Soc. Rev. 2014, 43, 6906.
Synlett 2013, 24, 145.

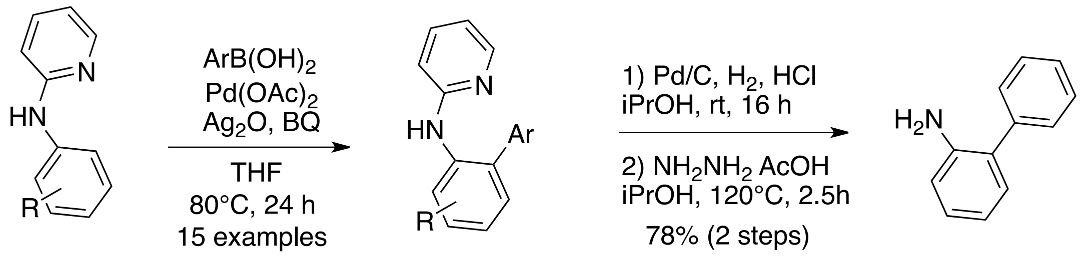
Removal of 2-pyridylsilyl group

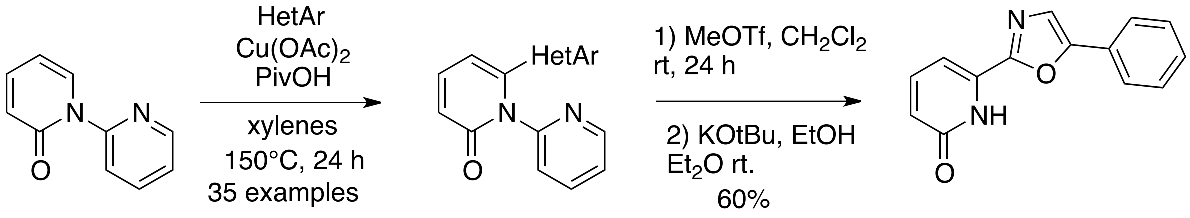


Chem. Soc. Rev. 2014, 43, 6906

2-Aminopyridine directing groups

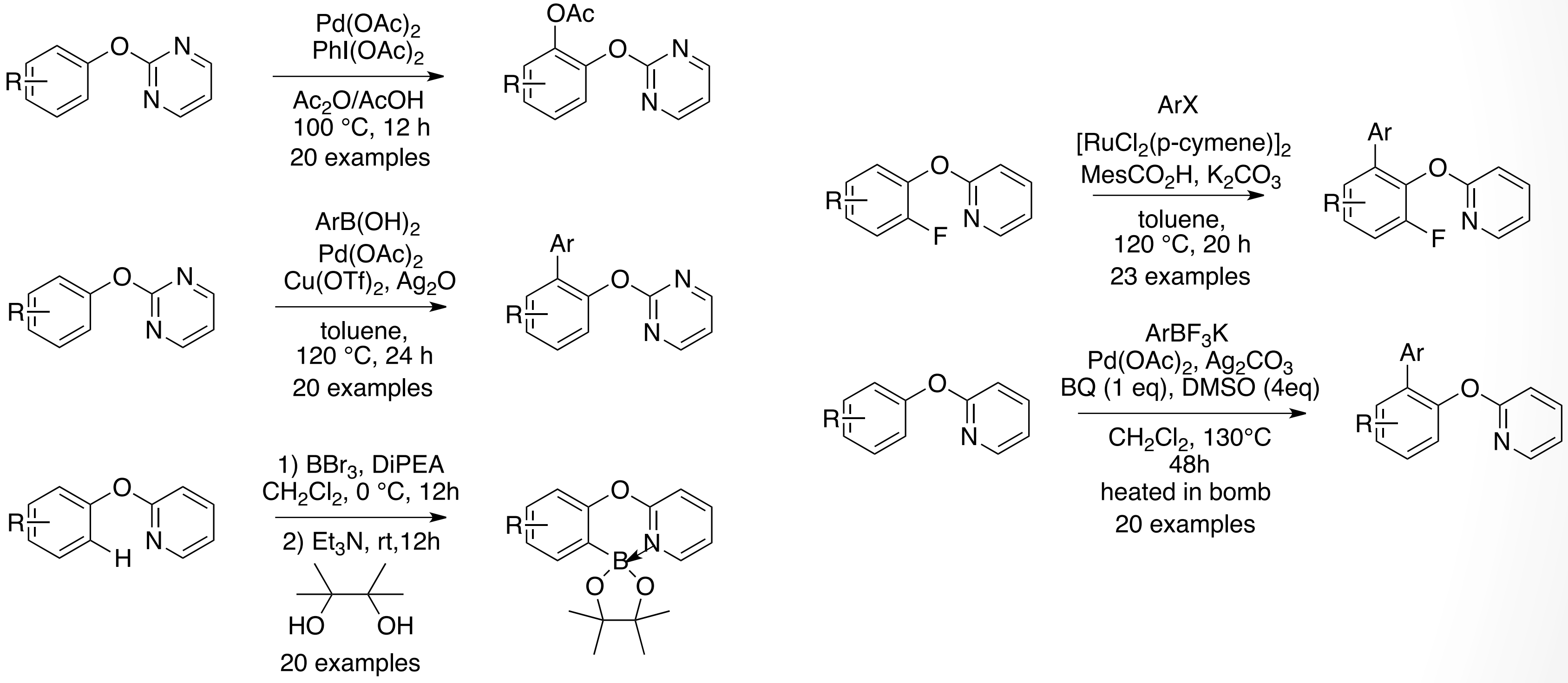






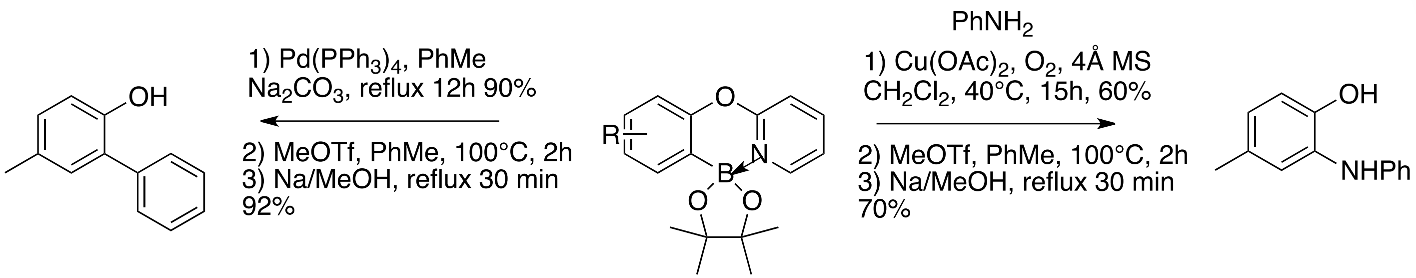
J. Am. Chem. Soc. 2010, 132, 8270
Angew. Chem., Int. Ed. 2010, 49, 8729.
Angew. Chem., Int. Ed. 2013, 52, 10800.

2-Pyridyloxy directing group



JACS. 2000, 122, 12882
JACS. 2001, 123, 10935
JACS. 2012, 134, 12924
OL. 2014, 16, 2748.
J. Organometallics 2013, 32, 272

Deprotection of 2-Pyridyloxy

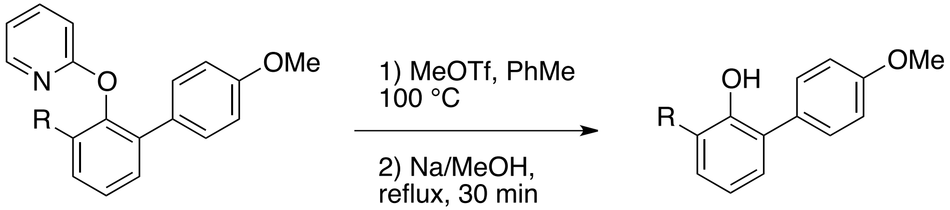


1) $Pd(PPh_3)_4$, PhMe
Na_2CO_3, reflux 12h 90%

2) MeOTf, PhMe, 100°C, 2h
3) Na/MeOH, reflux 30 min
92%

$PhNH_2$
1) $Cu(OAc)_2$, O_2, 4Å MS
CH_2Cl_2, 40°C, 15h, 60%

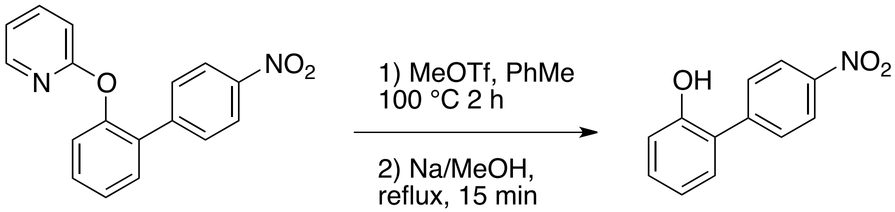
2) MeOTf, PhMe, 100°C, 2h
3) Na/MeOH, reflux 30 min
70%



1) MeOTf, PhMe
100 °C

2) Na/MeOH,
reflux, 30 min

R = H, 81%
R = F, 90%



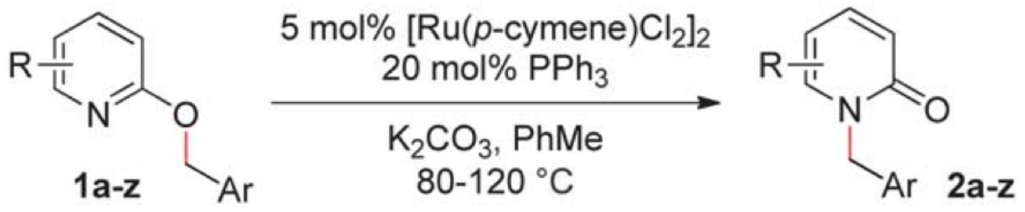
1) MeOTf, PhMe
100 °C 2 h

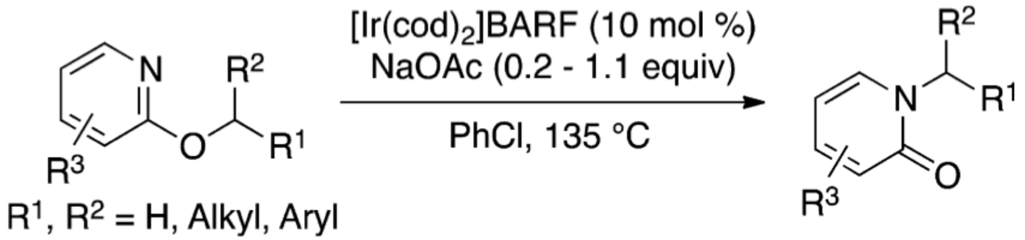
2) Na/MeOH,
reflux, 15 min

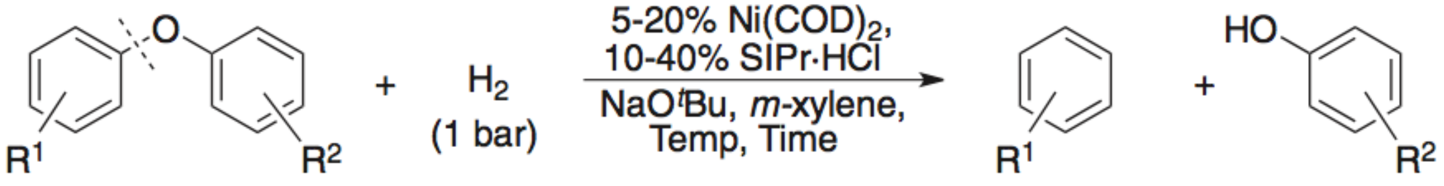
79%

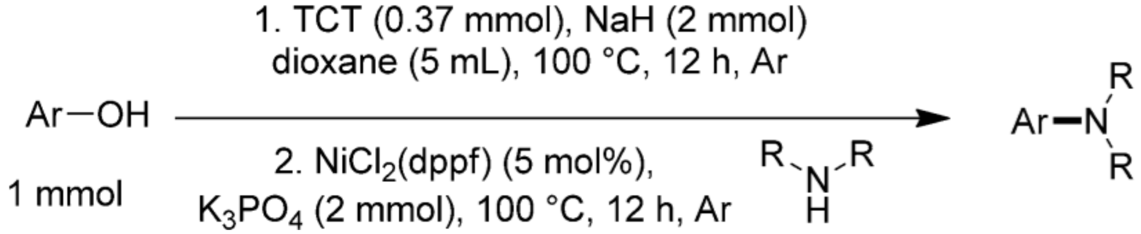
JOC. 2009, 74, 7203.
J. Organometallics 2010, 29, 4058.
OL. 2012, 14, 1154.

C-O bond cleavage

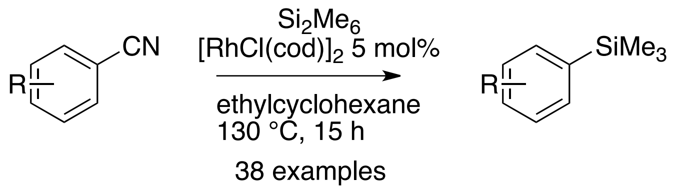


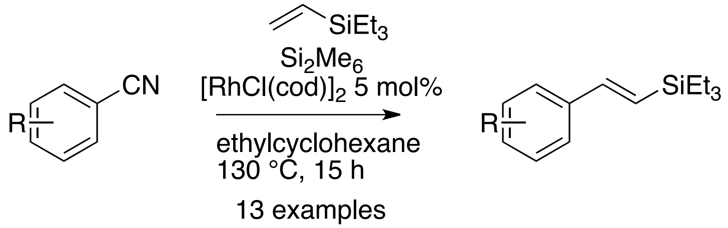


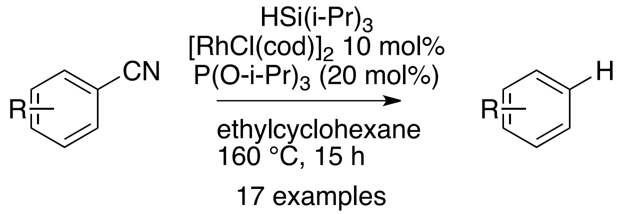


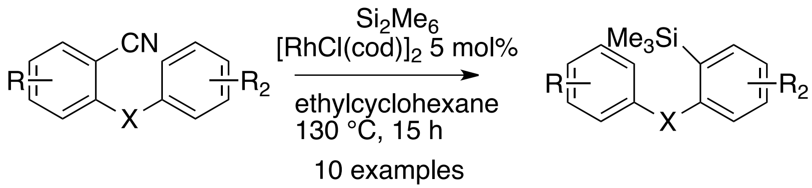


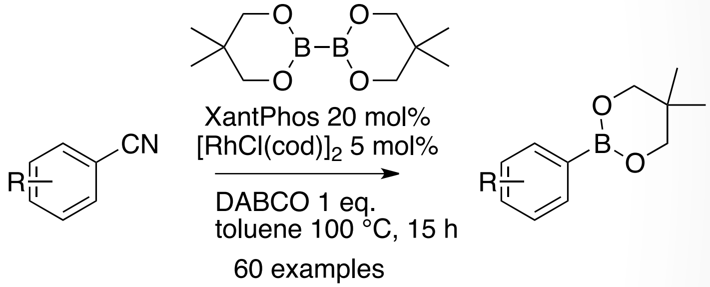
Early work





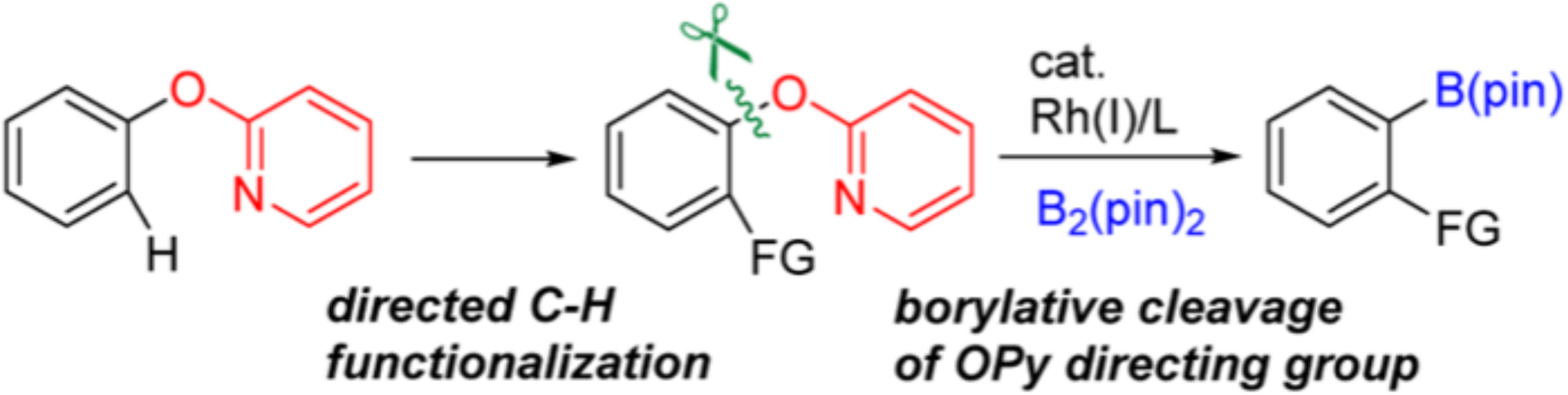


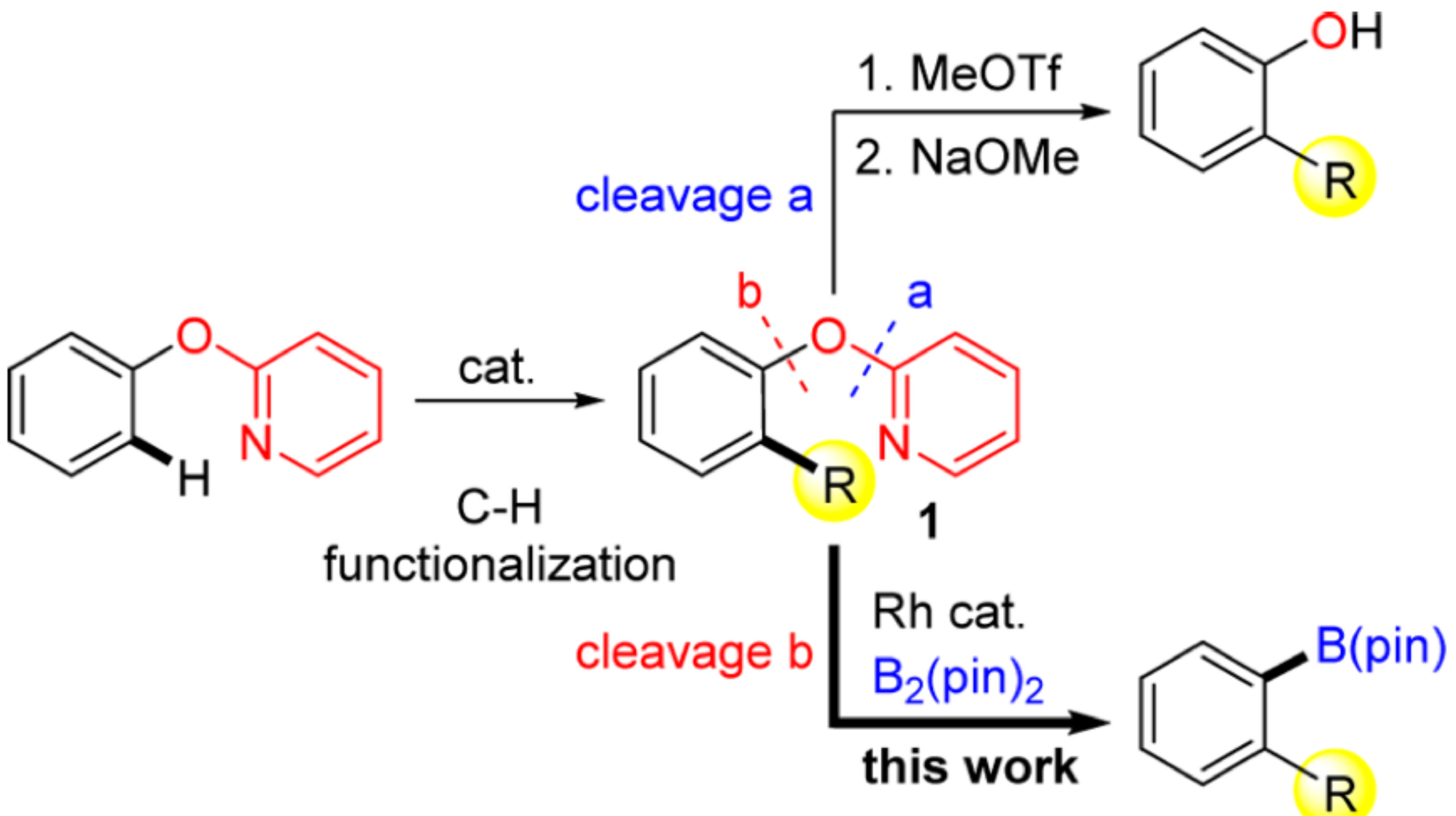




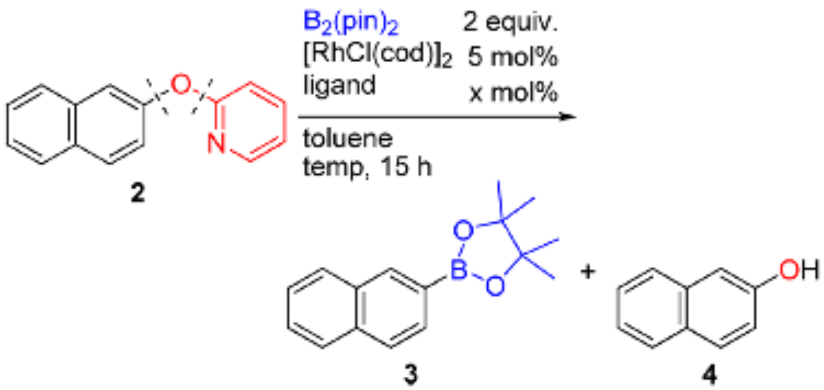
JACS. 2006, 128, 8152.
JACS. 2008, 130, 15982.
JACS. 2009, 131, 3174
Bull. Korean Chem. Soc. 2010, 31, 582.
JACS. 2012, 134, 115

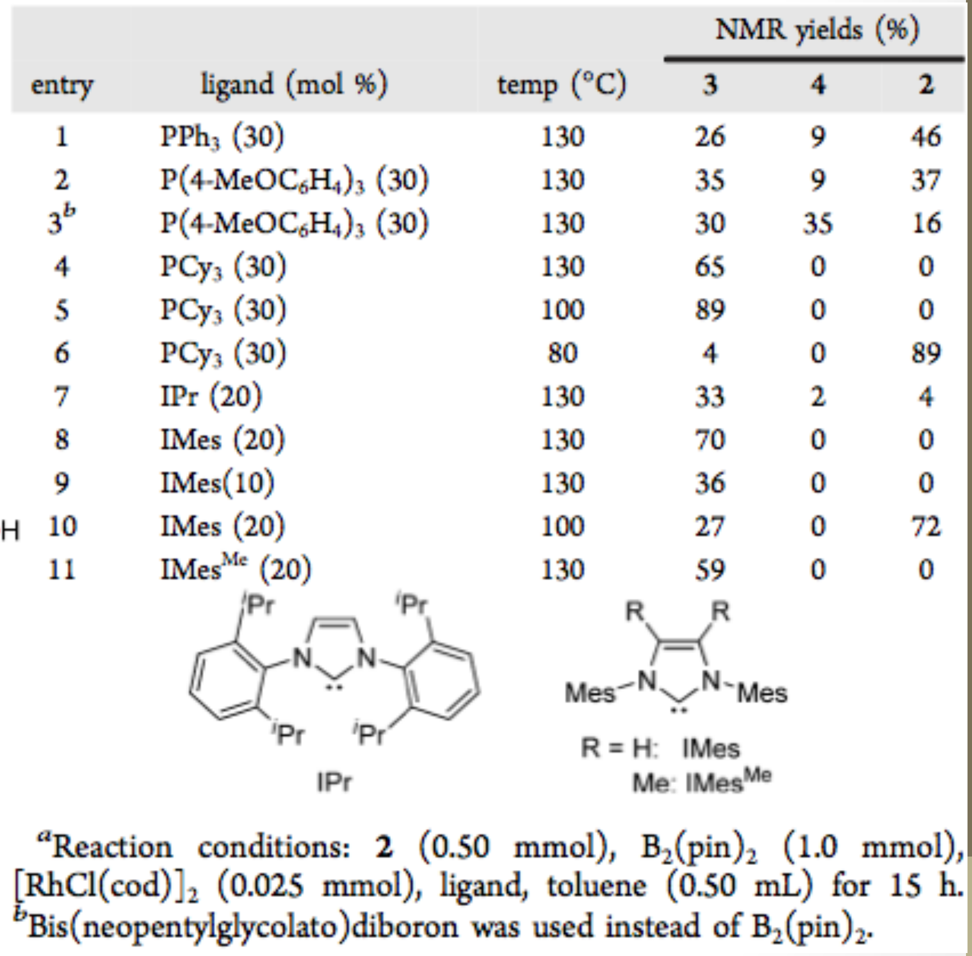
Title paper


H
FG
cat.
Rh(I)/L
$B_2(pin)_2$
B(pin)
FG
directed C-H functionalization
borylative cleavage of OPy directing group


1. MeOTf
2. NaOMe
cleavage a
OH
R
b
a
O
N
H
cat.
C-H
functionalization
R
1
Rh cat.
B₂(pin)₂
cleavage b
this work
B(pin)
R

Optimization of conditions

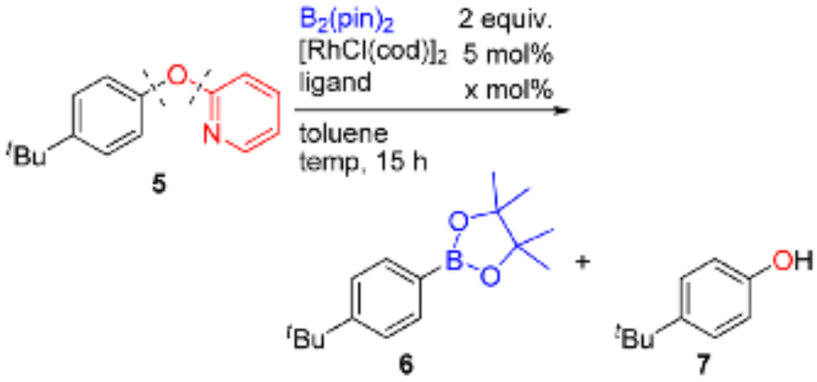




			NMR yields (%)		
entry	ligand (mol %)	temp (°C)	**3**	**4**	**2**
1	PPh_3 (30)	130	26	9	46
2	$P(4\text{-}MeOC_6H_4)_3$ (30)	130	35	9	37
3[b]	$P(4\text{-}MeOC_6H_4)_3$ (30)	130	30	35	16
4	PCy_3 (30)	130	65	0	0
5	PCy_3 (30)	100	89	0	0
6	PCy_3 (30)	80	4	0	89
7	IPr (20)	130	33	2	4
8	IMes (20)	130	70	0	0
9	IMes(10)	130	36	0	0
10	IMes (20)	100	27	0	72
11	$IMes^{Me}$ (20)	130	59	0	0

[a] Reaction conditions: **2** (0.50 mmol), $B_2(pin)_2$ (1.0 mmol), $[RhCl(cod)]_2$ (0.025 mmol), ligand, toluene (0.50 mL) for 15 h.
[b] Bis(neopentylglycolato)diboron was used instead of $B_2(pin)_2$.

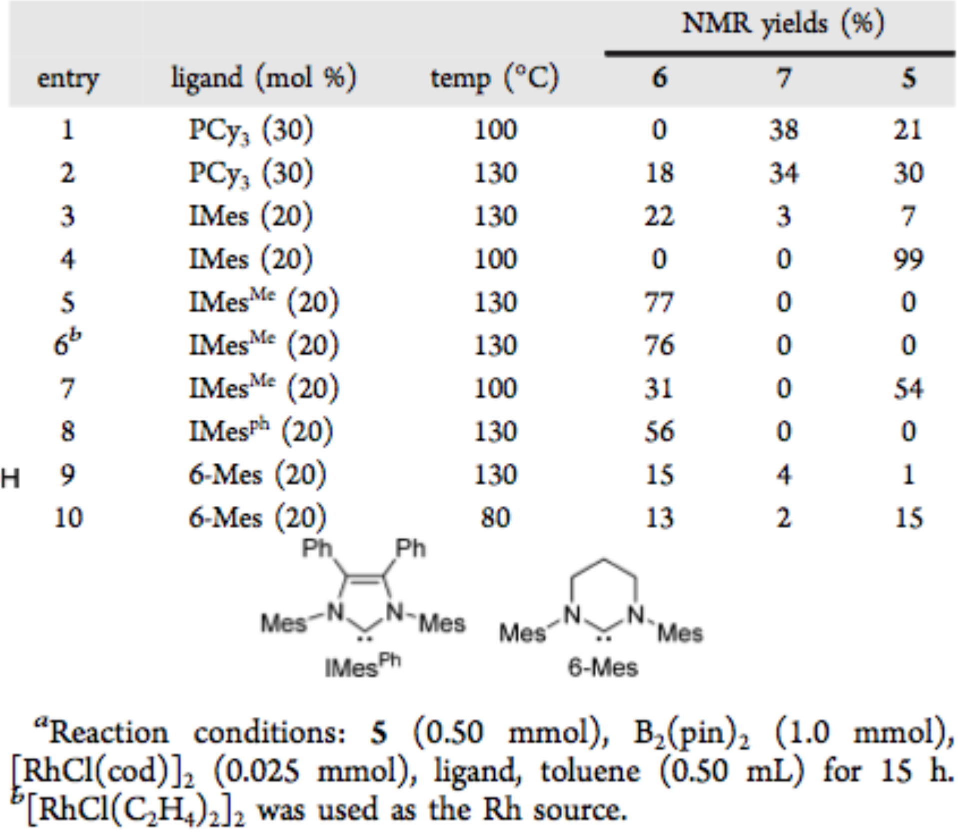
Optimization of conditions



5

6

7

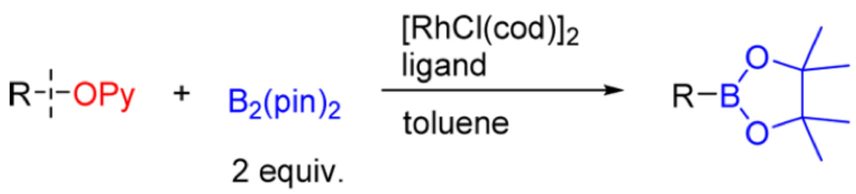


entry	ligand (mol %)	temp (°C)	NMR yields (%) 6	7	5
1	PCy_3 (30)	100	0	38	21
2	PCy_3 (30)	130	18	34	30
3	IMes (20)	130	22	3	7
4	IMes (20)	100	0	0	99
5	$IMes^{Me}$ (20)	130	77	0	0
6[b]	$IMes^{Me}$ (20)	130	76	0	0
7	$IMes^{Me}$ (20)	100	31	0	54
8	$IMes^{Ph}$ (20)	130	56	0	0
9	6-Mes (20)	130	15	4	1
10	6-Mes (20)	80	13	2	15

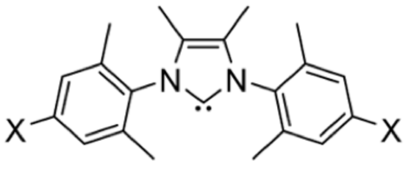
$IMes^{Ph}$

6-Mes

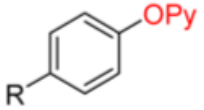
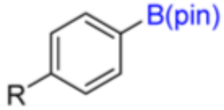
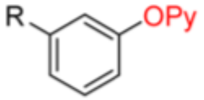
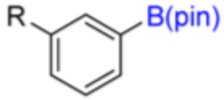
[a] Reaction conditions: 5 (0.50 mmol), $B_2(pin)_2$ (1.0 mmol), $[RhCl(cod)]_2$ (0.025 mmol), ligand, toluene (0.50 mL) for 15 h. [b] $[RhCl(C_2H_4)_2]_2$ was used as the Rh source.

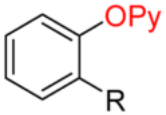
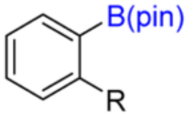
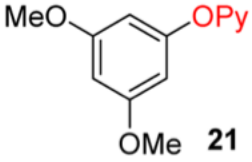
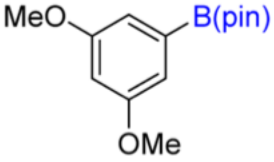
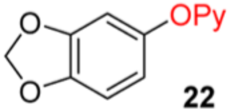
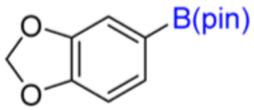
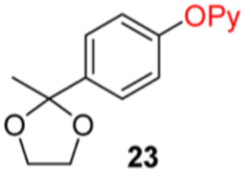
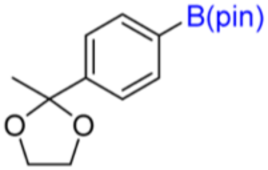


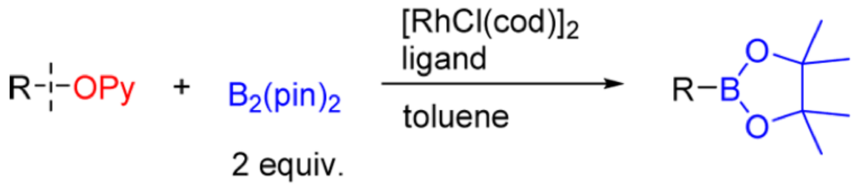
condition A: PCy_3, 100 °C
condition B: IMes^{Me}, 130 °C
condition C: IMXy^{Me}, 160 °C



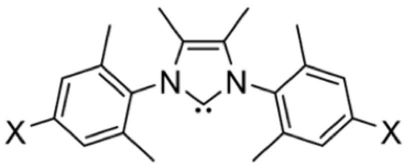
X = Me: IMes^{Me}
OMe: IMXy^{Me}

entry	ether	product	condition^a	yield (%)
				
1	R = ^{t}Bu (**5**)		B	77
2	Ph (**8**)		B	80
3	OMe (**9**)		B	68
4	OPh (**10**)		B	71
5	OCF_3 (**11**)		B	62
6	F (**12**)		B^{b,c}	70
7	Cl (**13**)		A	21^d
8			B	0
9	CF_3 (**14**)		A^e	65
10			B	61
11	CO_2Et (**15**)		A^e	75
12			B	30
				
13	R = OPiv (**16**)		A^{b,e}	72
14			B	0
15	$OCONMe_2$ (**17**)		A^{b,e}	66
16			B	0
17	NMe_2 (**18**)		B	68

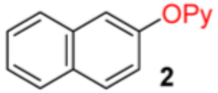
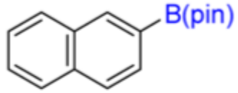
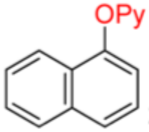
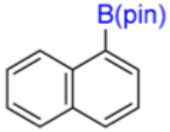
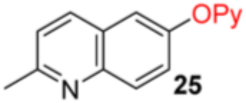
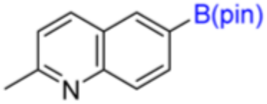
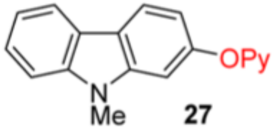
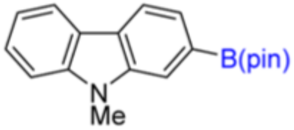
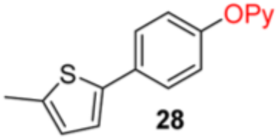
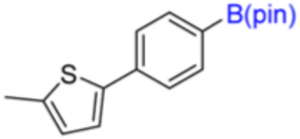
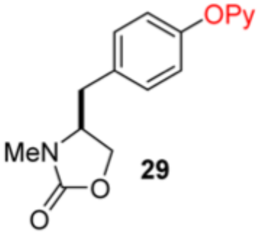
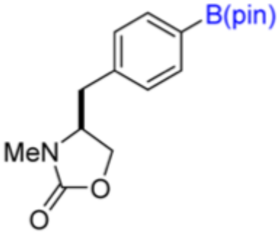
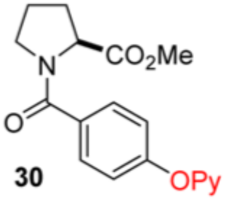
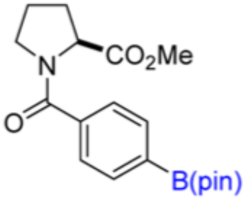
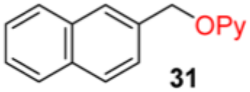
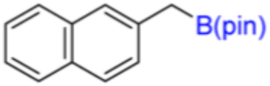
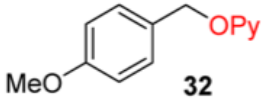
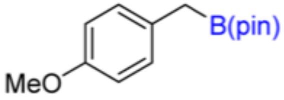
entry	ether	product	condition^a	yield (%)
				
18	R = Me (**19**)		B^f	42
19			C	63
20	Ph (**20**)		B^f	50
21			C	70
22	 **21**		B	40
23	 **22**		A^{c,e}	53
24			B	30
25	 **23**		B	60



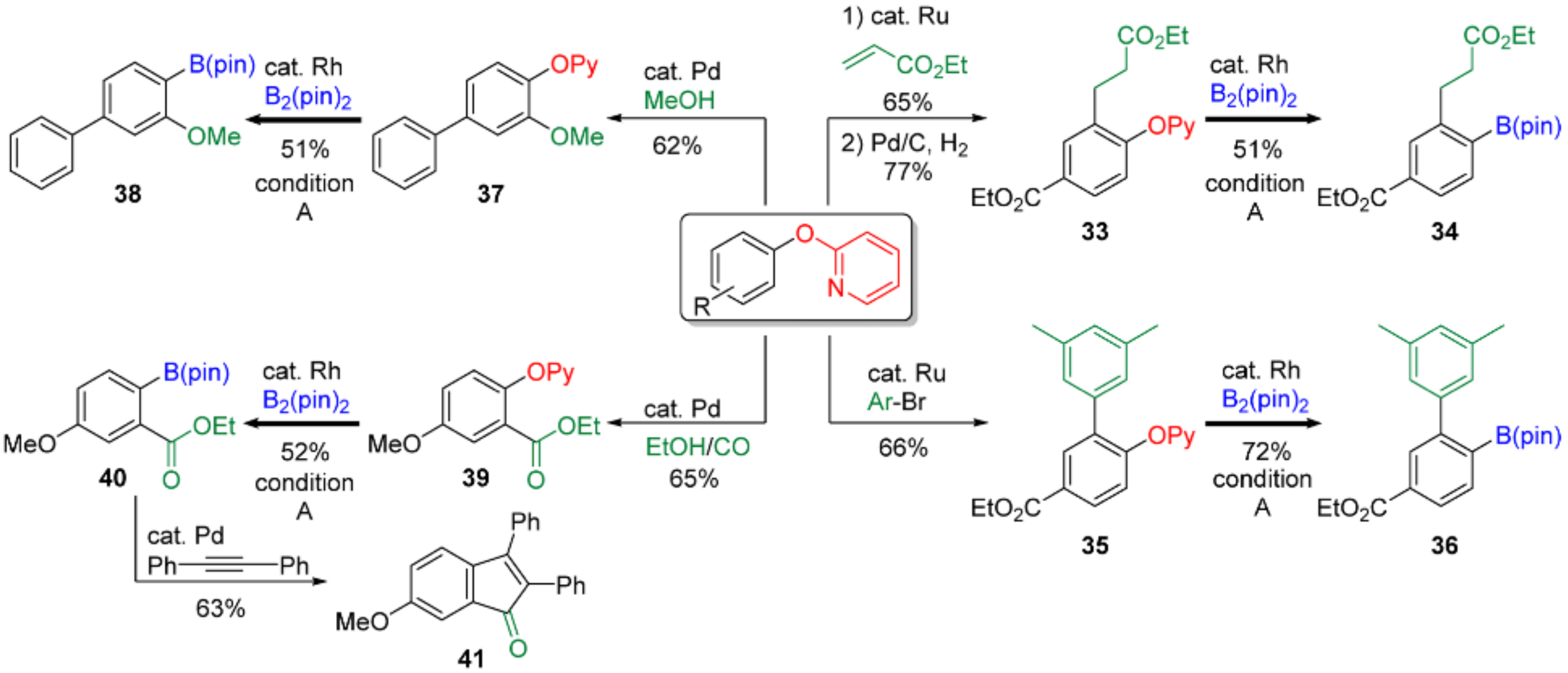
condition A: PCy_3, 100 °C
condition B: $IMes^{Me}$, 130 °C
condition C: $IMXy^{Me}$, 160 °C

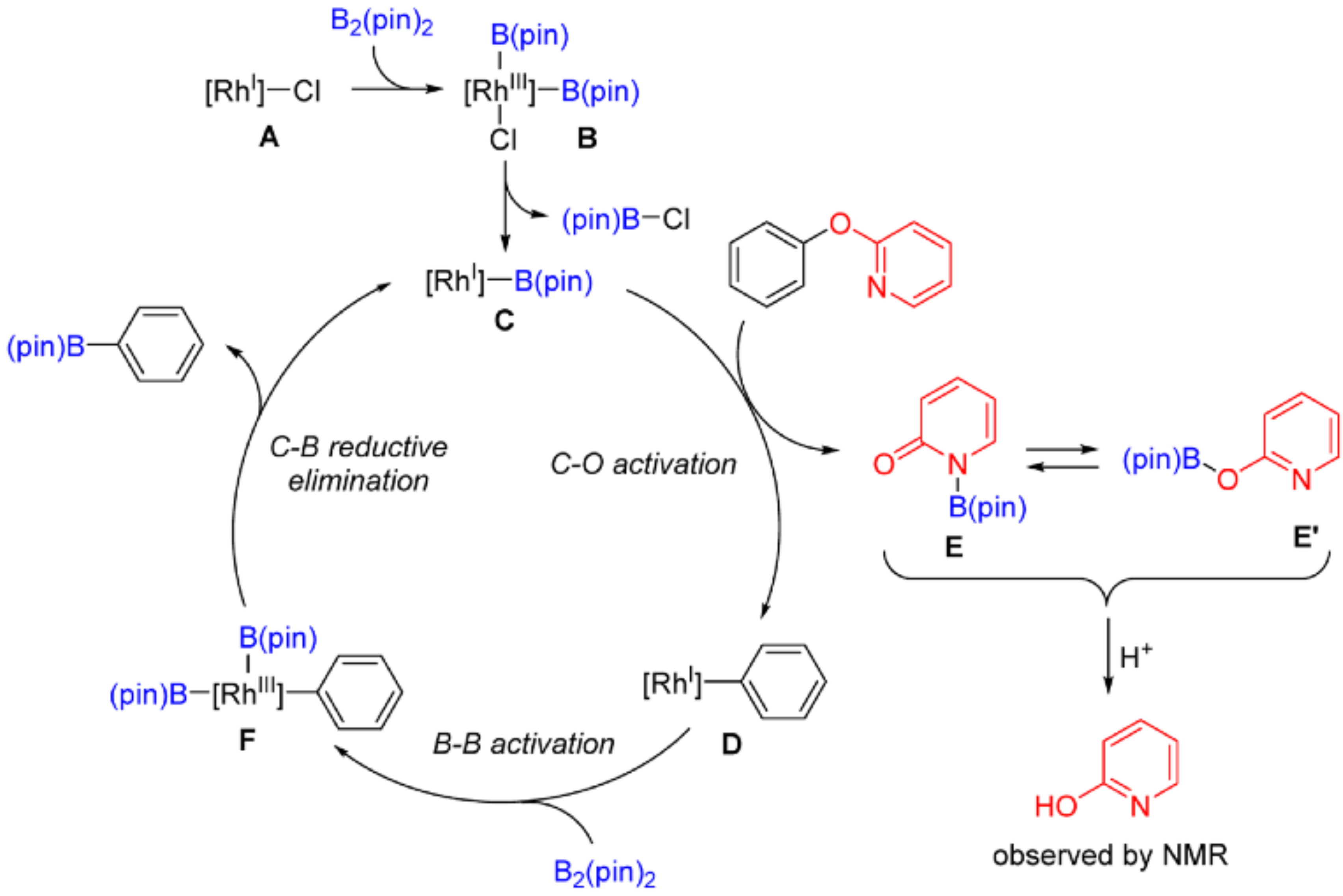


X = Me: $IMes^{Me}$
OMe: $IMXy^{Me}$

entry	ether	product	condition[a]	yield (%)
26	 **2**		A	89
27			B	59
28	 **24**		A	61
29			B	65
30	 **25**		B	82
31	 **26**		B	60
32	 **27**		B	60
33	 **28**		B[b,c]	65
34	 **29**		B	66
35	 **30**		A	68
36			B	21
37	 **31**		A	62
38			B	21
39	 **32**		B	68

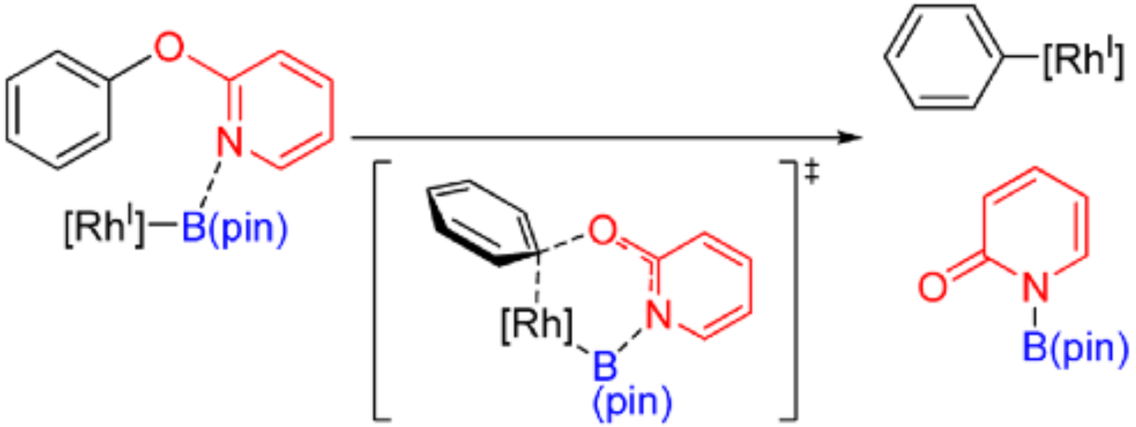
Sequential functionalization



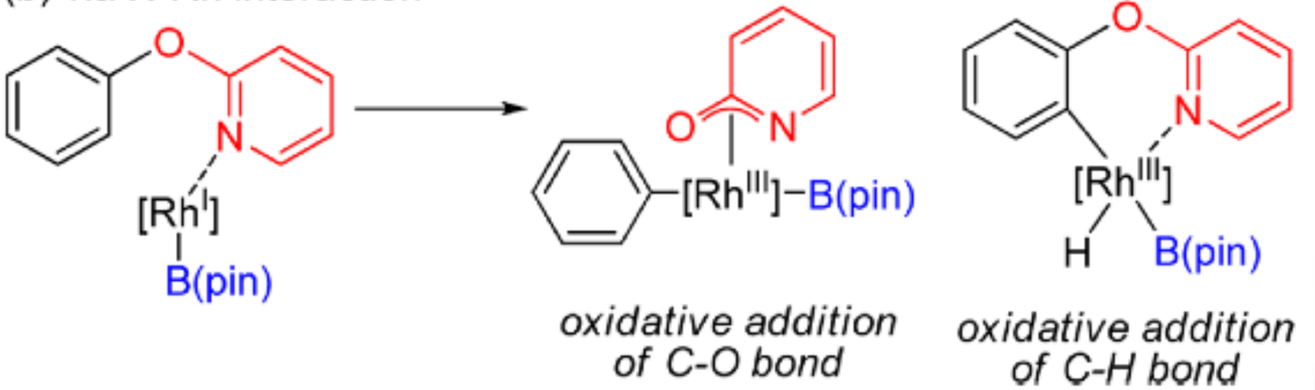

B2(pin)2
B(pin)
[RhI]—Cl
A
[RhIII]—B(pin)
Cl
B
(pin)B—Cl
[RhI]—B(pin)
C
O
N
(pin)B
C-B reductive elimination
C-O activation
O
N
B(pin)
E
(pin)B
O
N
E'
H+
HO
N
observed by NMR
B(pin)
(pin)B—[RhIII]
F
[RhI]
D
B-B activation
B2(pin)2

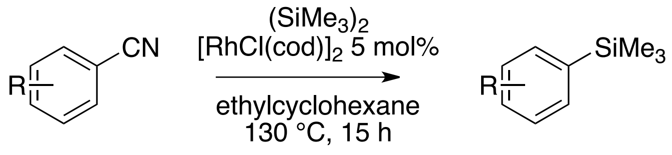
C-OPy cleavage

(a) via N-B interaction

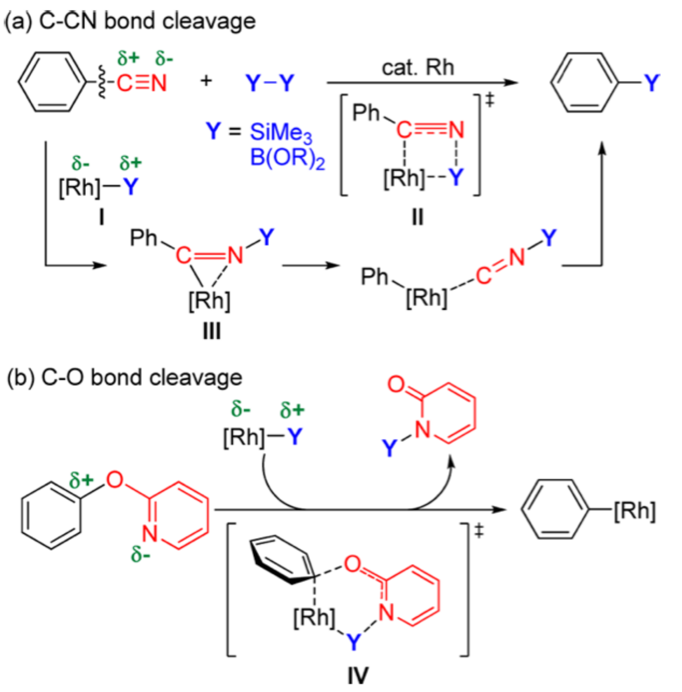


(b) via N-Rh interaction

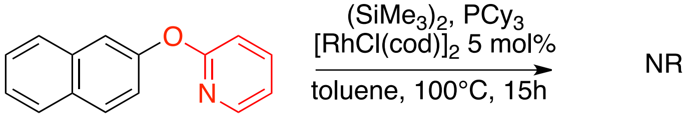




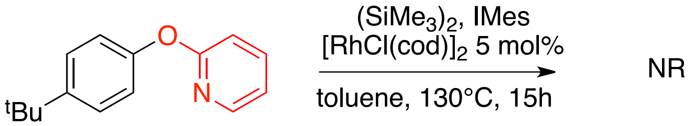
$(SiMe_3)_2$
$[RhCl(cod)]_2$ 5 mol%
ethylcyclohexane
130 °C, 15 h


(a) C-CN bond cleavage

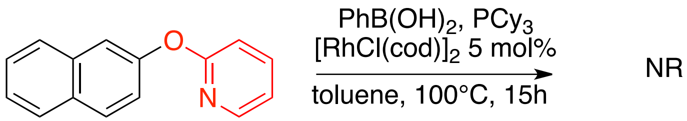
(b) C-O bond cleavage



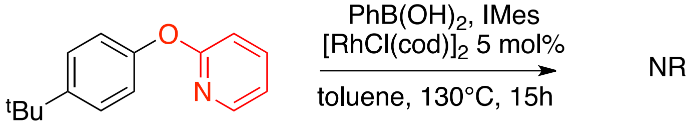
$(SiMe_3)_2$, PCy_3
$[RhCl(cod)]_2$ 5 mol%
toluene, 100°C, 15h



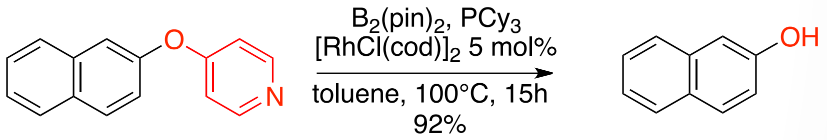
$(SiMe_3)_2$, IMes
$[RhCl(cod)]_2$ 5 mol%
toluene, 130°C, 15h



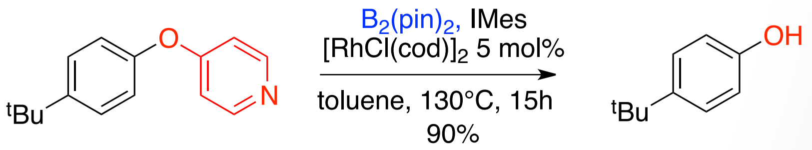
$PhB(OH)_2$, PCy_3
$[RhCl(cod)]_2$ 5 mol%
toluene, 100°C, 15h



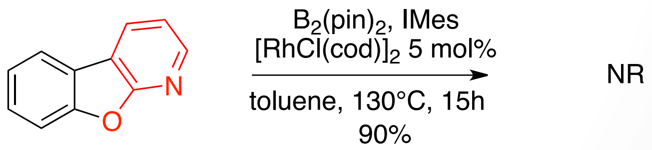
$PhB(OH)_2$, IMes
$[RhCl(cod)]_2$ 5 mol%
toluene, 130°C, 15h



$B_2(pin)_2$, PCy_3
$[RhCl(cod)]_2$ 5 mol%
toluene, 100°C, 15h
92%

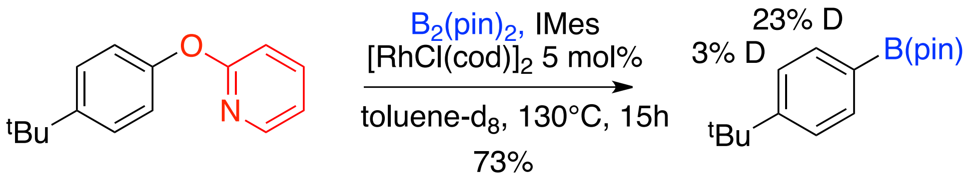


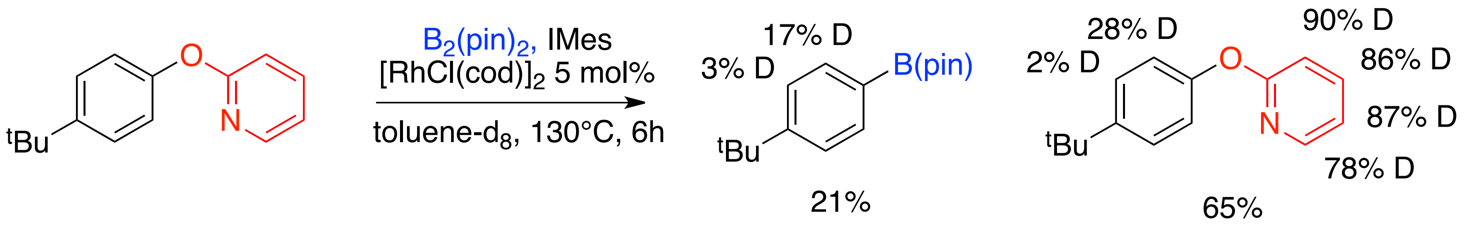
$B_2(pin)_2$, IMes
$[RhCl(cod)]_2$ 5 mol%
toluene, 130°C, 15h
90%

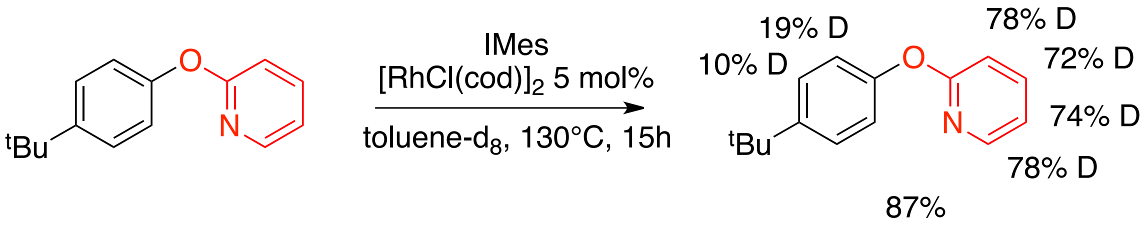


$B_2(pin)_2$, IMes
$[RhCl(cod)]_2$ 5 mol%
toluene, 130°C, 15h
90%

Deuterium Exchange







Conclusions

- Developed Rh-catalyzed borylation reaction for Ar-2-pyridyl ethers.
- A new application in directed C-H activation that can be used as a handle for further manipulation.