Roles of Bases in Transition-Metal Catalyzed Organic Reactions

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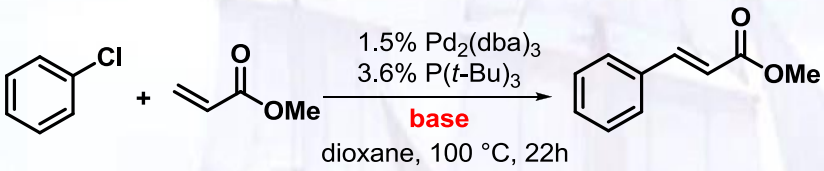
Outline

- **Background**
  1. Applications and influences of bases in transition-metal catalyzed organic reactions
  2. Factors influencing the performance of bases
- **Roles of Bases**
- **Summary**

Background

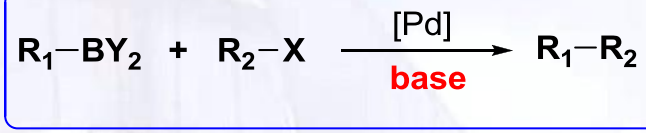
- Wide applications of bases in transition-metal catalyzed organic reactions

Heck Reaction

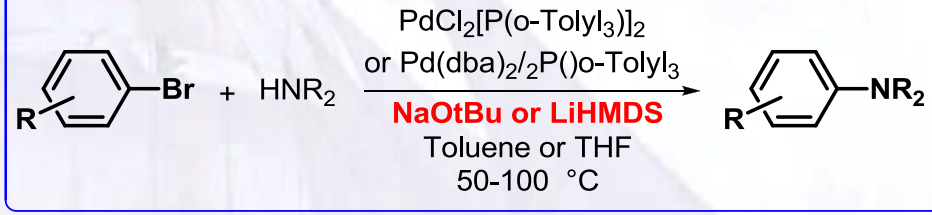


Entry	Base	%yield(GC)
1	None	5
2	K_2CO_3	9
3	NaOAc	21
4	NEt_3	37
5	K_3PO_4	50
6	Cs_2CO_3	56

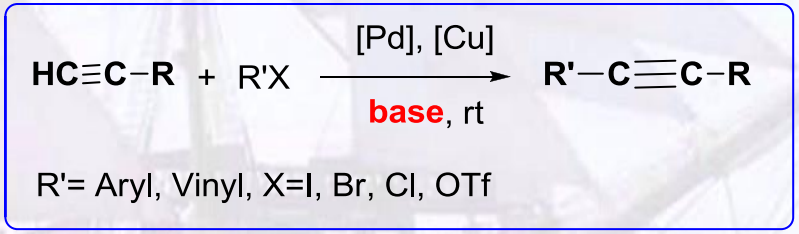
Suzuki Coupling Reaction



Buchwald–Hartwig amination



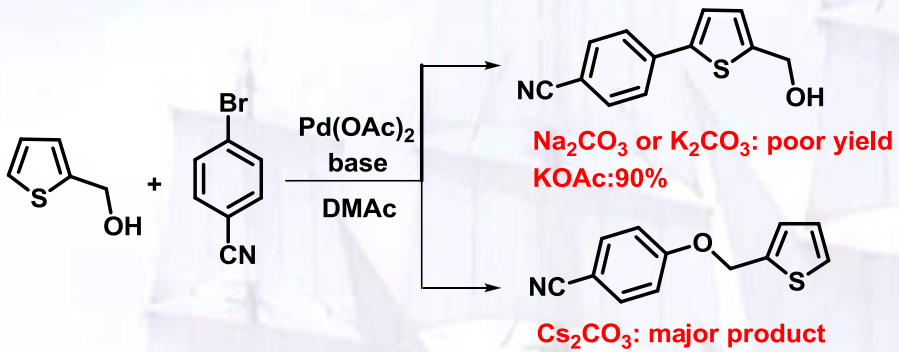
Sonogashira reaction



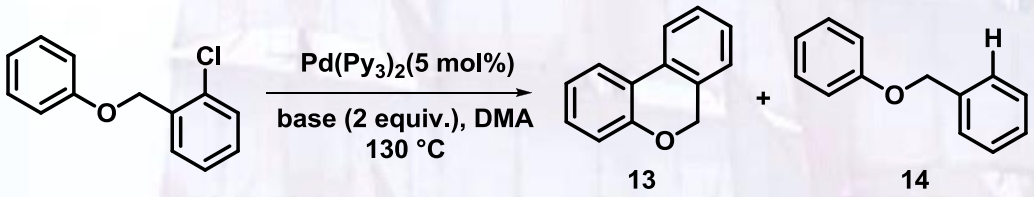
Littke, A. F.; Fu, G. C. *J. Org. Chem.* **1999**, *64*, 10. Louie, J.; Hartwig, J. F. *Tetrahedron Lett* **1995**, *36*, 3609. Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314.

Background

- Influence of bases on transition-metal catalyzed organic reactions



Different bases leads to different products.



Base	Conversion/ %	Ratio 13:14
Na_2CO_3	11	20:1
K_2CO_3	100	>99:1
Cs_2CO_3	25	15:1
KOAc	81	>99:1
NaOAc	41	28:1
Et_3N	3	2:1

Why different bases have different performance?

Roger, J.; Požgan, F.; Doucet, H. *Adv. Synth. Catal.* **2010**, *352*, 696.
Campeau, L.-C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128* , 581.

Background

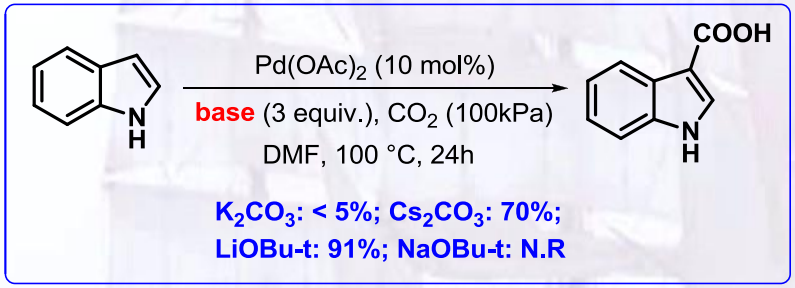
- Factors influencing the performance of bases

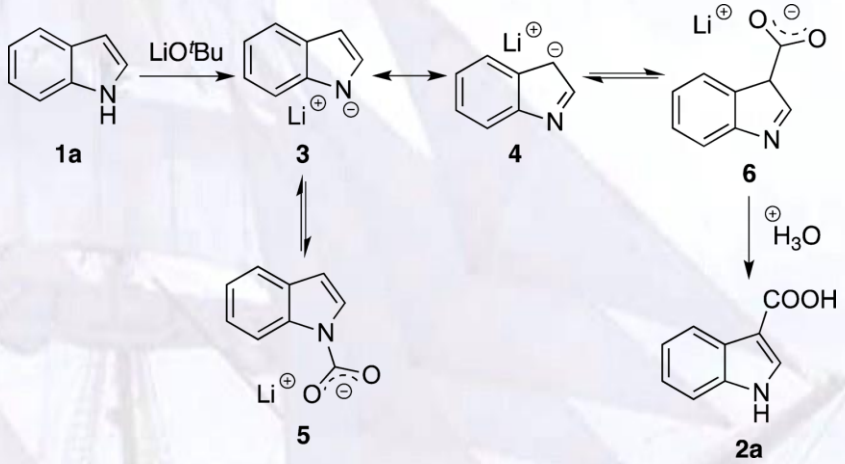
basicity, solvent, solubility, ionization ability, aggregation state

metal cations: size, Lewis acidity, the HSAB theory

counter anions: size, the coordination ability

- Effects of basicity





Yoo, W. J.; Capdevila, M. G.; Du, X.W.; Kobayashi, S. *Org. Lett.* **2012,** 14, 5326.

Background

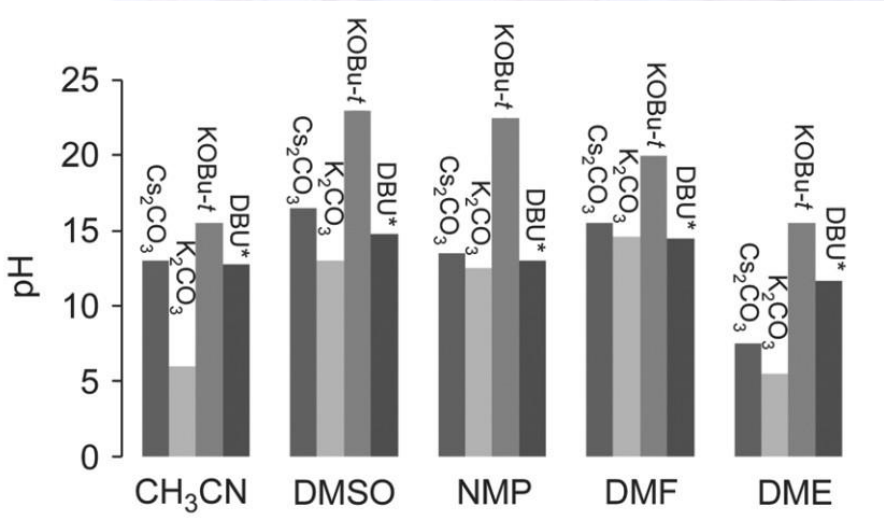
- Study of base is complex.

Table 1 Solubility of metal carbonate salts in dipolar aprotic solvents

Solvent	Li_2CO_3	Na_2CO_3	K_2CO_3	Cs_2CO_3
DMF	0.003	0.038	0.075	1.195
Me_2SO	0.014	0.143	0.470	3.625
DMAC	0.004	0.021	0.046	0.490
Sulfolane	0.021	0.031	0.160	3.950
NMP	0.014	0.208	0.237	7.224

[a] Solubilities in g/10 mL determined at ambient temperature by flame photometry.

Most of inorganic bases have poor solubility in organic solvents.



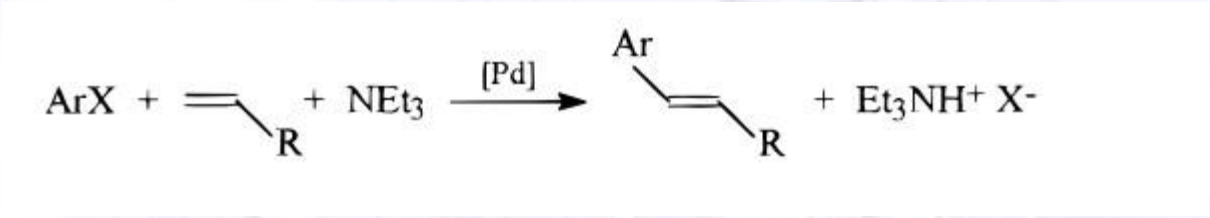
Basicity varies in different solvents.

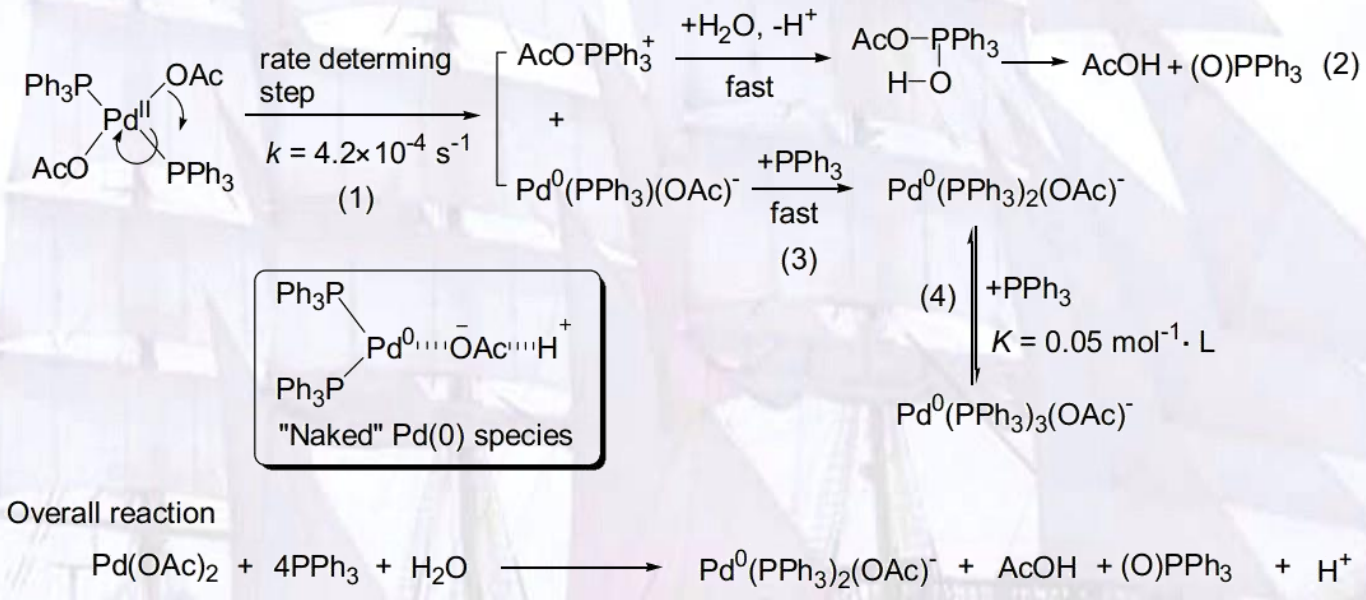
What's the role of base in transition-metal catalyzed reactions?
How do bases affect the reactions?

Olmstead, W. N.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3299;
Kuwano, R.; Utsunomiya, M.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 6479.

Roles of Bases

- Activate catalyst, neutralize acids

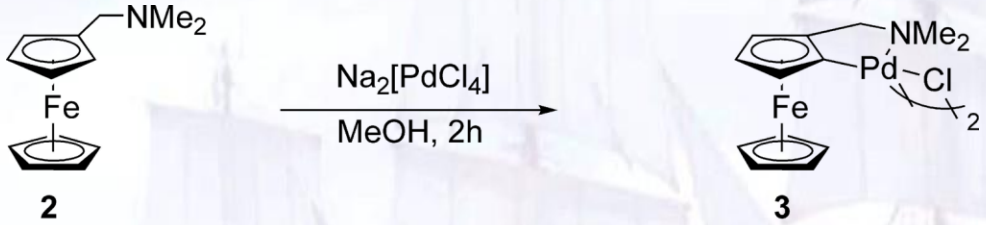




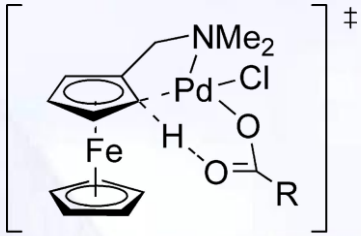
Amatore, C.; Jutand, A. *Acc. Chem. Res.* **2000**, *33*, 314.

Roles of Bases

- Deprotonation---base assisted deprotonation

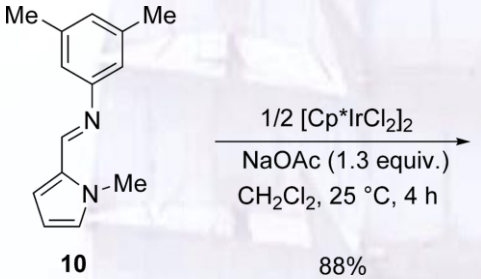


no additive: ---
NaOAc (1.0 equiv): 84%

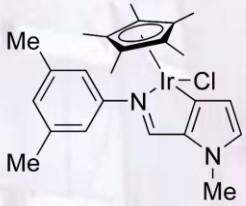


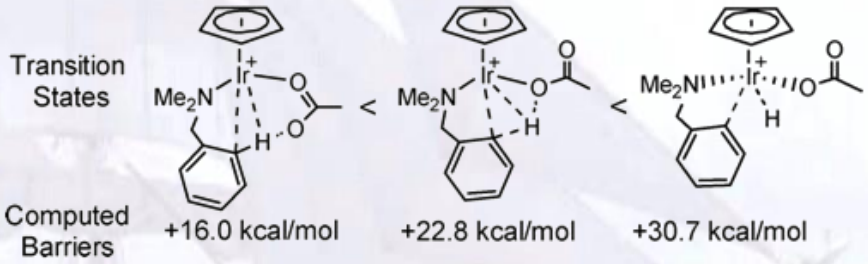
4

Transition state of a carboxylate-assisted cyclopalladation as proposed by Sokolov and Reutov (1979).



88%

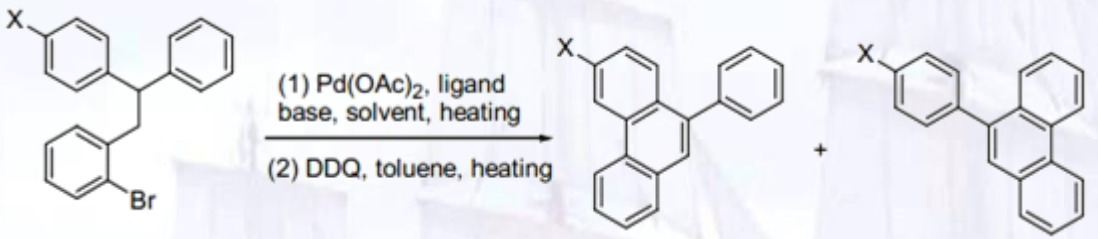




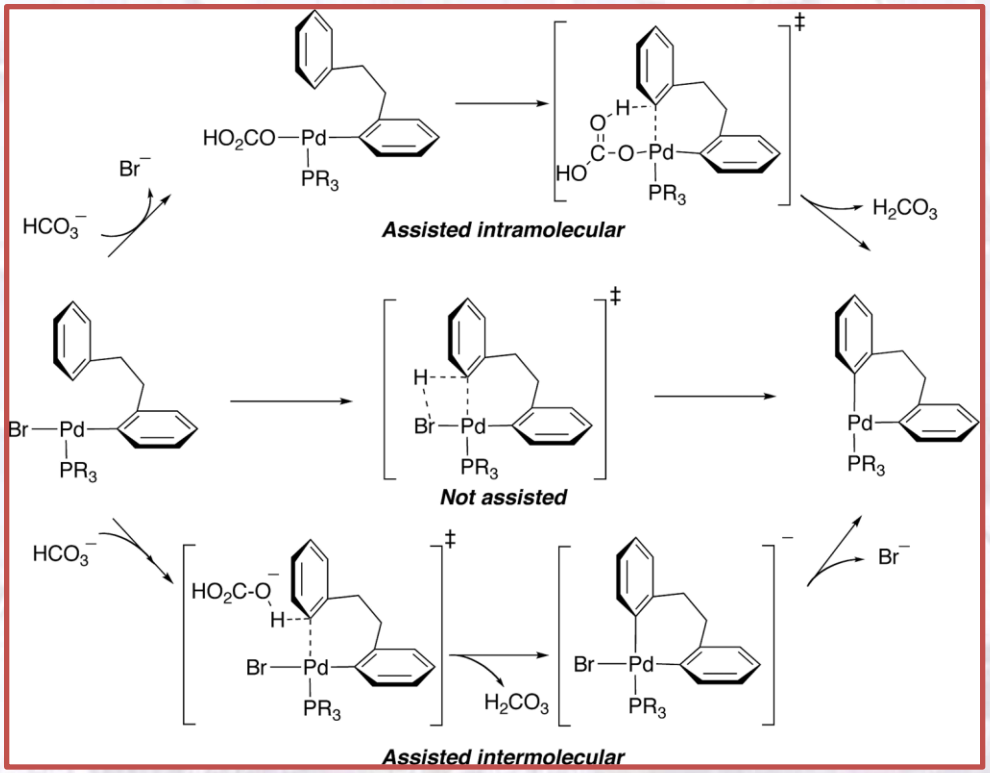
Gaunt, J. C.; Shaw, B. L. *J. Organomet. Chem.* **1975**, 102, 511.
Sokolov, V. I.; Troitskaya, L. L.; Reutov, O. A. *J. Organomet. Chem.* **1979**, *182*, 537.
Davies, D. L.; Donald, S. M. A.; Al-Duaij, O.; Macgregor, S. A.; Pölleth, M. *J. Am. Chem. Soc.* **2006**, *128*, 4210.

Roles of Bases

- Deprotonation---base assisted deprotonation



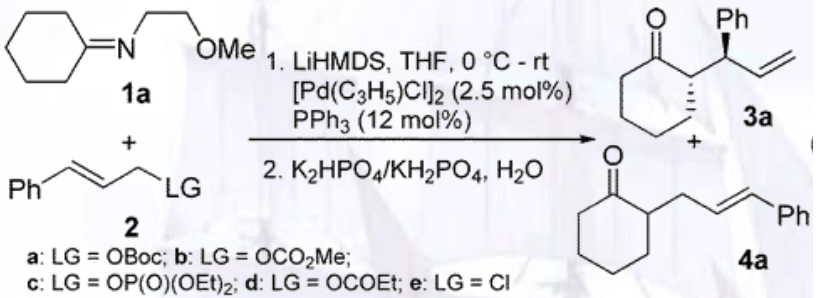
Base	Yield/%	**11/12** ratio
K_2CO_3	84	2:1
DBU	—	—
Et_3N	—	—
K_2CO_3/PivOH	>95	1.7:1



Garcia-Cuadrado, D.; de Mendoza, P.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2007**, *129* , 6880.

Roles of Bases

- Effects of cation



entry	base	2	% yield[b]	3a/4a[c]	3a anti/syn[c]
1	LiHMDS	2a	60	36/64	6/1
2	NaHMDS	2a	25	78/22	7/1
3	KHMDS	2a	12	68/32	7/1
4	*t*-BuONa	2a	26	98/2	9/1
5	*t*-BuOK	2a	51	99/1	7/1
6	*t*-BuOK	2b	60	98/2	7/1
7	*t*-BuOK	2c	64	98/2	24/1
8	*t*-BuOK	2d	17	95/5	13/1
9	*t*-BuOK	2e	70	99/1	32/1
10[d]	*t*-BuOK	2e	88	99/1	24/1
11[e]	*t*-BuOK	2a	48	95/5	4/1
12[e]	LiHMDS	2a	29	7/93	–
13[e]	*s*-BuLi	2a	61	12/88	–
14[e]	LDA	2a	77	8/92	–

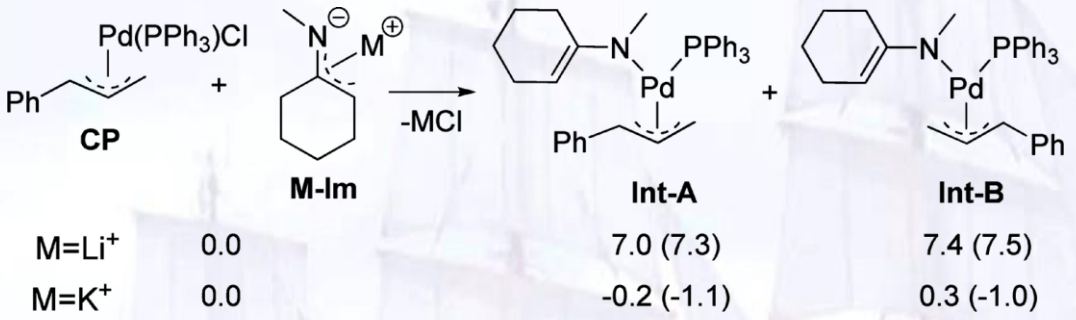
K salts get branched products

Li salts get linear products

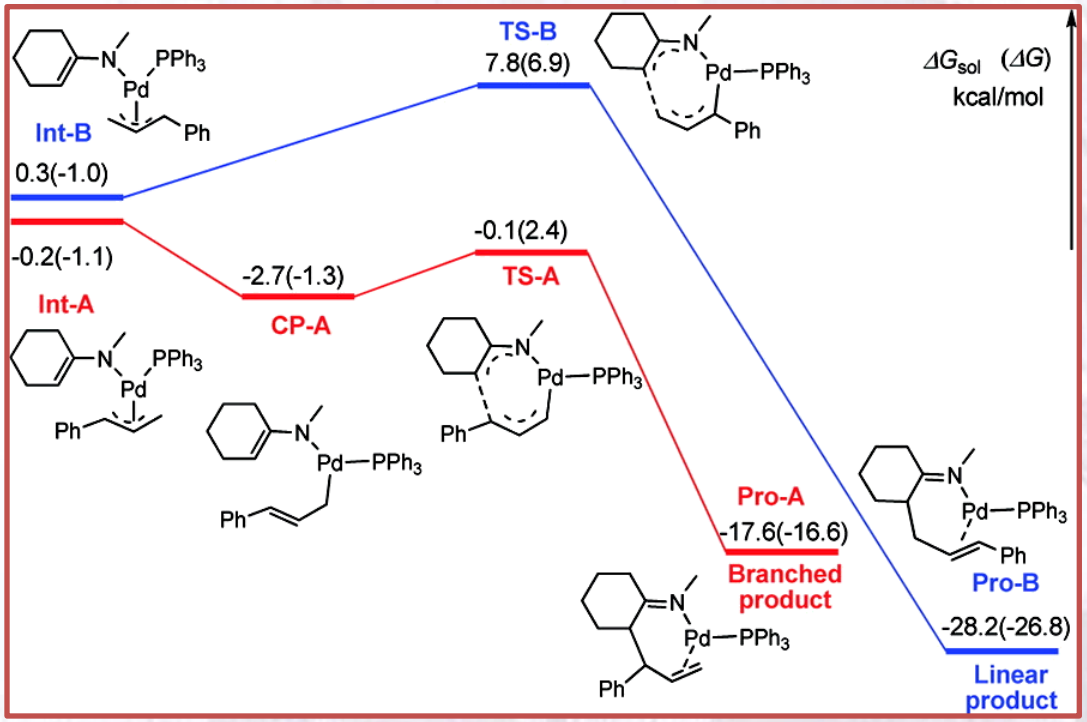
Why?

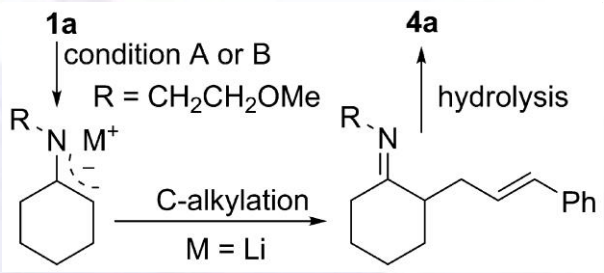
Chen, J.-P.; Peng, Q.; Lei, B.-L.; Hou, X.-L.; Wu, Y.-D. *J. Am. Chem. Soc.* **2011**, *133*, 14180.

Roles of Bases



The transmetalation reaction between CP and M-Im is favorable if the metal ion is the soft acid K^+.

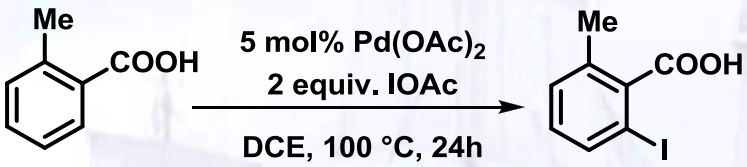


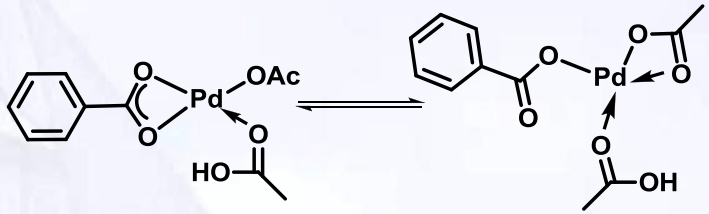


Chen, J.-P.; Peng, Q.; Lei, B.-L.; Hou, X.-L.; Wu, Y.-D. *J. Am. Chem. Soc.* **2011**, *133*, 14180.

Roles of Bases

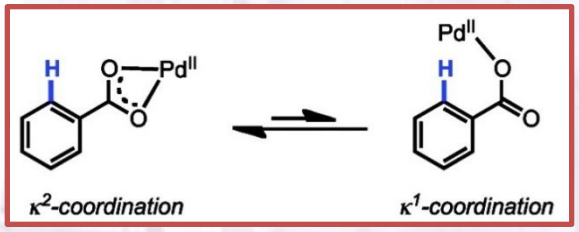
- Effects of cation---interact with substrate ?

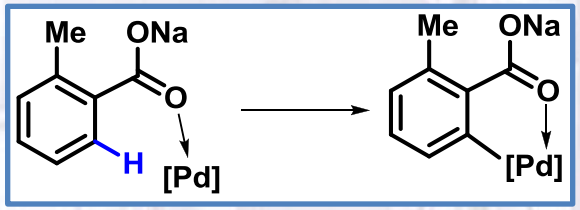


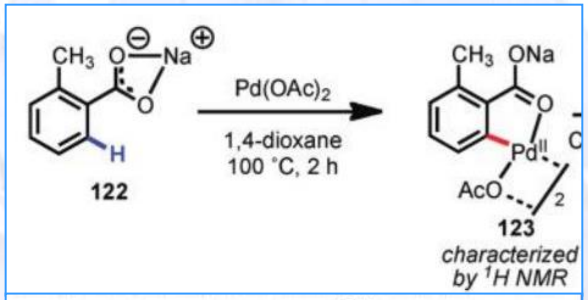


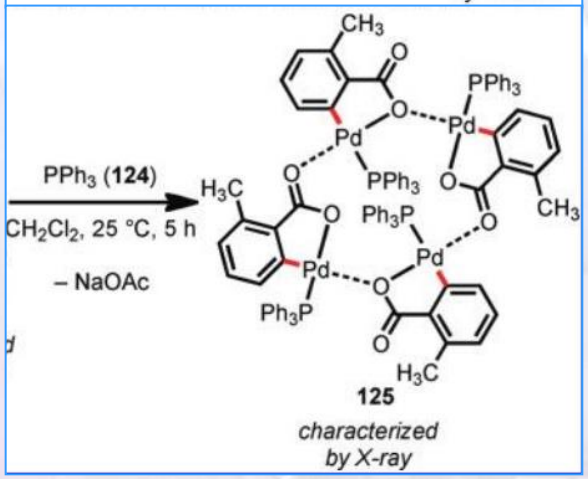
$\Delta G(\Delta E) = -0.03(-0.01)$ **kcal/mol**

Base	Yield [%]
none	5
NaOAc	85









Mei, T.-S.; Giri, R.; Maugel, N.; Yu, J.-Q. *Angew. Chem. Intern. Ed.* **2008**, *47*, 5215.
Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082.

Summary

- Bases influence catalytic reaction efficiency, yield, selectivity…
- Factors influencing the performance of bases

basicity, solvent, solubility, ionization ability, aggregation state

metal cations: size, Lewis acidity, the HSAB theory

counter anions: size, the coordination ability

- Study of base is complex and limited.
- Roles of base: (1) Activate catalyst, neutralize acids
  (2) base assisted deprotonation
  (3) interact with substrate

Thanks for your attention!