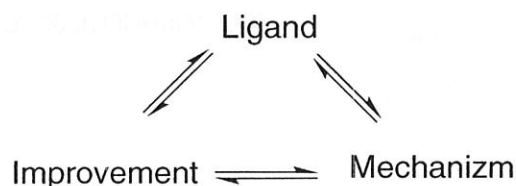
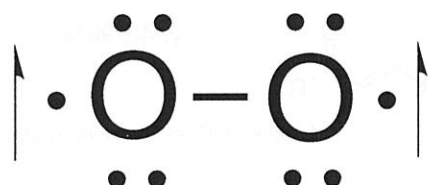


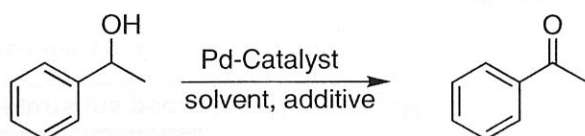
Ligand Caused Dynamic Change in Catalyst Profile

~Improvement in Pd Catalyzed Aerobic Alcohol Oxidation~

-Triplet oxygen



-Recent Advances

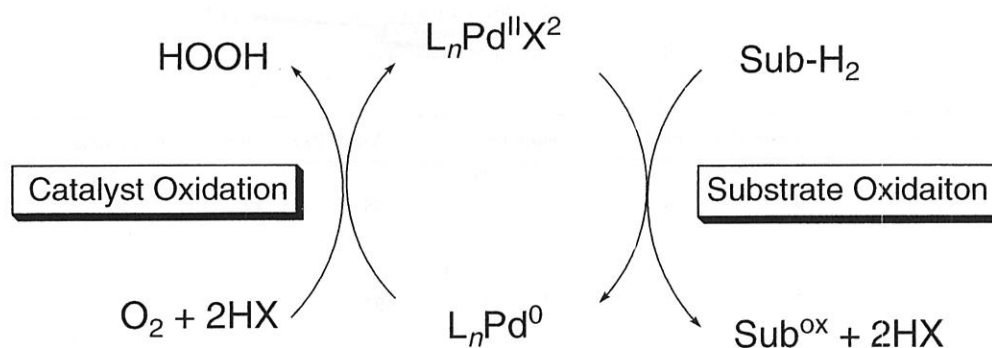


Pyridine: 5 mol % Pd, O₂, 80 °C

Triethylamine: 3 mol % Pd, O₂, rt

NHC: 1 mol % Pd, Air, rt

-Oxidase Type Reaction



CONTENTS

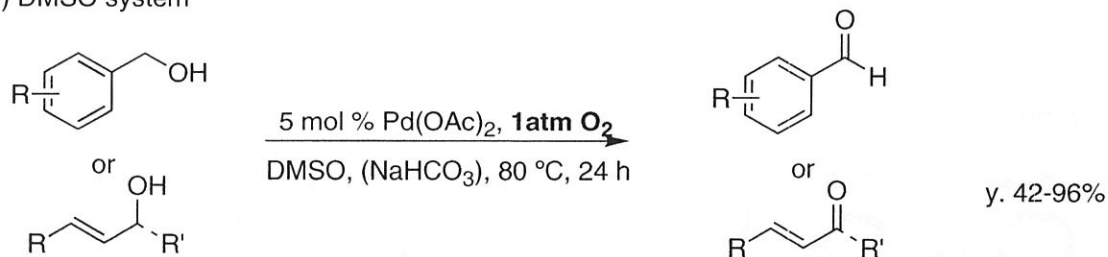
1. Introduction
2. Ligand Effect in Alcohol Oxidation Part
3. Ligand Effect in Catalyst Oxidation Part

1. Introduction

1-1 Property of Pd-Catalyzed Aerobic Alcohol Oxidations

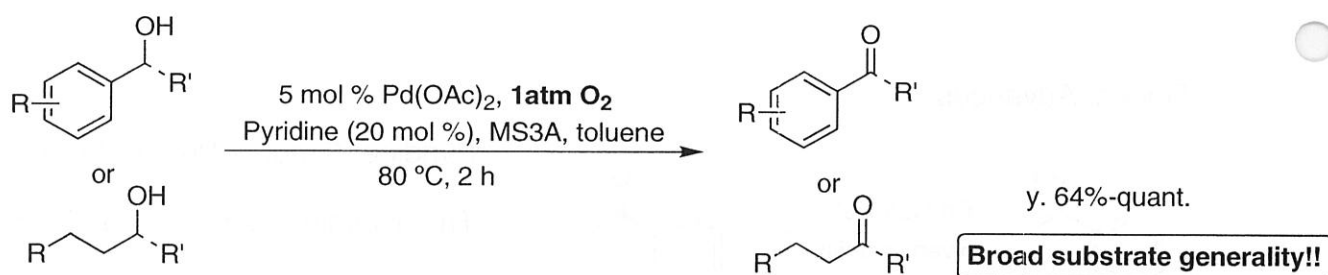
-Benchmarks in catalyst development

i) DMSO system



Larock, R. C. et al. *J. Org. Chem.* **1998**, *63*, 3185

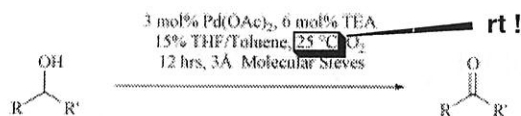
ii) Pyridine system



Uemura, S. et al. *J. Org. Chem.* **1999**, *64*, 6750

-Recently advanced milder conditions

iii) Triethylamine system

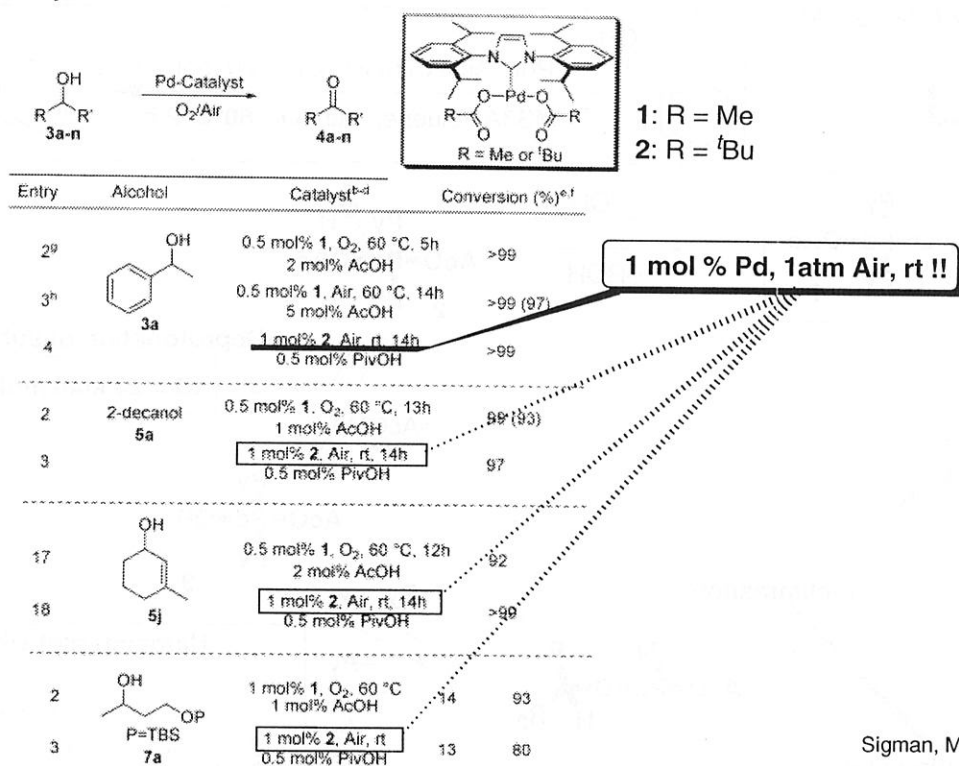


Entry	Substrate	Yield ^b (%)	Entry	Substrate	Yield ^b (%)	Entry	Substrate	Yield ^b (%)
1		93	6		95	12		98
2		96	7		97	13		81
3		95	8		93	14		90 ^c
4		85	9		0	15		93
5		50 ^c	10	2-Decanol	97	16		30 ^f
			11	1-Dodecanol	88 ^d	17		39 ^g

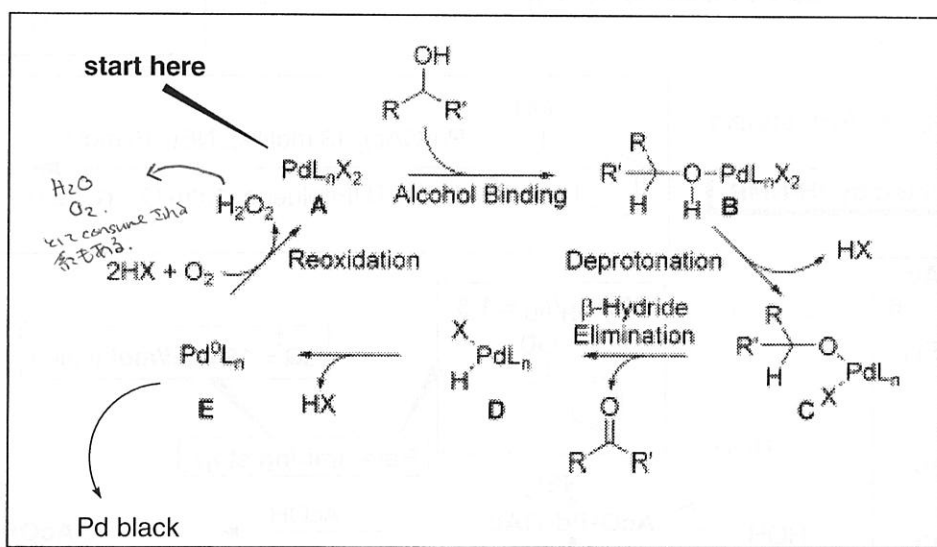
^a All products have been previously reported in the literature. ^b Average of two experiments. ^c 36 h. ^d 0.1 M alcohol. ^e Product is the corresponding lactone. ^f 5 mol % Pd(OAc)₂ and 50 mol % TEA. ^g 5 mol % Pd(OAc)₂ and 300 mol % TEA.

Reaction proceeds at rt, 1 atm O₂ !!

Sigman, M.S. et al. *Chem. Commun.* **2002**, 3034



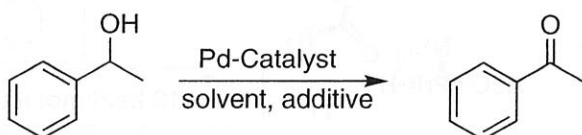
1-2 Proposed General Mechanism



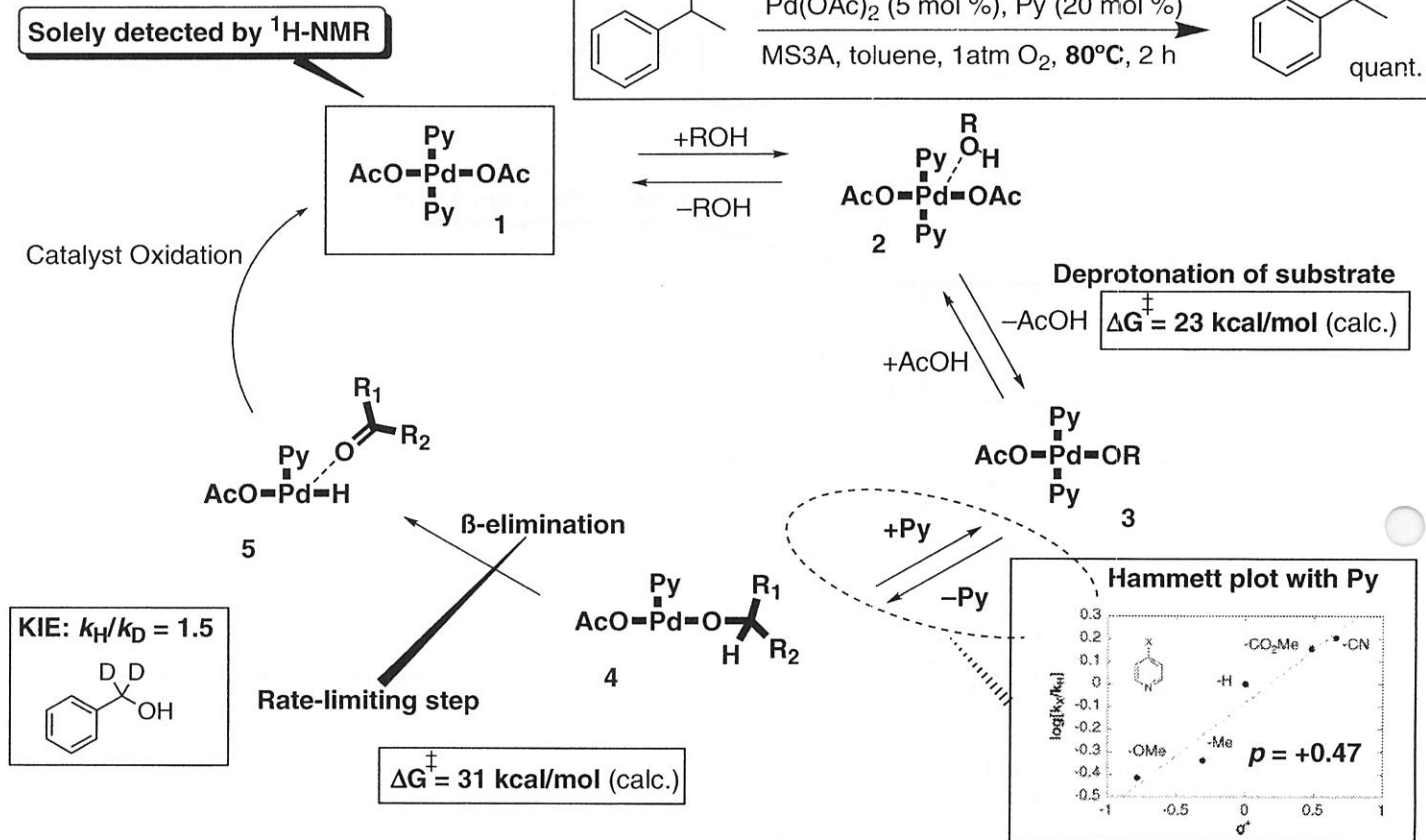
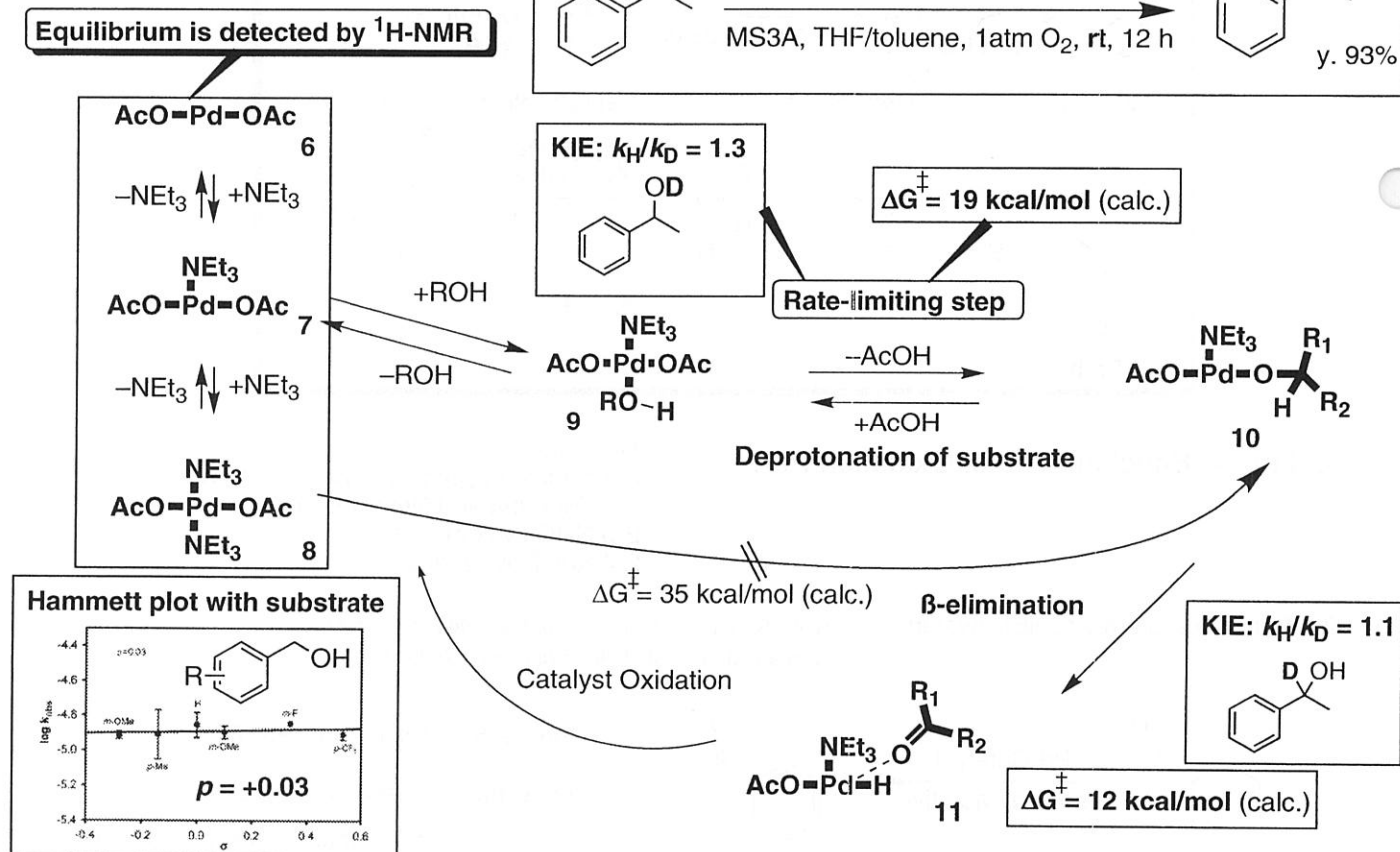
2. Ligand Effect in Alcohol Oxidation Part

contents

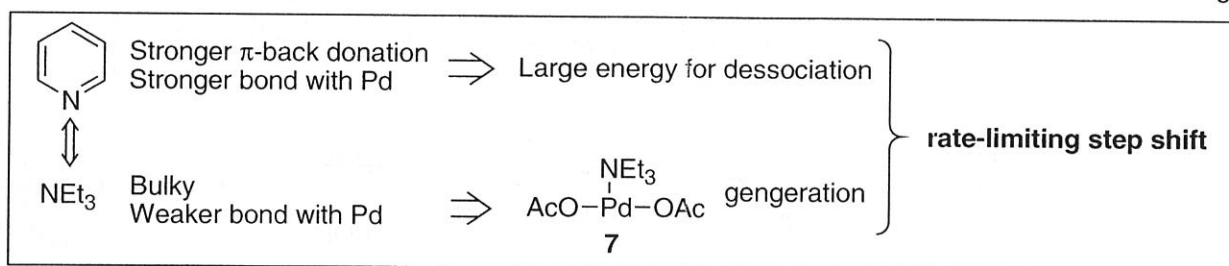
- 2-1 Pyridine system v.s. NEt₃ system
- 2-2 Dilemma and New Design
- 2-3 NHC system
- 2-4 Key Role of Acid

2-1 Pyridine system v.s. NEt₃ systemStahl, S. S. et al. *J. Am. Chem. Soc.* **2004**, *126*, 11268Sigman, M. S. et al. *J. Am. Chem. Soc.* **2005**, *127*, 8499Pyridine: 5 mol % Pd, O₂, 80 °CTriethylamine: 3 mol % Pd, O₂, rtWhat makes the difference??

-Proposed mechanism for pyridine system

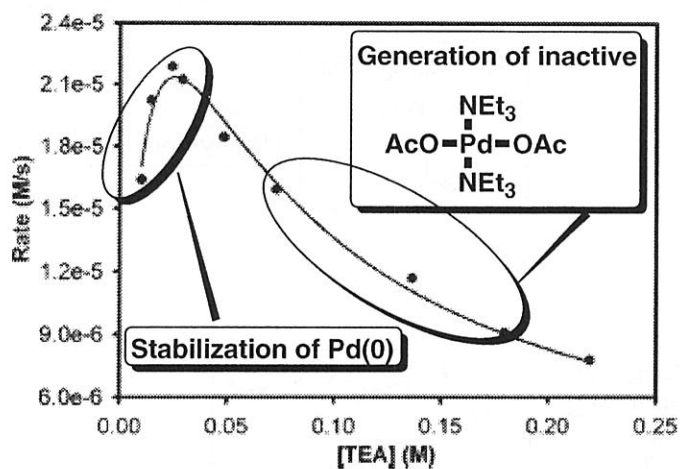
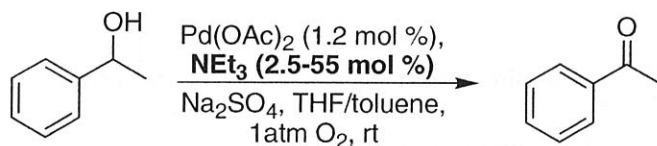
-Proposed mechanism for NEt₃ system

+Conclusion

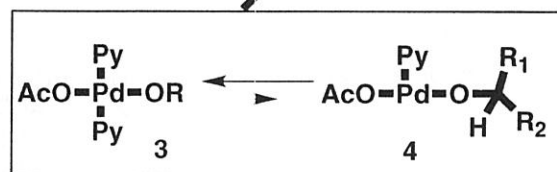
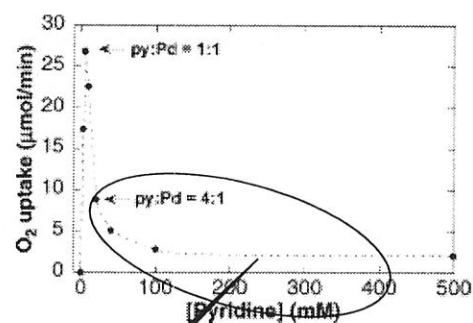
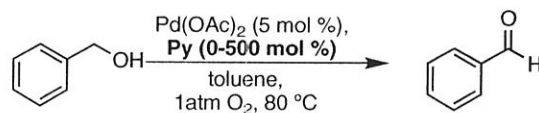


2-2 Dilemma and New Design

-Reaction rate dependency on ligand loading



-Same dilemma was seen in Py system



-New Catalyst Design

Sigman, M. S. et al. *Angew. Chem. Int. Ed.* **2003**, 42, 3810
 Carreira, E. M. et al. *Angew. Chem. Int. Ed.* **2008**, 47, 4482

-Monodentate ligand

-Strong bonding to stabilize Pd(0)

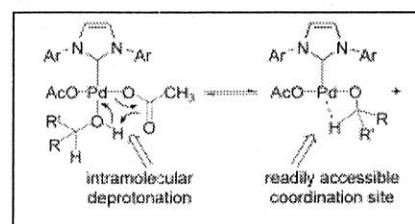
 \Rightarrow NHC ligands

L	donation	back-donation	L	bonding energy
C ₂ H ₄	0.36	0.13	C ₂ H ₄	-27.6
C ₂ H ₂	0.16	0.12	C ₂ H ₂	-26.6
CO	0.27	0.22	CO	-34.2
PMe ₃	0.53	0.16	PMe ₃	-43.8
imidazol-2-ylidene	0.36	0.12	imidazol-2-ylidene	-52.7
NMe ₃	0.20	0.01	NMe ₃	-29.9

back-donation

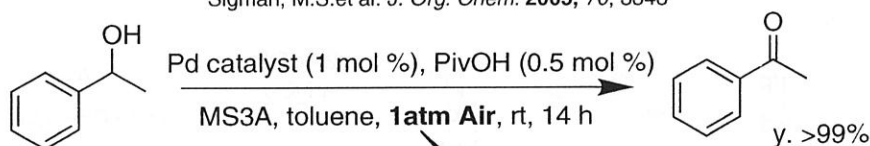
strong bond

-Design

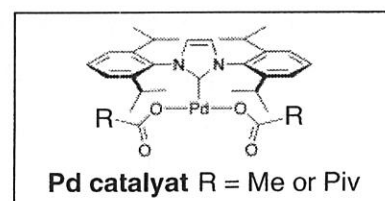


2-3 NHC system

Sigman, M.S. et al. *J. Am. Chem. Soc.* **2004**, 126, 9724
 Sigman, M.S. et al. *J. Org. Chem.* **2005**, 70, 3343

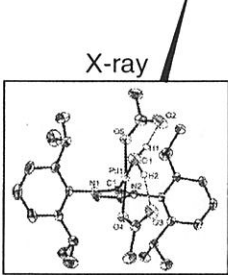
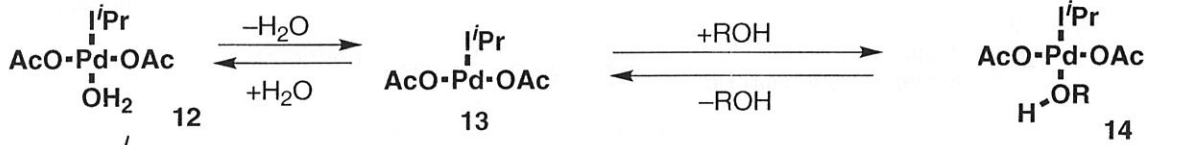
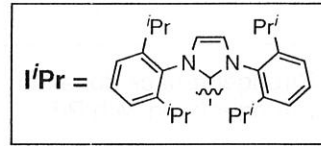


What makes this possible ??



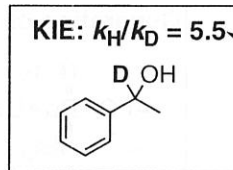
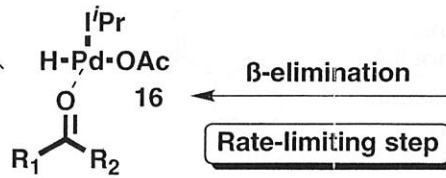
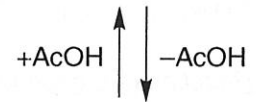
-Proposed mechanism of alcohol oxidation part

Sigman, M. S. et al. *J. Am. Chem. Soc.* 2004, 126, 9724

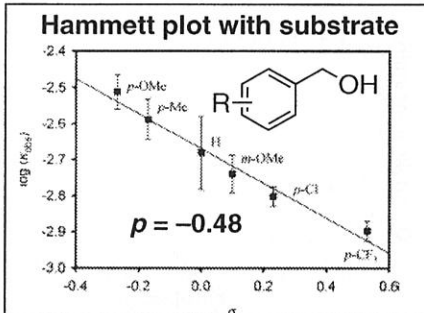


Catalyst Oxidation

$\Delta G^\ddagger = 21 \text{ kcal/mol (exp.)}$

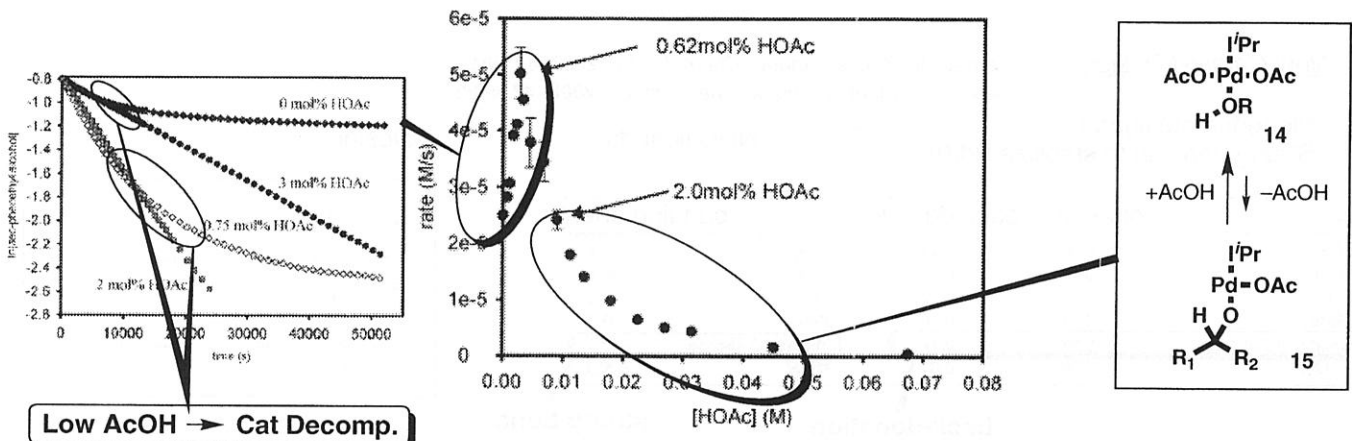
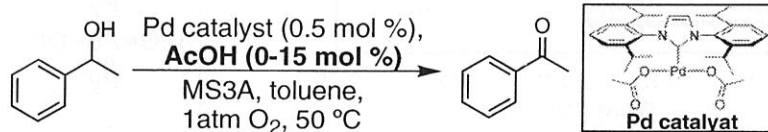


Py system: 1.3



2-4 Key Role of Acid

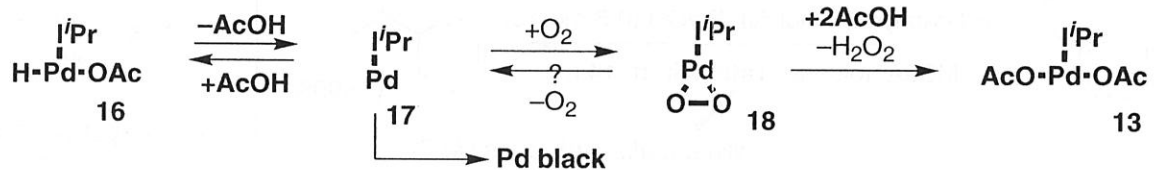
-Another dilemma



-Why acid prevent the catalyst from decomposition ?

-Sigman's Proposal

-Proposed catalyst oxidation step



-Change of Rate-Limiting Step

Kinetics study without AcOH

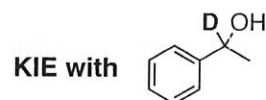
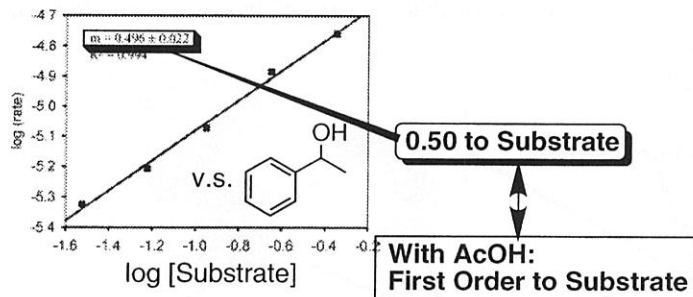


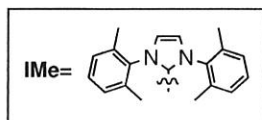
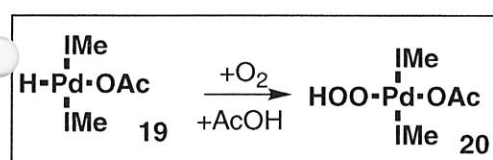
Table 3. KIE Values at Various HOAc Concentrations

[HOAc] (mM)	KIE value	[HOAc] (mM)	KIE value	[HOAc] (mM)	KIE value
0	1.7	2.79	3.1	6.75	5.2
2.12	2.7	4.50	3.4	9.00	5.5

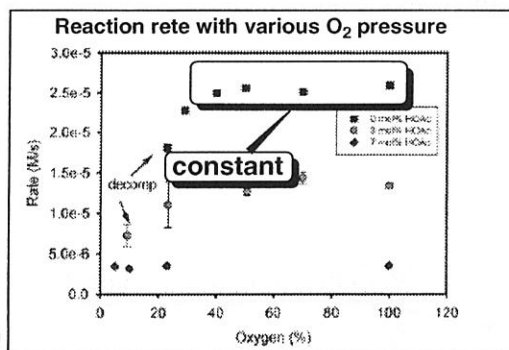
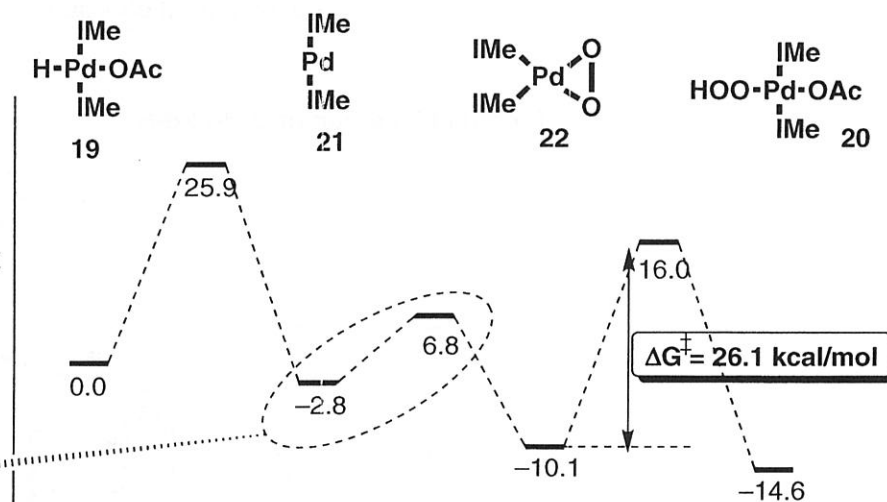
Different between 0 mol % AcOH and 2 mol % AcOH

-Energy Profile for Catalyst Oxidation

Stahl, S. S. et al. *J. Am. Chem. Soc.* 2007, 129, 4410



ΔG_{298K}



-Conclusion

-Relatively stable Pd(0) state $\begin{array}{c} \text{iPr} \\ | \\ \text{Pd} \end{array}$

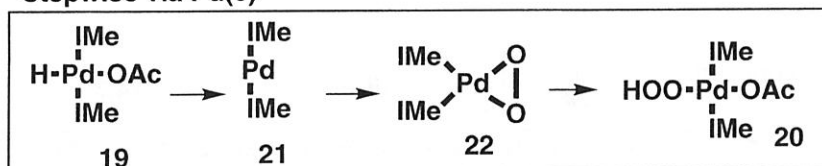
-Acid to promote protonation of $\begin{array}{c} \text{iPr} \\ | \\ \text{Pd} \\ | \\ \text{O-O} \end{array} \Rightarrow$ Rate-Limiting step shift.

3. Ligand Effect in Catalyst Oxidation Part

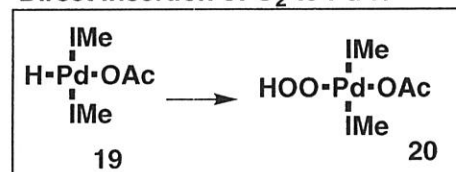
3-1 Major Reaction Mechanisms and Similarity of Them

-Two Commonly Proposed Mechanisms

Stepwise via Pd(0)



Direct insertion of O₂ to Pd-H

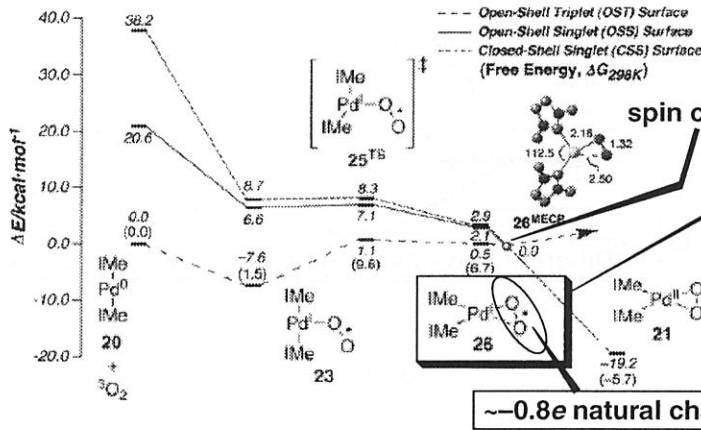


-Why Triplet O₂ can React with Pd Catalyst ?

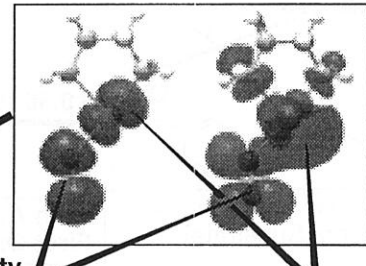
Stahl, S. S. et al. *J. Am. Chem. Soc.* **2004**, *124*, 16302

Stahl, S. S. et al. *J. Am. Chem. Soc.* **2007**, *129*, 4410

Reaction profile for stepwise via Pd(0)



Electronic structure of two unpaired electrons

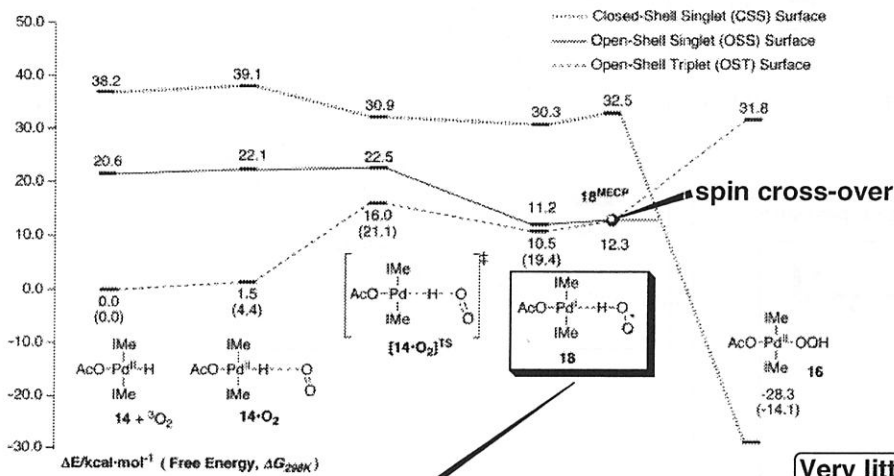


Spin density

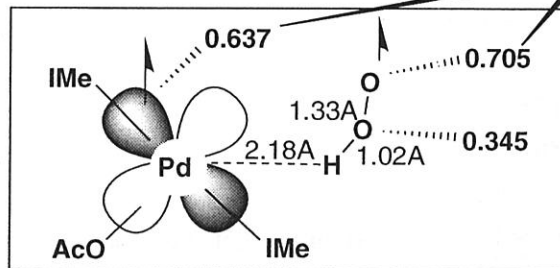
On Oxygen: 0.91 On Pd: 0.75

- Spin delocalization
- Separation of two electrons

Reaction profile for direct insertion of O₂ to Pd-H



Spin density on 18

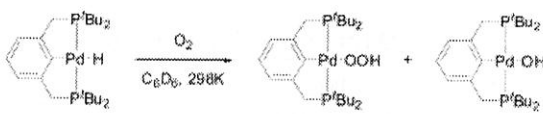


Very little communication

3-2 Relationship between Ligand and Mechanism

-Electron-Rich Catalyst Prefers Direct Insertion of O₂ to Pd-H

Goldberg, K. I. et al. *J. Am. Chem. Soc.* **2006**, *128*, 2508



Direct insertion mechanism is proposed.

mimic

Complex	via Pd(0):	ΔG [‡] (kcal/mol)
IMe AcO-Pd-H IMe		9.6 (25.9 for red. elim.)
	direct:	21.1
IMe CH ₃ -Pd-H IMe	direct:	14.7

Stahl, S. S. et al. *J. Am. Chem. Soc.* **2007**, *129*, 4410