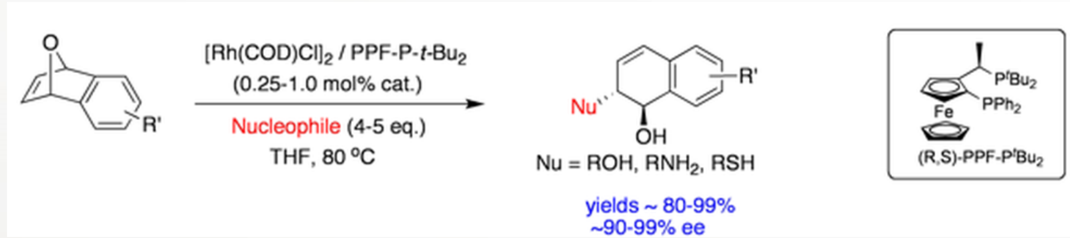
From Reversible Oxidative Addition to Catalytic Carbon-Halogen Bond Formation

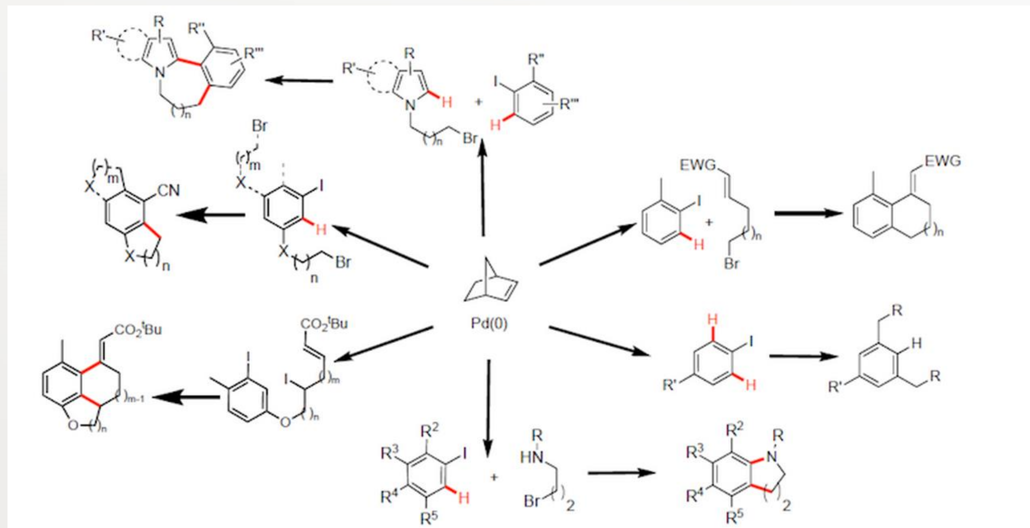
Mark Lautens*

RSC **2015**, *New Trends in Cross-Coupling*, 276-321

In Memory of Prof. Heck

Report: Zhe Dong
Advisor: Prof. Guangbin Dong
Oct 10st 2015





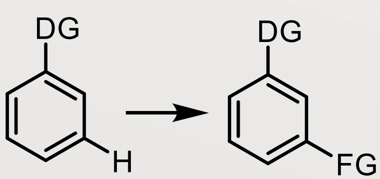
Mark Lautens

(1959 - now)

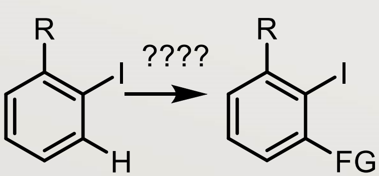
BS in chemistry, Guelph University 1981
PHD : Prof. B. M. Trost UWM 1981-1985
Postdoc: D. A. Evans 1985-1987
Assistant Professor at University of Toronto 1987-1992
Associate Pull Professor, 1992-1995
Full Professor 1995 –

Mark Lautens

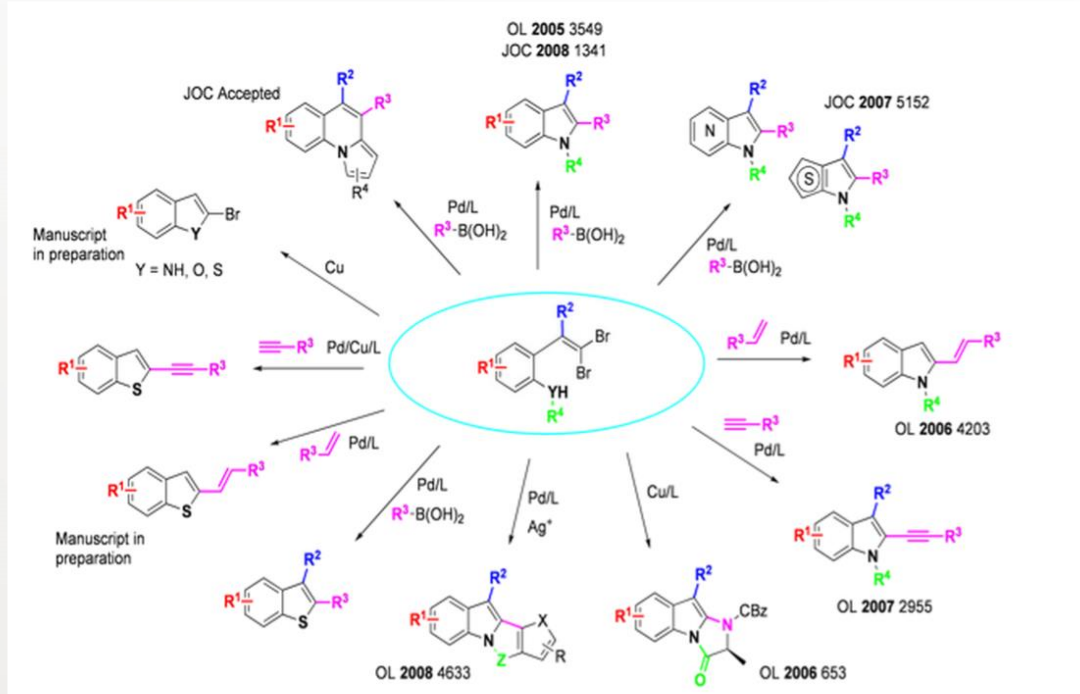
(1959 - now)

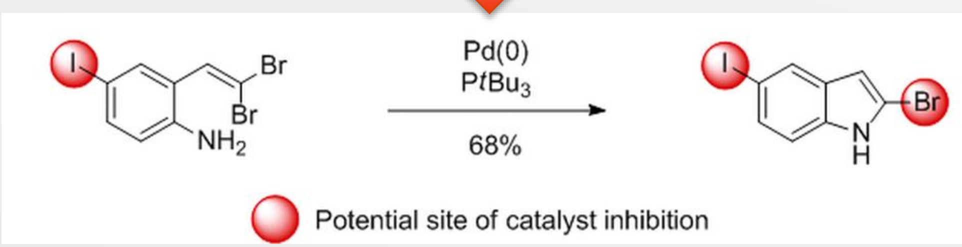


Traceless



Ideal Traceless system





????

Outline:

1. Early discovery and Stoichiometry study

2. The Reversible and Selective Oxidative Addition

3. Catalytic Reaction: From Aryl Iodide to Alkyl Iodide

4. Vinyl Halide to alkyl halide

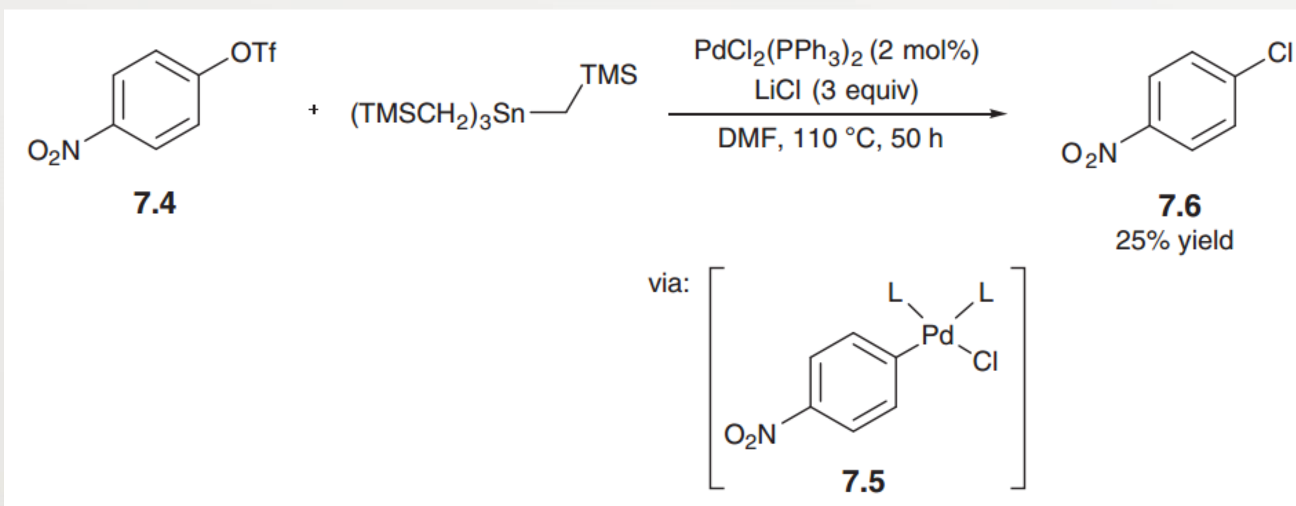
5. Conclusion and Outlook

Early Discovery:

$$\underset{\textbf{7.1}}{[\mathrm{Pt(PEt_3)_2Ph_2I_2}]} + \mathrm{solvent} \xrightarrow{-\mathrm{I}^-} \underset{\textbf{7.2}}{[\textit{trans}\text{-}[\mathrm{Pt(PEt_3)_2Ph_2I(solvent)}]]}$$

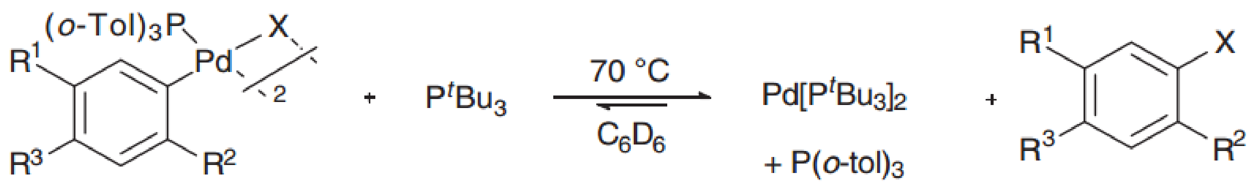
$$\xrightarrow{-\mathrm{PhI}} \underset{\textbf{7.3}}{\textit{trans}\text{-}[\mathrm{Pt(PEt_3)_2PhI}]}$$

R. Ettorre, *Inorg. Nucl. Chem. Lett.*, **1968**, 5, 45.



A. M. Echavarren and J. K. Stille, *J. Am. Chem. Soc.,* **1987**, 109, 5478.

Stoichiometry study:

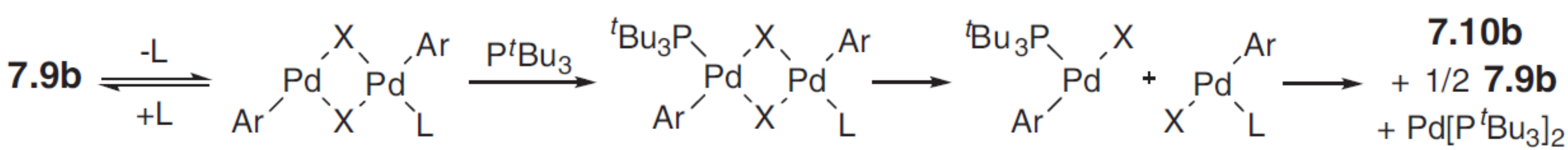


R^1 = ^{t}Bu, R^2 = Me, R^3 = H
X = Cl: **7.9a**
X = Br: **7.9b**
X = I: **7.9c**

R^1 = R^2 = H, R^3 = ^{t}Bu
X = Cl: **7.9d**
X = Br: **7.9e**

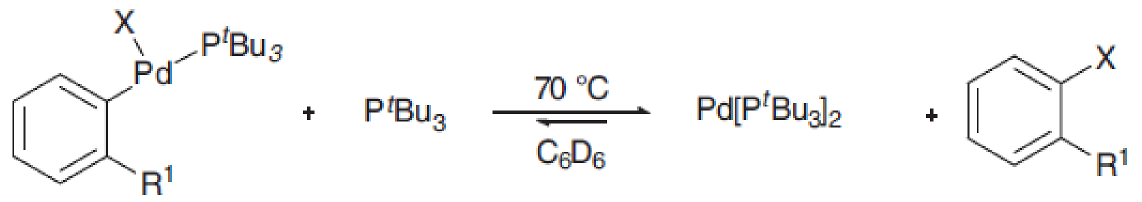
7.10a-e

X	Yield of **7.10** (%)	K_{eq}
7.7a (X = Cl)	70	$9(3)\times10^{-2}$
7.7b (X = Br)	70	$2.3(3)\times10^{-3}$
7.7c (X = I)	39	$3.7(2)\times10^{-5}$
7.7d (X = Cl)	30	Not measured
7.7e (X = Br)	75	$3.3(6)\times10^{-4}$



A. H. Roy and J. F. Hartwig, *J. Am. Chem. Soc.*, **2001**, 123, 1232.

Stoichiometry study:

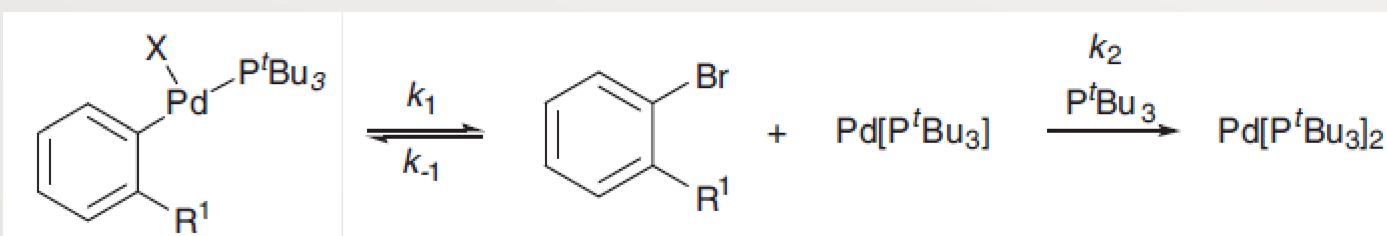


R^1 = Me
X = Cl: **7.12a**
X = Br: **7.12b**
X = I: **7.12c**

R^1 = H
X = Br: **7.12d**
X = I: **7.12e**

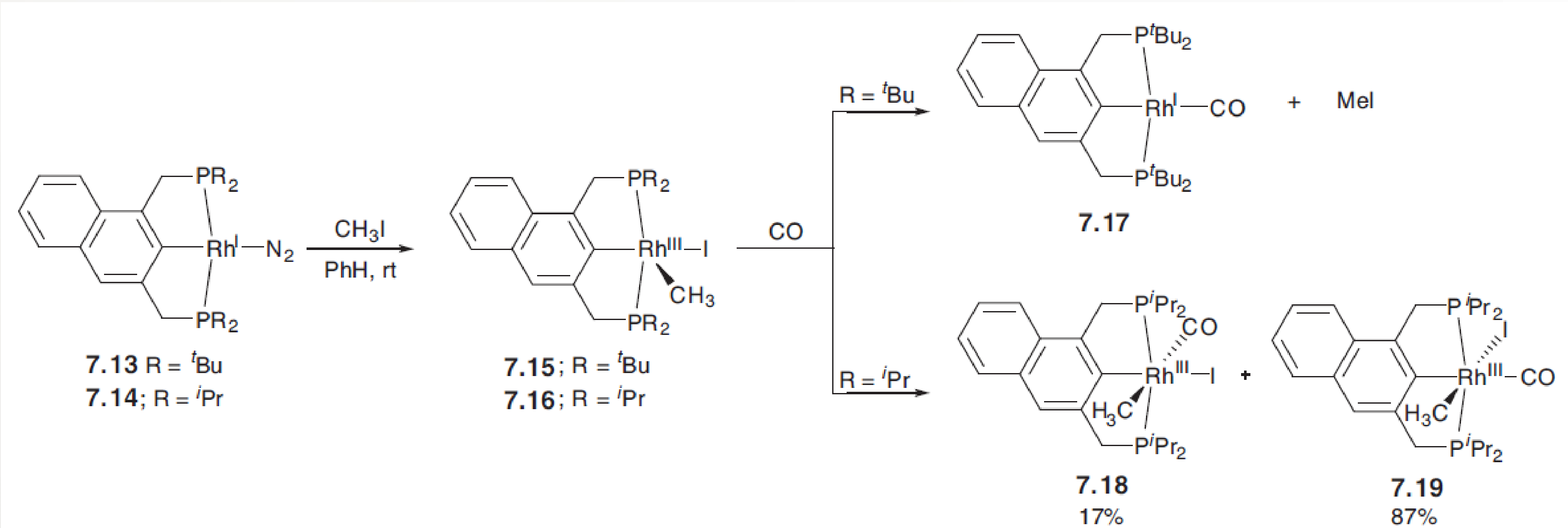
7.13a–e

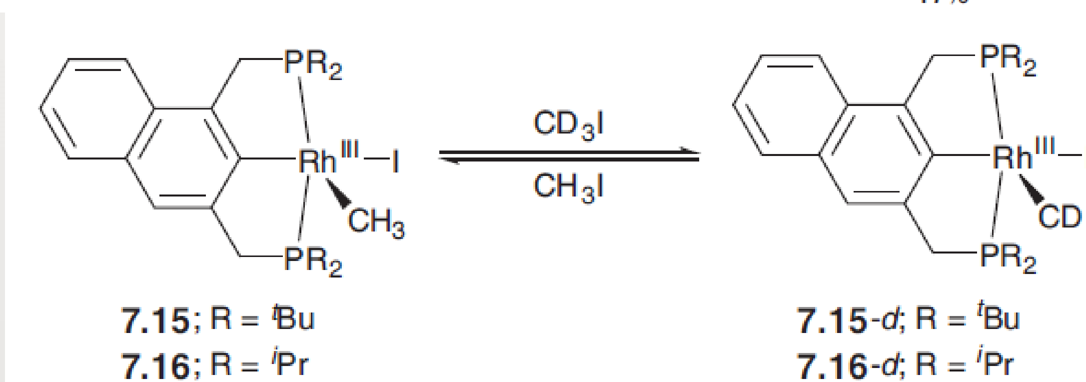
X	Yield of **7.13** (%)	K_{eq}
7.12a (X = Cl)	76	10.9×10^{2}
7.12b (X = Br)	98	32.7×10^{-1}
7.12c (X = I)	79	1.79×10^{-1}
7.12d (X = Br)	68	13.4×10^{-1}
7.12e (X = I)	60	0.51×10^{-1}



A. H. Roy, J. F. Hartwig, *J. Am. Chem. Soc.* **2003**, *125*, 13944.

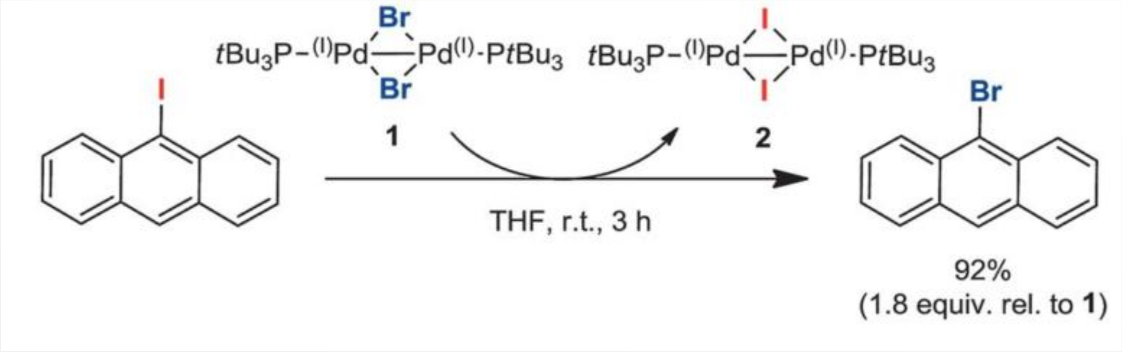
Stoichiometry study:

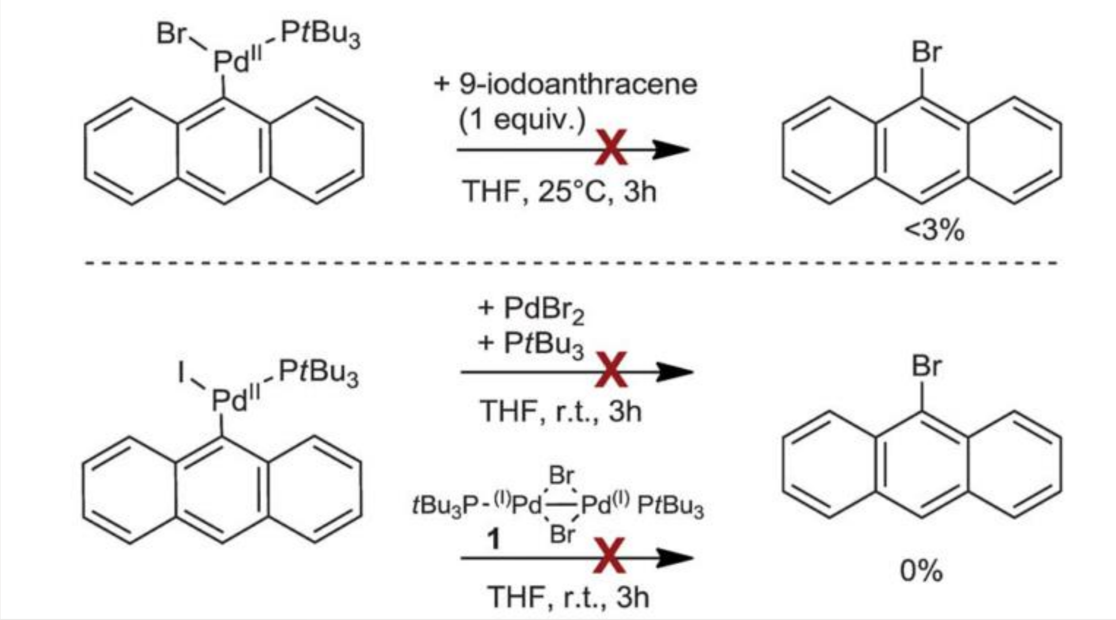




C. M. Frech, D. Milstein, *J. Am. Chem. Soc.* **2006**, *128*, 12434.
M. Feller, Y. Diskin-Posner, G. Leitus, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2013**, *135*, 11040.

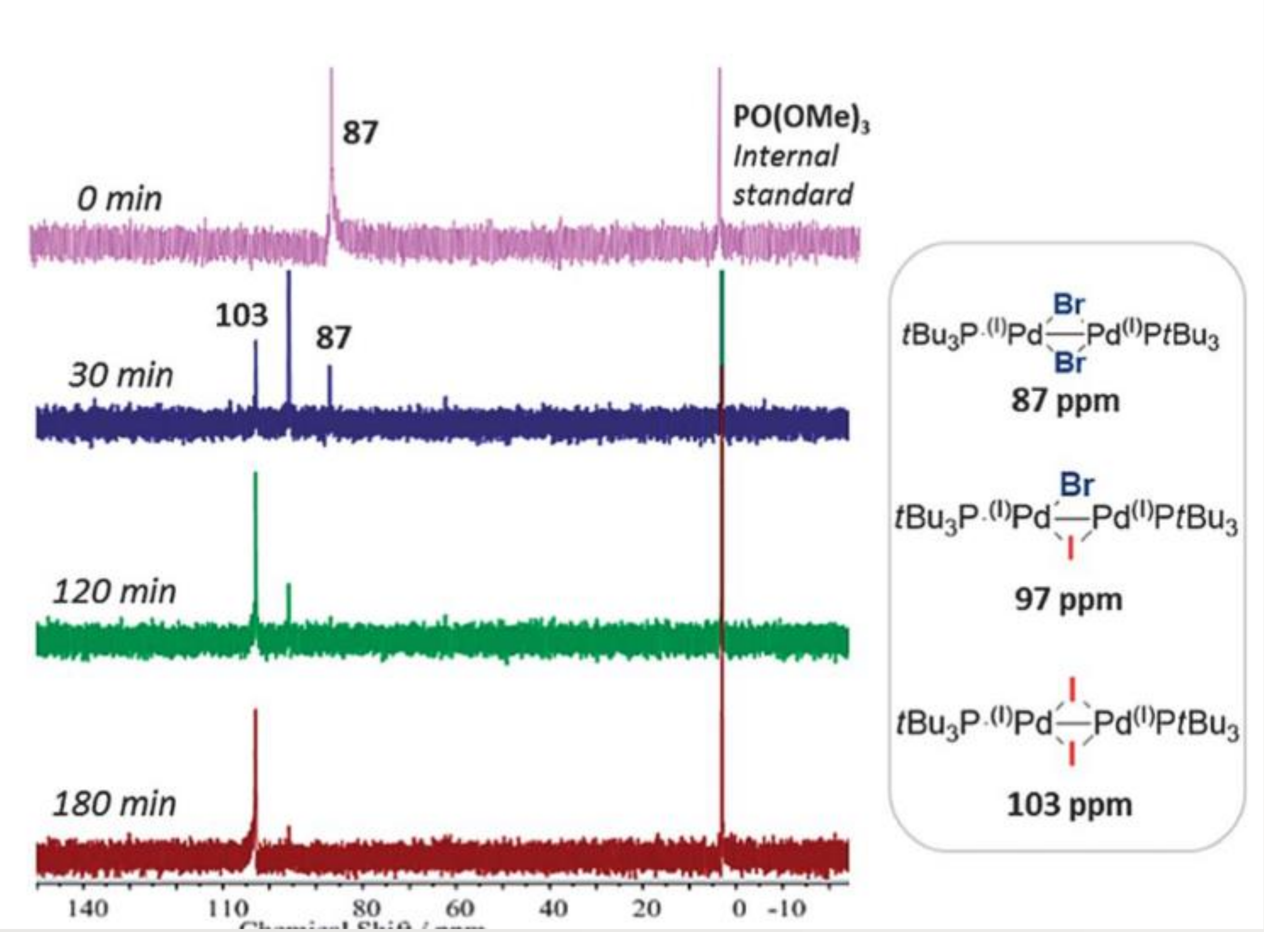
Stoichiometry study to Catalysis:





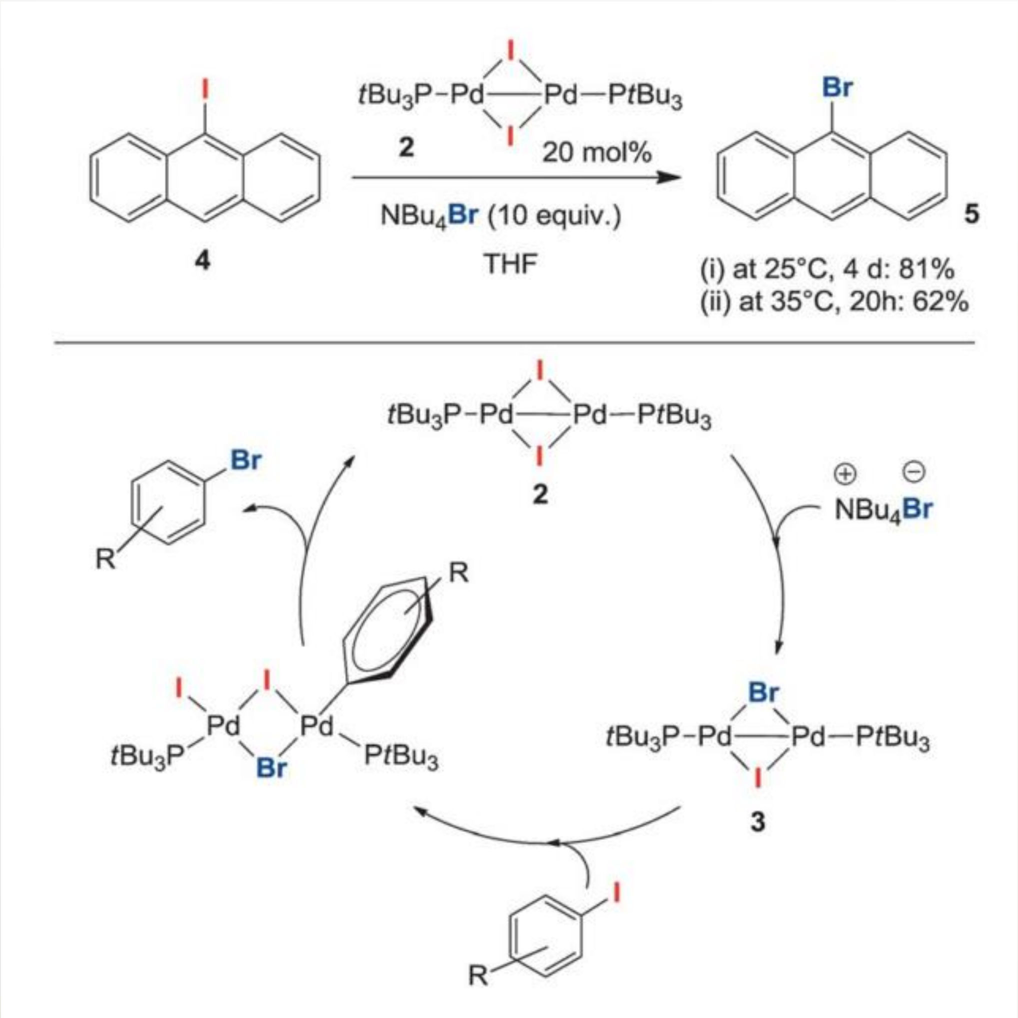
K. J. Bonney, F. Proutiere, F. Schoenebeck, *Chem. Sci.* **2013**, *4*, 4434.

Stoichiometry study to Catalysis :



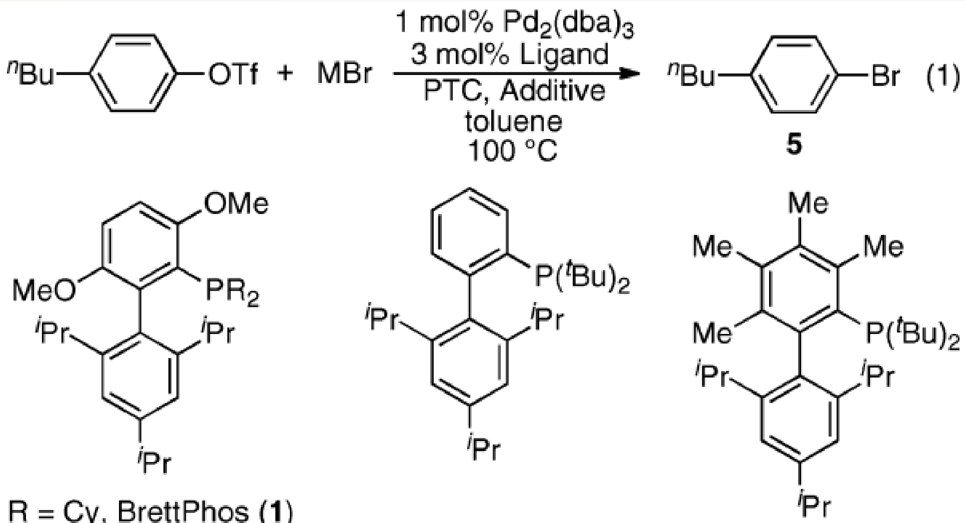
K. J. Bonney, F. Proutiere, F. Schoenebeck, *Chem. Sci.* **2013**, *4*, 4434.

Stoichiometry study to Catalysis :



K. J. Bonney, F. Proutiere, F. Schoenebeck, *Chem. Sci.* **2013**, *4*, 4434.

Catalysis :

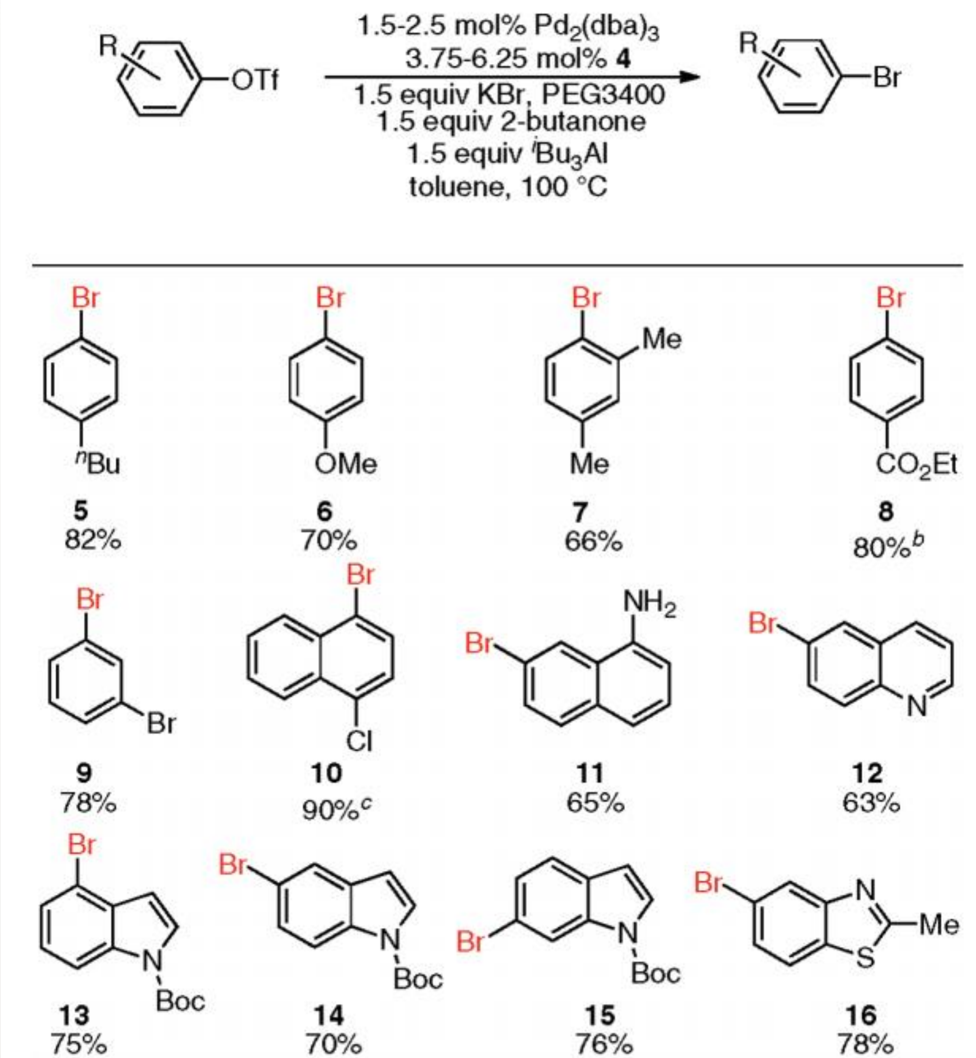


R = Cy, BrettPhos (**1**)
R = ^{t}Bu, ^{t}BuBrettPhos (**4**)
^{t}BuXPhos (**2**)
(**3**)

entry	MBr	ligand	PTC	additive	yield (%) [b]
1	Bu_4NBr	**1**			1[c]
2	Bu_4NBr	**2**			2[c]
3	Bu_4NBr	**3**			3[c]
4	Bu_4NBr	**4**			6[c]
5	KBr	**4**			11[c]
6	KBr	**4**	PEG		32[c]
7	KBr	**4**	PEG	KOTf[c,d]	1[c]
8	KBr	**4**	PEG	Et_3B	50[c]
9	KBr	**4**	PEG	$^iBu_2AlF$	54[e]
10	KBr	**4**	PEG	$^iBu_3Al$	41[e]
11	KBr	**4**	PEG	$(^iPrO)_3Al$	1[c]
12	KBr	**4**	PEG	$^iPr_3Al$[f]	25[g]
13	KBr	**4**	PEG	$^iBu_3Al$/2-butanone[h]	92

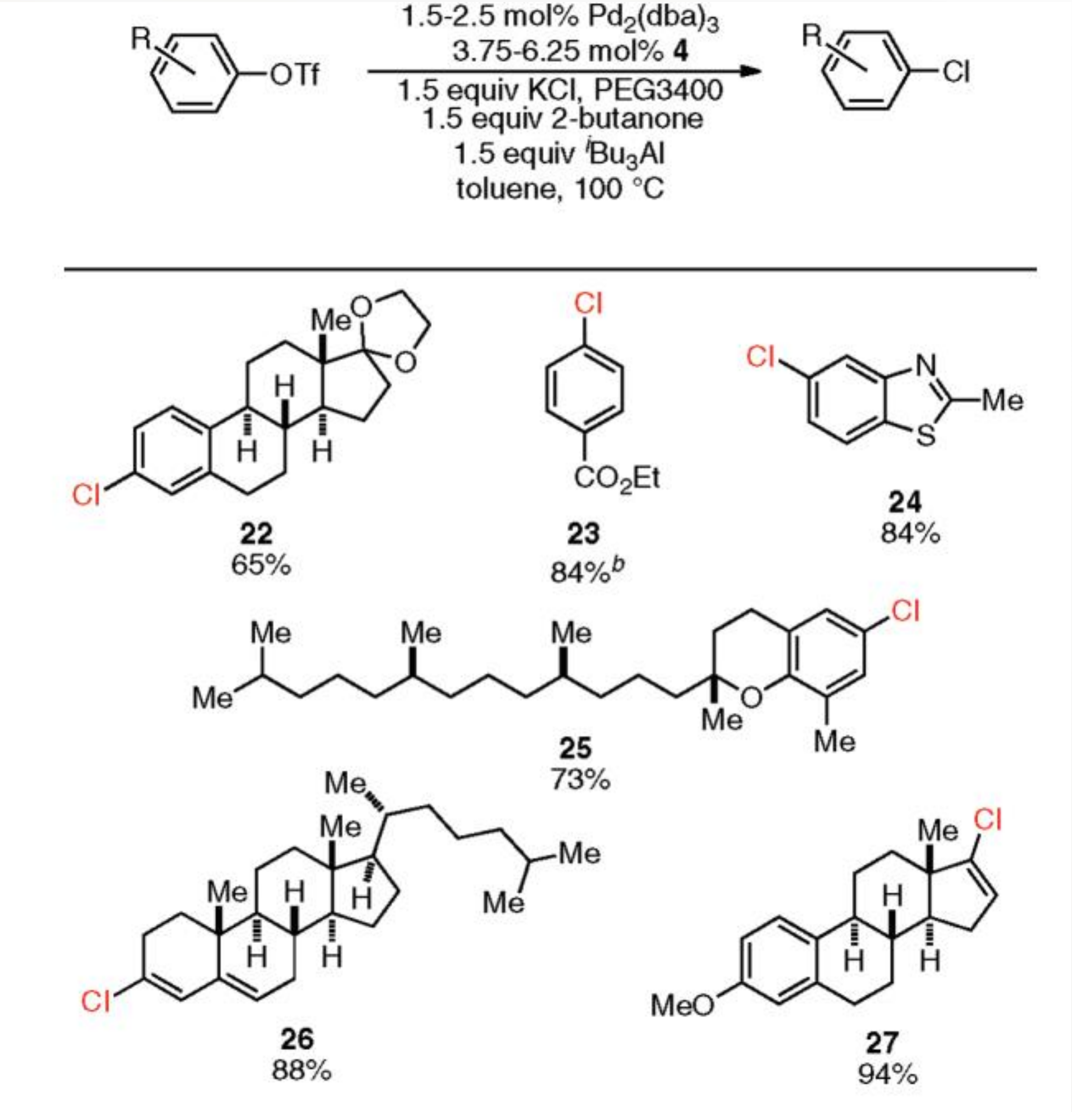
X. Shen, A. M. Hyde, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 14076.

Catalysis :



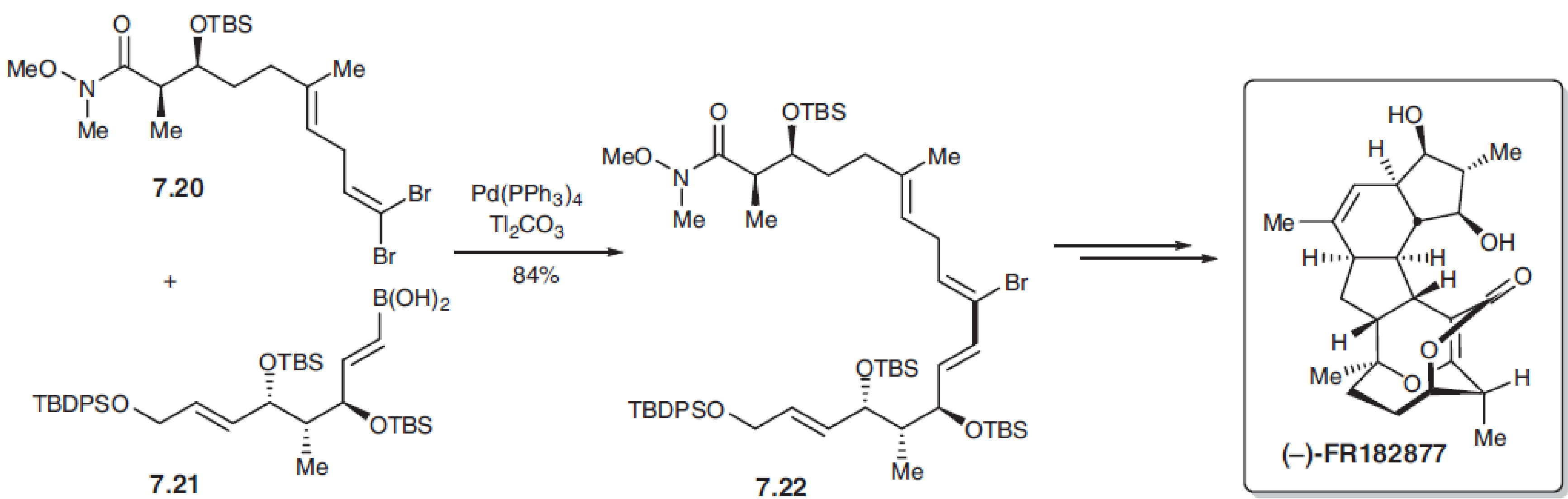
X. Shen, A. M. Hyde, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 14076.

Catalysis :



X. Shen, A. M. Hyde, S. L. Buchwald, *J. Am. Chem. Soc.* **2010**, *132*, 14076.

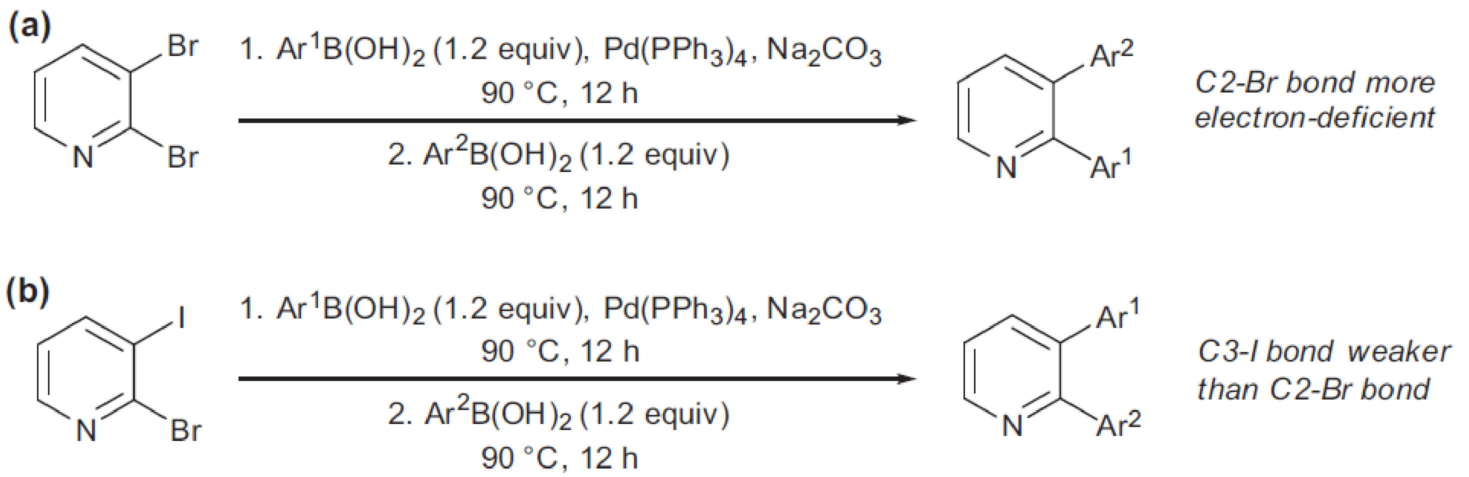
Reversible and Selective Oxidative Addition:



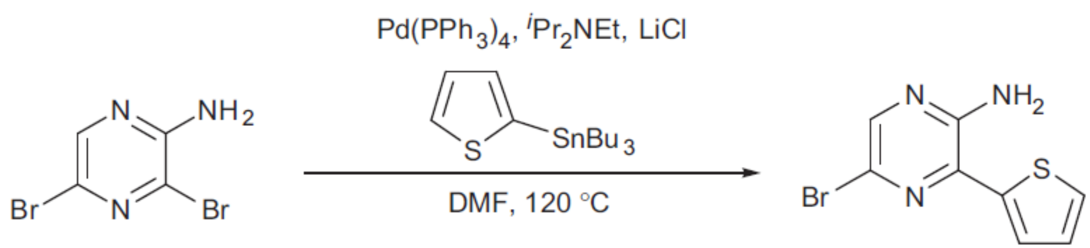
Scheme 7.9 Total synthesis of (–)-FR182877 featuring selective cross-couplings of *gem*-dibromoolefin 7.20.

D. A. Evans and J. T. Starr, *Angew. Chem. Int. Ed.*, **2002**, 41, 1787.

Reversible and Selective Oxidative Addition:



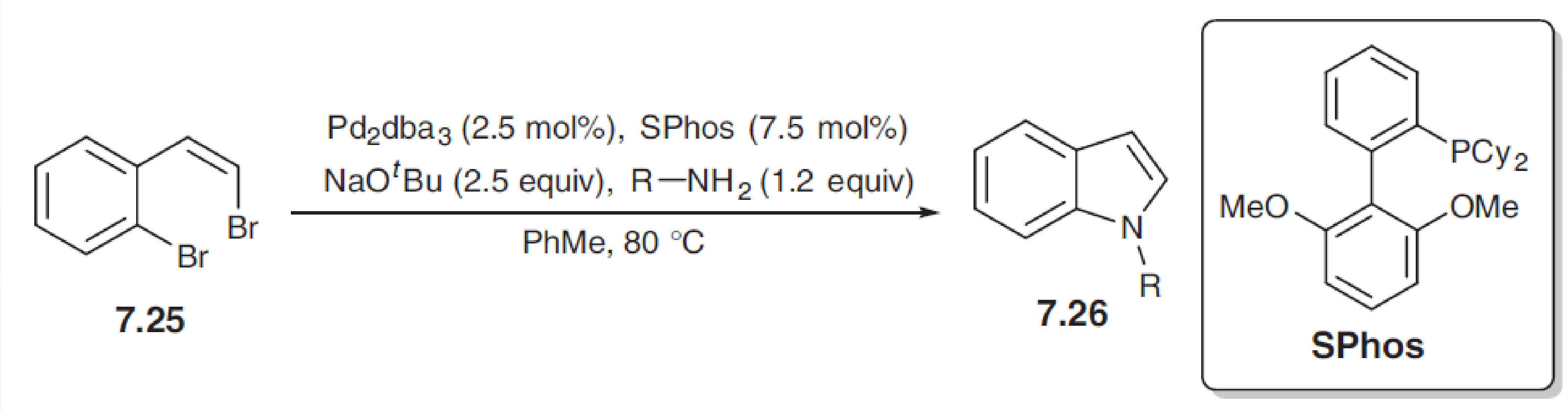
Scheme 7.10 Switch in regioselectivity based on differences in electronic effects and bond dissociation energies.



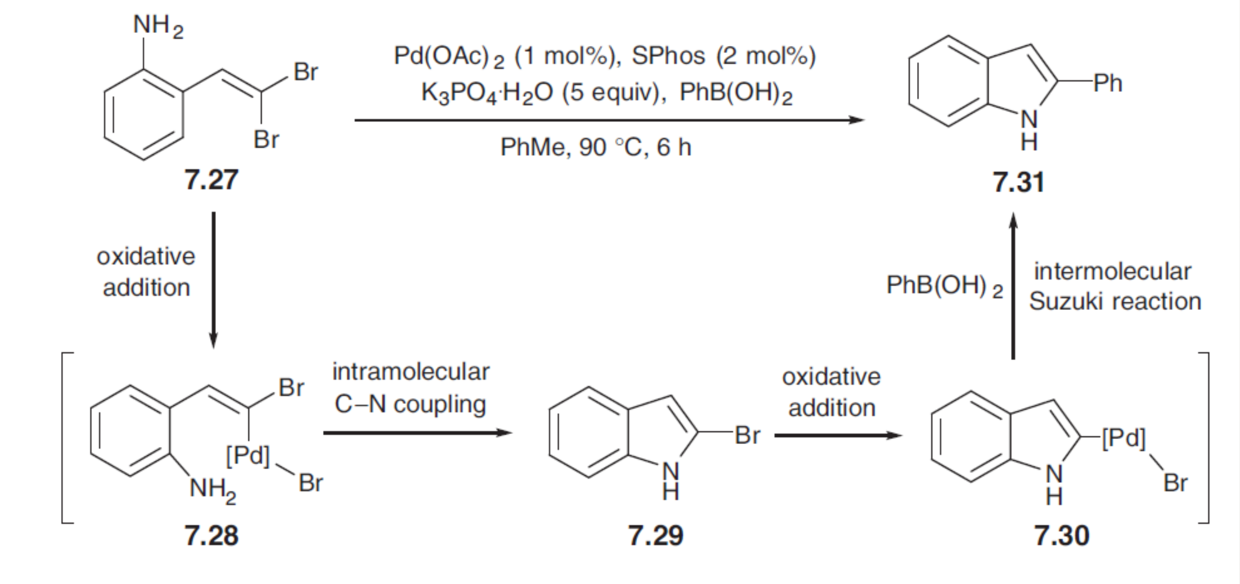
7.23 7.24 74%

S. T. Handy, T. Wilson, A. Muth, *J. Org. Chem.* **2007**, *72*, 8496.
H. Nakamura, D. Takeuchi and A. Murai, *Synlett*, **1995**, 1227.

Reversible and Selective Oxidative Addition:

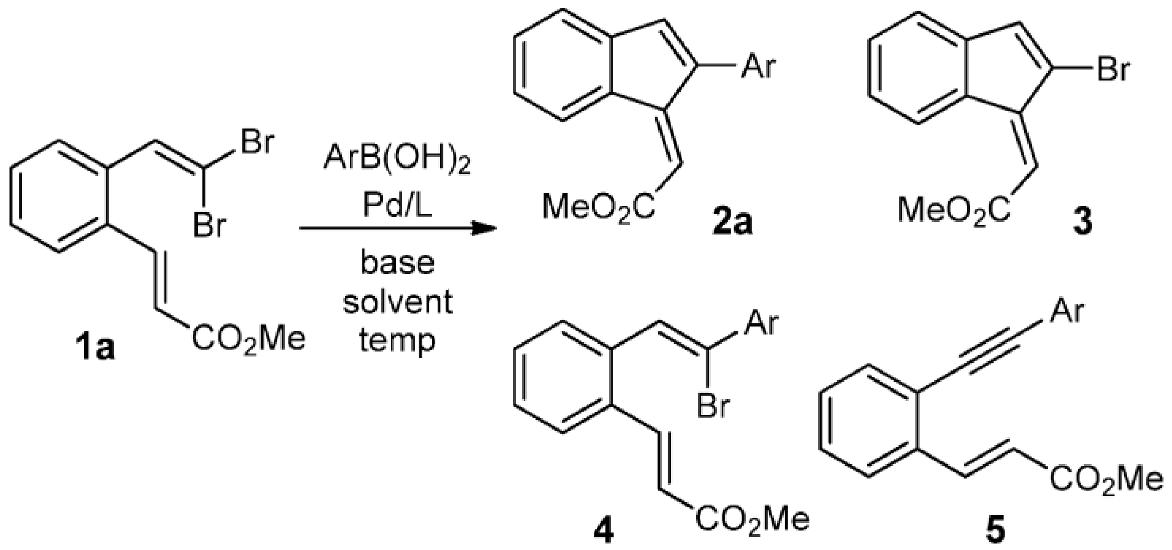


M. C. Willis, G. N. Brace, T. J. K. Findlay and I. P. Holmes, *Adv. Synth.Catal.*, **2006**, 348, 851.



Y.-Q. Fang and M. Lautens, *J. Org. Chem.*, **2008**, 73, 538;

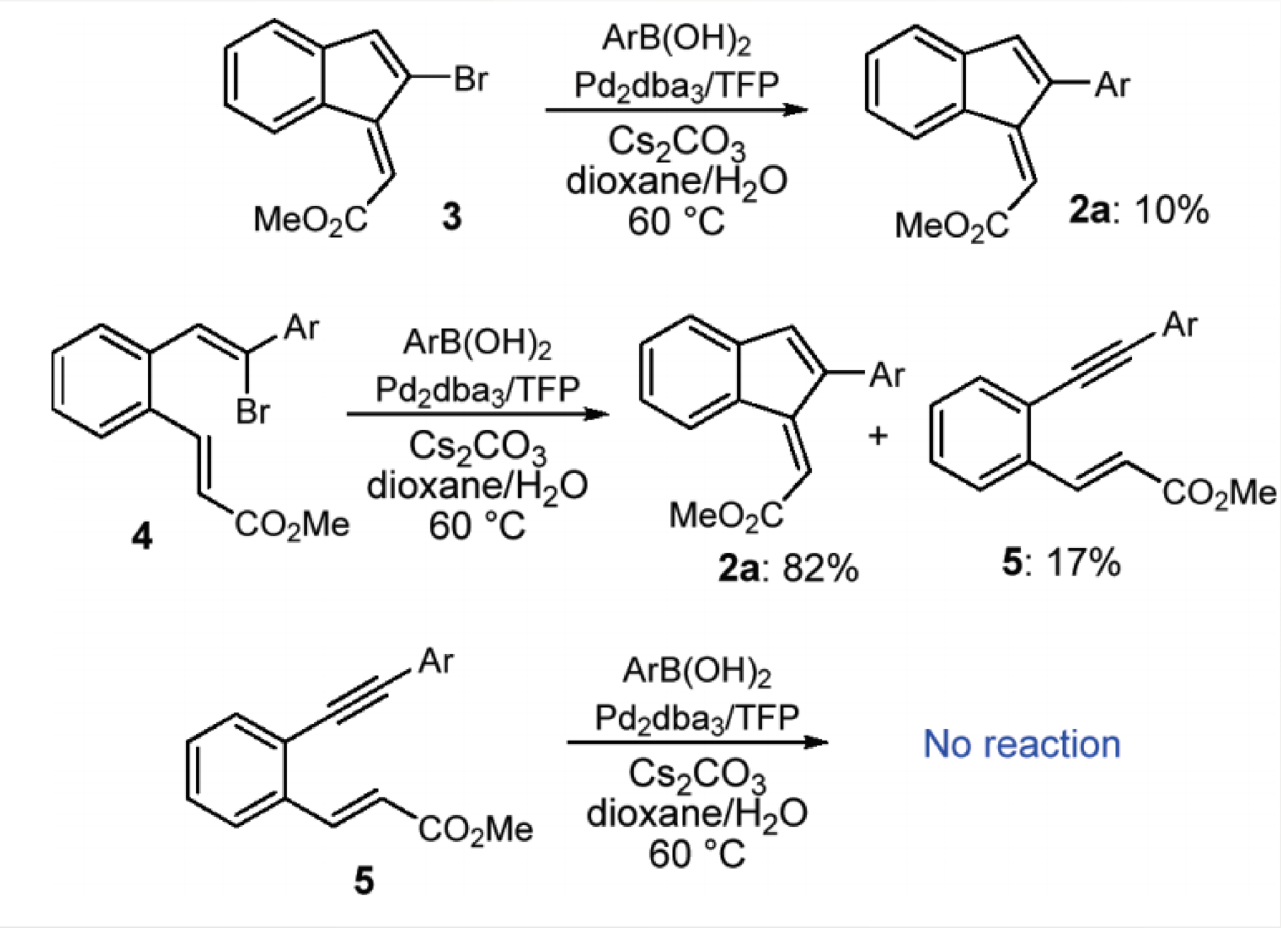
Reversible and Selective Oxidative Addition:



entry	ligand	base	temp (°C)	**2a**:**3**:**4**:**5**[b]
1	SPhos	K_3PO_4	110	0:15:0:0
2	Bu_4NBr[c]	K_3PO_4/Et_3N	110	0:24:0:0
3[d,e]	TFP	Na_2CO_3	60	31:0:55:nd
4[e]	TFP	Na_2CO_3	60	64:0:0:nd
5[e]	TFP	Cs_2CO_3	60	77:0:0:16
6	$^tBu_3PHBF_4$	Cs_2CO_3	110	0:45:0:0

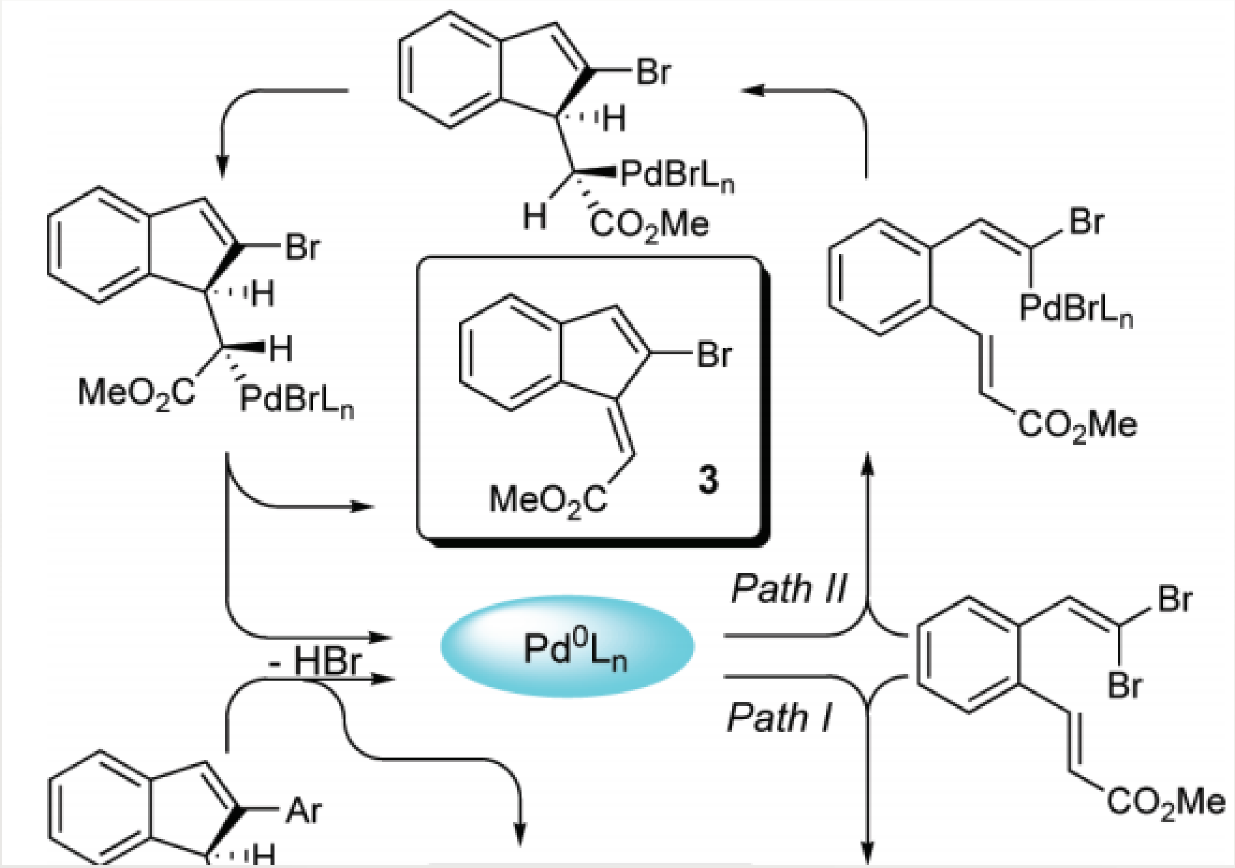
C. S. Bryan, M. Lautens, *Org. Lett.* **2010**, *12*, 2754..

Reversible and Selective Oxidative Addition:



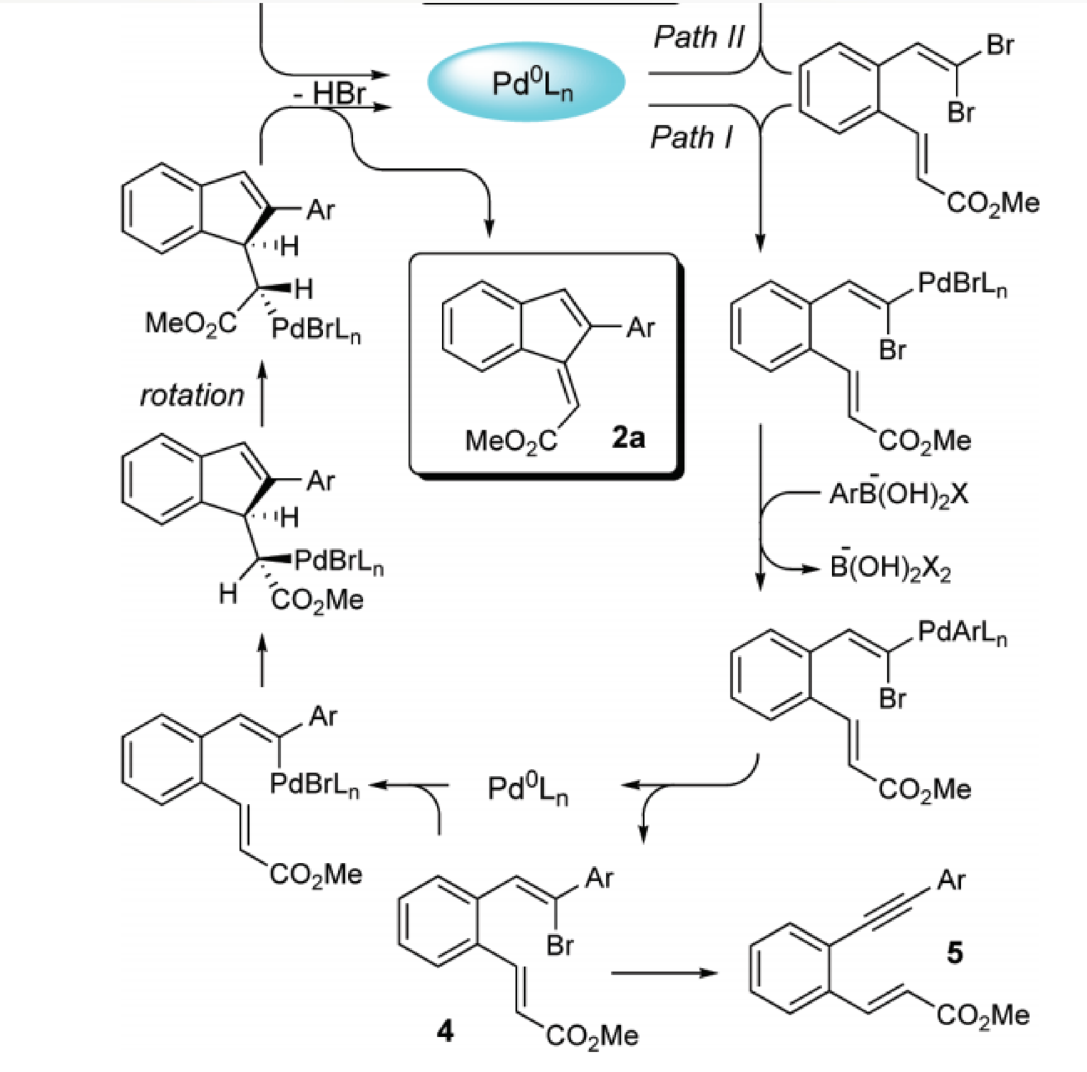
C. S. Bryan, M. Lautens, *Org. Lett.* **2010**, *12*, 2754..

Reversible and Selective Oxidative Addition:



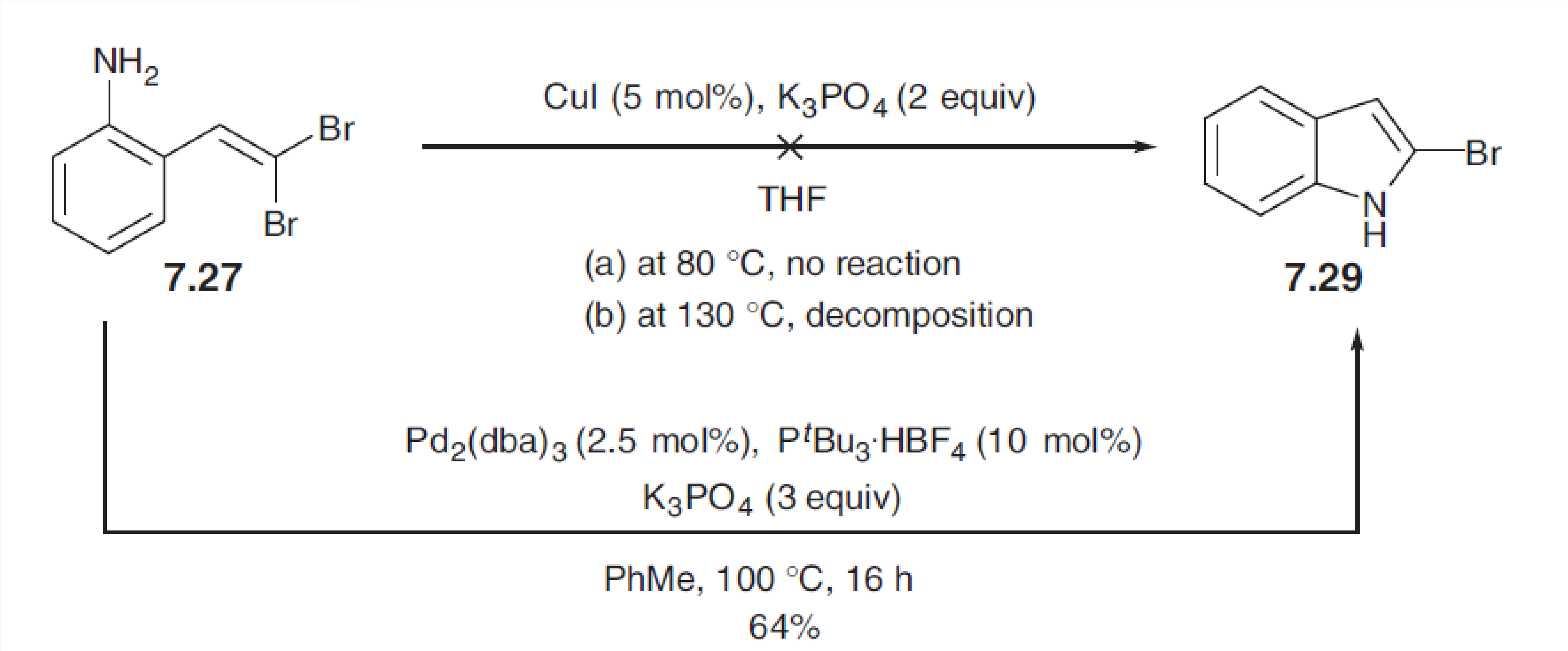
C. S. Bryan, M. Lautens, *Org. Lett.* **2010**, *12*, 2754..

Reversible and Selective Oxidative Addition:



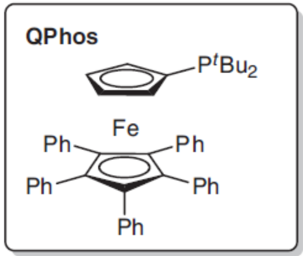
C. S. Bryan, M. Lautens, *Org. Lett.* **2010**, *12*, 2754..

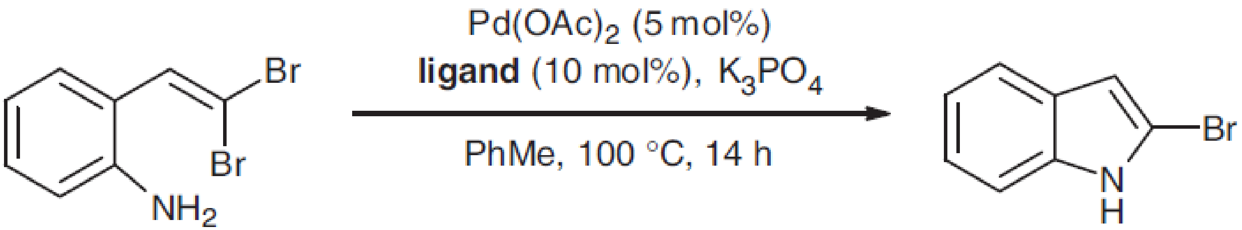
Reversible and Selective Oxidative Addition:



S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2010**, *132*, 11416.

Reversible and Selective Oxidative Addition:





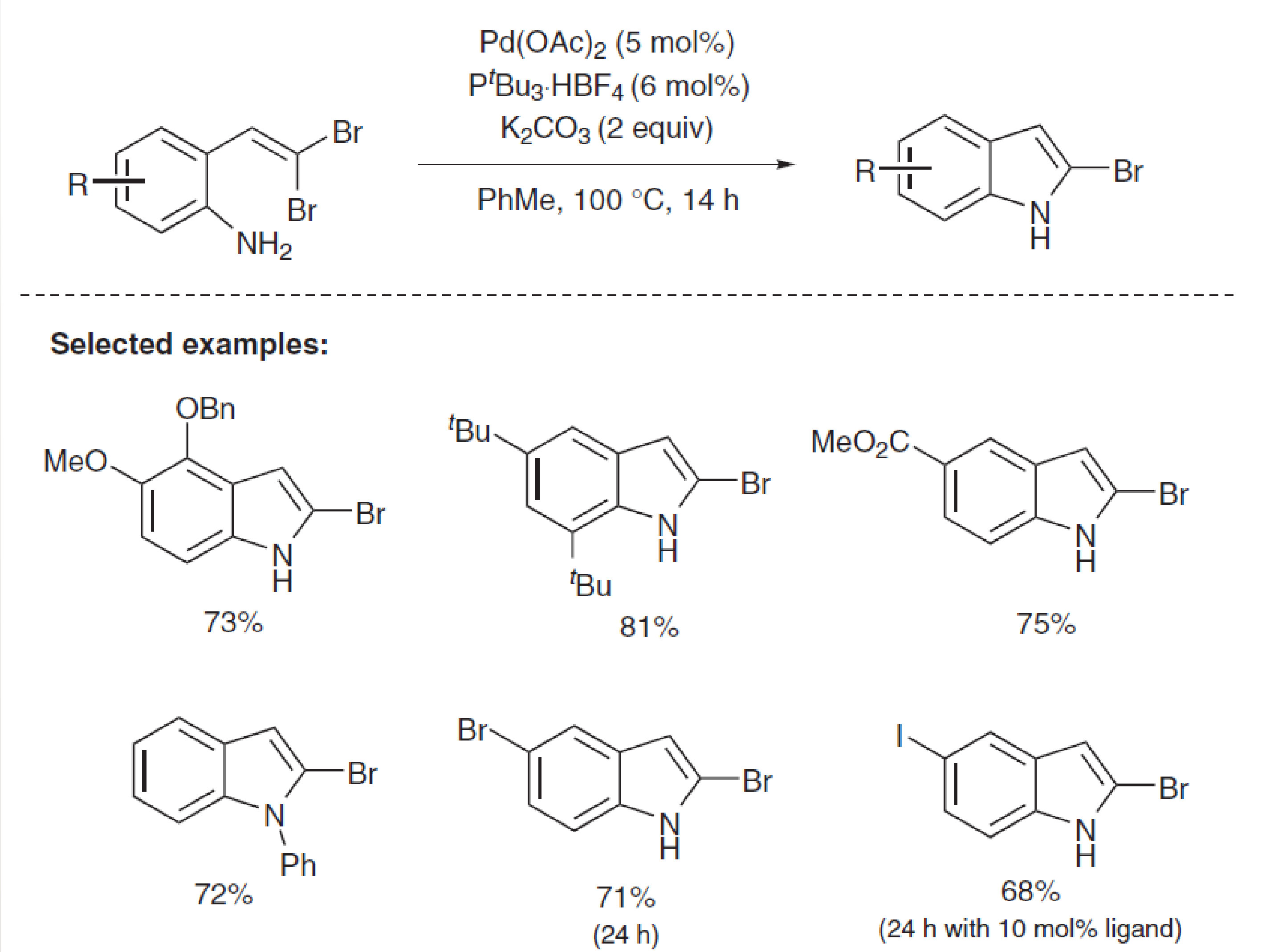
7.27 **7.29**

Ligand	Yield (%)
P^{t}Bu$_3$	64 (81)[a]
QPhos	17
PPh$_3$, PBu$_3$, PCy$_3$, SPhos, JohnPhos, BINAP, Xantphos, P(*o*-tol)$_3$, dppf	< 5

[a]Using optimized conditions: Pd(OAc)$_2$ (5 mol%), P^{t}Bu$_3$·HBF$_4$ (6 mol%), K$_2$CO$_3$ (2 equiv), PhMe, 100 °C, 14 h.

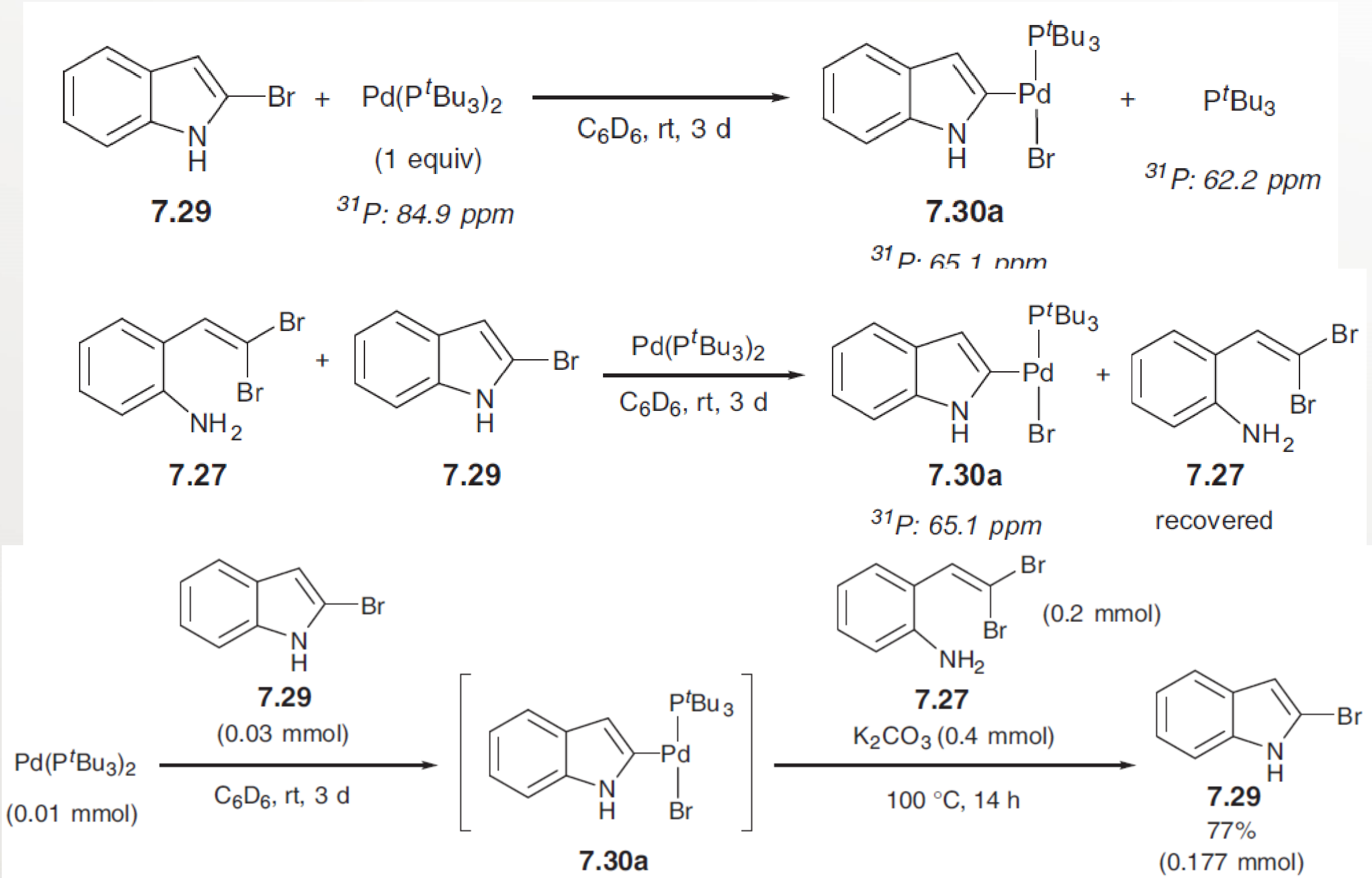
S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2010**, *132*, 11416.

Reversible and Selective Oxidative Addition:



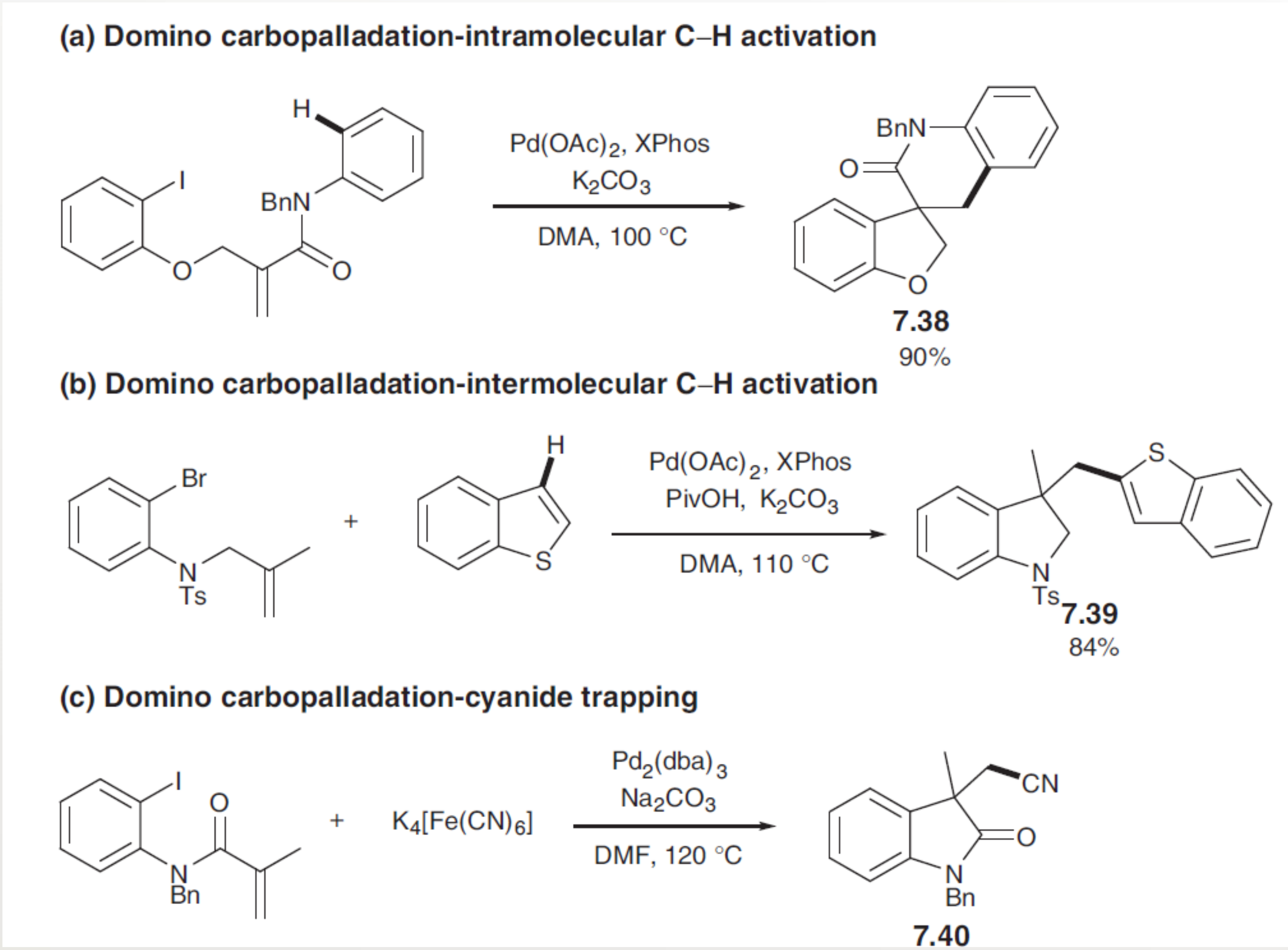
S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2010**, *132*, 11416.

Reversible and Selective Oxidative Addition:



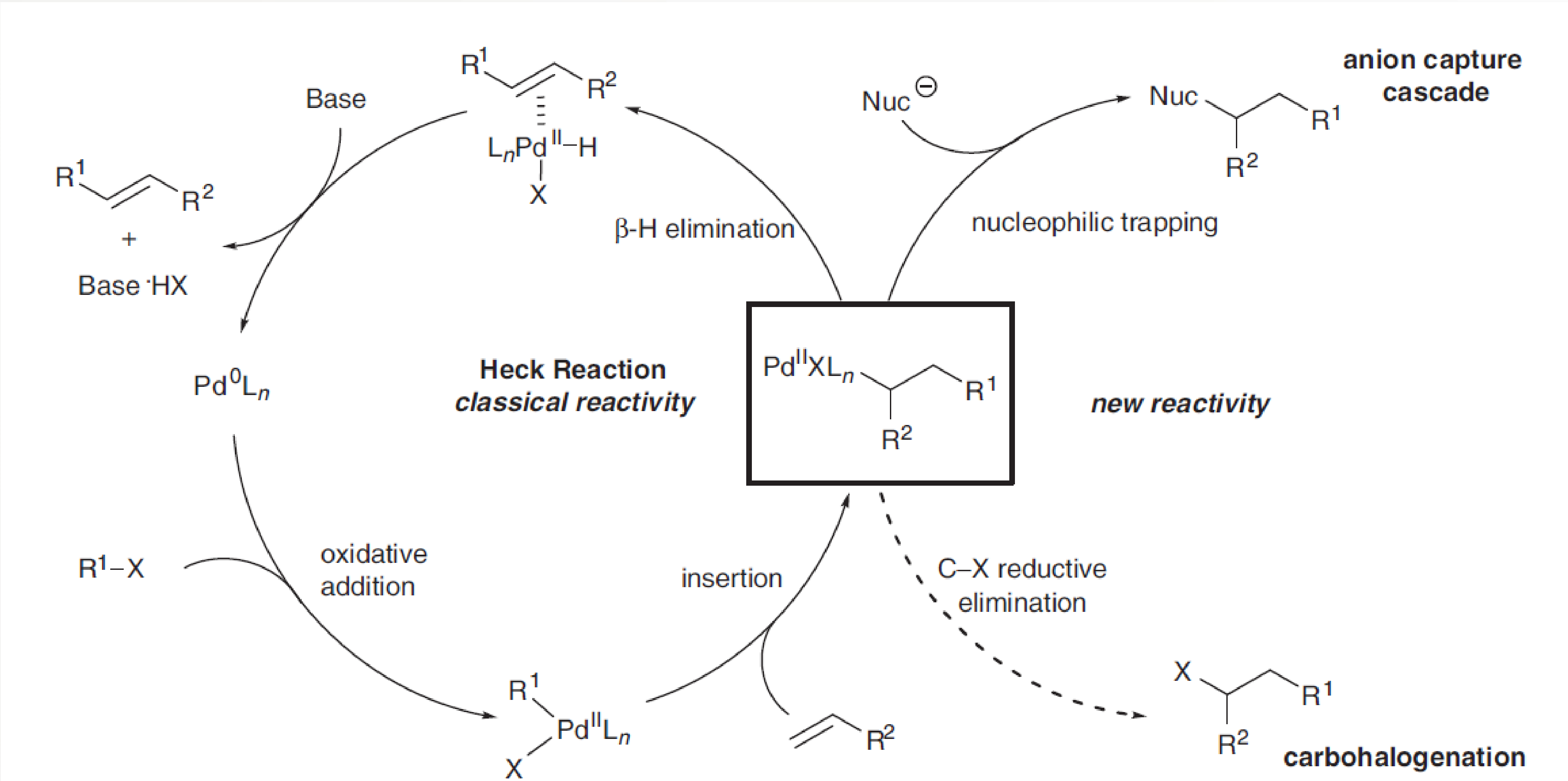
S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2010**, *132*, 11416.

C-I Bond R.E. : Reaction Design



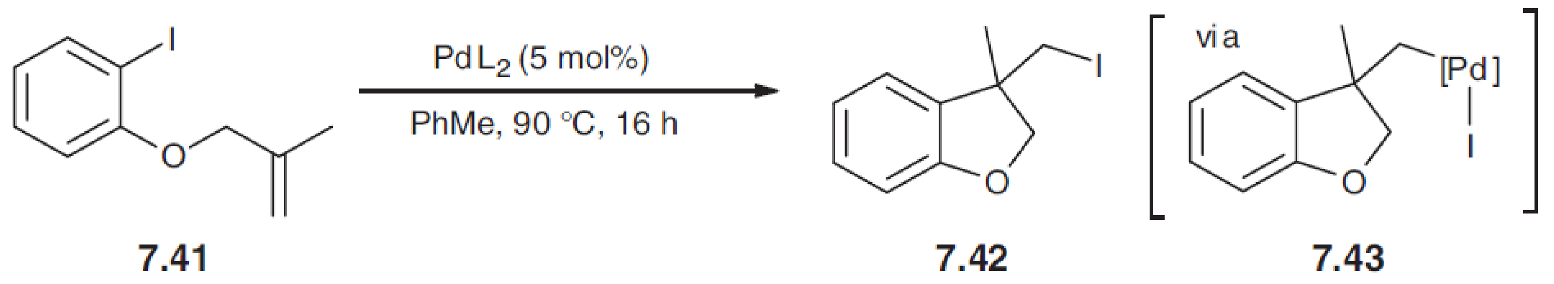
Fangnou and. Lautens's Group's result.

C-I Bond R.E. : Reaction Design

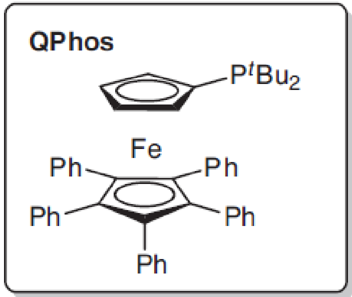


S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 1778.

C-I Bond R.E. : Reaction Design

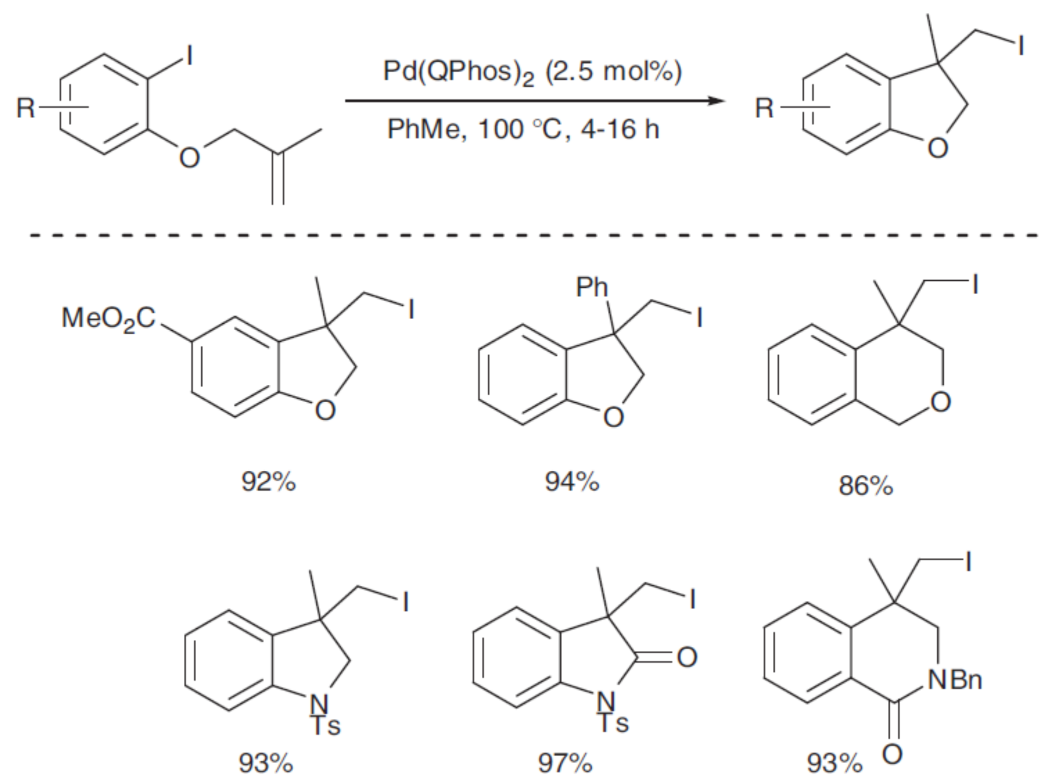


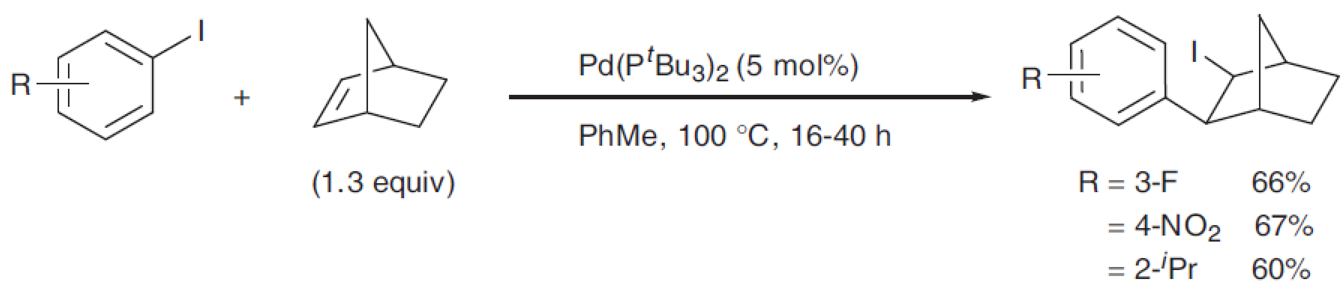
Entry	Ligand	Yield (%)
1	QPhos	82 (95)[a]
2	P^tBu_3	61
3	$PhP(P^tBu_3)_2$	76
4	PCy_3	0
5	$P(o\text{-tol})_3$	0



S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 1778.

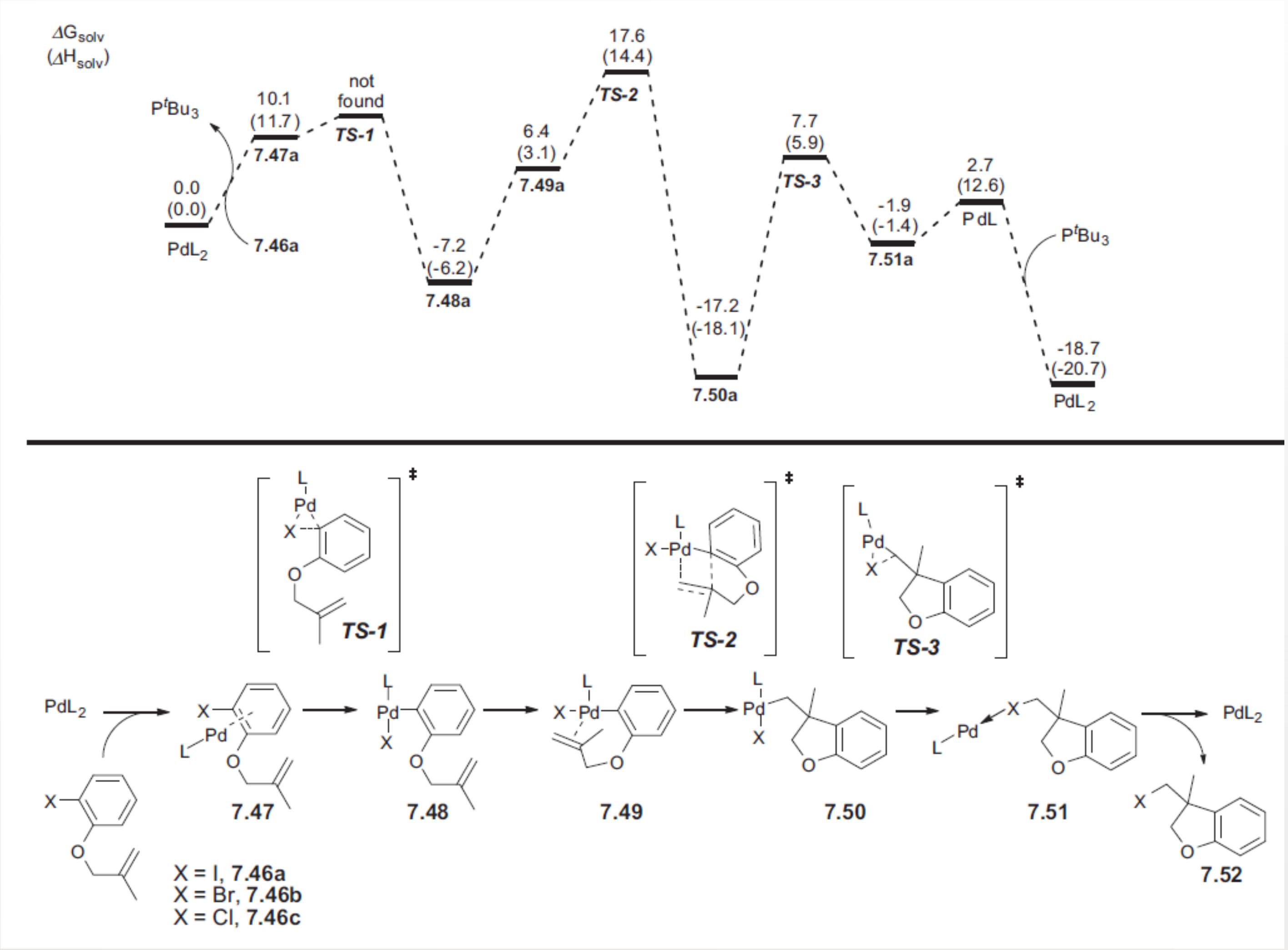
C-I Bond R.E. : Reaction Scope





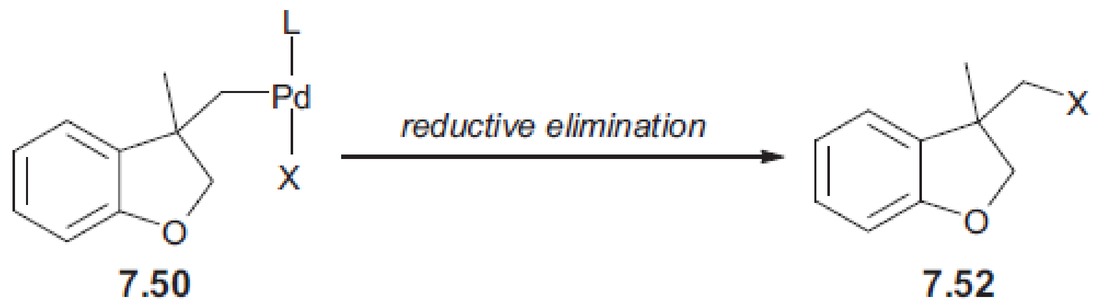
S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 1778.

C-I Bond R.E. : Mechanism

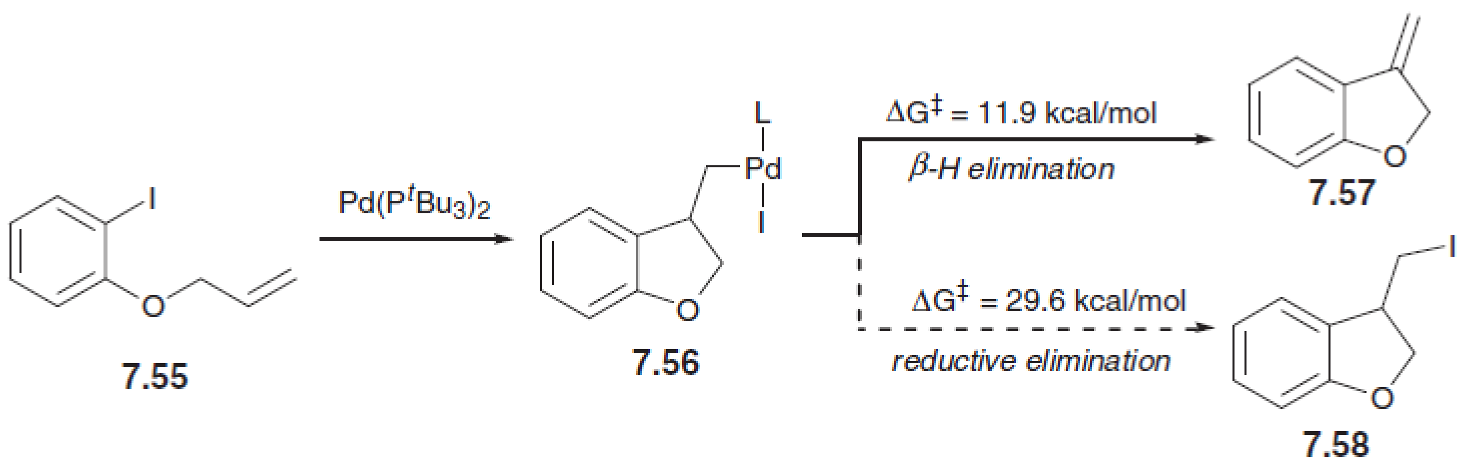


Y. Lan, P. Liu, S. G. Newman, M. Lautens, K. N. Houk, *Chem. Sci.* **2012**, *3*, 1987.

C-I Bond R.E. : Mechanism

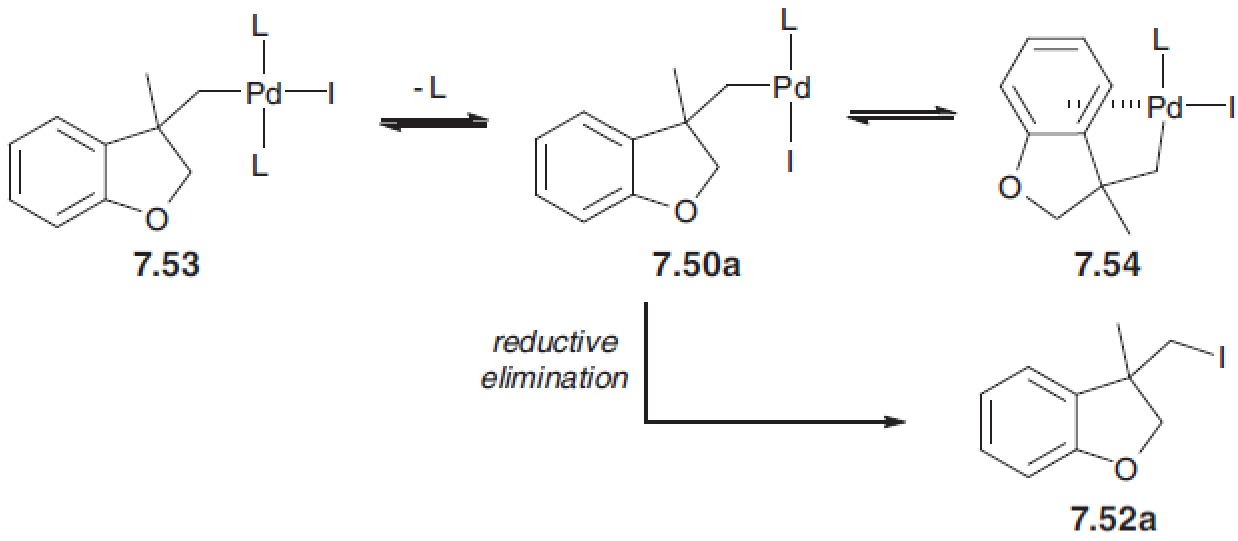


BDE (kcal/mol)		ΔG‡ (kcal/mol)	BDE (kcal/mol)	
Pd–I:	72.8	24.9	C–I:	65.7
Pd–Br:	81.1	27.4	C–Br:	75.0
Pd–Cl:	91.9	27.9	C–Cl:	91.0



Y. Lan, P. Liu, S. G. Newman, M. Lautens, K. N. Houk, *Chem. Sci.* **2012**, *3*, 1987.

C-I Bond R.E. : Mechanism

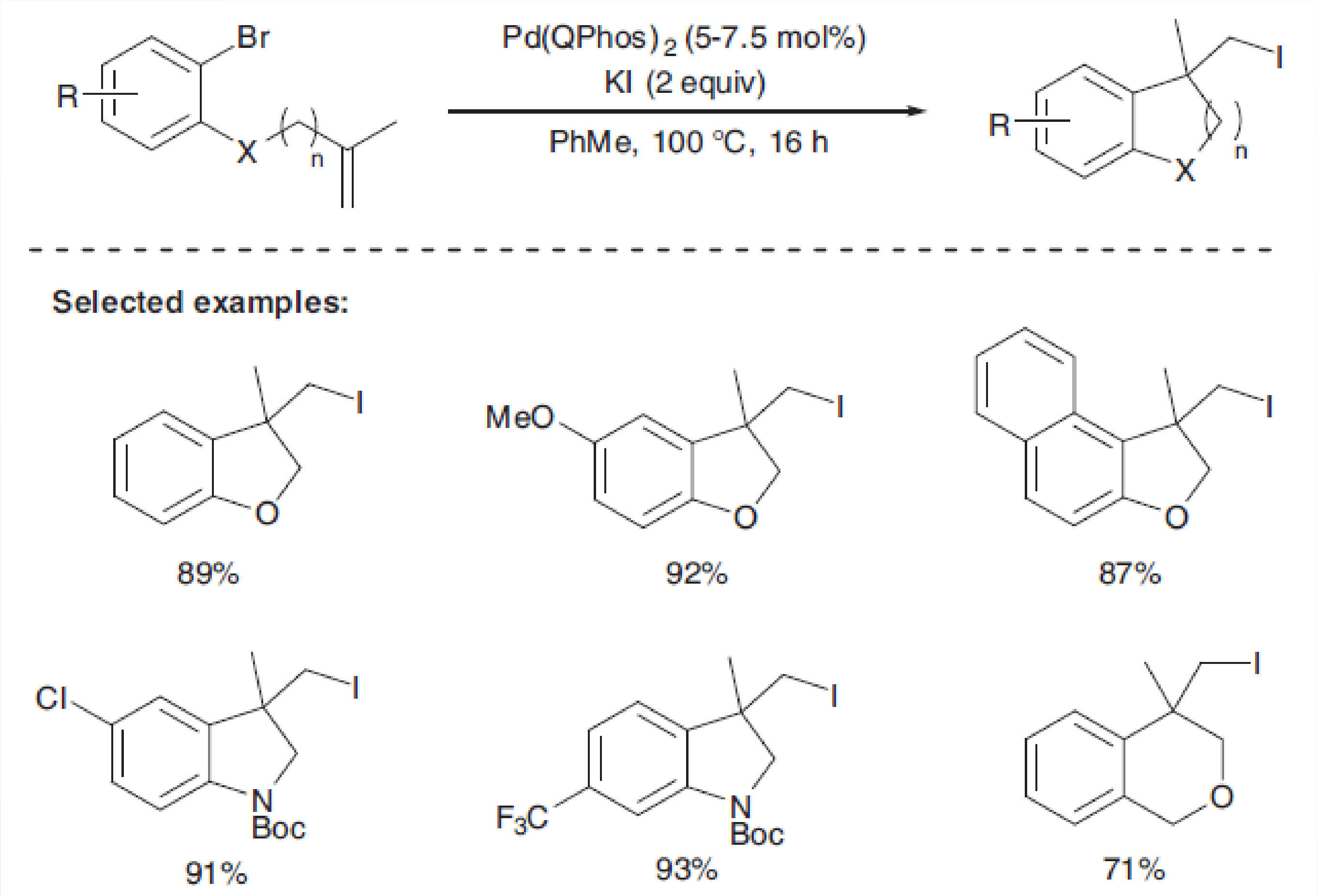


Entry	Ligand (%)	$\Delta G^{\ddagger}$ (kcal mol^{-1})
1	P^tBu_3	24.9
2	FcP^tBu_2	23.7
3	P^iPr_3	26.3
4	$P(OMe)_3$[a]	26.9
5	PMe_3[a]	36.9
6	PH_3[a]	30.5

[a]Resting state is a $Pd^{II}L_2$ species.

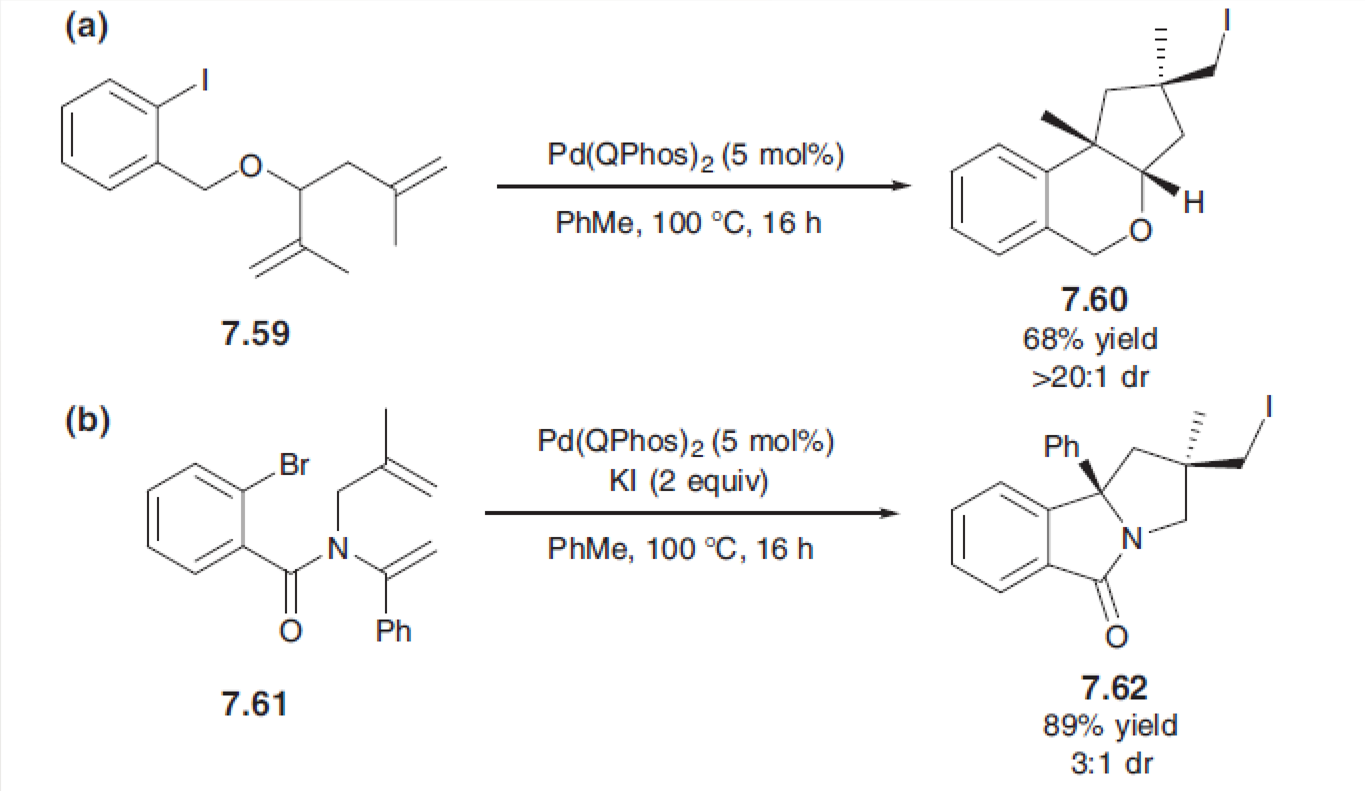
Y. Lan, P. Liu, S. G. Newman, M. Lautens, K. N. Houk, *Chem. Sci.* **2012**, *3*, 1987.

C-I Bond R.E. : In-Situ Exchange



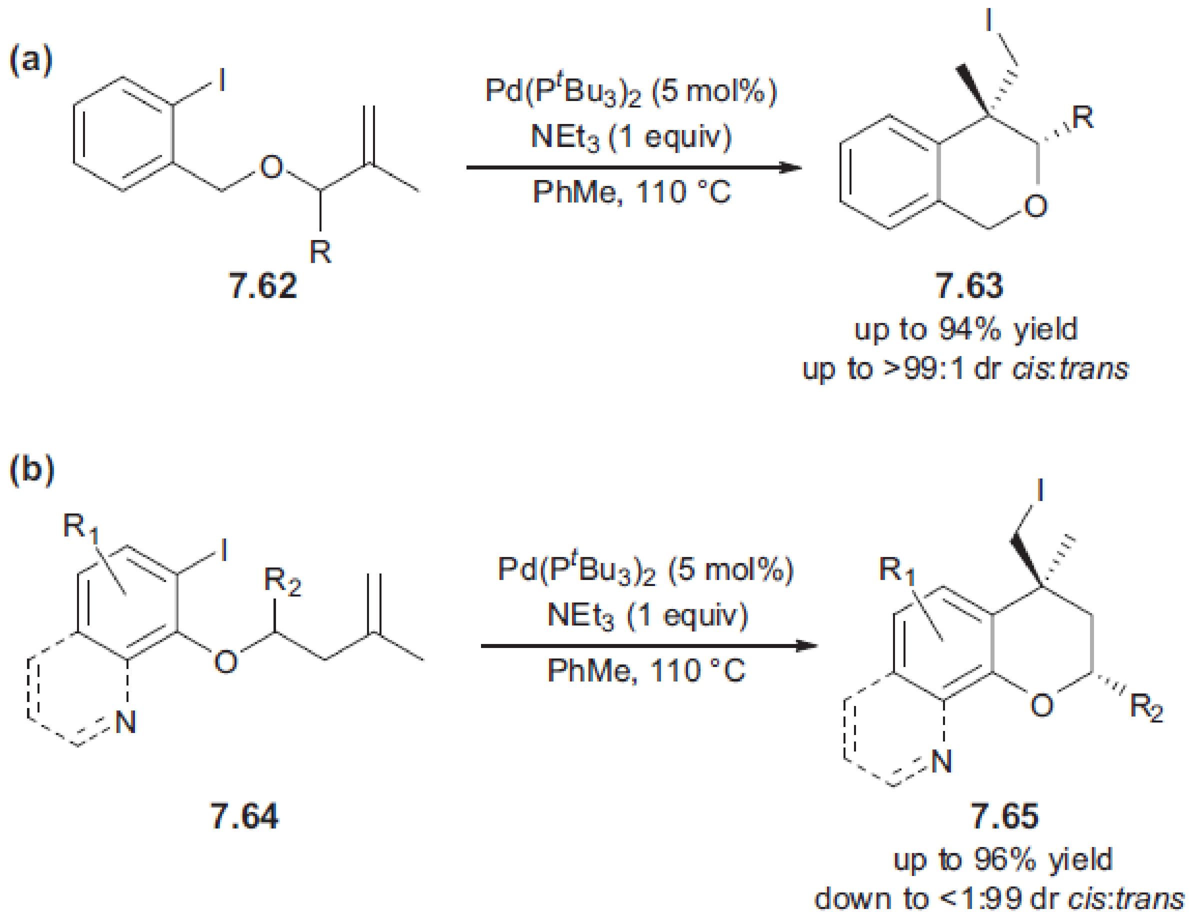
S. G. Newman, J. K. Howell, N. Nicolaus, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 14916.

C-I Bond R.E. : Cascade Insertion



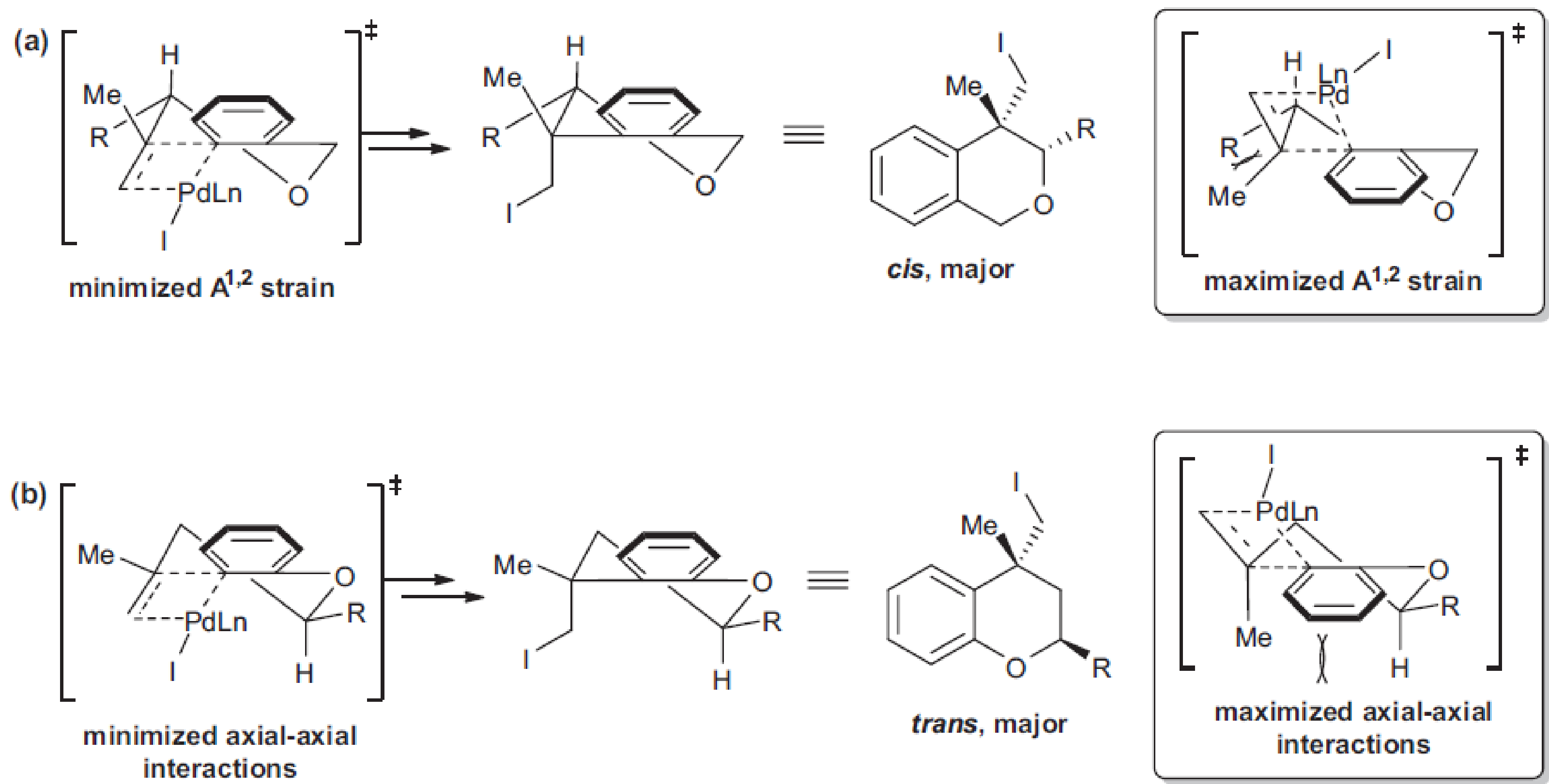
S. G. Newman, J. K. Howell, N. Nicolaus, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 14916.

C-I Bond R.E. : Diastereoselectivity



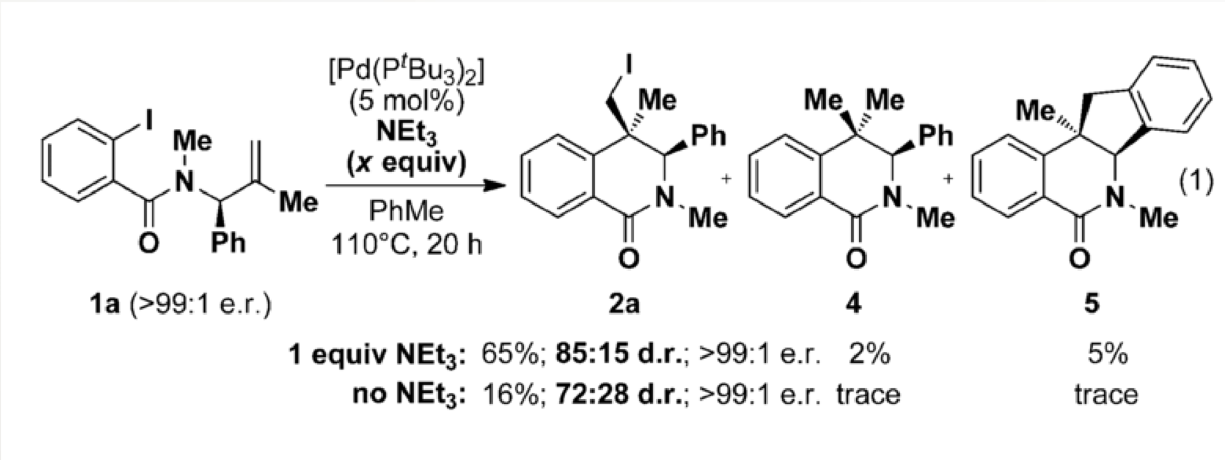
D. A. Petrone, H. A. Malik, A. Clemenceau, M. Lautens, *Org. Lett.* **2012**, *14*, 4806.

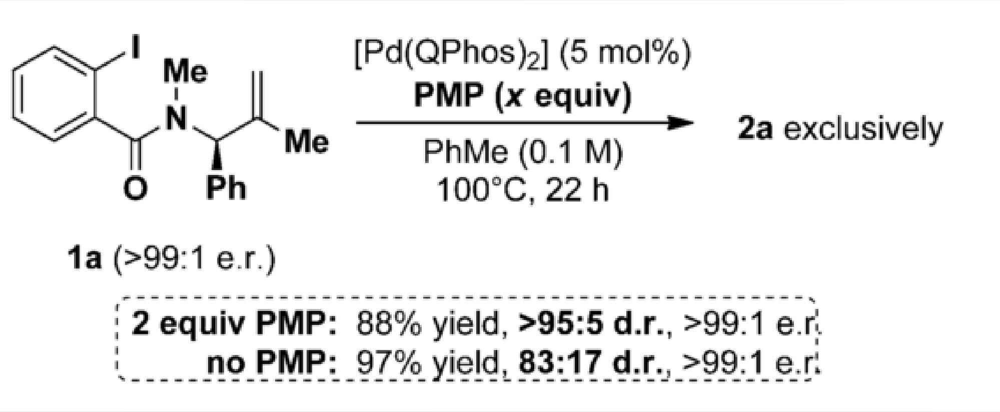
C-I Bond R.E. : Diastereoselectivity



D. A. Petrone, H. A. Malik, A. Clemenceau, M. Lautens, *Org. Lett.* **2012**, *14*, 4806.

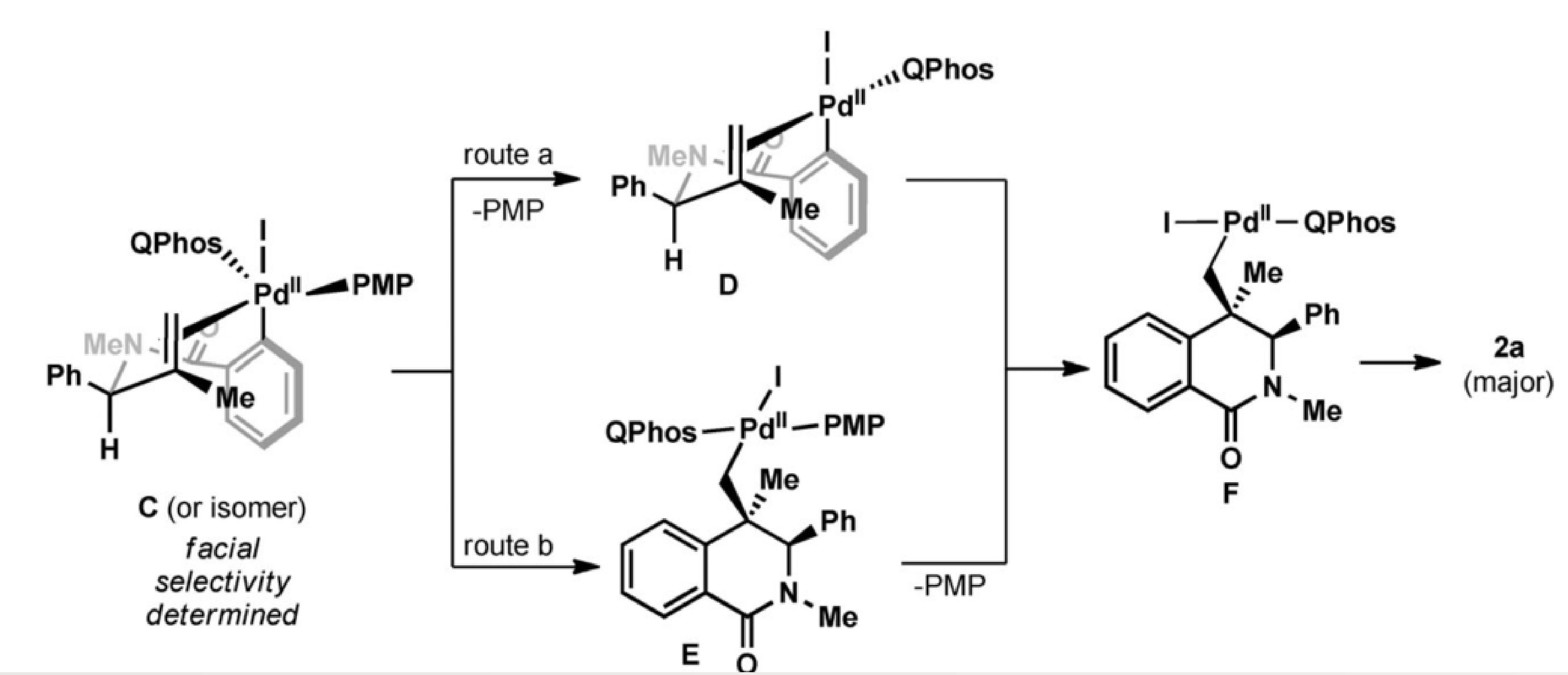
C-I Bond R.E. : Diastereoselectivity





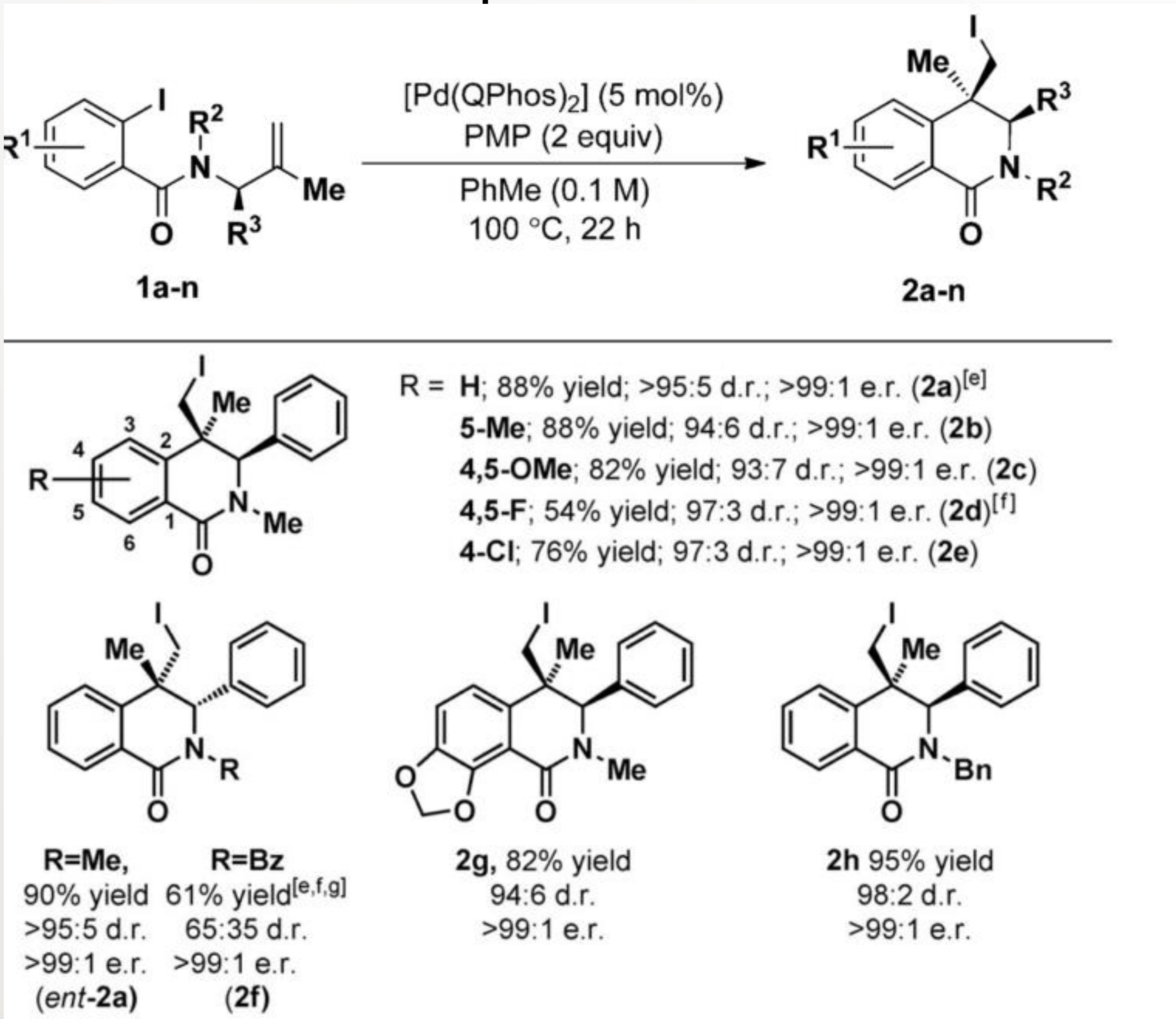
D. A. Petrone, H. Yoon, H. Weinstabl, M. Lautens, *Angew. Chem. Int. Ed.* **2014**, *53*, 7908.

C-I Bond R.E. : Diastereoselectivity



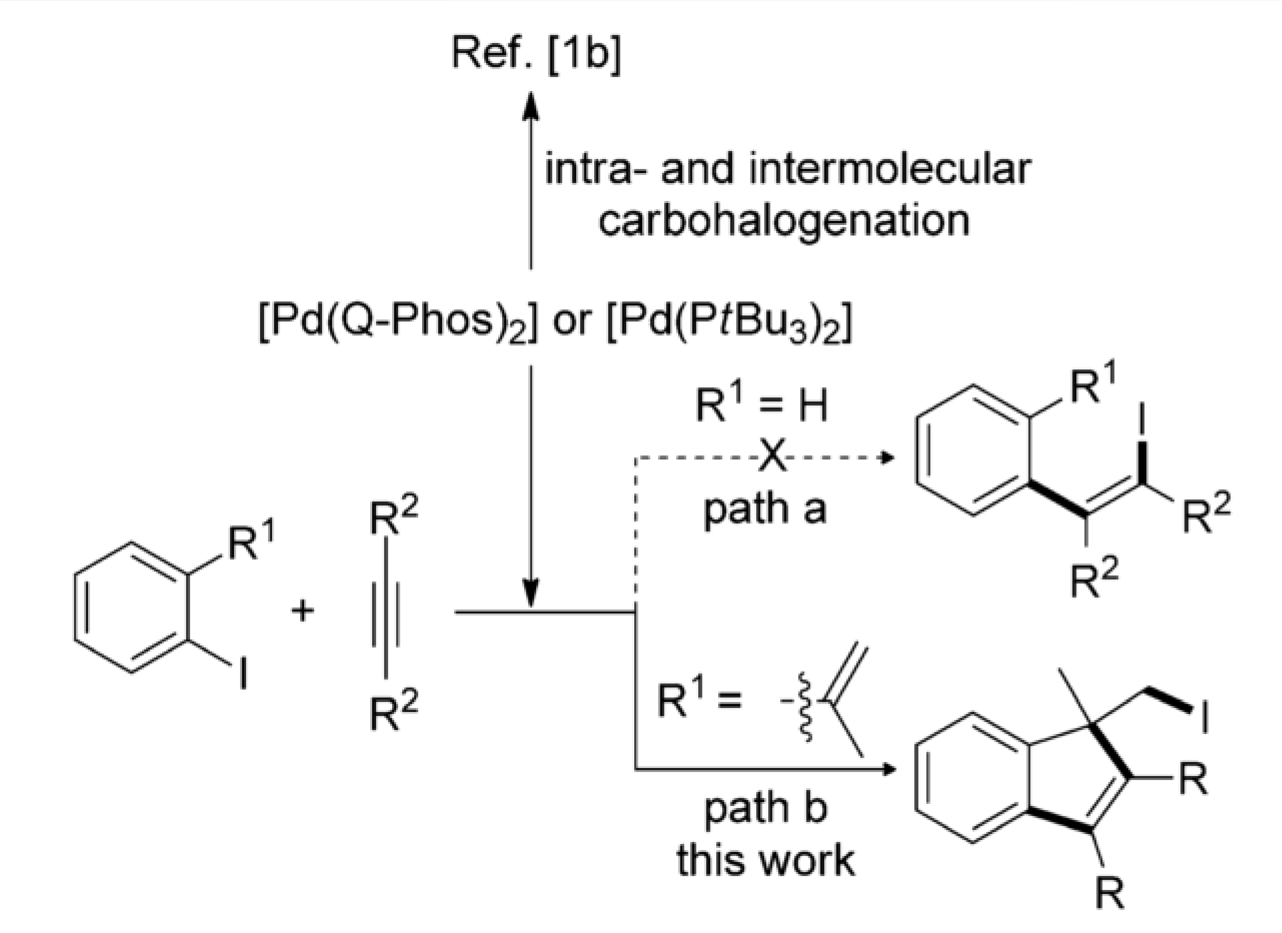
D. A. Petrone, H. Yoon, H. Weinstabl, M. Lautens, *Angew. Chem. Int. Ed.* **2014**, *53*, 7908.

C-I Bond R.E. : Reaction Scope



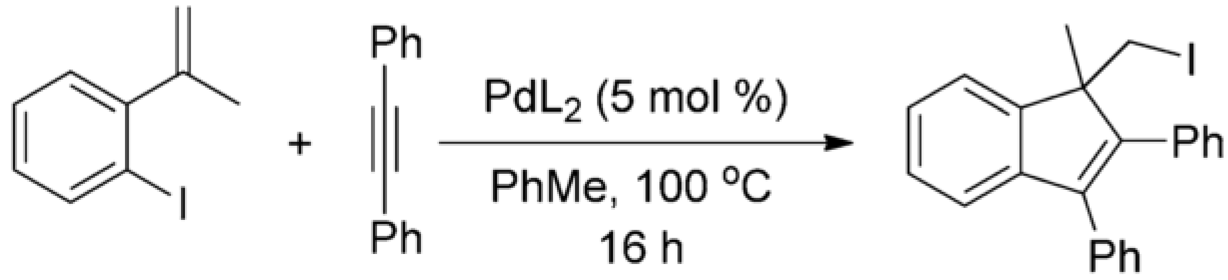
D. A. Petrone, H. Yoon, H. Weinstabl, M. Lautens, *Angew. Chem. Int. Ed.* **2014**, *53*, 7908.

C-I Bond R.E. : Intramolecular Reaction

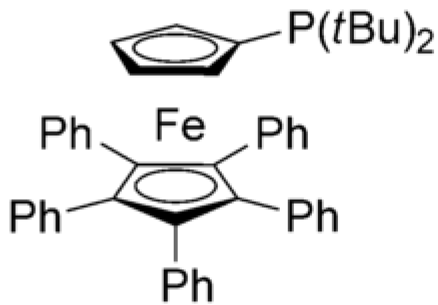


X. Jia, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2012**, *51*, 9870.

C-I Bond R.E. : Intramolecular Reaction



1a **2a** **3a**

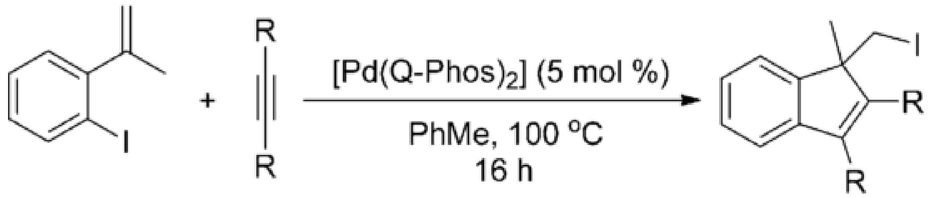


Q-Phos

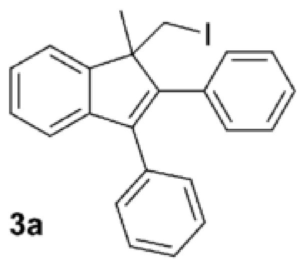
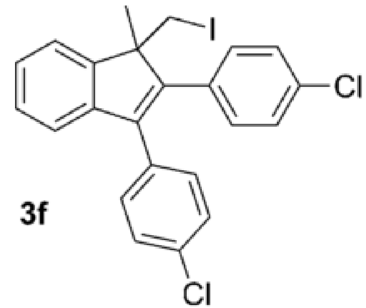
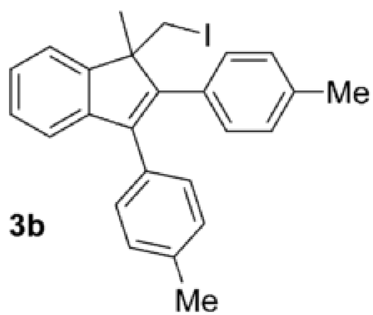
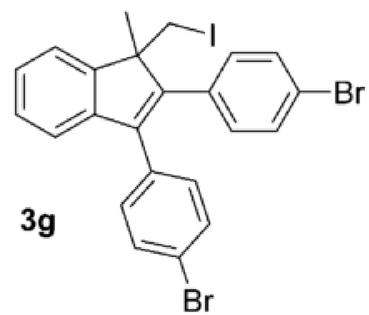
Ligand	Yield
Q-Phos	96%
P(*t*Bu)$_3$	55%
PhP(*t*Bu)$_2$	32%
P(*o*-tol)$_3$	8%
PCy_3	0%

X. Jia, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2012**, *51*, 9870.

C-I Bond R.E. : Reaction Scope

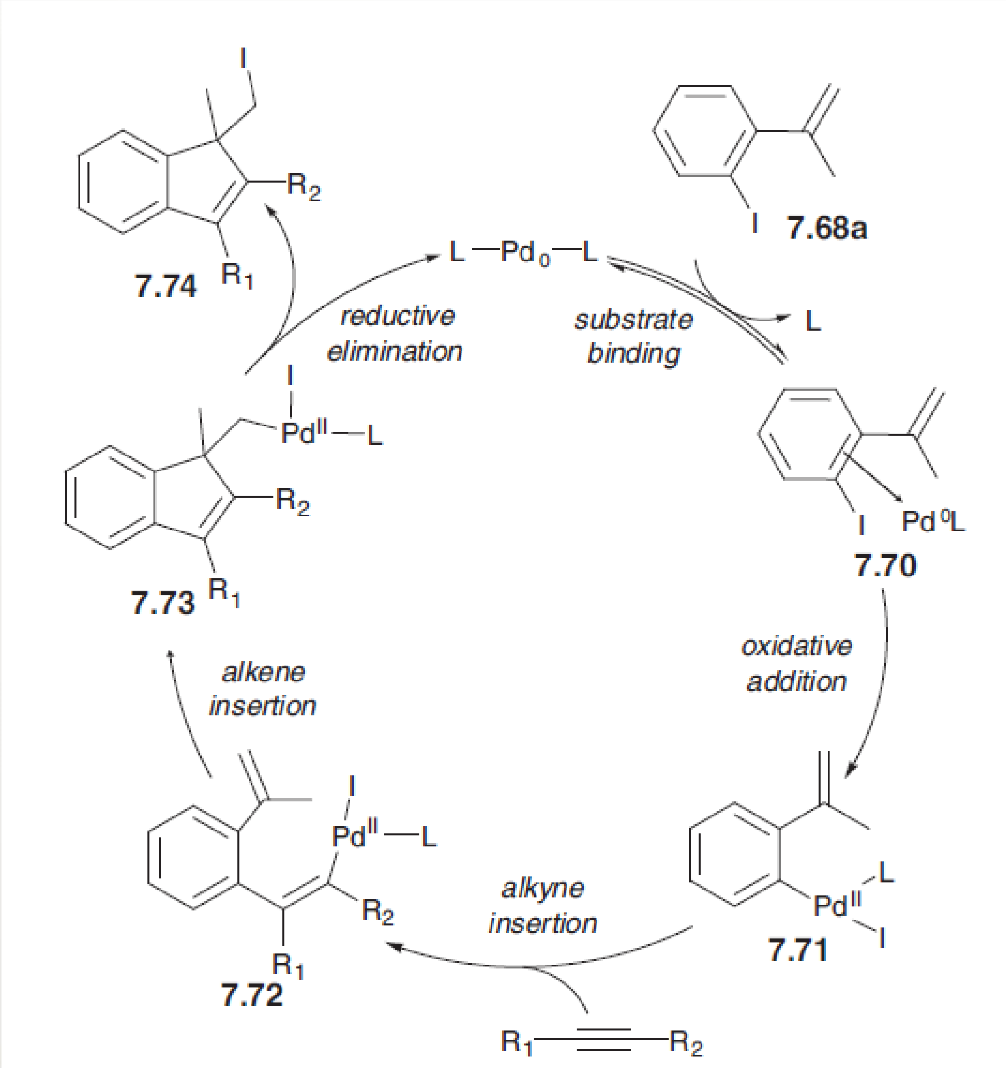


1a 2 3

Entry	Product	Yield [%]	Entry	Product	Yield [%]
1	 3a	96	6	 3f	92
2	 3b	93	7	 3g	57[b]

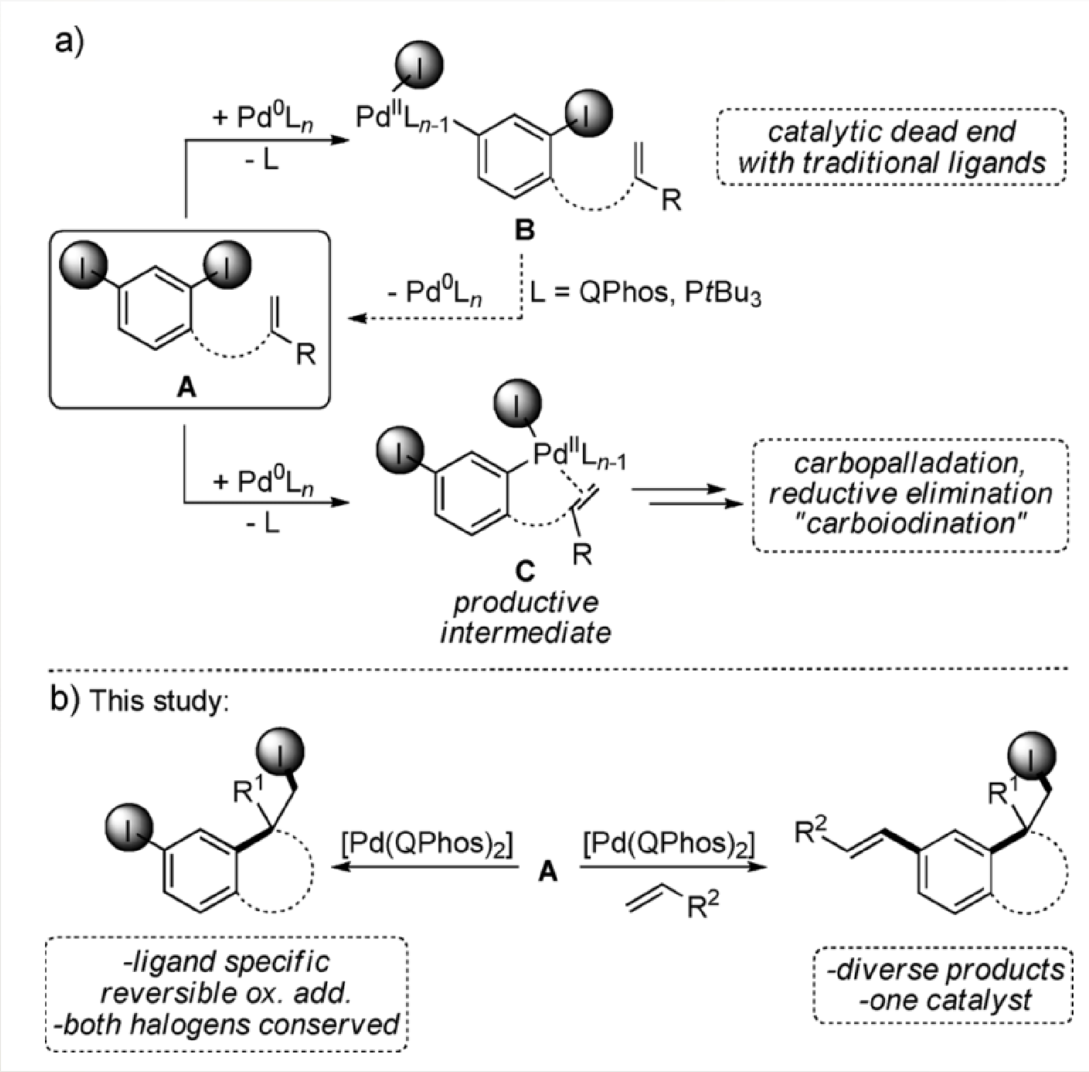
X. Jia, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2012**, *51*, 9870.

C-I Bond R.E. : Reaction Mechanism



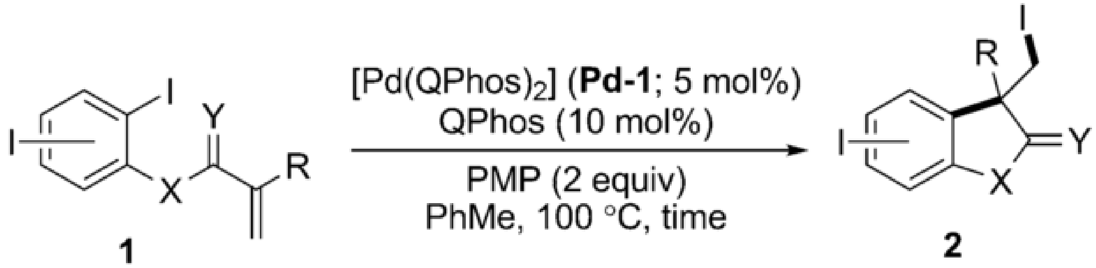
X. Jia, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2012**, *51*, 9870.

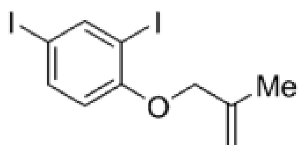
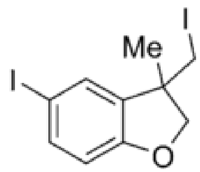
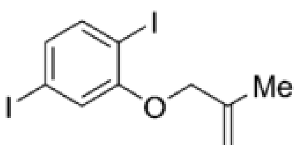
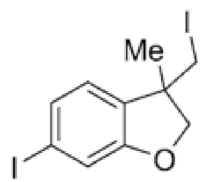
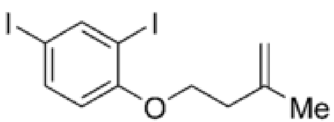
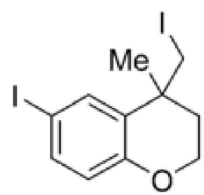
C-I Bond R.E. : Selectivity?



D. A. Petrone, M. Lischka, M. Lautens, *Angew. Chem. Int. Ed.* **2013**, *52*, 10635.

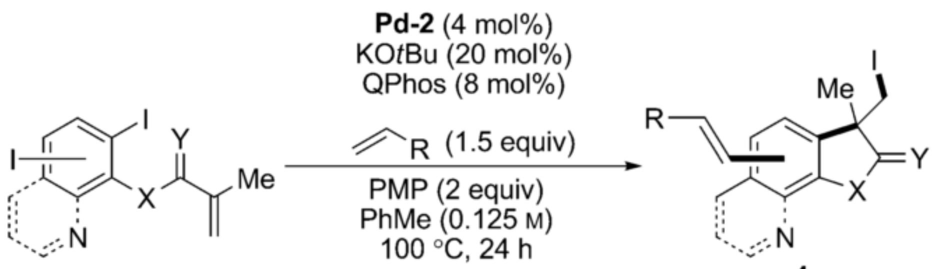
C-I Bond R.E. : Reaction Scope

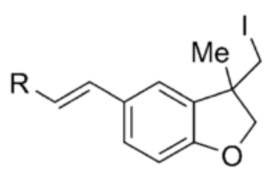
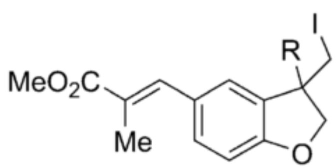
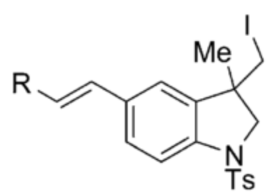


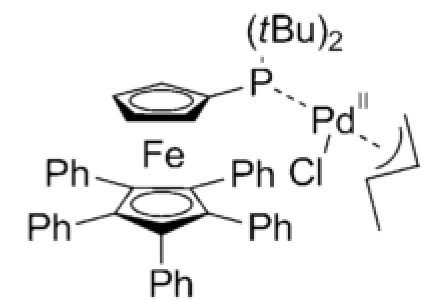
Entry	Substrate **1**	Product **2**	*t* [h]	Yield [%][b]
1	 **1a**	 **2a**	5	74 (67)[c]
2	 **1b**	 **2b**	7	76
3	 **1c**	 **2c**	8	74

D. A. Petrone, M. Lischka, M. Lautens, *Angew. Chem. Int. Ed.* **2013**, *52*, 10635.

C-I Bond R.E. : Reaction Scope

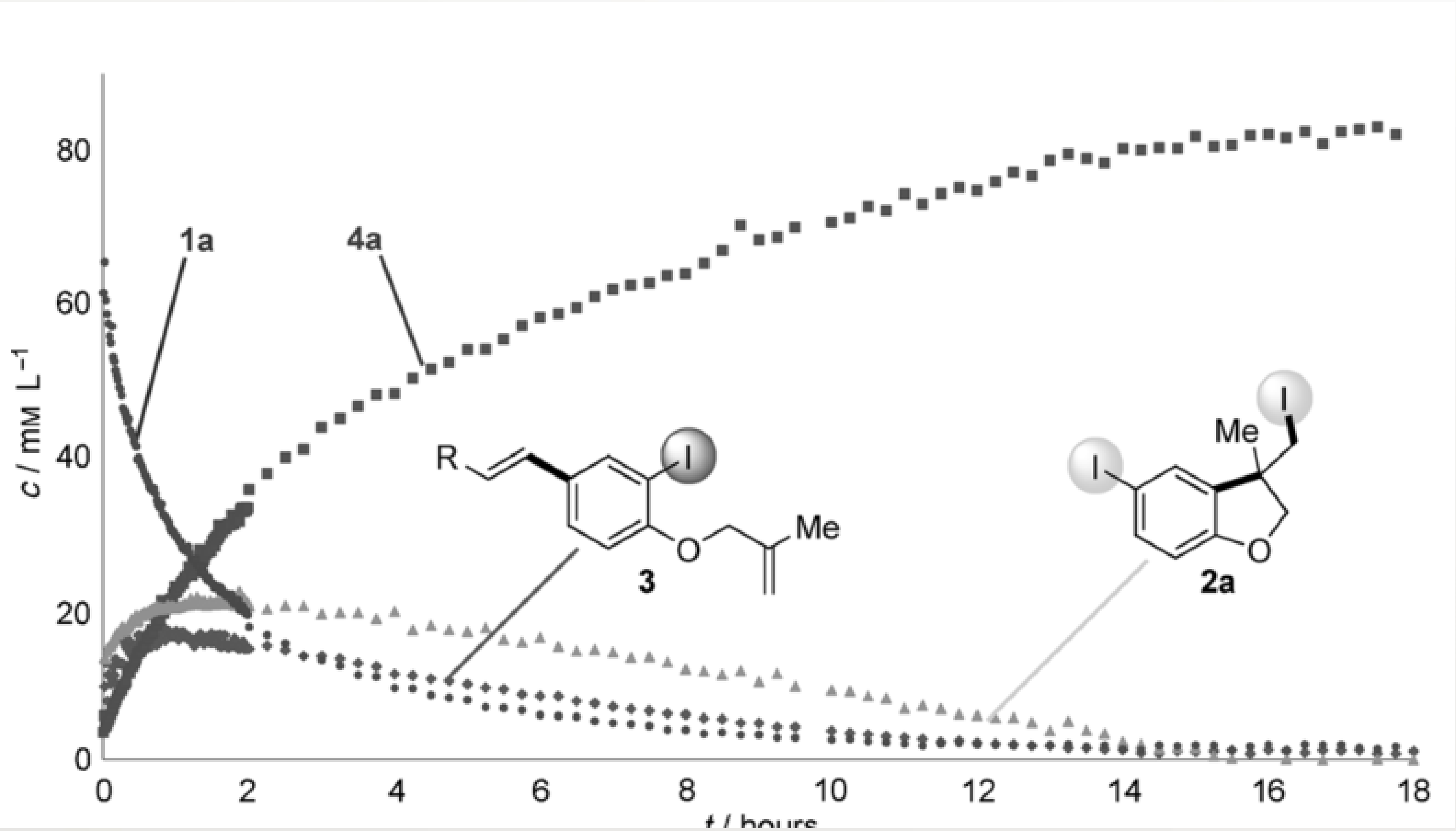


Entry	Product	4	Yield [%][b]
1	R = CO_2tBu	4a	88 (79)[c]
2	R = CO_2Me	4b	83
3[c]	R = $CONMe_2$	4c	73
4	R = Ph	4d	82
5	R = CN 	4e (4:1 E/Z)	90[d]
6		4f (R = Me)	77
7		4f' (R = Ph)	25
8[e]	R = CO_2tBu	4g	86
9	R = 2-py 	4h	84



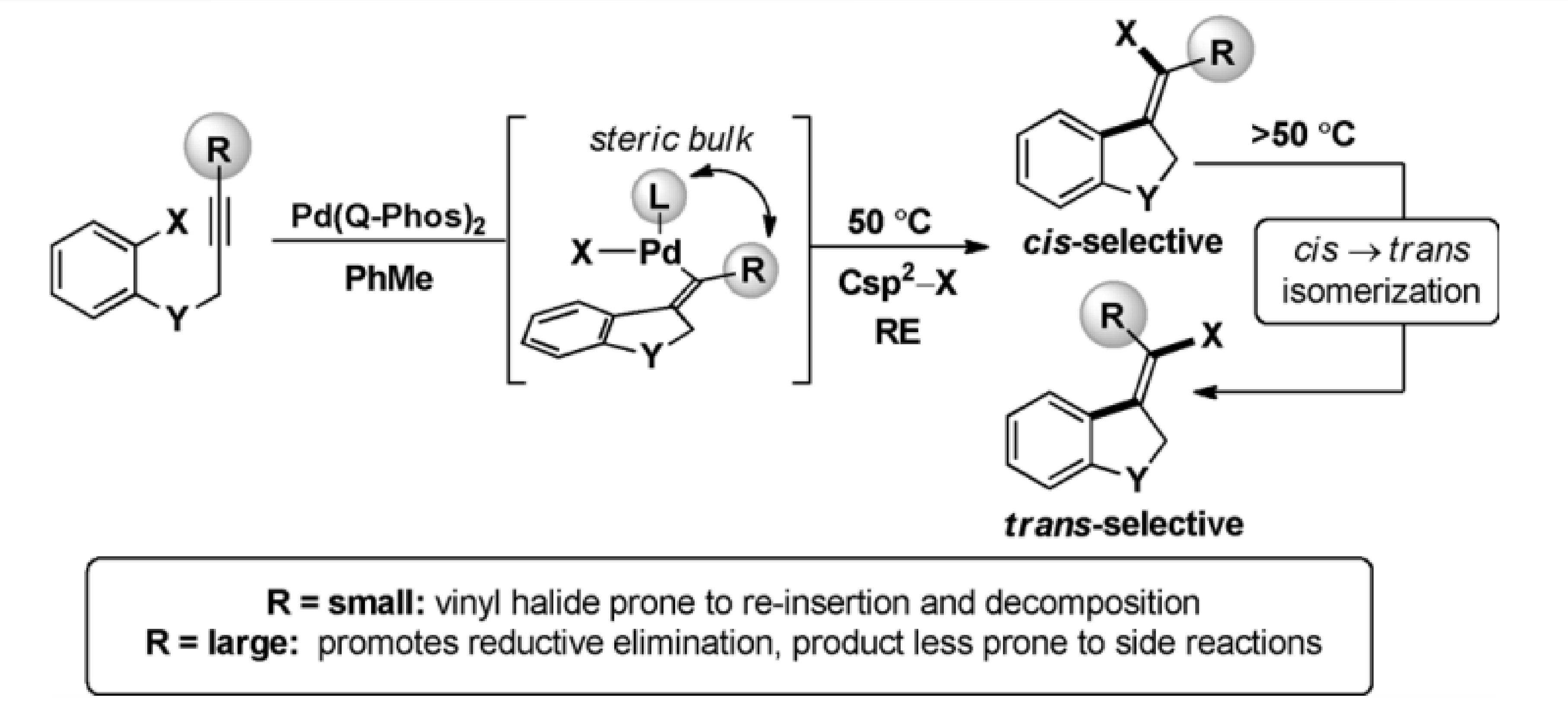
D. A. Petrone, M. Lischka, M. Lautens, *Angew. Chem. Int. Ed.* **2013**, *52*, 10635.

C-I Bond R.E. :   Kinetic Study



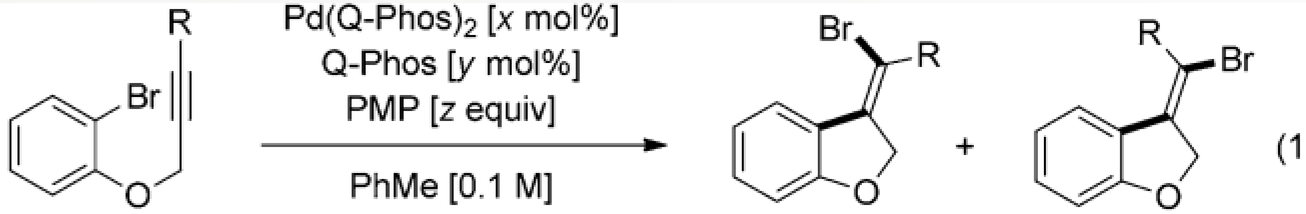
D. A. Petrone, M. Lischka, M. Lautens, *Angew. Chem. Int. Ed.* **2013**, *52*, 10635.

C-I Bond R.E. : Sp2-carbon iodide R.E.



C. M. Le, P. J. C. Menzies, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2015**, *54*, 254.

C-I Bond R.E. : Reaction Scope

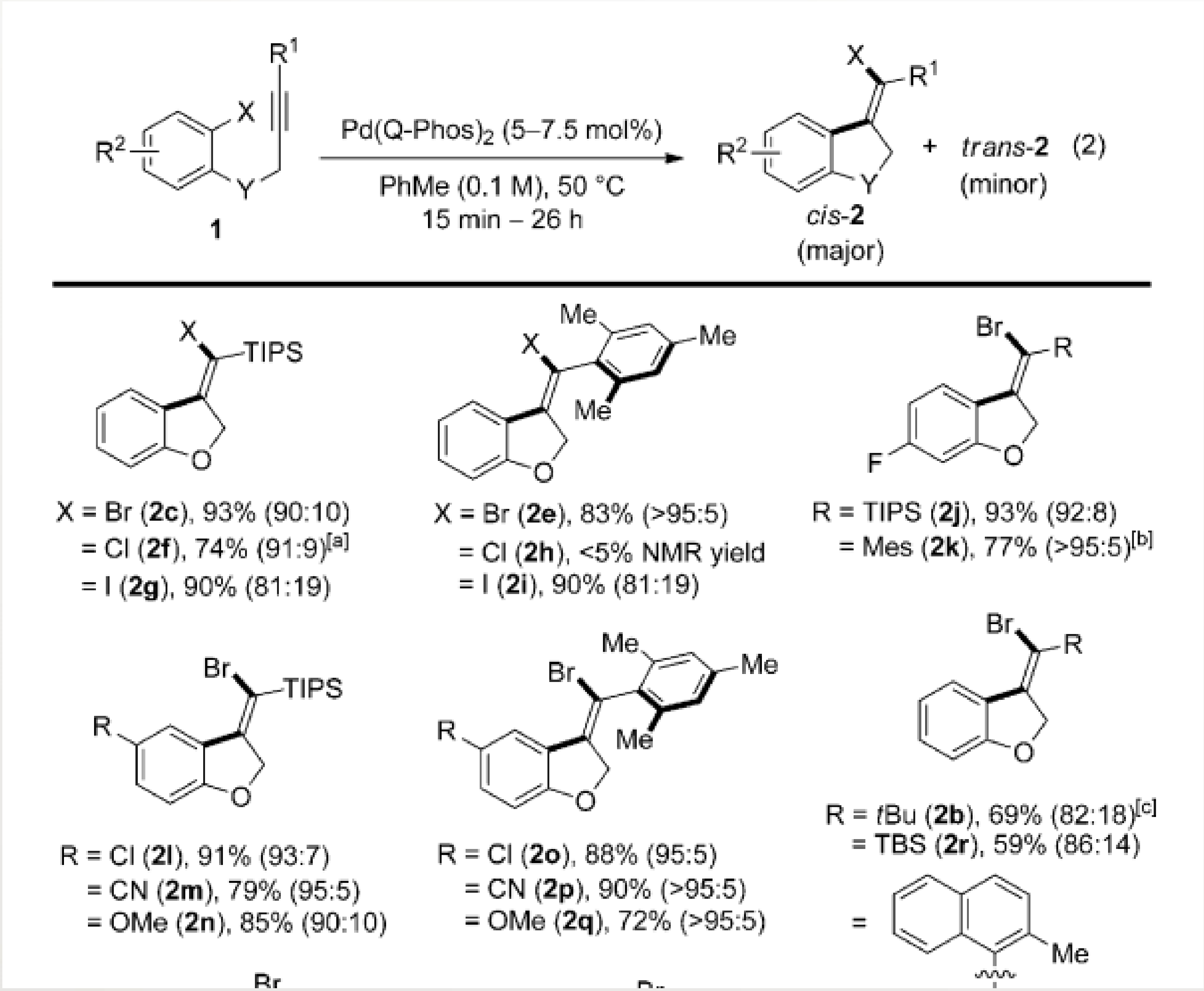


1   *cis*-**2**   *trans*-**2**

Entry	R (**1**)	*x* [mol%]	Temp [°C]/ (Time [h])	Yield[a] [%]	*cis/trans*[a]
1[b]	Me (**1a**)	5.0	110 (1.0)	40	N/D
2[b]	*t*Bu (**1b**)	5.0	110 (1.0)	83	82:18
3[b]	TIPS (**1c**)	5.0	110 (1.0)	94	87:13
4[c]	**TIPS (1c)**	**7.5**	**50 (0.25)**	**96**	**90:10**
5[c]	TIPS (**1c**)	0	50 (0.25)	0	N/D
6[b]	Ph (**1d**)	5.0	110 (1.0)	<5	N/D
7[c]	**mesityl (1e)**	**5.0**	**50 (18)**	**85**	**>95:5**
8[c]	**mesityl (1e)**	**5.0**	**100 (18)**	**90**	**10:90**

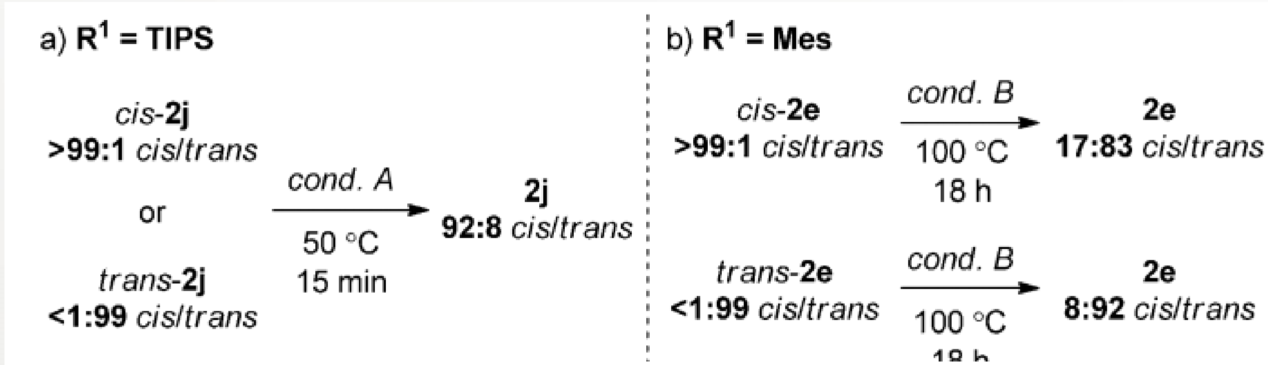
C. M. Le, P. J. C. Menzies, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2015**, *54*, 254.

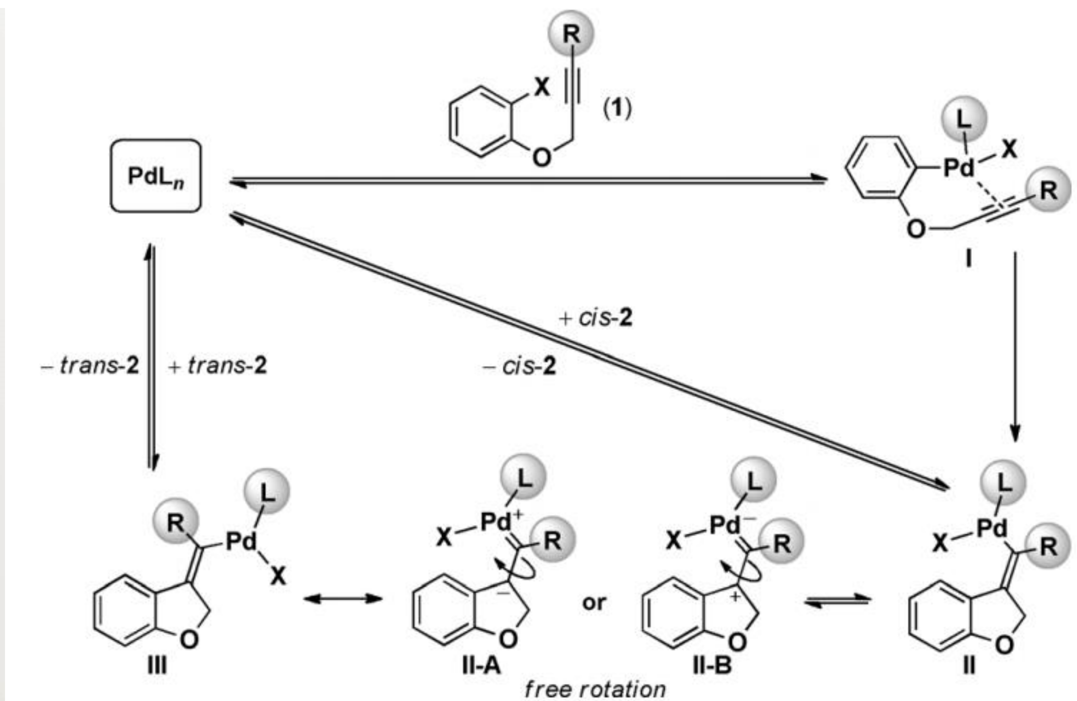
C-I Bond R.E. : Reaction Scope



C. M. Le, P. J. C. Menzies, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2015**, *54*, 254.

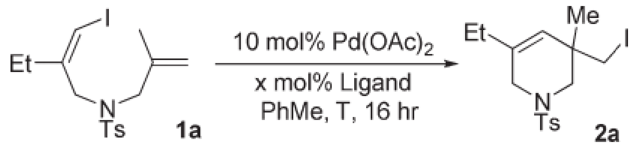
C-I Bond R.E. : Cis/Trans isomerization



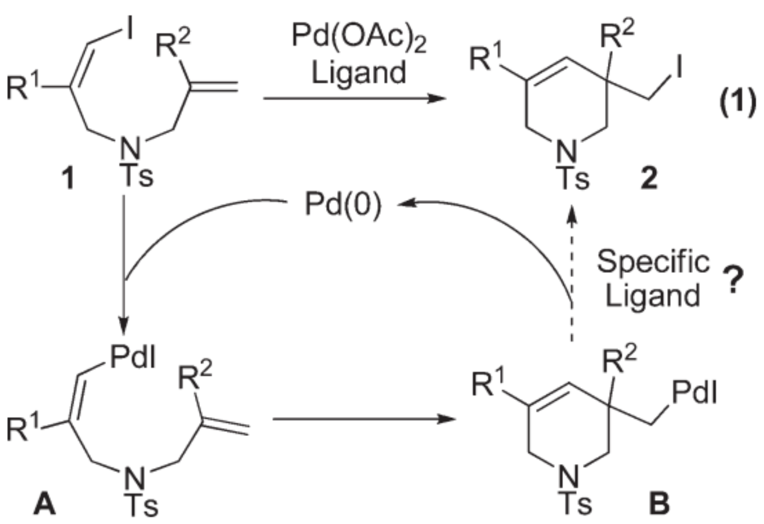


C. M. Le, P. J. C. Menzies, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2015**, *54*, 254.

C-I Bond R.E. : Reaction Design

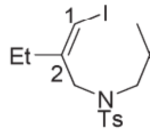
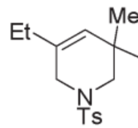
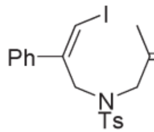
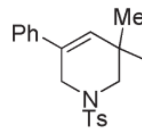
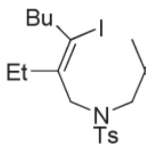
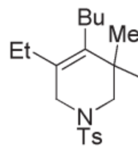
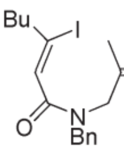
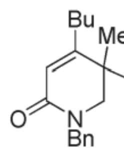
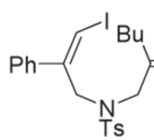
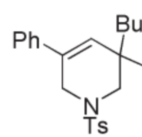
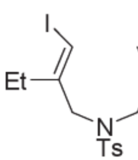


entry	ligand	x	T (°C)	yield (%)[b]
1	P(*t*-Bu)$_3$[c]	100	80	34
2	P(*t*-Bu)$_3$	100	reflux	41
3	P(*t*-Bu)$_3$	120	reflux	39
4	P(*t*-Bu)$_3$	60	reflux	27
5	P(*t*-Bu)$_3$	30	reflux	trace
6[d]	P(*t*-Bu)$_3$	100	reflux	ND[g]
7[e]	–	–	reflux	ND[g]
8[f]	–	–	reflux	ND[g]
9	PPh$_3$	100	reflux	23
10	P(*n*-Bu)$_3$	100	reflux	15
11	DPPE	50	reflux	trace
12	BINAP	50	reflux	10
13	DPPP	50	reflux	25
14	DPPB	50	reflux	36
15	DPPF	50	reflux	74
16	DPPF	70	reflux	75
17	DPPF	100	reflux	73
18	DPPF	20	reflux	trace
19	DPPF	25	reflux	43
20	**DPPF**	**30**	**reflux**	**84**
21	DPPF	40	reflux	71

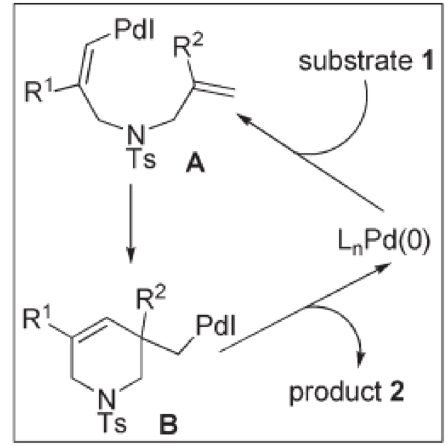


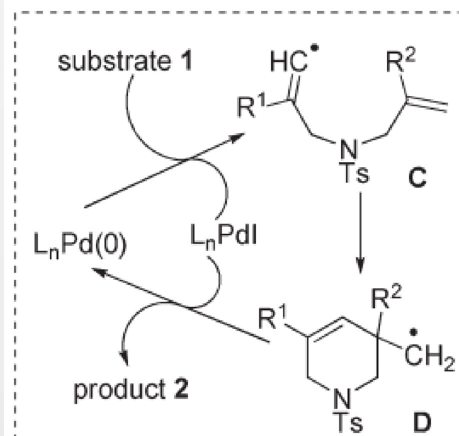
H. Liu, C. Li, D. Qiu, X. Tong, *J. Am. Chem. Soc.* **2011**, *133*, 6187.

C-I Bond R.E. : Reaction Scope

1	 1a	 2a	84
2	 1b	 2b	75
3	 1c	 2c	NR[c]
4	 1d	 2d	43
5	 1e	 2e	87
12	 (E)-1a	--	--

Cycle I

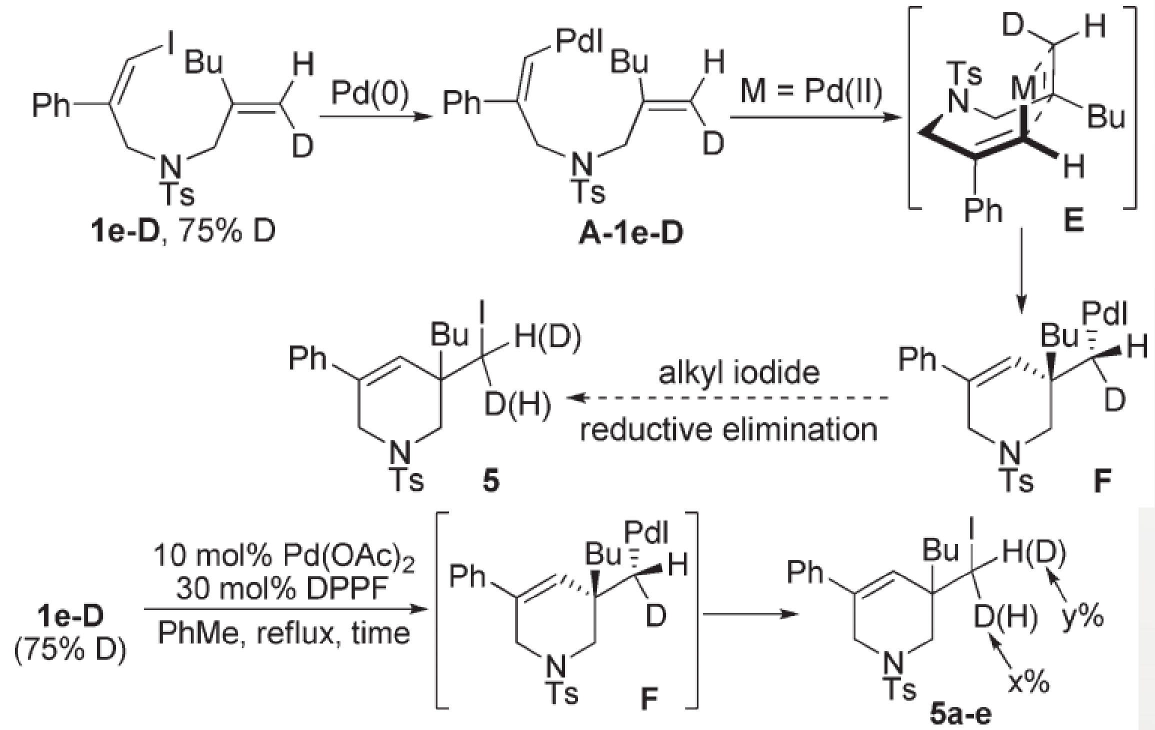




Cycle II

H. Liu, C. Li, D. Qiu, X. Tong, *J. Am. Chem. Soc.* **2011**, *133*, 6187.

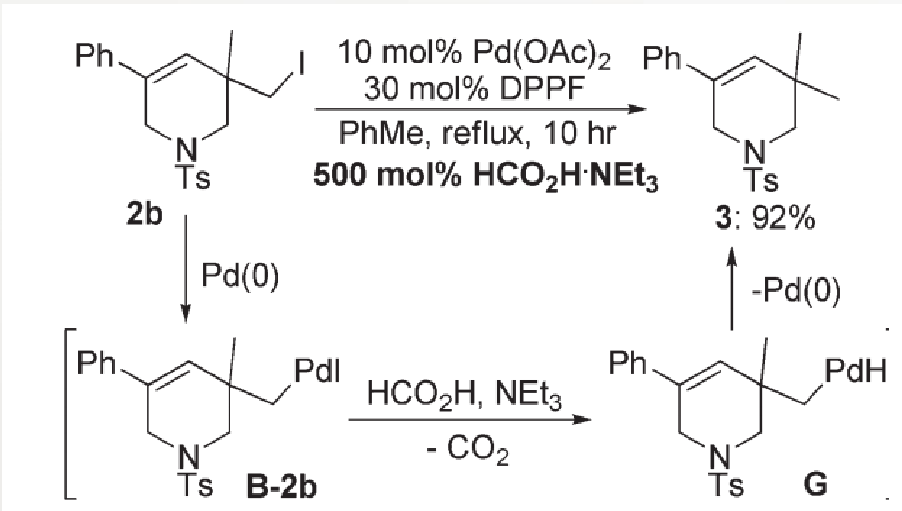
C-I Bond R.E. : Mechanism Study

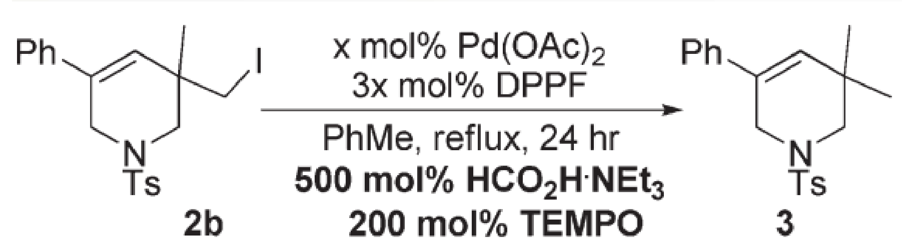


entry	time	1e-D recovery	product	isolated yield
1	2 hr	33%	**5a** (x = 75, y = 0)	60%
2	6 hr	20%	**5b** (x = 73, y = 2)	64%
3	10 hr	5%	**5c** (x = 71, y = 4)	75%
4	16 hr	0%	**5d** (x = 58, y = 17)	79%
5	24 hr	0%	**5e** (x = 40, y = 35)	72%

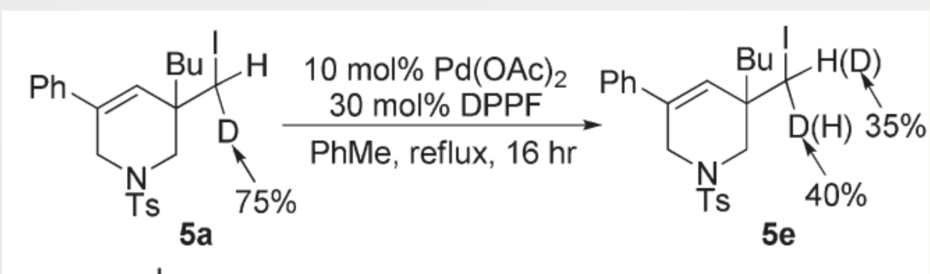
H. Liu, C. Li, D. Qiu, X. Tong, *J. Am. Chem. Soc.* **2011**, *133*, 6187.

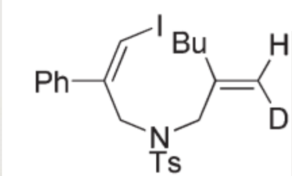
C-I Bond R.E. : Mechanism Study

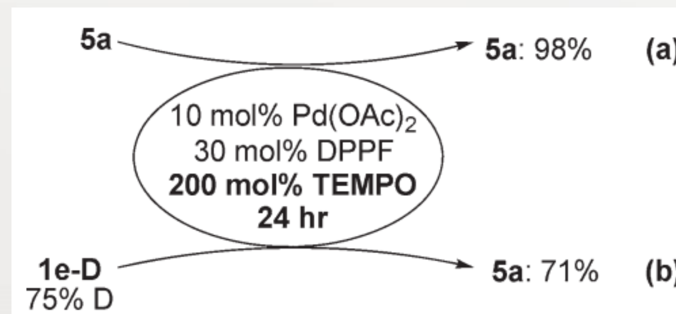




entry	x	yield (%) 3	yield (%) 2b
1	10	63	27
2	20	89	0

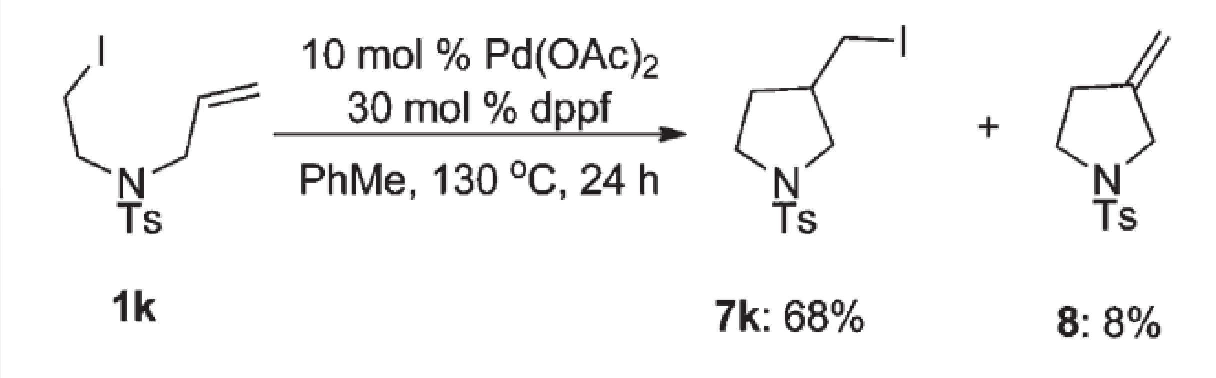


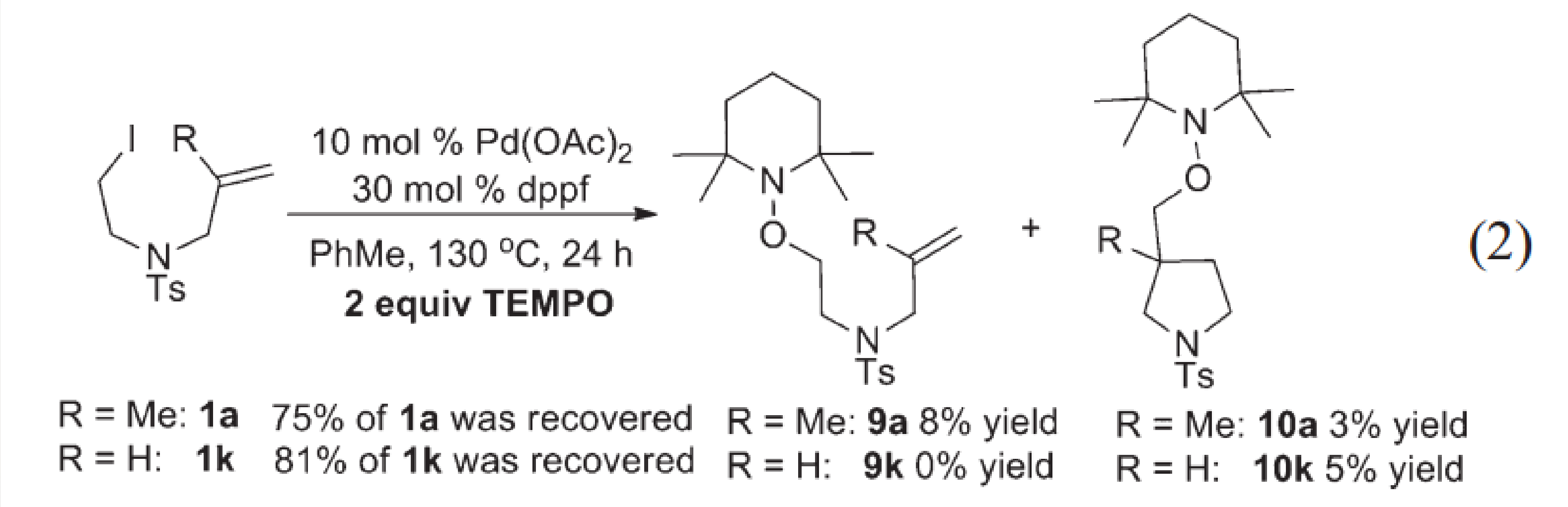




H. Liu, C. Li, D. Qiu, X. Tong, *J. Am. Chem. Soc.* **2011**, *133*, 6187.

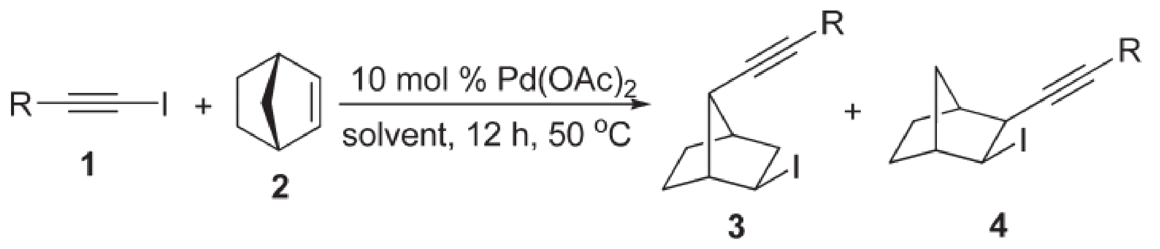
C-I Bond R.E. : Reaction Scope





H. Liu, Z. Qiao, X. Jiang, *Org. Biomol. Chem.;* **2012**, *10*, 7274.

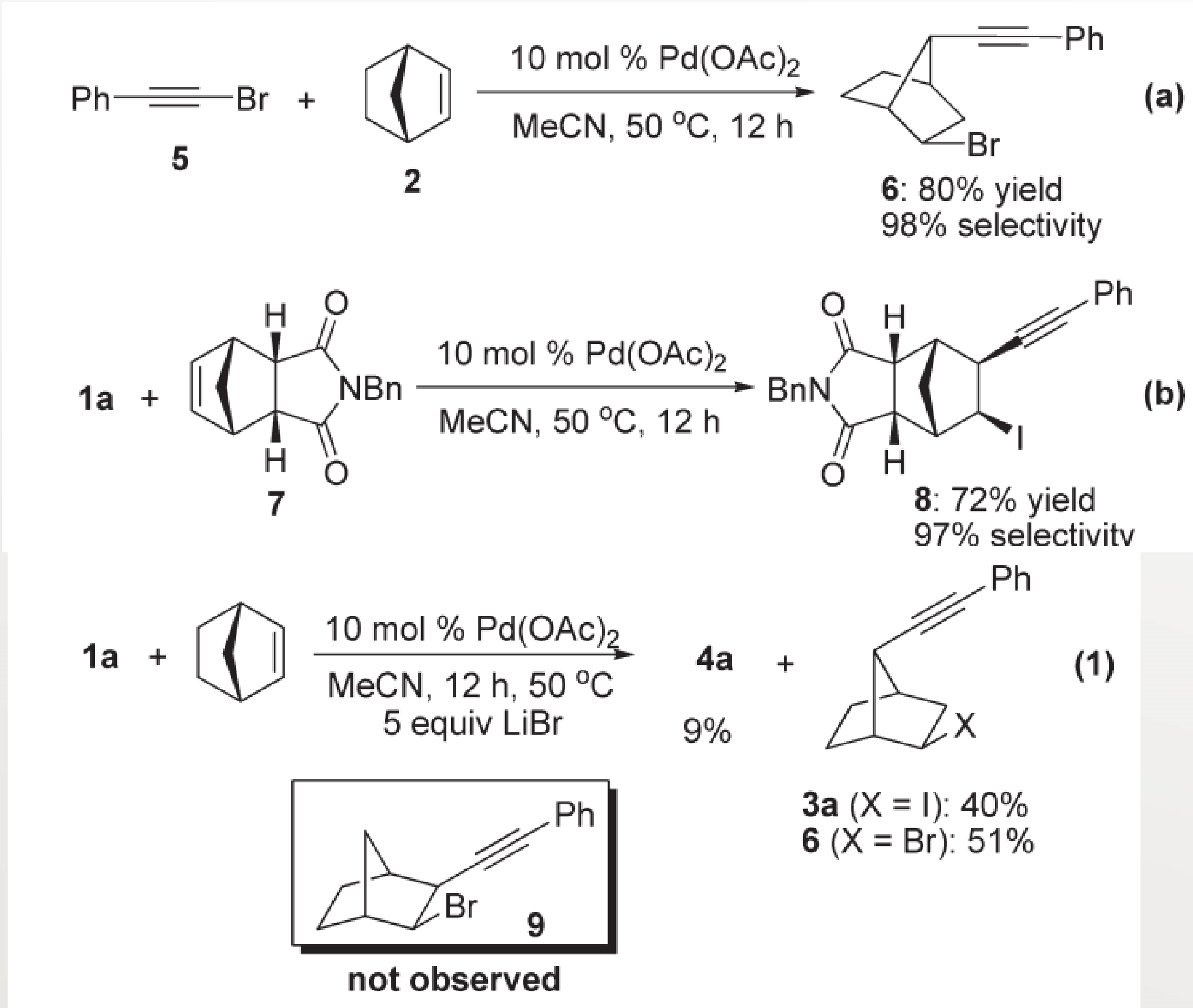
C-I Bond R.E. : Reaction Scope



entry	R	In CCl_4: 4 (yield)[b]	In CCl_4: 4:3	In MeCN: 3 (yield)[b]	In MeCN: 3:4
1	Ph	**4a** (75%)	98:2	**3a** (82%)	97:3
2	4-Me-C_6H_4	**4b** (73%)	99:1	**3b** (75%)	99:1
3	3-Me-C_6H_4	**4c** (62%)	88:12	**3c** (58%)	96:4
4	4-MeO-C_6H_4	**4d** (58%)	89:11	**3d** (61%)	92:8
5	2-Br-C_6H_4	**4e** (97%)	94:6	**3e** (95%)	99:1
6	4-Br-C_6H_4	**4f** (65%)	91:9	**3f** (64%)	96:4
7	4-Cl-C_6H_4	**4g** (70%)	97:3	**3g** (86%)	98:2
8	4-F-C_6H_4	**4h** (52%)	97:3	**3h** (58%)	97:3
9	2-thietyl	**4i** (66%)	98:2	**3i** (73%)	96:4
10	*n*-Bu	**4j** (31%)	94:6	**3j** (41%)	80:20

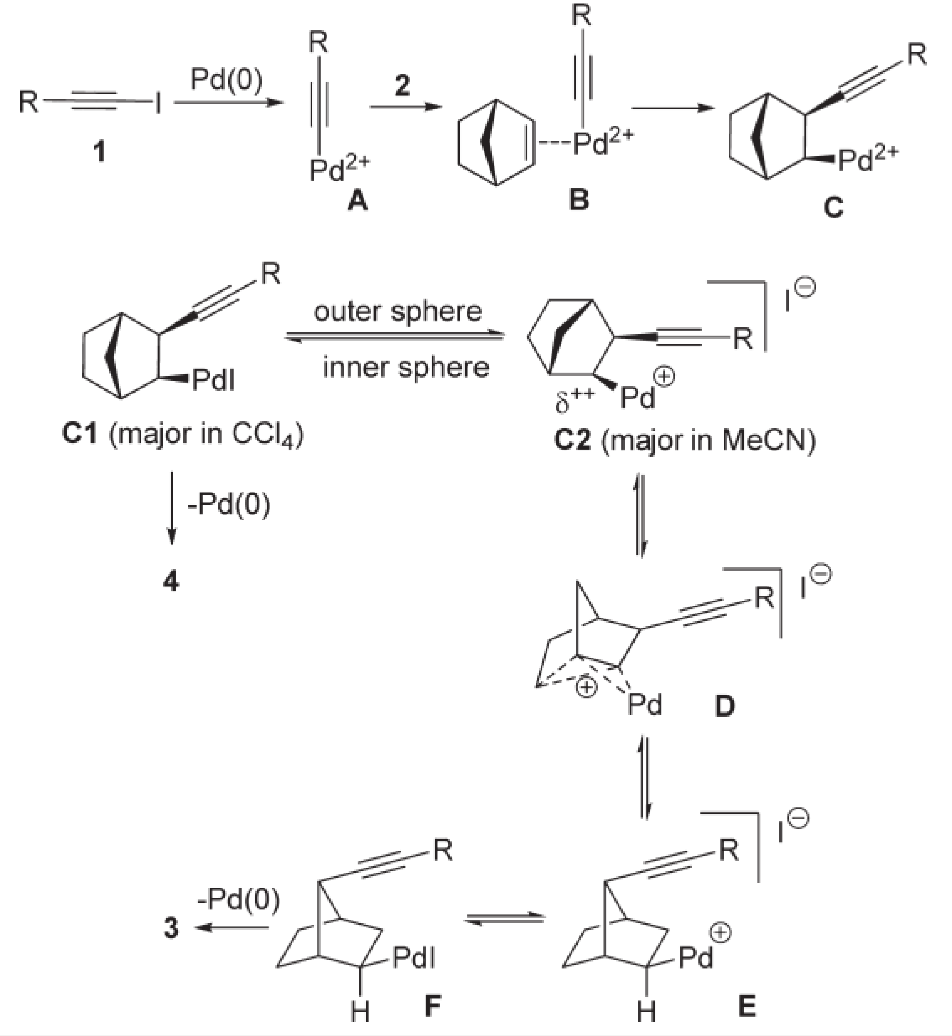
H. Liu, C. Chen, L. Wang, X. Tong, *Org. Lett.* **2011**, *13*, 5072.

C-I Bond R.E. : Reaction Scope



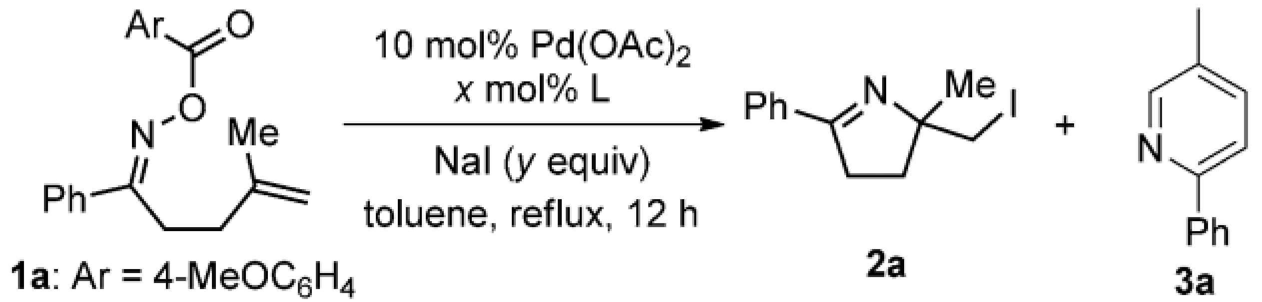
H. Liu, C. Chen, L. Wang, X. Tong, *Org. Lett.* **2011**, *13*, 5072.

C-I Bond R.E. : Mechanism



H. Liu, C. Chen, L. Wang, X. Tong, *Org. Lett.* **2011**, *13*, 5072.

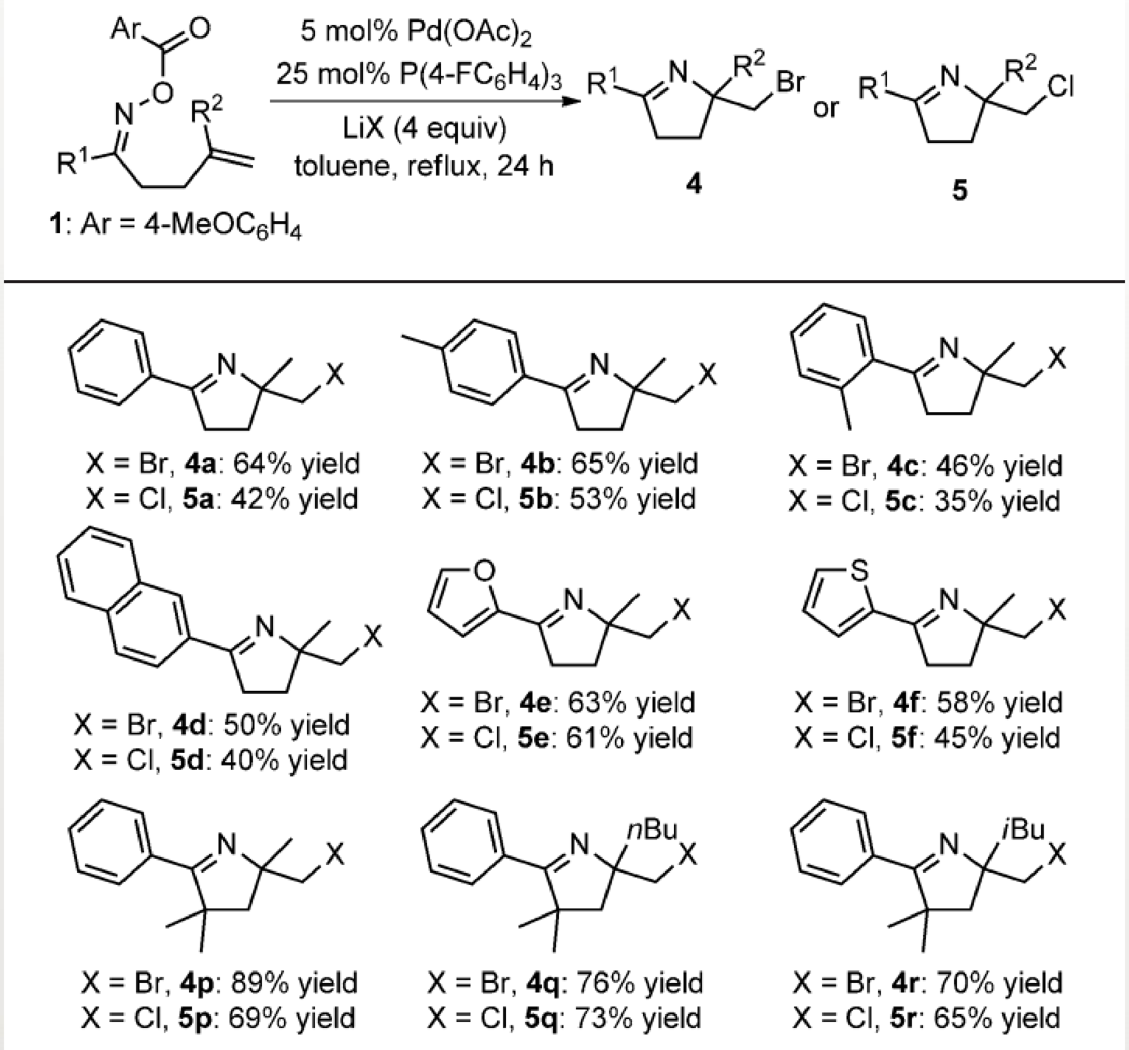
C-I Bond R.E. : Reaction Optimization



Entry	L (*x*)	NaI (*y*)	Yield [%][b] 2a	3a
1	$P(4\text{-}FC_6H_4)_3$ (20)	NaI (2)	15	35
2	$P[3,5\text{-}(CF_3)_2C_6H_3]_3$ (20)	NaI (2)	15	29
3	$P(4\text{-}FC_6H_4)_3$ (50)	NaI (2)	62	8
4	$P[3,5\text{-}(CF_3)_2C_6H_3]_3$ (50)	NaI (2)	37	14
5	$P(4\text{-}FC_6H_4)_3$ (50)	NaI (4)	77	<5
6	$P(4\text{-}FC_6H_4)_3$ (50)	NaI (6)	78	<5
7[c]	$P(4\text{-}FC_6H_4)_3$ (25)	NaI (4)	75	<5

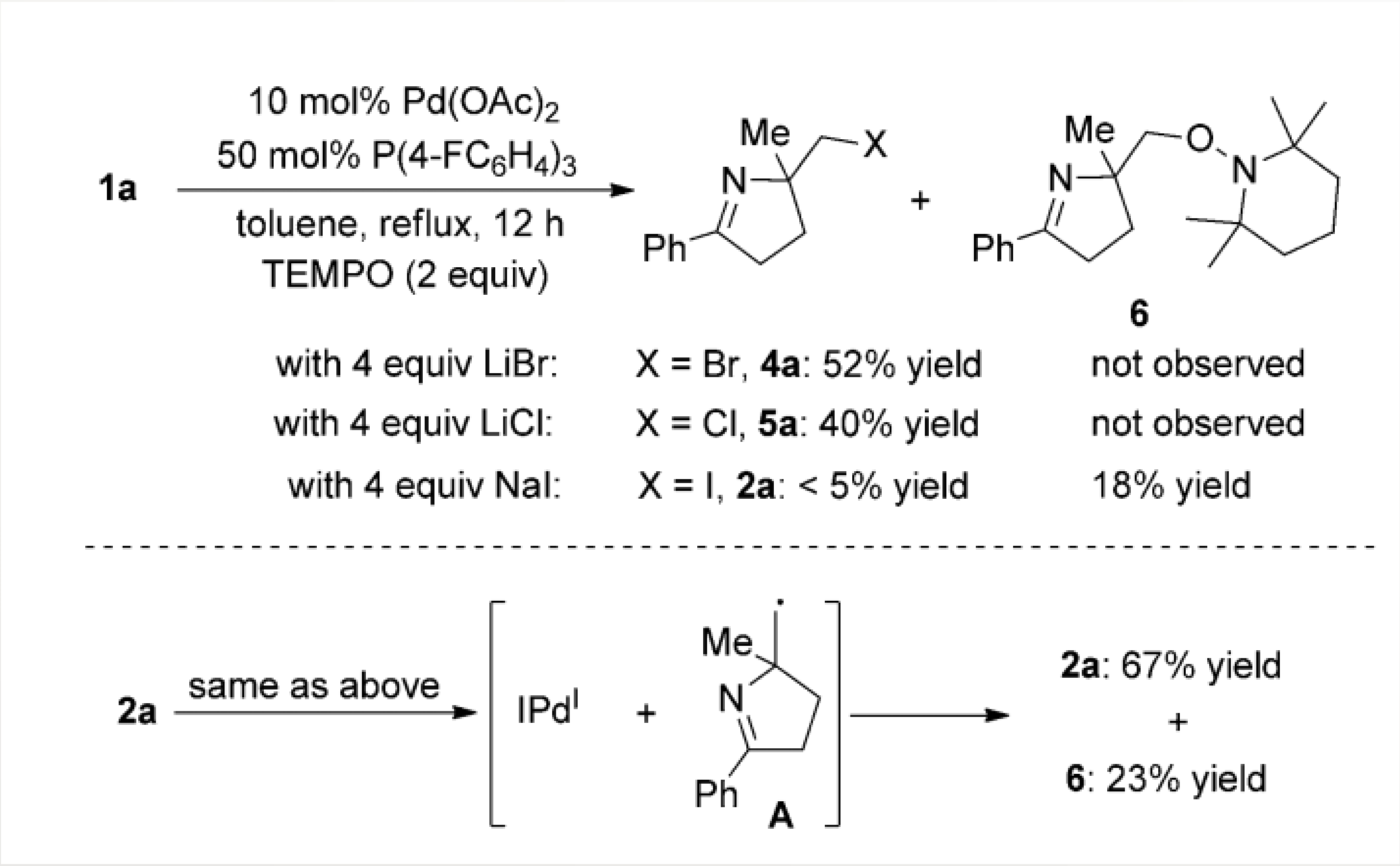
C. Chen, L. Hou, M. Cheng, J. Su, X. Tong, *Angew. Chem. Int. Ed.* **2015**, *54*, 3092.

C-I Bond R.E. : Reaction Scope



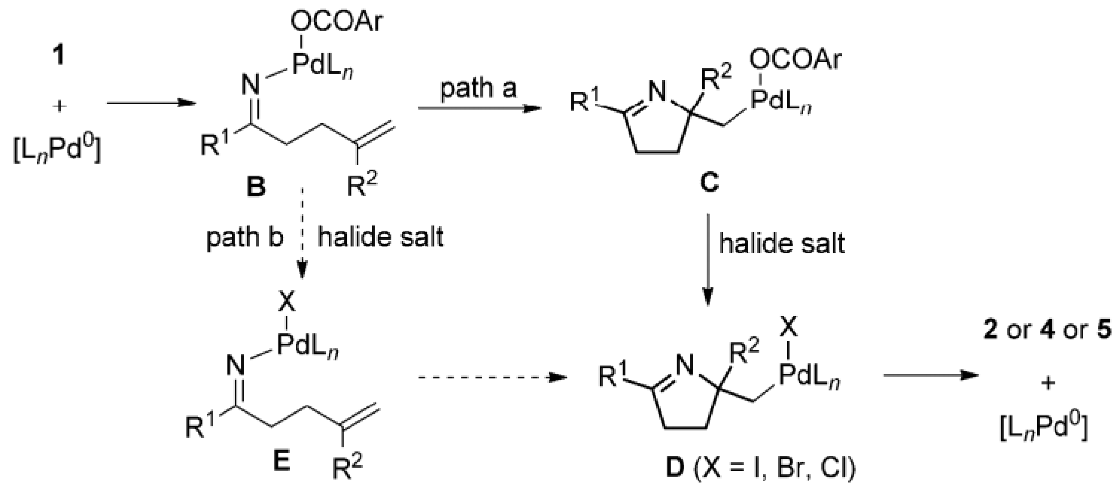
C. Chen, L. Hou, M. Cheng, J. Su, X. Tong, *Angew. Chem. Int. Ed.* **2015**, *54*, 3092.

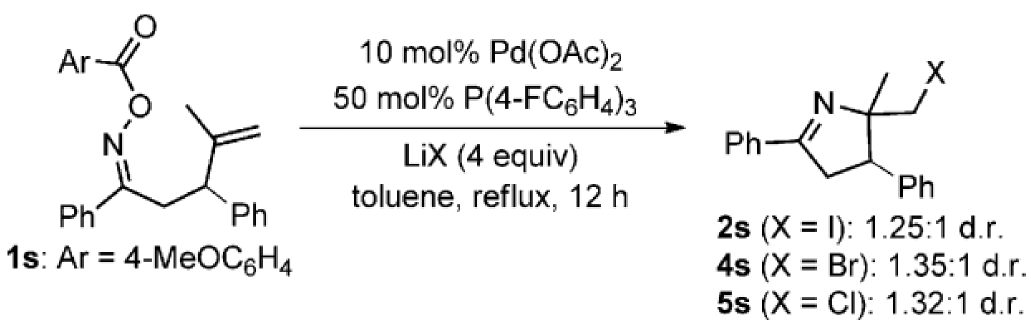
C-I Bond R.E. : Mechanism Study



C. Chen, L. Hou, M. Cheng, J. Su, X. Tong, *Angew. Chem. Int. Ed.* **2015**, *54*, 3092.

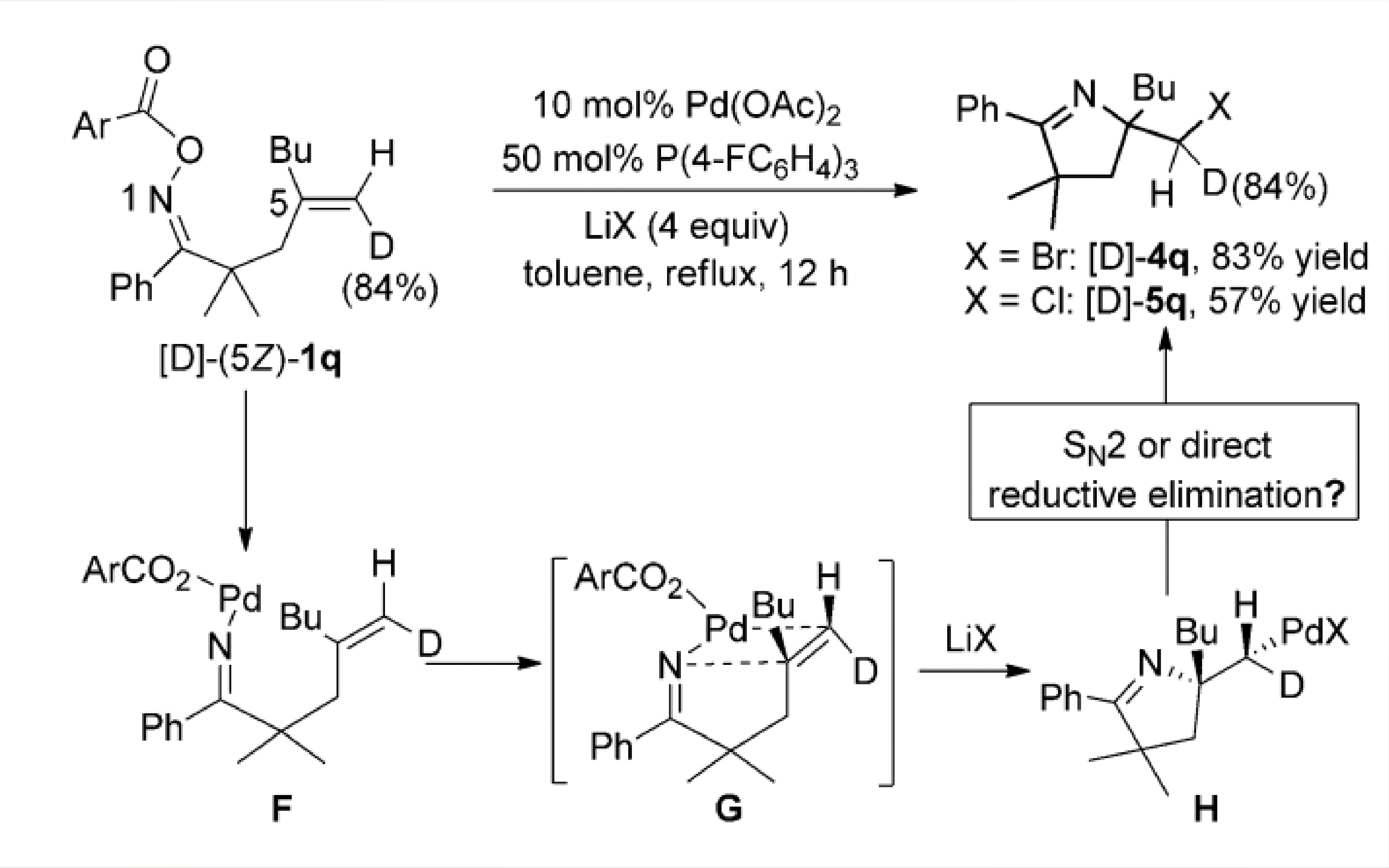
C-I Bond R.E. : Mechanism Study





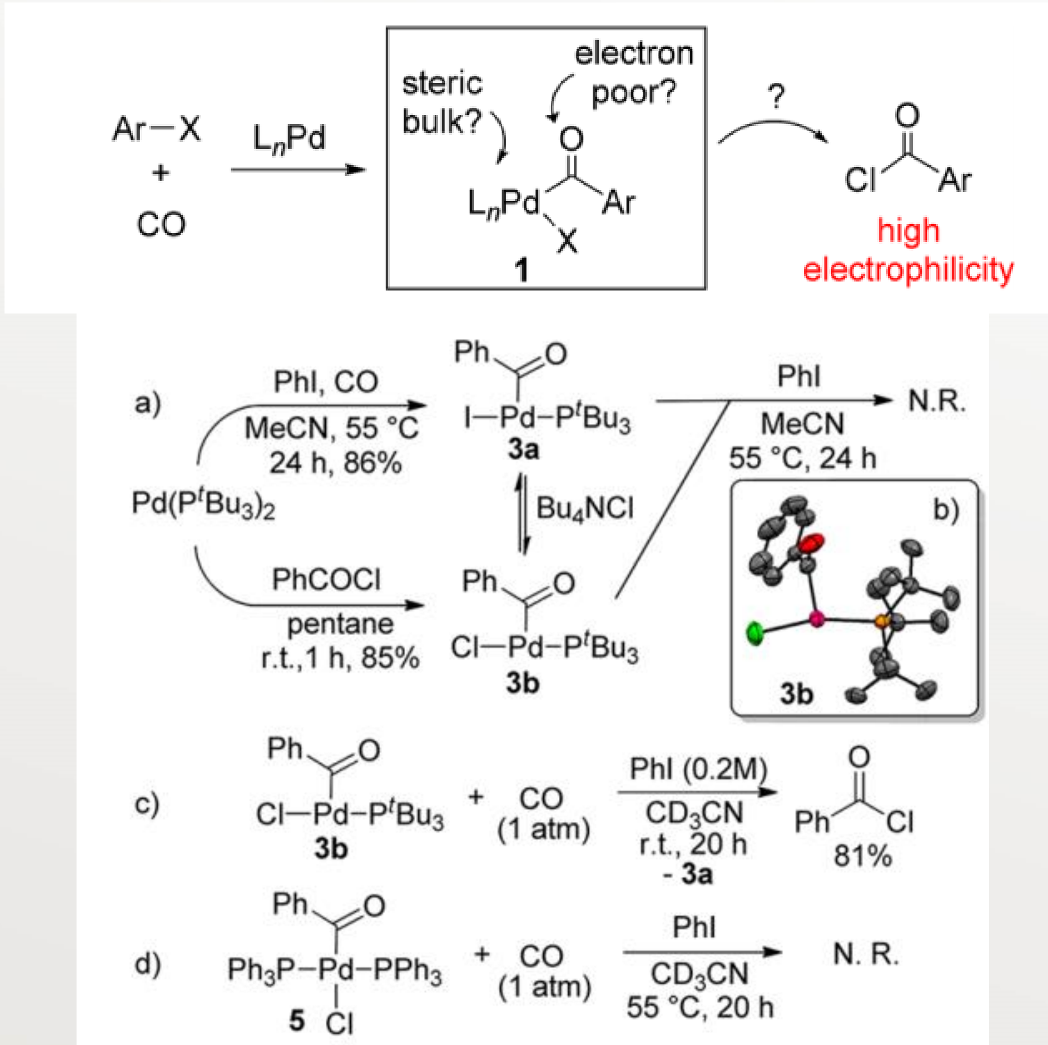
C. Chen, L. Hou, M. Cheng, J. Su, X. Tong, *Angew. Chem. Int. Ed.* **2015**, *54*, 3092.

C-I Bond R.E. : Mechanism Study



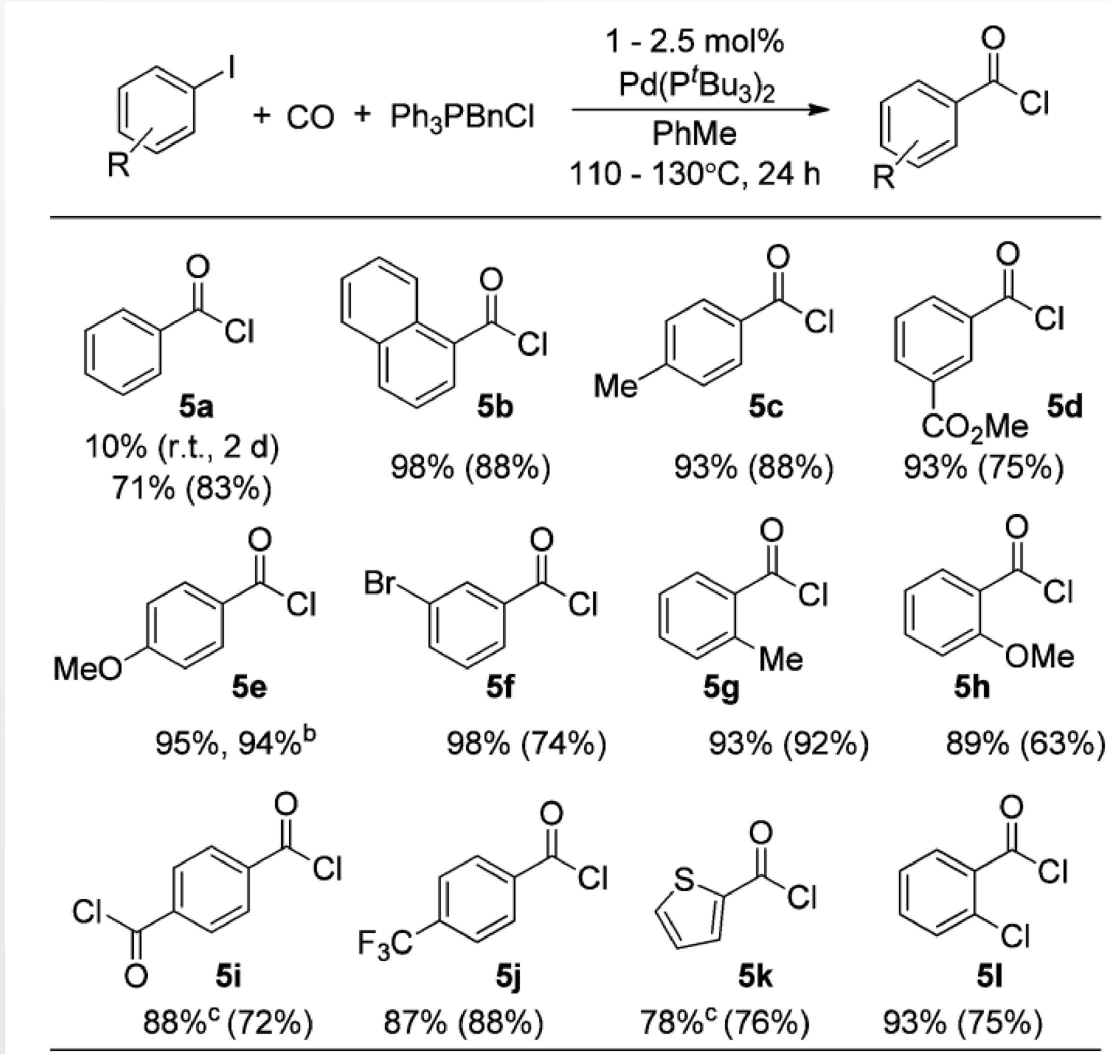
C. Chen, L. Hou, M. Cheng, J. Su, X. Tong, *Angew. Chem. Int. Ed.* **2015**, *54*, 3092.

C-I Bond R.E. : Reaction Design



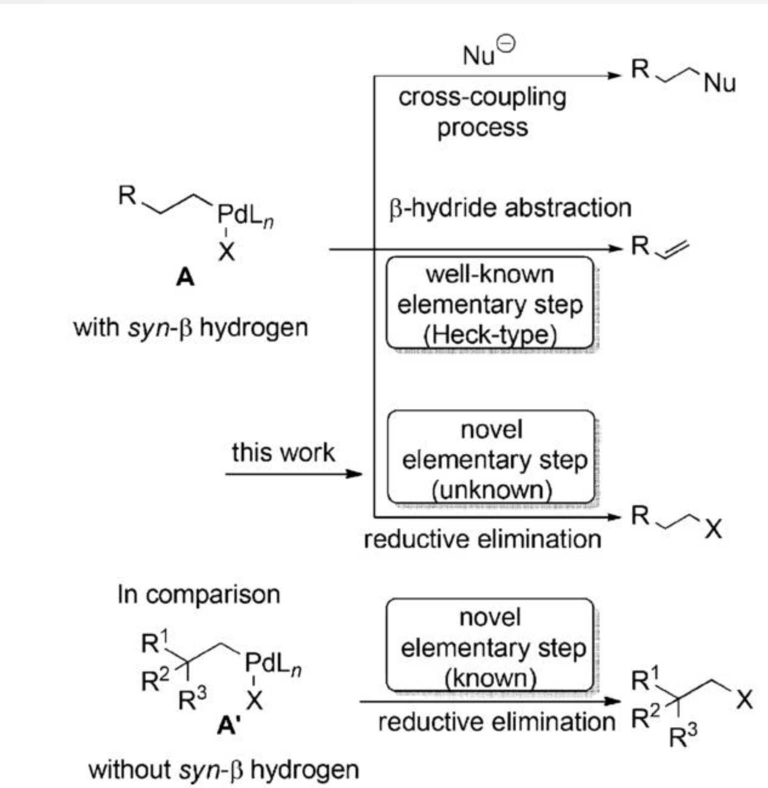
J. S. Quesnel, B. A. Arndtsen, *J. Am. Chem. Soc.* **2013**, *135*, 16841

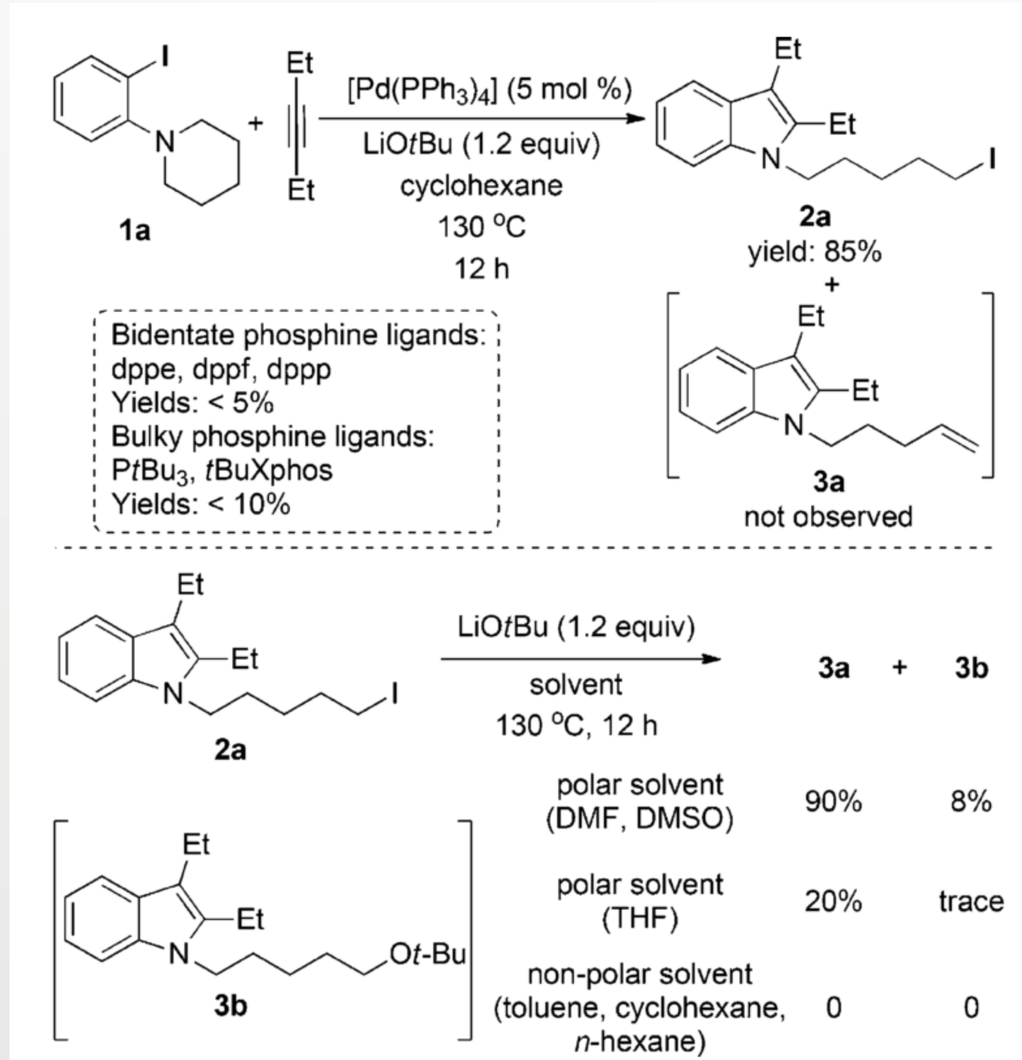
C-I Bond R.E. : Reaction Scope



J. S. Quesnel, B. A. Arndtsen, *J. Am. Chem. Soc.* **2013**, *135*, 16841

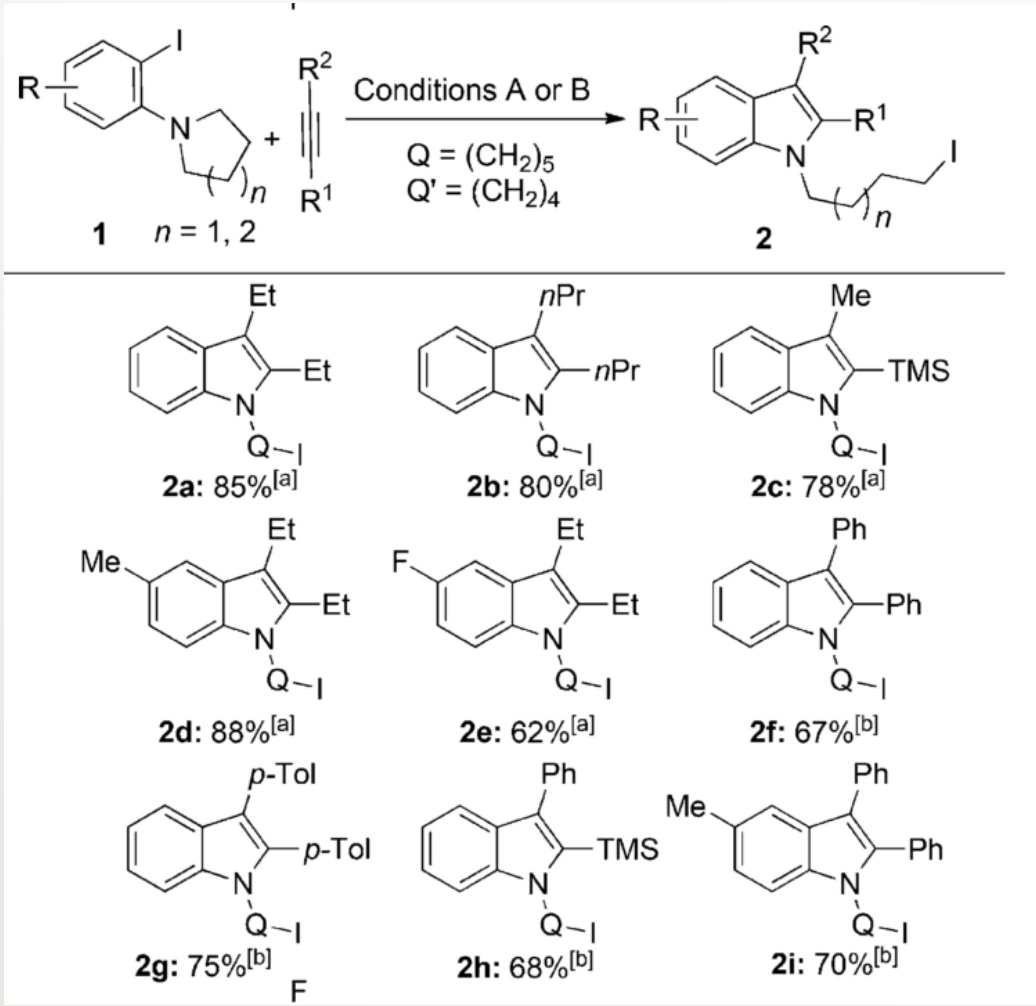
C-I Bond R.E. : Reaction Scope





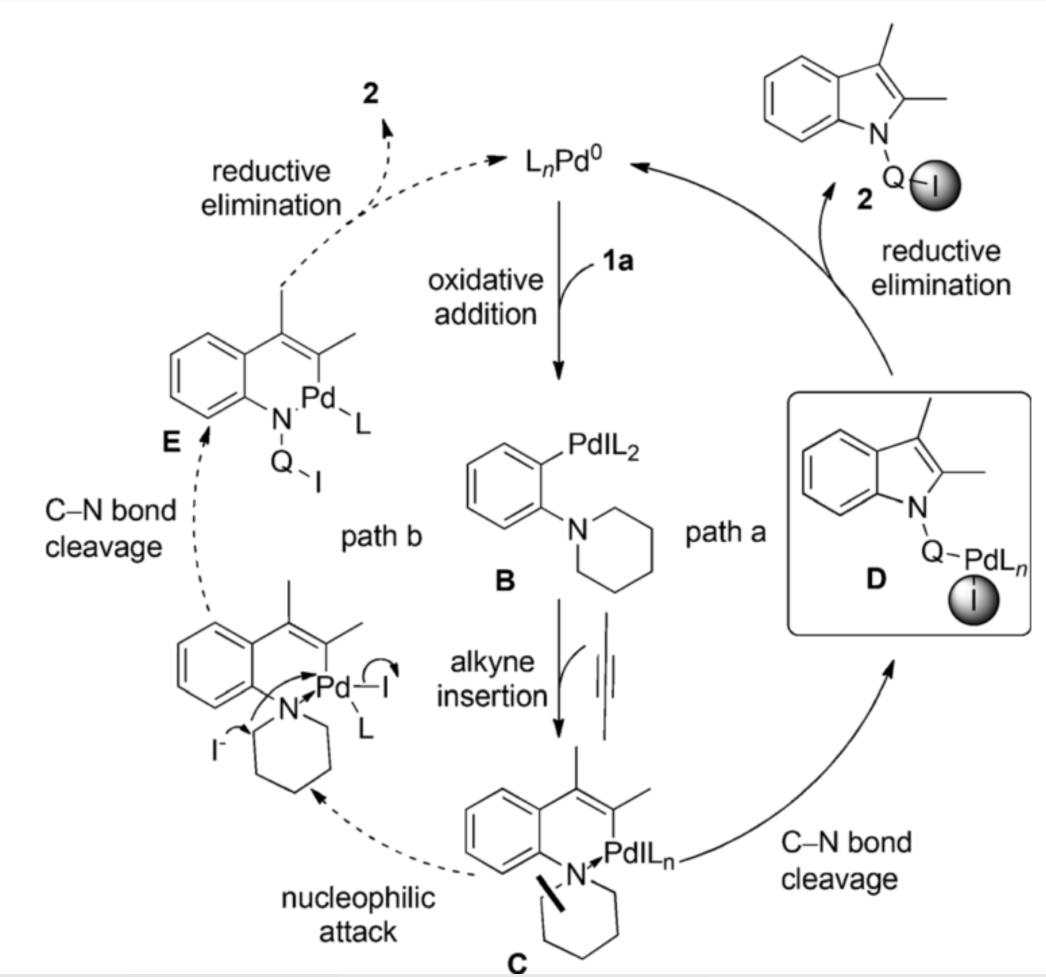
W. Hao, J. Wei, W. Geng, W.-X. Zhang, Z. Xi, *Angew. Chem. Int. Ed.* **2014**, *53*, 14533.

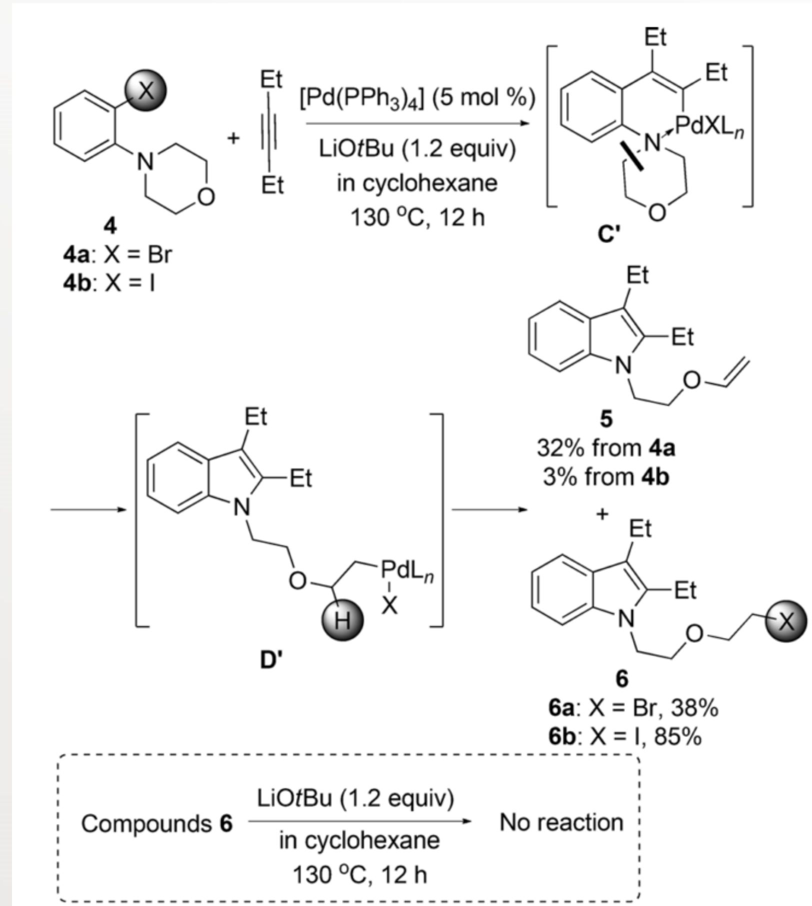
C-I Bond R.E. : Reaction Scope



W. Hao, J. Wei, W. Geng, W.-X. Zhang, Z. Xi, *Angew. Chem. Int. Ed.* **2014**, *53*, 14533.

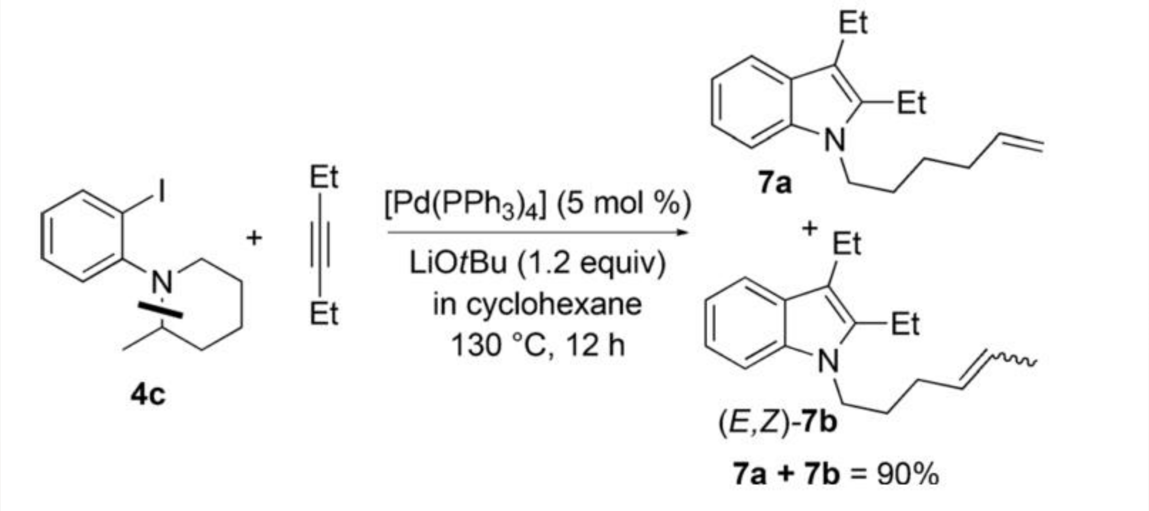
C-I Bond R.E. : Mechanism Study

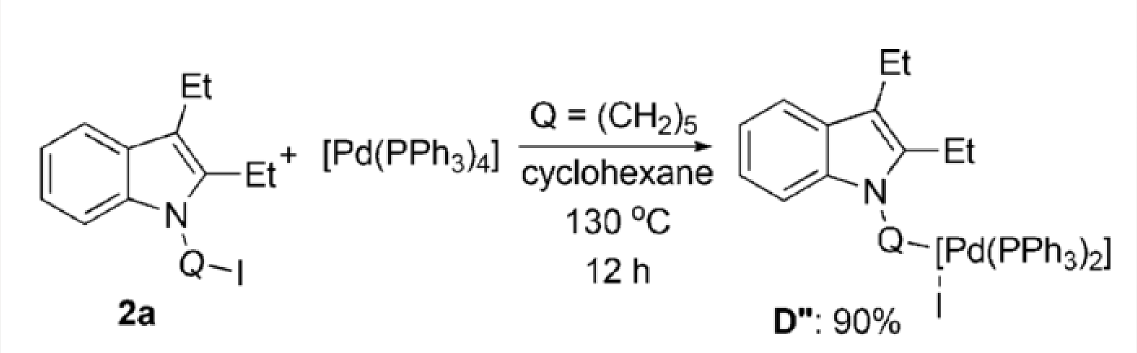




W. Hao, J. Wei, W. Geng, W.-X. Zhang, Z. Xi, *Angew. Chem. Int. Ed.* **2014**, *53*, 14533.

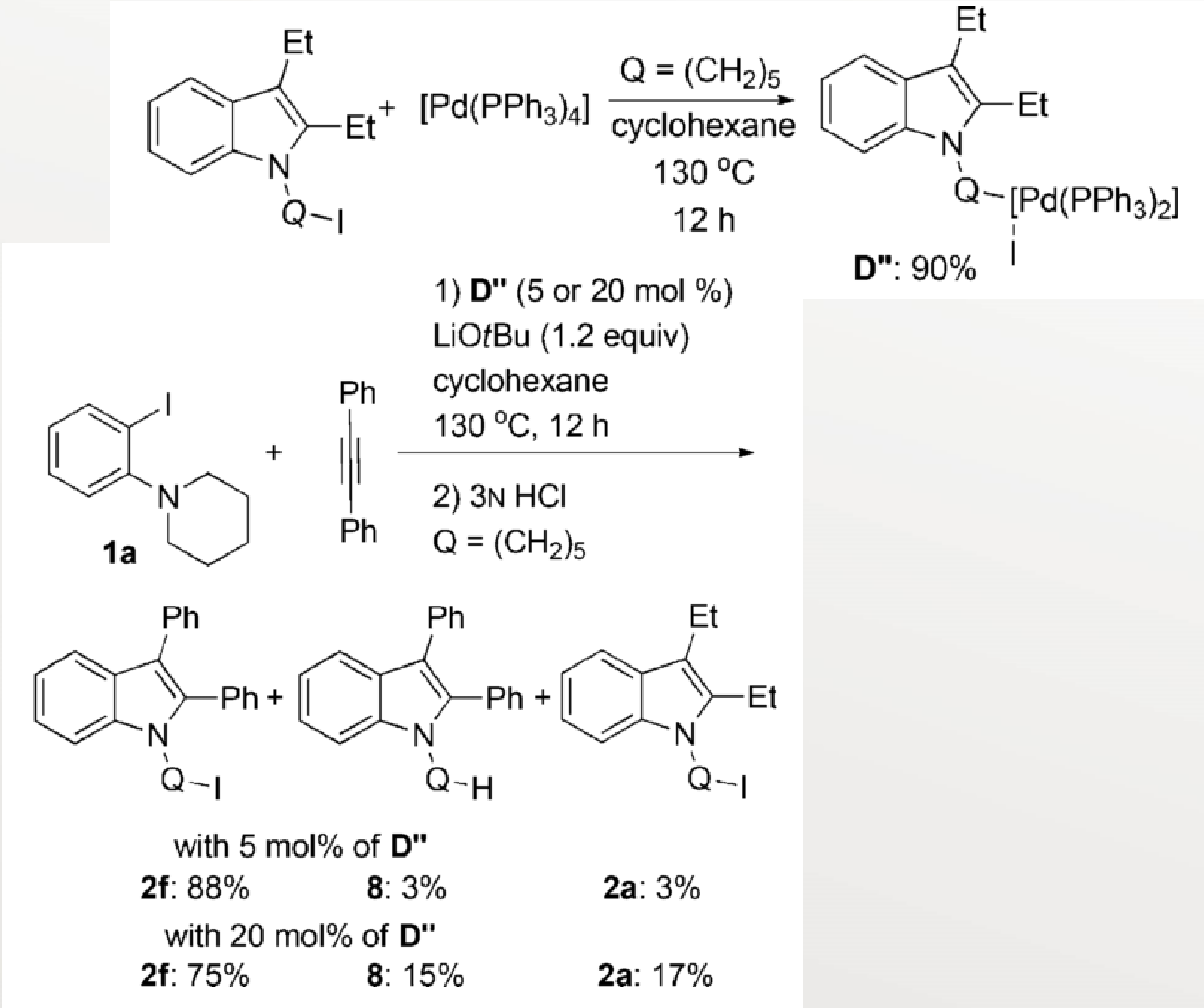
C-I Bond R.E. :   Mechanism Study





W. Hao, J. Wei, W. Geng, W.-X. Zhang, Z. Xi, *Angew. Chem. Int. Ed.* **2014**, *53*, 14533.

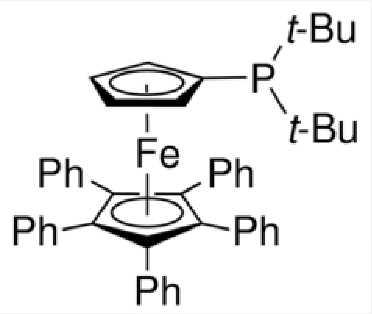
C-I Bond R.E. : Mechanism Study



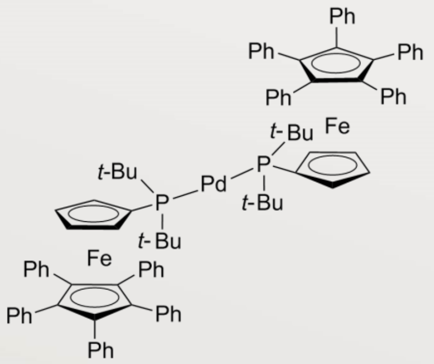
W. Hao, J. Wei, W. Geng, W.-X. Zhang, Z. Xi, *Angew. Chem. Int. Ed.* **2014**, *53*, 14533.

Summary:

1. Extreme Bulky(expensive) Phosphine Ligand Enabled Reaction

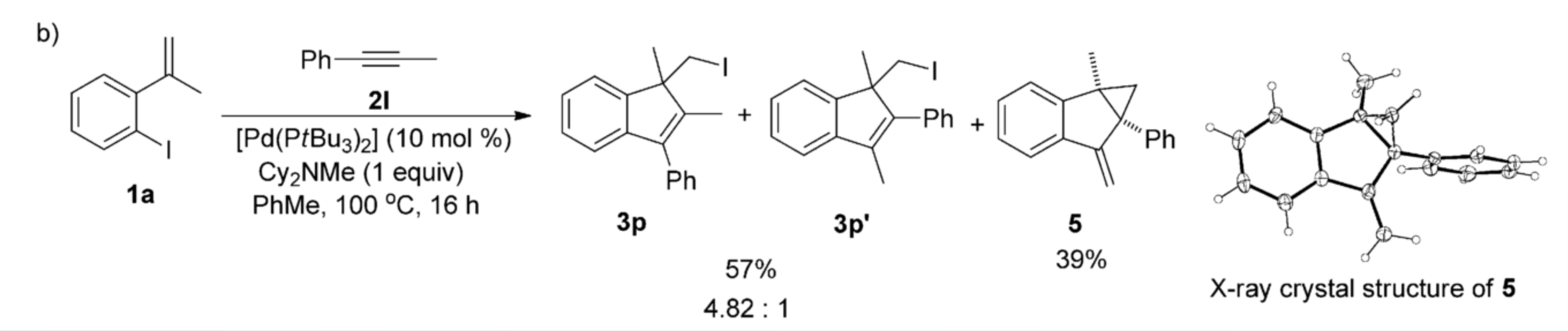


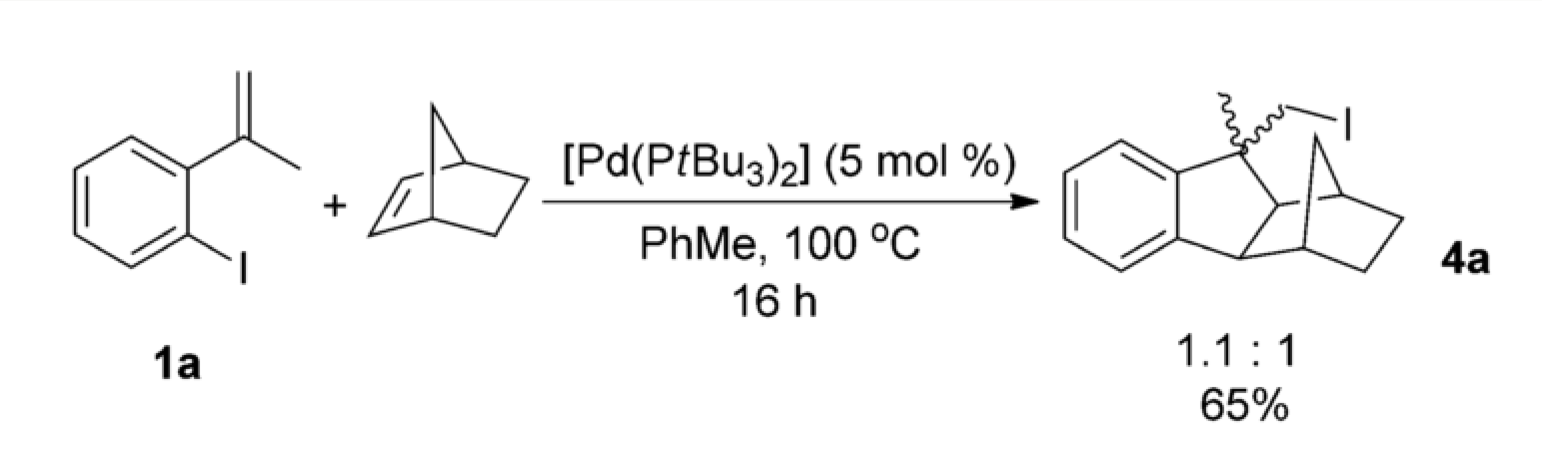
0.5 grams 269.50 dollars
MW: 710

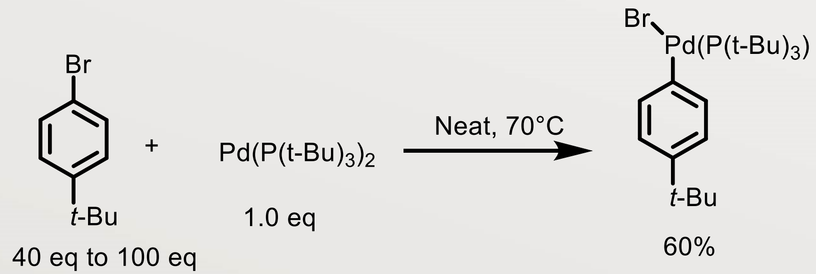


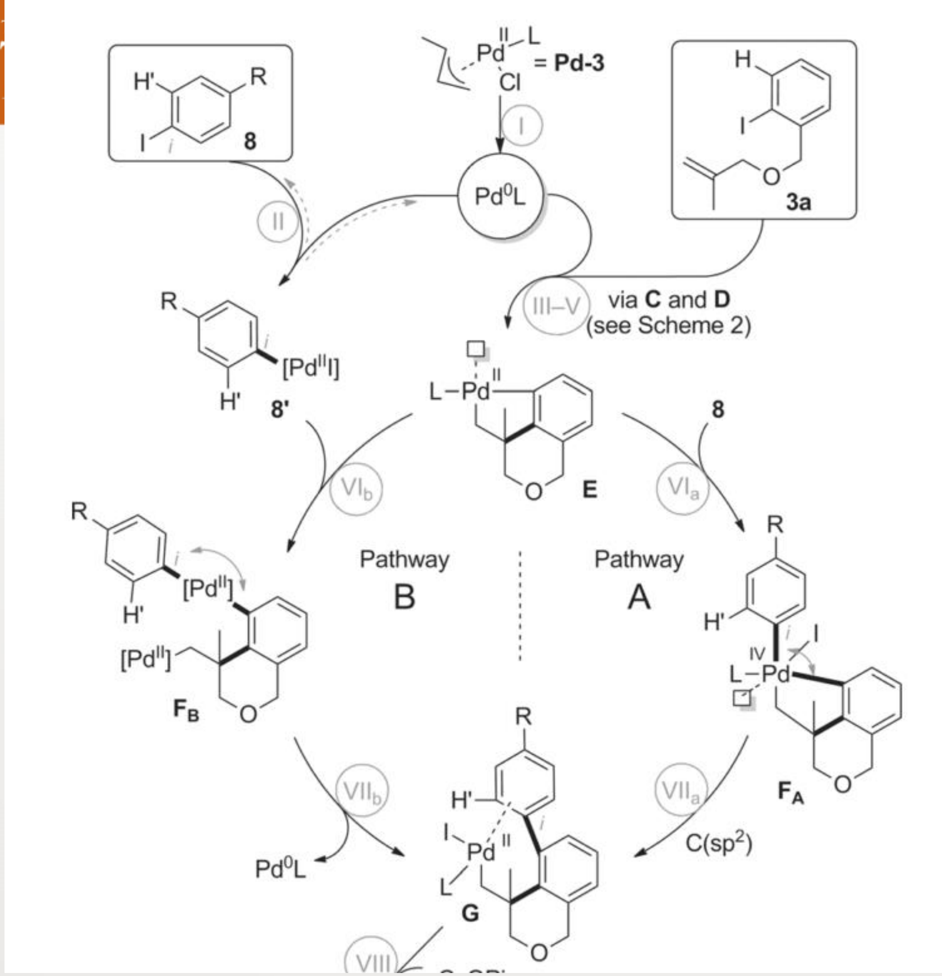
1 grams 671 dollars
MW: 1527

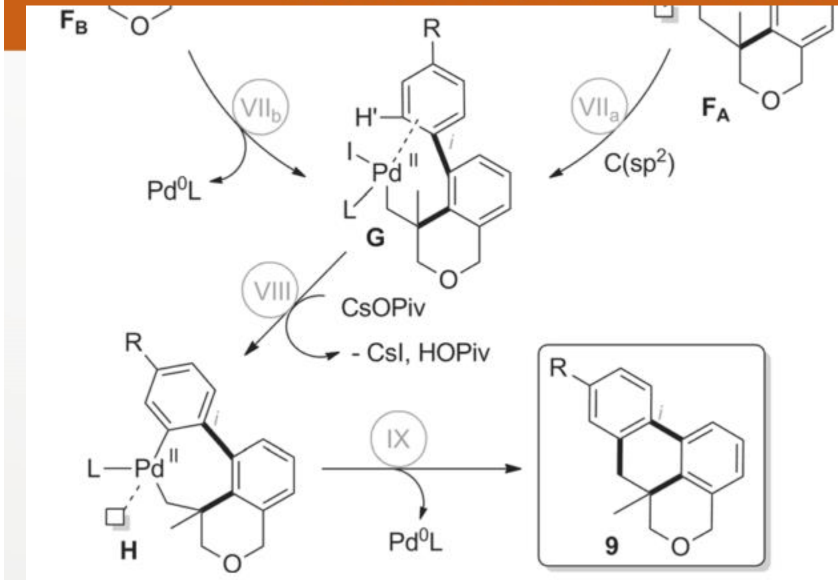
Thank you for your attention

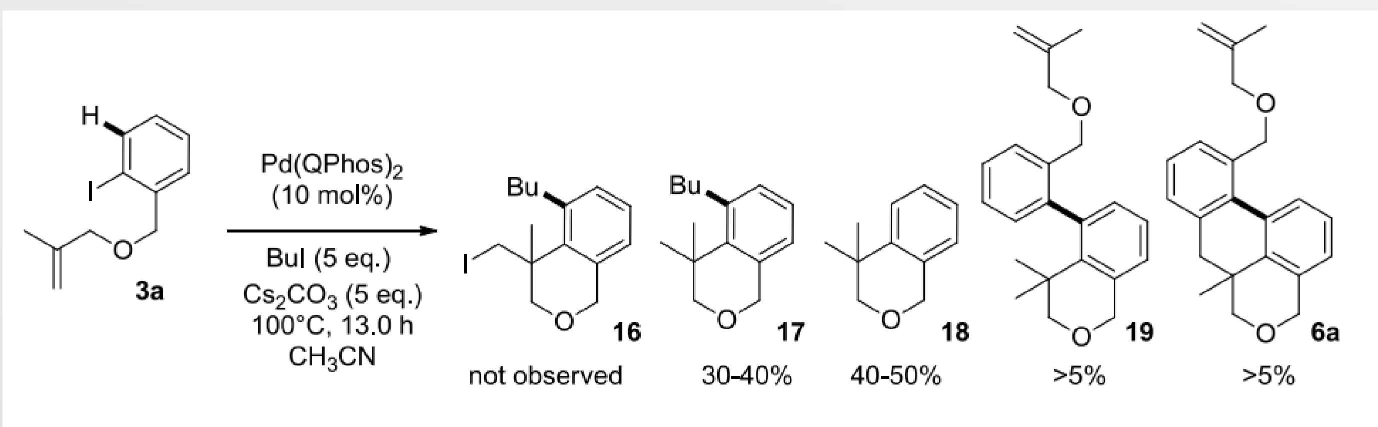

b)
Ph
2l
[Pd(PtBu3)2] (10 mol %)
Cy2NMe (1 equiv)
PhMe, 100 °C, 16 h
1a
I
I
Ph
Ph
Ph
3p
3p'
5
57%
4.82 : 1
39%
X-ray crystal structure of 5


[Pd(PtBu3)2] (5 mol %)
PhMe, 100 °C
16 h
1a
I
I
4a
1.1 : 1
65%


Br
t-Bu
40 eq to 100 eq
Pd(P(t-Bu)3)2
1.0 eq
Neat, 70°C
Br
Pd(P(t-Bu)3)
t-Bu
60%


Pd-3
8
3a
Pd0L
I
II
III–V
via C and D
(see Scheme 2)
8'
E
VIb
VIa
Pathway
B
Pathway
A
FB
FA
VIIb
VIIa
C(sp2)
G
VIII


FB
FA
VIIb
VIIa
C(sp2)
Pd0L
G
VIII
CsOPiv
- CsI, HOPiv
H
IX
9


3a
Pd(QPhos)2
(10 mol%)
BuI (5 eq.)
Cs2CO3 (5 eq.)
100°C, 13.0 h
CH3CN
16
not observed
17
30-40%
18
40-50%
19
>5%
6a
>5%