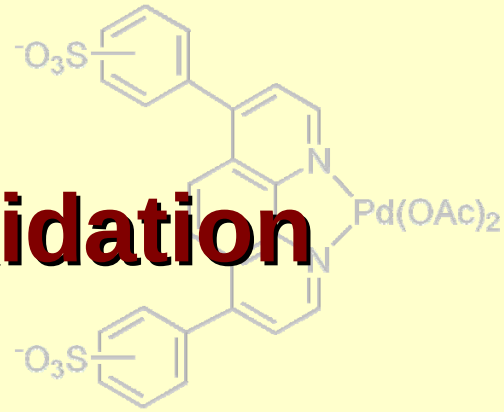
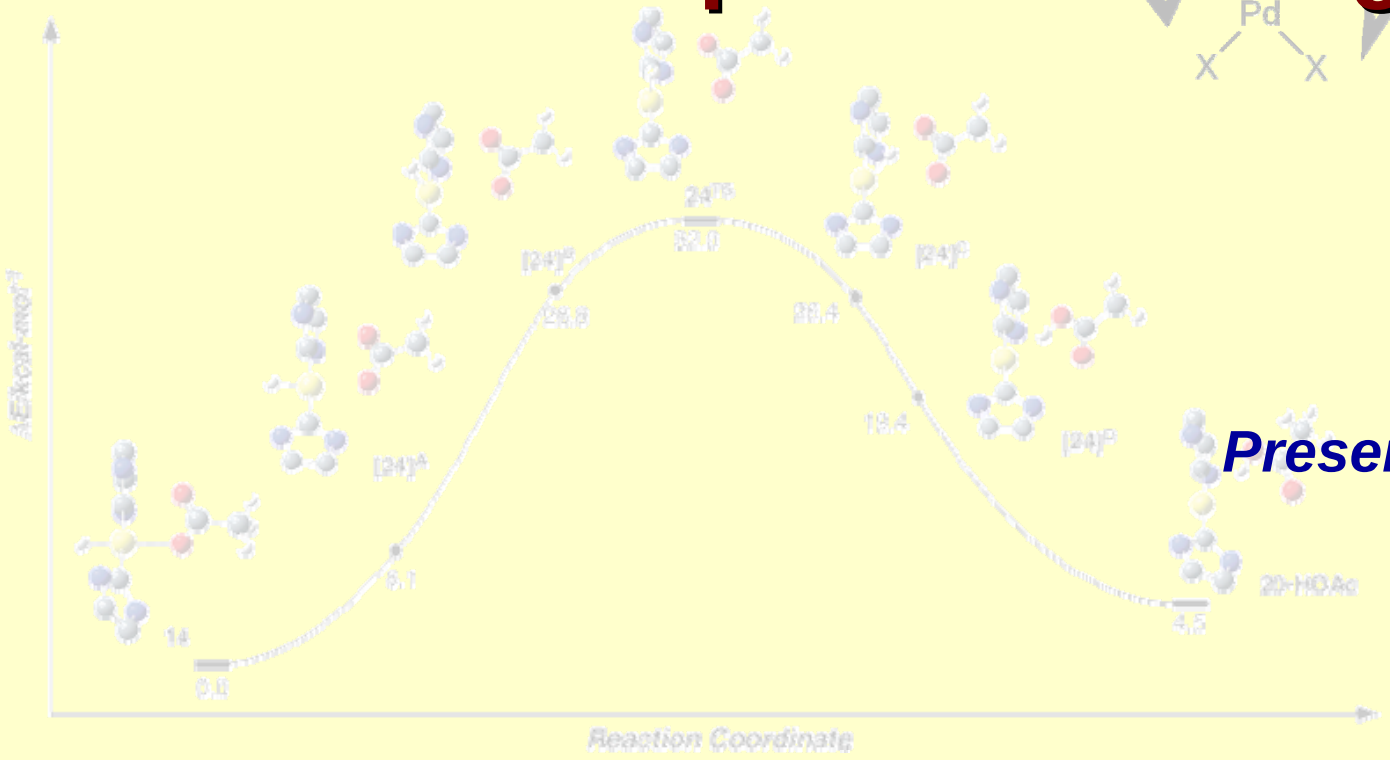
Palladium-Catalyzed Oxidation of Alcohols by Molecular Oxygen: Recent Computational Insights

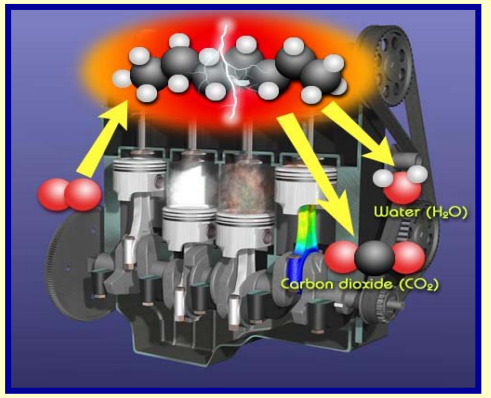




Presented by Dice

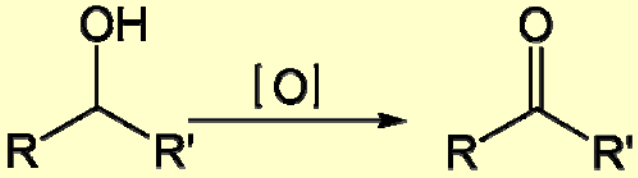
OUTLINE

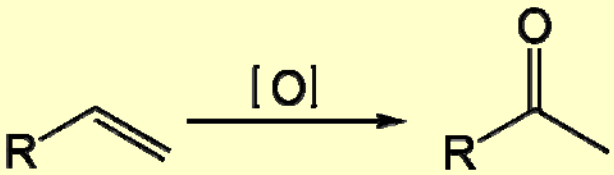
- Background
- Palladium Catalyst Systems for aerobic oxidation
  - 1. $Pd(OAc)_2$ / DMSO Catalyst System
  - 2. $Pd(OAc)_2$ / Pyridine Catalyst System
  - 3. $Pd(OAc)_2$ / NEt_3(TEA) Catalyst System
  - 4. $Pd(OAc)_2$ / Bathophenanthroline Catalyst System
  - 5. PdX_2 / (-)-Sparteine Catalyst System
  - 6. Palladacycle 6 Catalyst System
  - 7. $Pd(OAc)_2$ / NHC Catalyst System
- Summary

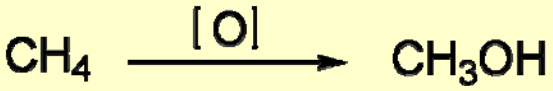


O_2 is essential for us!

Chemical Transformations involving Oxidation

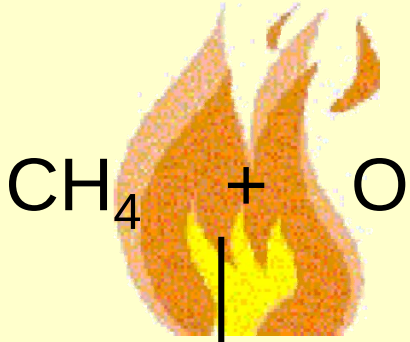






If [O] = O_2,
availability,
inexpensive,
environmentally friendly

However…



$$CH_4 + O_2 \longrightarrow CO_2 + H_2O$$

$$CH_4 \xrightarrow{\text{catalyst}} CH_3OH$$

Dioxygen activation

The catalytic activation of dioxygen continues to attract interest both due to its biological importance and synthetic potential.

(a) Metal-Dioxygen Complexes, *Chem. Rev.* **1994**, *94*, Issue 3.
(b) Kopp, D. A.; Lippard, S. J. *Curr. Opin. Chem. Biol*. **2002**, *6*, 568.
(c) Que, L., Jr.; Tolman, W. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 1114.
(d) The Activation of Dioxygen and Homogeneous Catalytic Oxidation, Barton, D. H. R.; Martell, A. E.; Sawyer, D. T. Eds, Plenum: New York, **1993**.
(e) Advances in Catalytic Activation of Dioxygen by Metal Complexes, László I. Simándi eds, Kluwer: **2003**
(f) Dioxygen Chemistry: *Account of Chemical Research*, **2007** *ASAP*

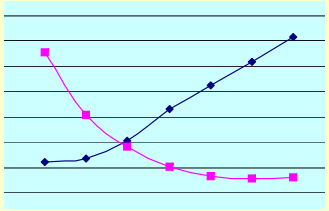
Spin state conversion hindered the theoretical studies

O_2

$^3\Sigma_g^-$

Binding mode of dioxygen with the metal complexes

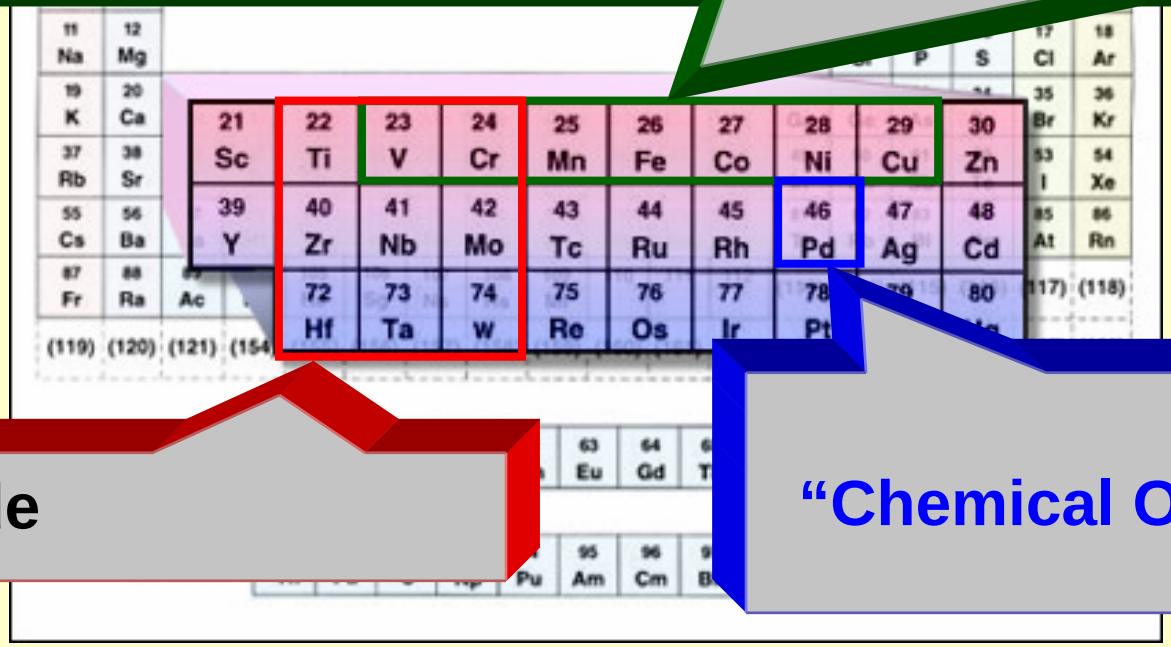
(a) Bytheway, I.; Hall, M. B. *Chem. Rev.* **1994**, *94*, 639.
(b) Cramer, C. J.; Smith, B. A. Tolman, W. B. *J. Am. Chem. Soc.* **1996**, *118*, 11283.
(d) Franzen, S. *Proc. Natl. Acad. Sci. USA.* **2002**, *99*, 16754
(d) Cramer, C.J.; Tolman, W.B.; Theopold, K. H.; Rheingold, A. *Proc. Natl. Acad. Sci. USA.* **2002**, *99*, 16754
(f) Jensen, K. P.; Ryde, U. *J. Biol. Chem.* **2004**, *279*, 14561



Dioxygen activation by the metal complexes

(a) Yoshizawa, K.; Ohta, T.; Yamabe, T. Hoffmann, R. *J. Am. Chem. Soc.* **1997**, *119*, 12311.
(b) Brunold, T. C.; Solomon, E. I. *J. Am. Chem. Soc.* **1999**, *121*, 8277.
(d) Wirstam, M.; Lippard, S. J.; Friesner, R. A. *J. Am. Chem. Soc.* **2003**, *125*, 3980.
(e) Gherman, B. F.; Baik, M-H.; Lippard, S. J.; Friesner, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 2978.
(f) Thepold, K. H. *Top. Organomet. Chem.* **2007**, *22*, 17

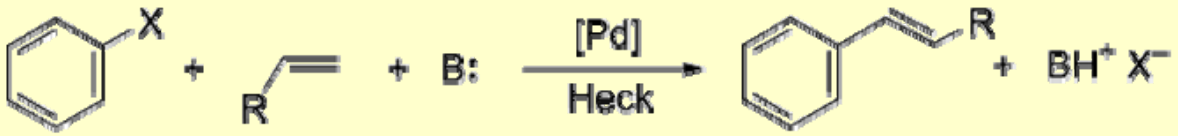
P450; Methane Monoxygenase… biomimetic complexes
Complicated structures, spin states…

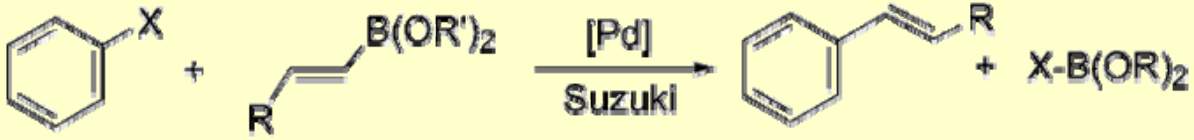


Metal Oxide

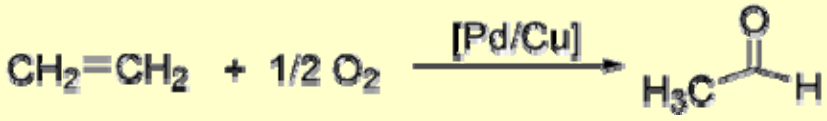
“Chemical Oxidase”

Palladium-Catalyzed Reactions

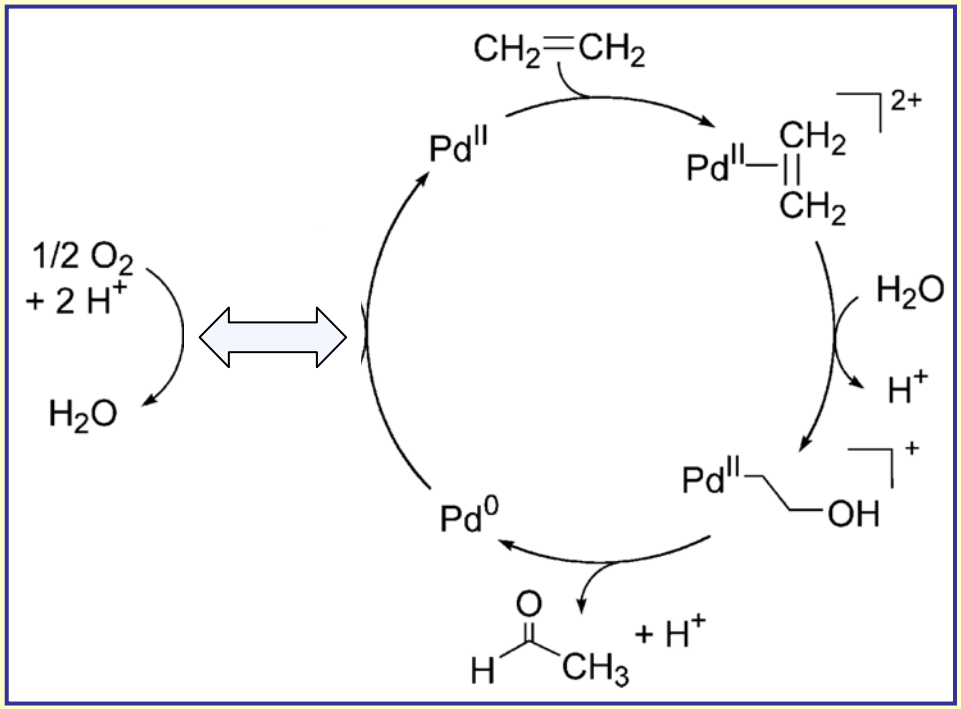




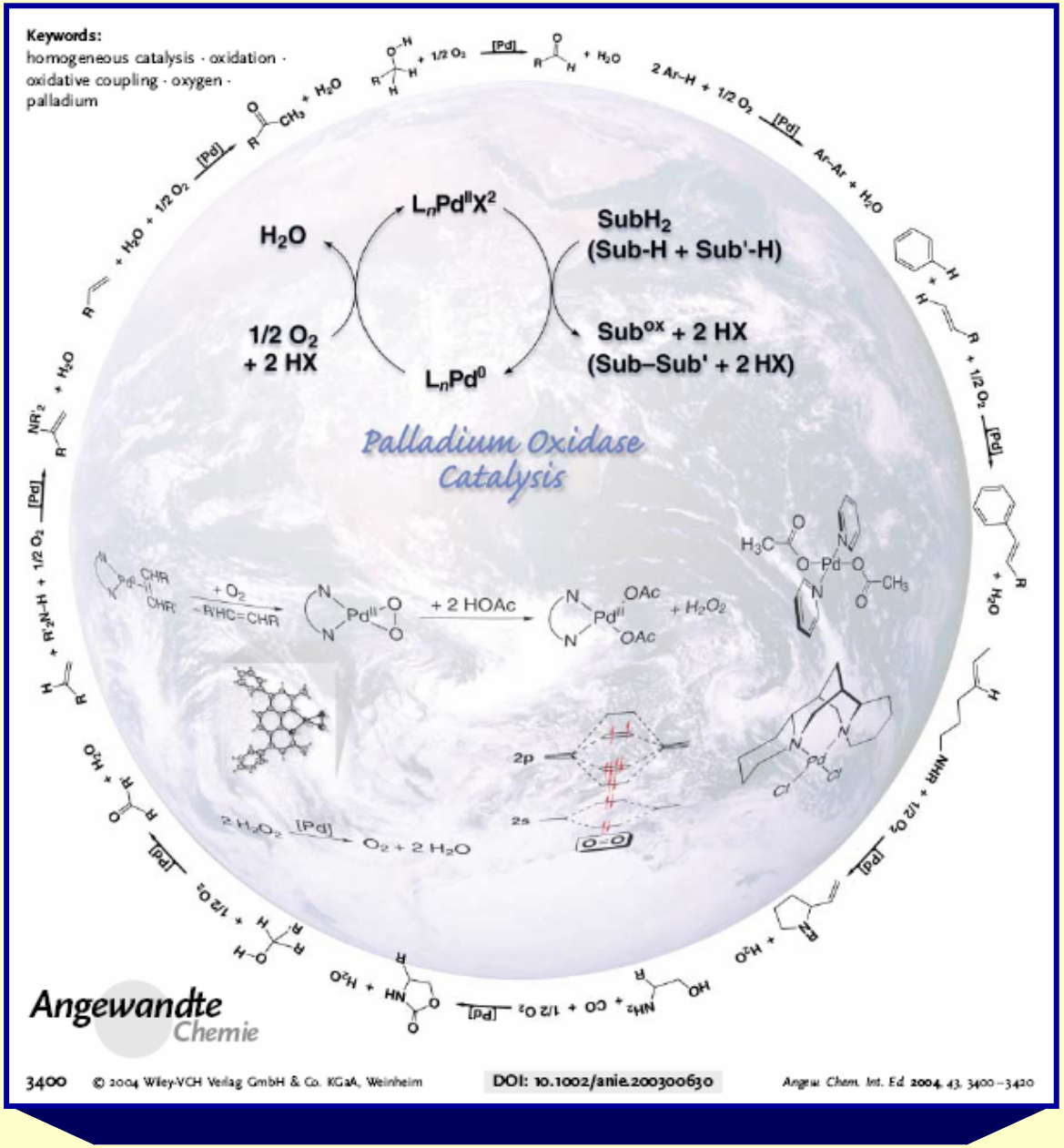
Cross-Coupling



Wacker Process



Takacs, J. M.; Jiang, X.T.
Curr. Org. Chem. **2003**, *7*, 369

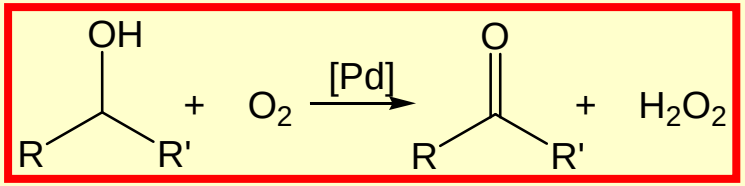


Sheldon, R. A.; Arends, IWCE.; ten Brink, G.-J.; Dijksman, A. *Acc. Chem. Res,* **2002**, 774

Stahl, S. S. *Angew. Chem. Int. Ed.* **2004**, 3400

Stahl, S. S. *Science,* **2005**, *309*, 1824

Sigman, M. S.; Jensen, D. R. *Acc. Chem. Res,* **2006**, 221



Representative Palladium Catalyst Systems

$Pd(OAc)_2$ (5%) + Na_2CO_3 (10%) / DMSO

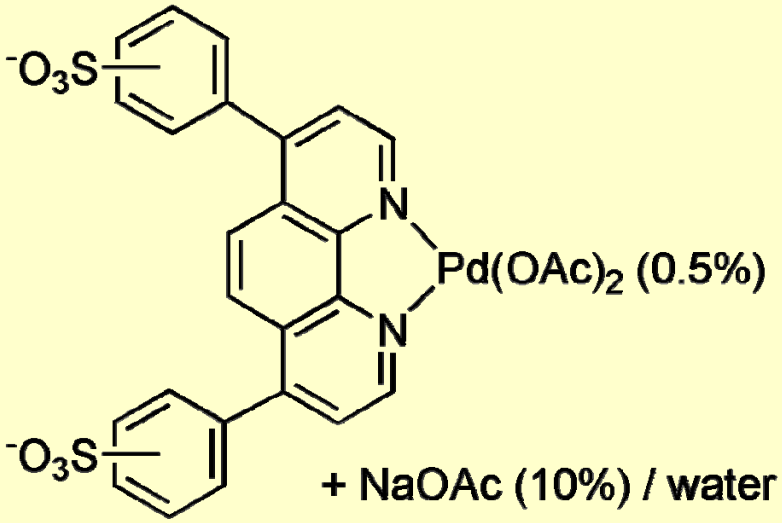
1

$Pd(OAc)_2$ (5%) + pyridine (20%) /toluene

2

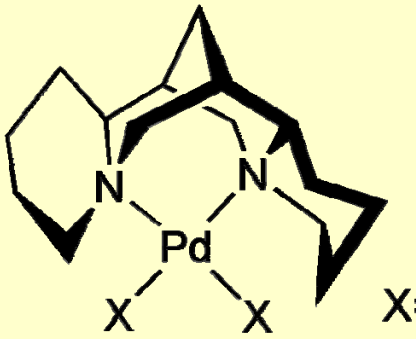
$Pd(OAc)_2$ (3%) + NEt_3 (6%) /toluene

3



+ NaOAc (10%) / water

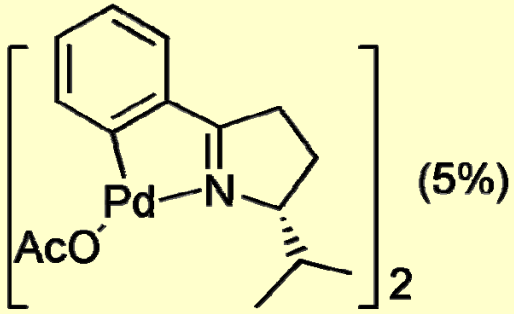
4



X=Cl, OAc, O_2CCF_3

+ (-)-sparteine (20%) /toluene

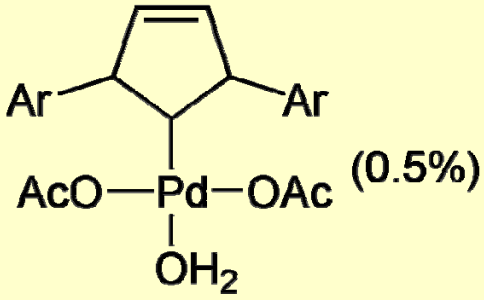
5



(5%)

+ pyridine (20%) /toluene

6

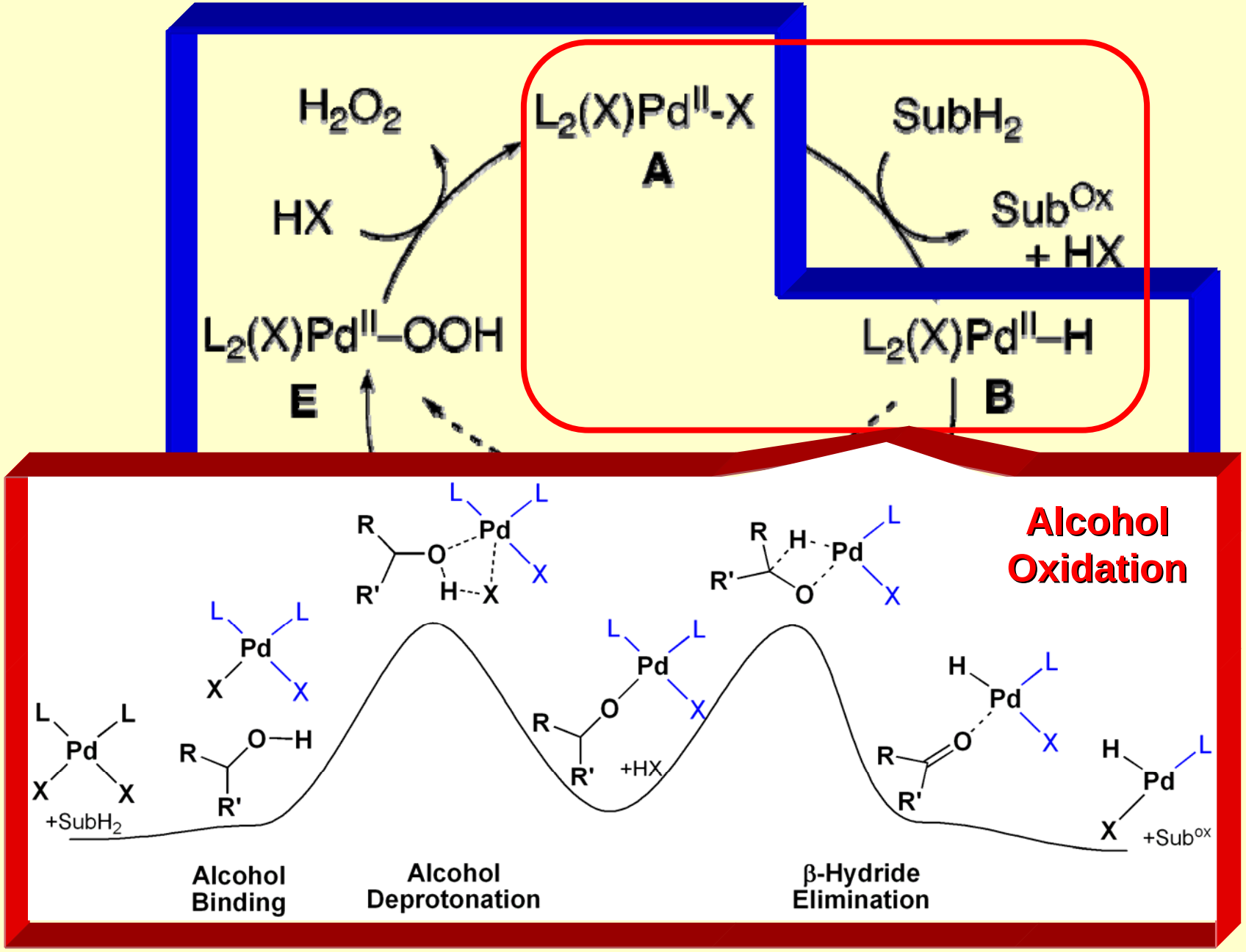


(0.5%)

+ HOAc (5%) / toluene

7

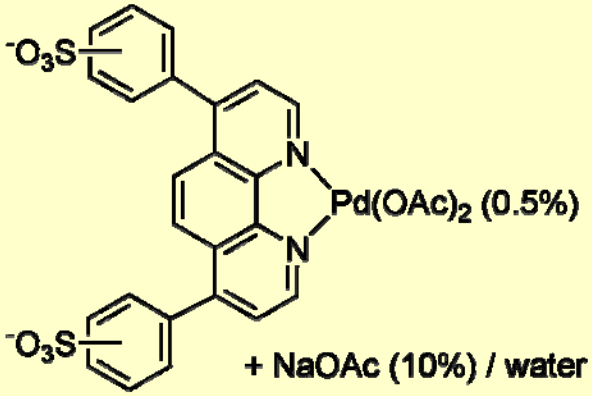
Mechanism of Pd Catalyzed Oxidation by O_2



Overview of Palladium Catalyst Systems

$Pd(OAc)_2$ (5%) + Na_2CO_3 (10%) / DMSO

1

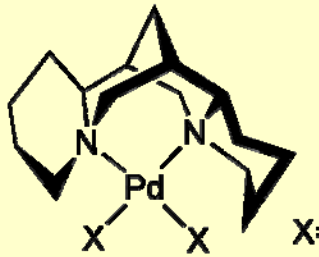


+ NaOAc (10%) / water

4

$Pd(OAc)_2$ (5%) + pyridine (20%) /toluene

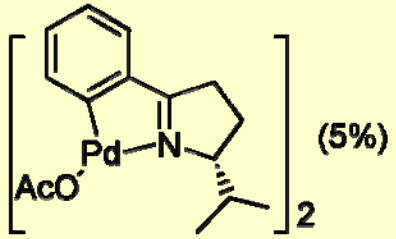
2



X=Cl, OAc, O_2CCF_3

+ (-)-sparteine (20%) /toluene

5

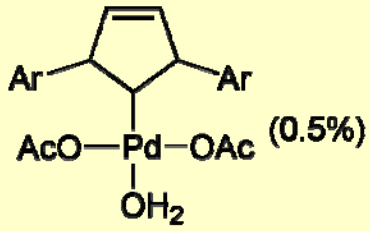


+ pyridine (20%) /toluene

6

$Pd(OAc)_2$ (3%) + NEt_3 (6%) /toluene

3



+ HOAc (5%) / toluene

7

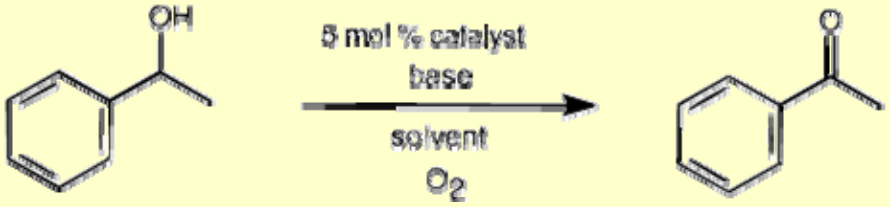
Entry	Alcohol scope	O_2 p	Loading	Temp	Time	Ref
1	A [a] and B [b]	1atm	5mol%	80	72h	Larock, *JOC*, **1998**, 3185
2	1º, 2º, A and B	air	5mol%	80	2h	Uemura, *TL*, **1998**, 6011
3	1º, 2º and B	1atm	3mol%	r.t.	12h	Sigman, *CC*, **2002**, 3034
4	1º, 2º, A and B	30bar	0.5mol%	100	100TO/h	Sheldon, *Science*, **2000**, 287
5	2º, A and B	1atm	5mol%	80	24h	Stoltz, *JACS*, **2001**, 7725
6	1º, 2º and B	air	5mol%	80	24h	Moberg, *Adv. Synth. Catal.* **2001**, 260
7	1º, 2º, A and B	air	0.5mol%	60	14h	Sigman, *Angew*, **2003**, 3810

a. A for allylic; b. B for benzylic

1. $Pd(OAc)_2$ / DMSO Catalyst System

$Pd(OAc)_2$ (5%) + Na_2CO_3 (10%) / DMSO

First Breakthrough!



1. The reactions are relative slow (< 1 TOh^{-1})
2. Other Pd sources: $PdCl_2$, $Pd(OCCF_3)_2$ were significantly less effective
3. Other solvents: CH_3CN, DMSO/H_2O mixture led to lower yield.

Peterson, K. P.; Larock, R. C. *J. Org. Chem.* **1998**, *63*, 3185

Mechanistic Study

- Kinetic studies indicate that oxidation of Pd(0) is the turnover-limiting step.
- DMSO may be important to hinder the decomposition of Pd(0) into bulk metal

Steinhoff, B. A.; Fix, S. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2002**, *124*, 766

2. $Pd(OAc)_2$ / Pyridine Catalyst System

$Pd(OAc)_2$ (5%) + pyridine (20%) / toluene

Most Versatile and simple!

1. Primary, secondary, benzylic, and allylic alcohols are oxidized
2. Other Pd sources: $PdCl_2$, $Pd(OCCF_3)_2$, $Pd(PPh_3)_4$ were ineffective
3. Other pyridine ligand were less effective, 2,2'-bipyridine inhibited the reaction

Nishimura, T.; Onoue, T.; Ohe, K.; Uemura, S. *Terahedron Lett.* **1998**, *39*, 6011

3. $Pd(OAc)_2$ / NEt_3(TEA) Catalyst System

$Pd(OAc)_2$ (3%) + TEA (6%) / DCE or toluene

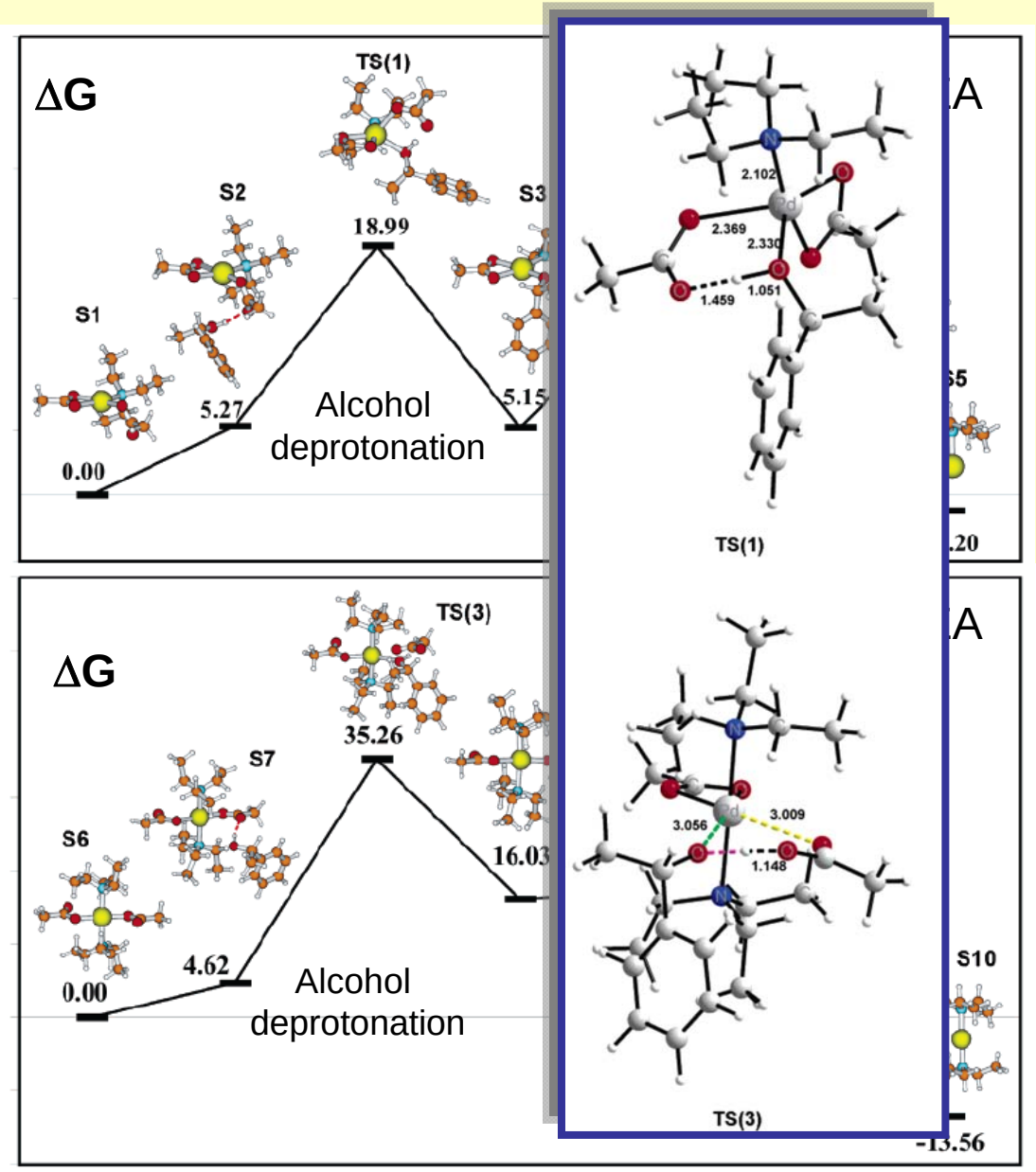
Room Temperature, Mildest!

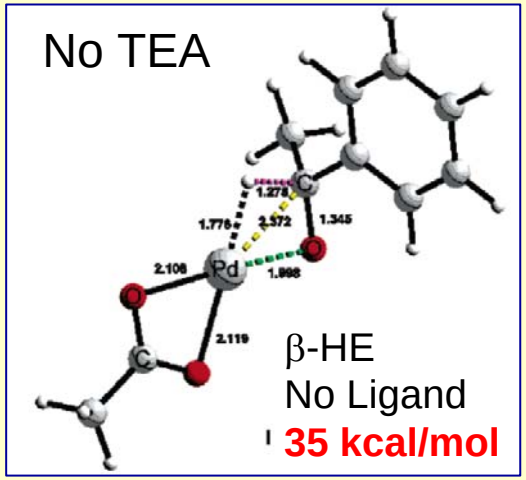
1. Primary, secondary and benzylic alcohols are oxidized
2. Effective at room temperature

Schultz, M. J. Park, C. C.; Sigman, M. S. *Chem. Commun.* **2002**, *39*, 3034

Mechanistic and Computational Studies of System 2 and 3

3
TEA





Path with ONE TEA is most favorable.

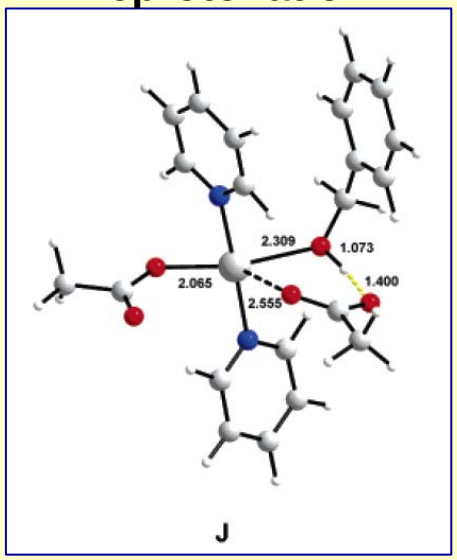
Rate-determining is alcohol deprotonation.

Schultz, M. J.; Adler, R. S.; Ziekiewicz, W.; Privalov, T.; Sigman, M. S. *JACS*, **2005**, *127*, 8499

Mechanistic and Computational Studies of System 2 and 3

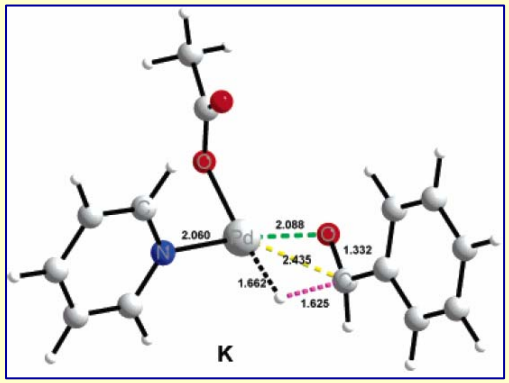
System 2
Pyridine

Alcohol Deprotonation



23 kcal/mol

β-Hydride Elimination



31 kcal/mol

Barrier is higher than TEA

Rate-determining is β-HE

bulky TEA is easier departed

$$\underset{\mathbf{1}}{Pd(OAc)_2} \rightleftharpoons \underset{\mathbf{2}}{Pd(OAc)_2(TEA)} \rightleftharpoons \underset{\mathbf{3}}{Pd(OAc)_2(TEA)_2}$$

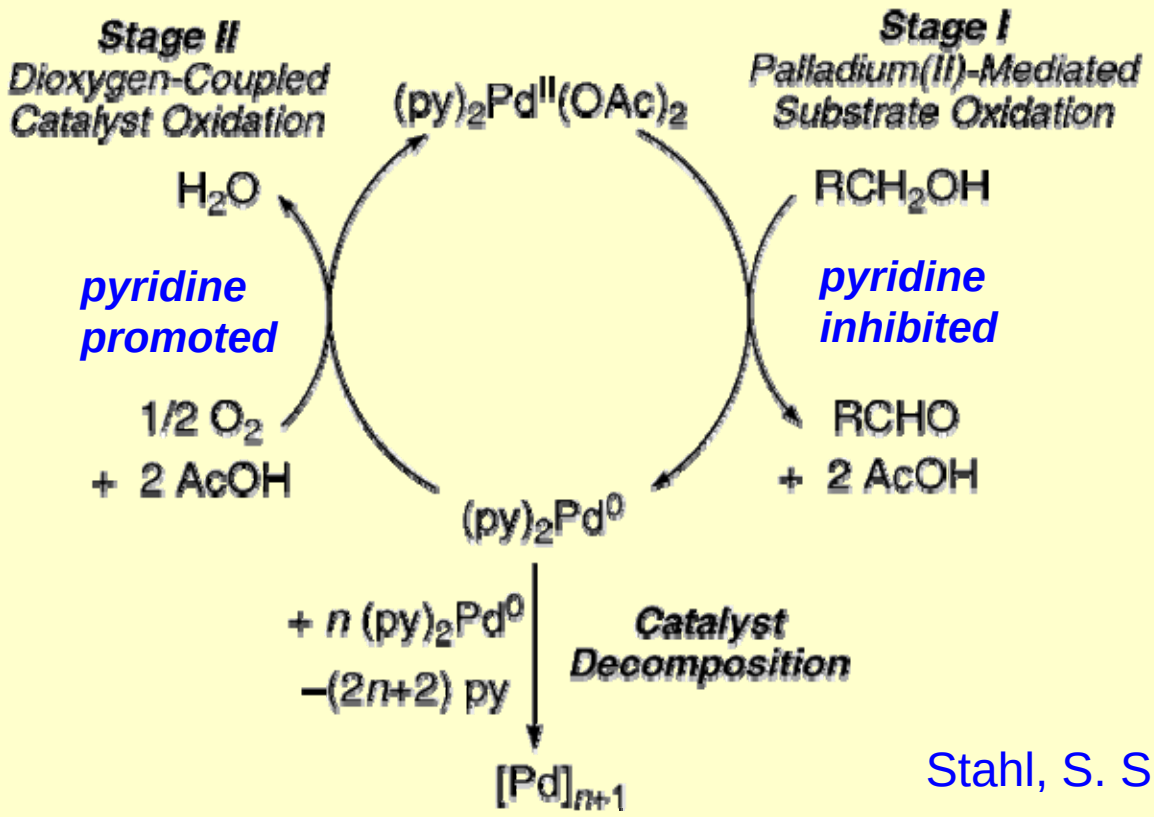
$$\underset{\mathbf{1}}{Pd(OAc)_2} \rightleftharpoons \underset{\mathbf{4}}{Pd(OAc)_2(pyridine)_2}$$

pyridine coordination hinders β-HE

2,2'-bipyridine inhibited the reaction

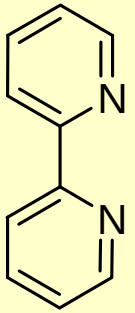
Stahl, S. S.; et.al *JACS*, **2004**, *126*, 11268

Schultz, M. J.; Adler, R. S.; Ziekiewicz, W.; Privalov, T.; Sigman, M. S. *JACS*, **2005**, *127*, 8499

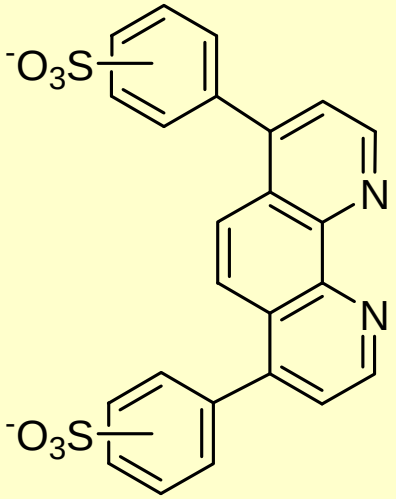


Stahl, S. S. *JACS*, **2004**, *126*, 11268

2,2'-bipyridine inhibits the reaction



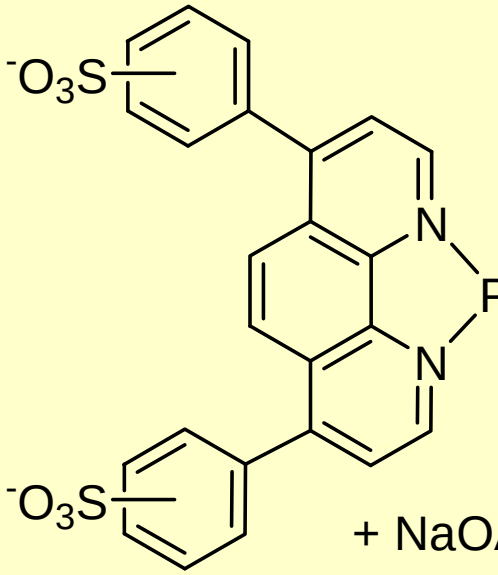
2,2'-bipyridine



bathophenanthroline disulfonate

4. $Pd(OAc)_2$ / Bathophenanthroline Disulfonate Catalyst System

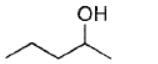
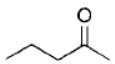
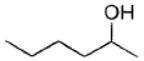
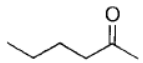
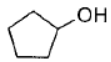
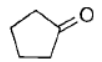
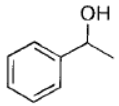
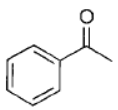
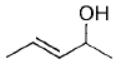
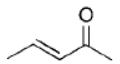
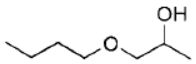
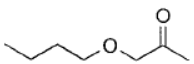
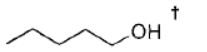
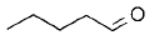
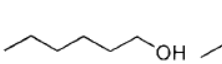
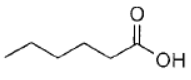
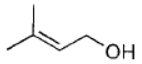
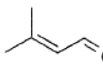
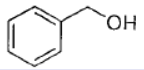
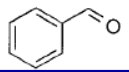
Aqueous! Low cat. loading!



$Pd(OAc)_2$ (0.5%)

+ NaOAc (10%) / water

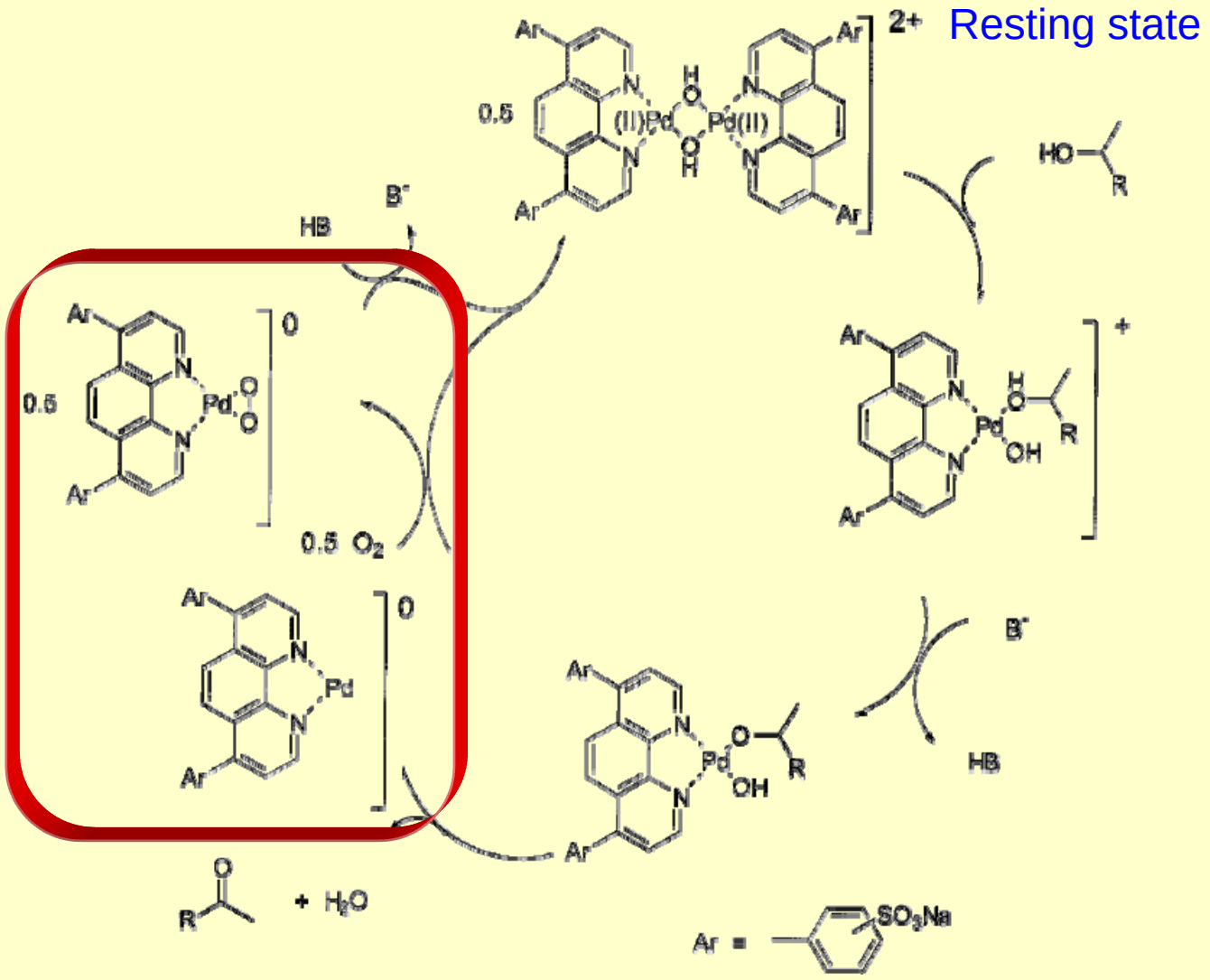
4

Substrate	Product	Time (hour)	Conversion (%)	Selectivity (%)	Isolated yield (%)
		5	100	100	90
		10	100	100	90
		5	100	100	90
		10	90	100	85
		10	95	83*	79
		10	100	100	92
 †		15	98	97‡	90
		12	95	90§	80
		10	100	96‡	88
		10	100	99.8‡	93

1. **Aqueous solution!**
2. Primary, secondary, benzylic, and allylic alcohols are oxidized
3. Catalytic rate (up to 100TOh^{-1}) and turnover numbers (200-400) are higher
4. Non-coordinating anions, like triflate, lead to Pd black deposition.

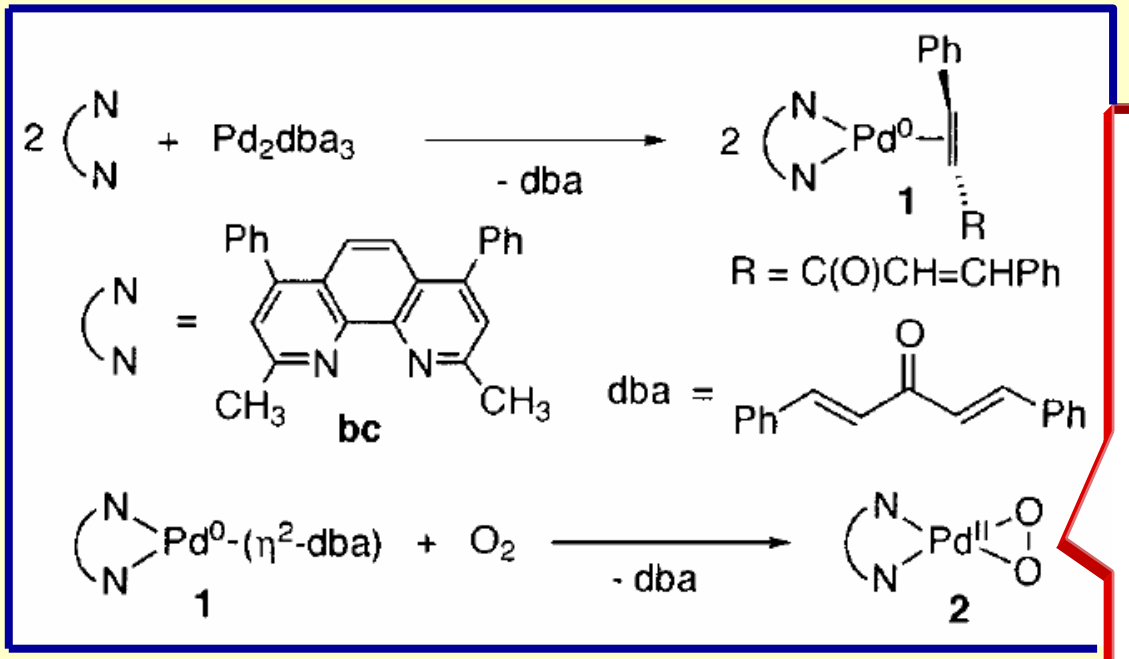
ten Brink, G.-J. Arends, I. W. C. E.; Sheldon, R. A. *Science,* **2000**, *287*, 1636

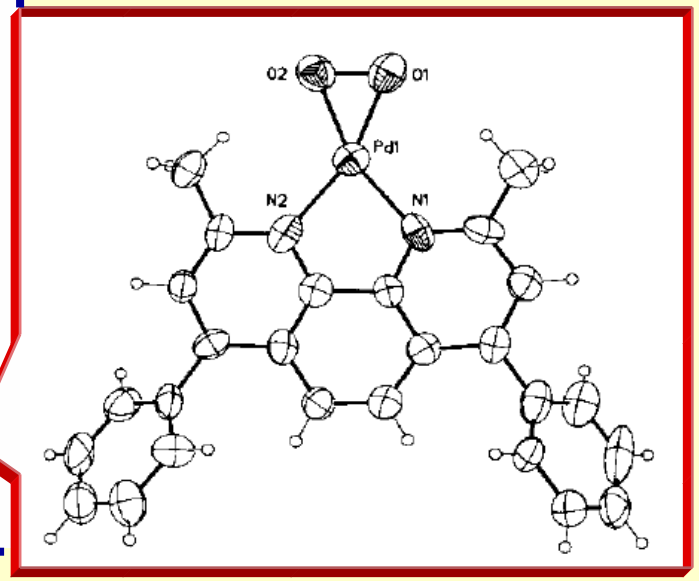
Mechanistic and Computational Studies of System 4

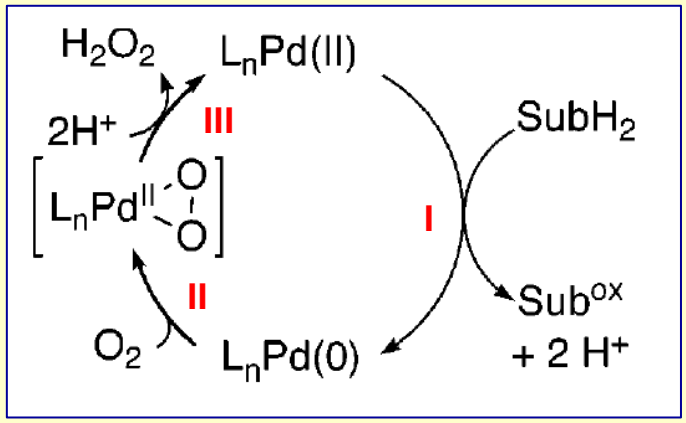


ten Brink, G.-J. Arends, I. W. C. E.; Sheldon, R. A. *Science,* **2000**, *287*, 1636

Mechanistic Studies of System 4



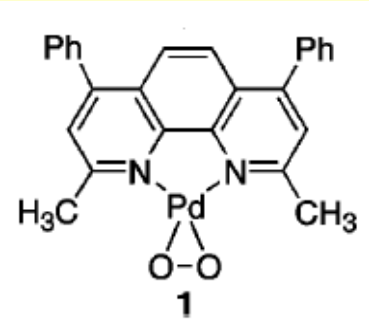


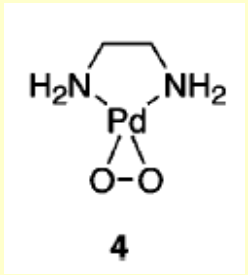


The chemistry here demonstrates the chemical viability of steps II and III of the proposed mechanism.

Stahl, S. S.; Thorman, J. L.; Nelson, R. C.; Kozee, M. A. *JACS*, **2001**, *123*, 7188

Computational Studies of System 4





This “spin-forbidden” reaction is accessible

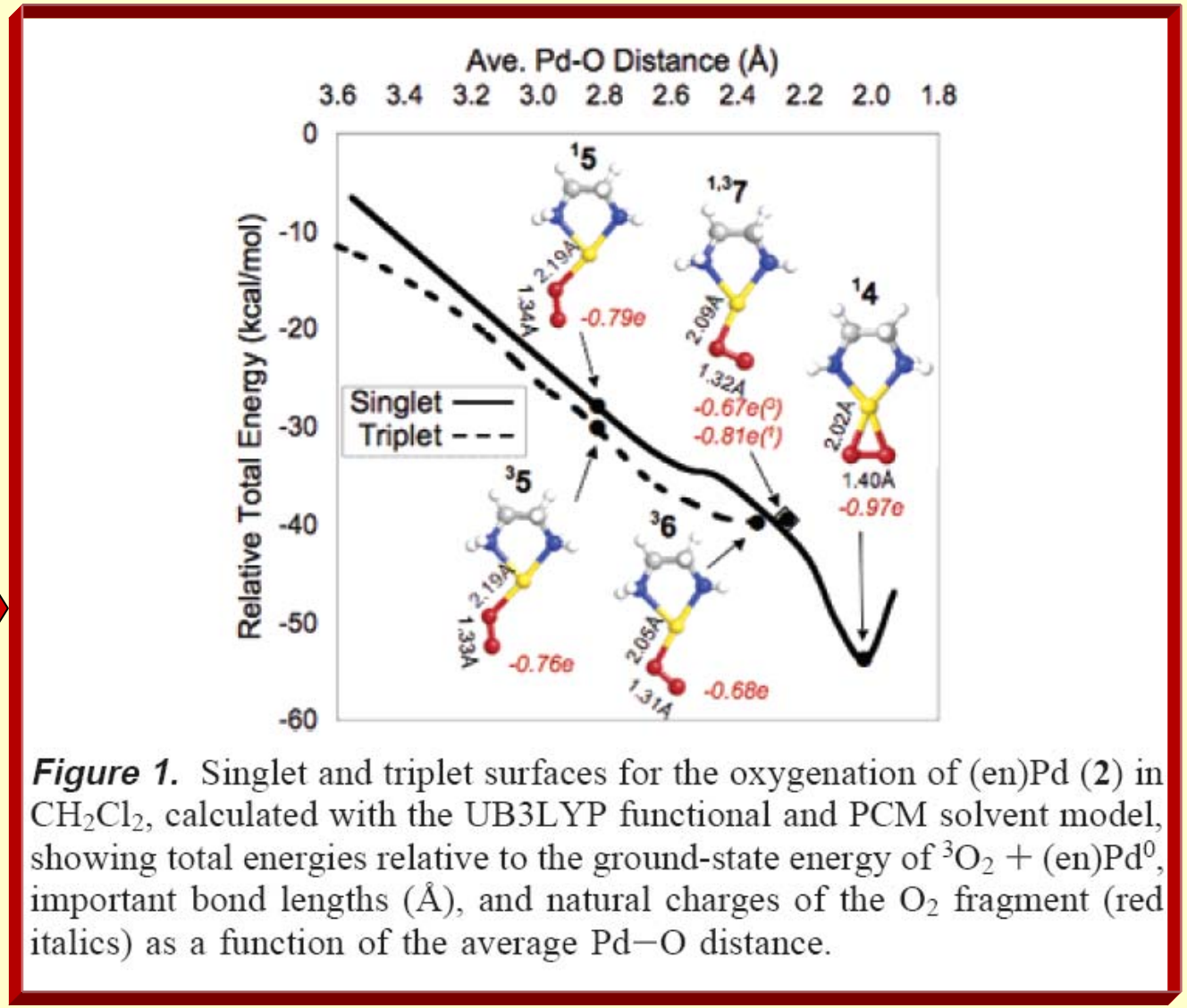


Figure 1. Singlet and triplet surfaces for the oxygenation of (en)Pd (**2**) in CH_2Cl_2, calculated with the UB3LYP functional and PCM solvent model, showing total energies relative to the ground-state energy of $^3O_2$ + (en)Pd^0, important bond lengths (Å), and natural charges of the O_2 fragment (red italics) as a function of the average Pd–O distance.

Landis, C. R.; Morales, C. M.; Stahl, S. S. *JACS*, **2004**, *126*, 16302

Computational Studies of System 4

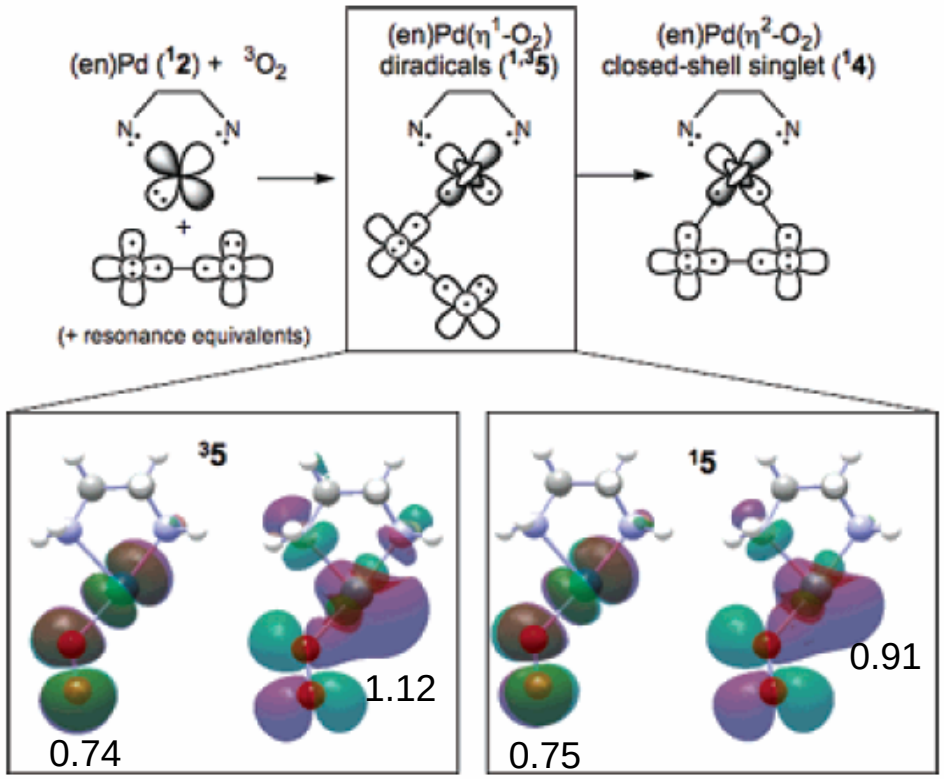


Figure 2. Evolution of the electronic structure during the oxygenation of **¹2** expressed in terms of generalized valence bond Lewis-like diagrams (top) and surface plots of Kohn−Sham orbitals bearing unpaired spin density (bottom) that demonstrate the similarity of singlet and triplet states at the geometry of **5**. The Pd-centered dark and light lobes of the Lewis representations of **4** and **5** represent pairs of s−d hybridized orbitals with perpendicular, in-plane directionalities.

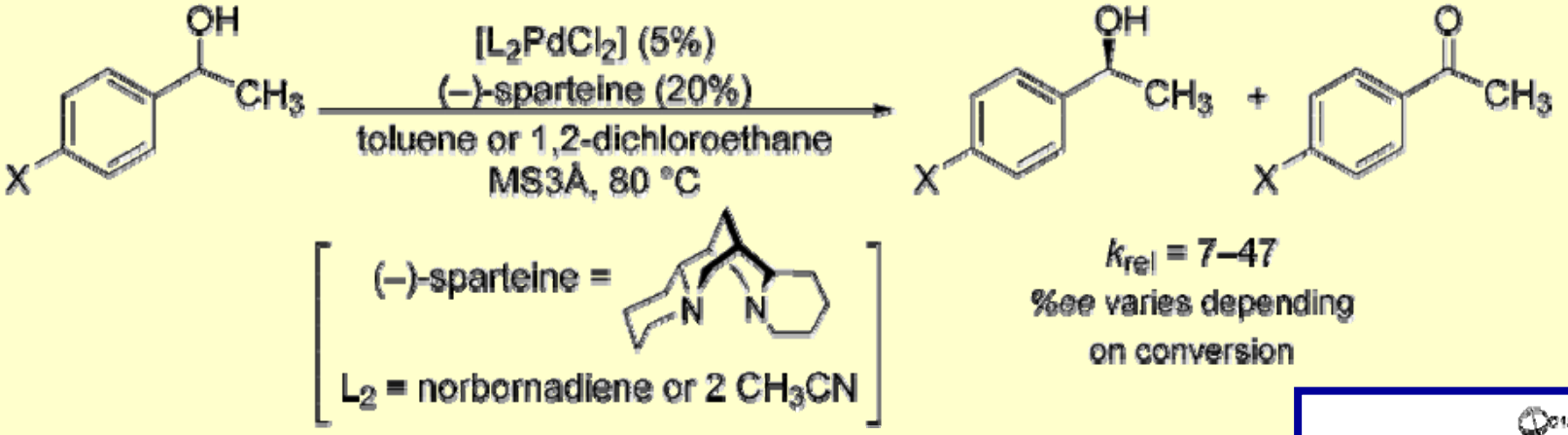
Single electron transfer from Pd^0 to O_2, results in a triplet diradical with one spin localized on Pd and one on O_2.

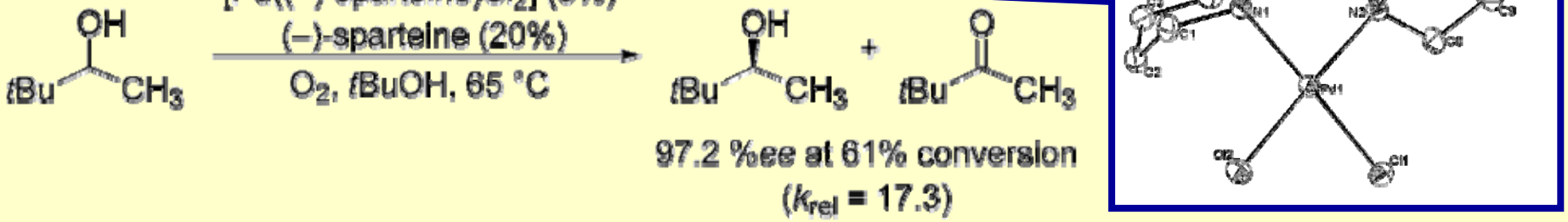
This “spin-forbidden” reaction is accessible

Landis, C. R.; Morales, C. M.; Stahl, S. S. *JACS*, **2004**, *126*, 16302

5. PdX_2 / (-)-Sparteine Catalyst System

Asymmetric! More Pd source



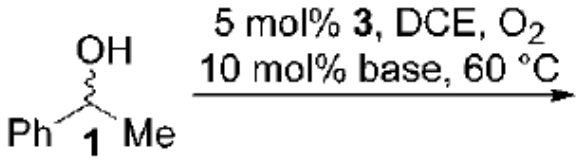


Kinetic Resolution

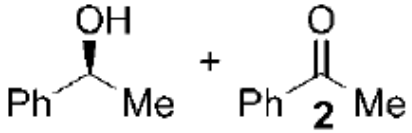
Ferreira, E. M.; Stoltz, B. M. *JACS*, **2001**, *123*, 7725

Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *JACS*, **2001**, *123*, 7475

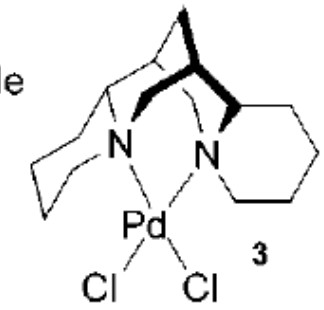
Mechanistic Studies of System 5



5 mol% **3**, DCE, O_2
10 mol% base, 60 °C



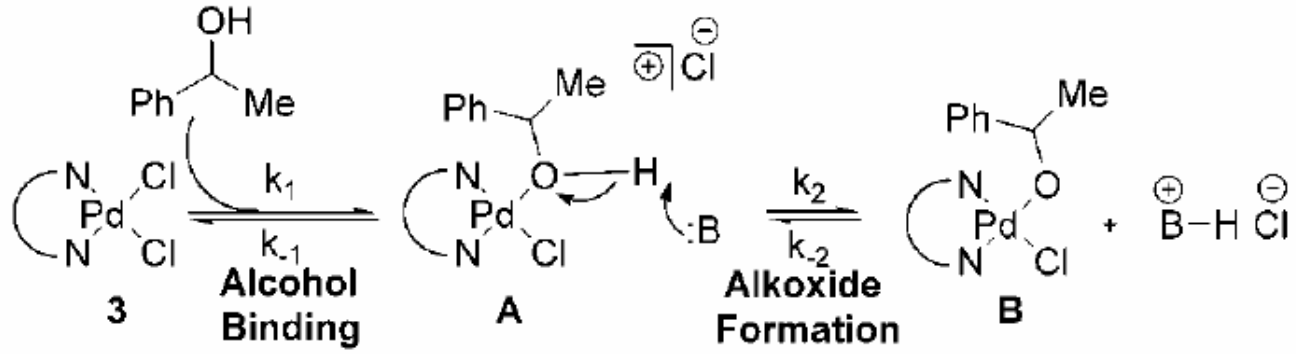
Entry	Base	%conv(%ee)	k_{rel}
1	no base	<1(--)	---
2	(-)-sparteine	51.5(82.4)	20.1

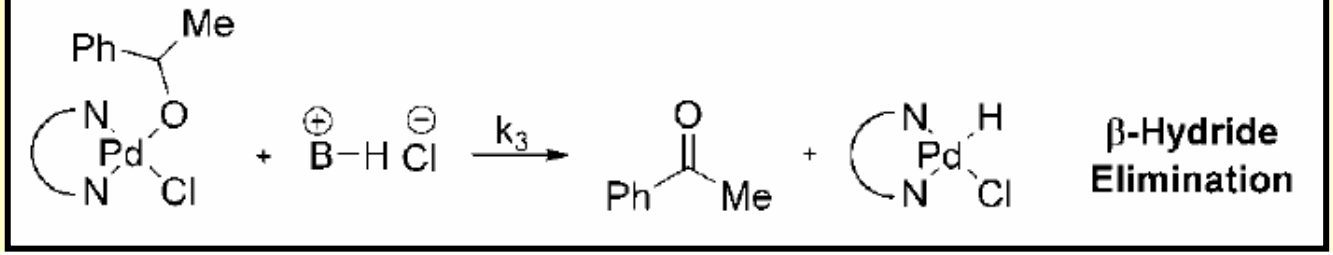


Dual roles of Sparteine:
1. Exogenous base to help alkoxide fomation
2. Chiral Ligand for kinetic resolution

(–)-sparteine (mol %)	k_{obs} *R*-(**1**)	k_{obs} *S*-(**1**)	intrinsic k_{rel}	racemate k_{rel}[c]
4[a]	1.9×10^{-5}	3.1×10^{-6}	6.1	7.6 ± 2.0
50[b]	7.5×10^{-5}	7.1×10^{-6}	11	25 ± 4.6

Rate-determining step is deprotonation of alcohol at low base con. RDS is β-Hydride elimination at high base con.

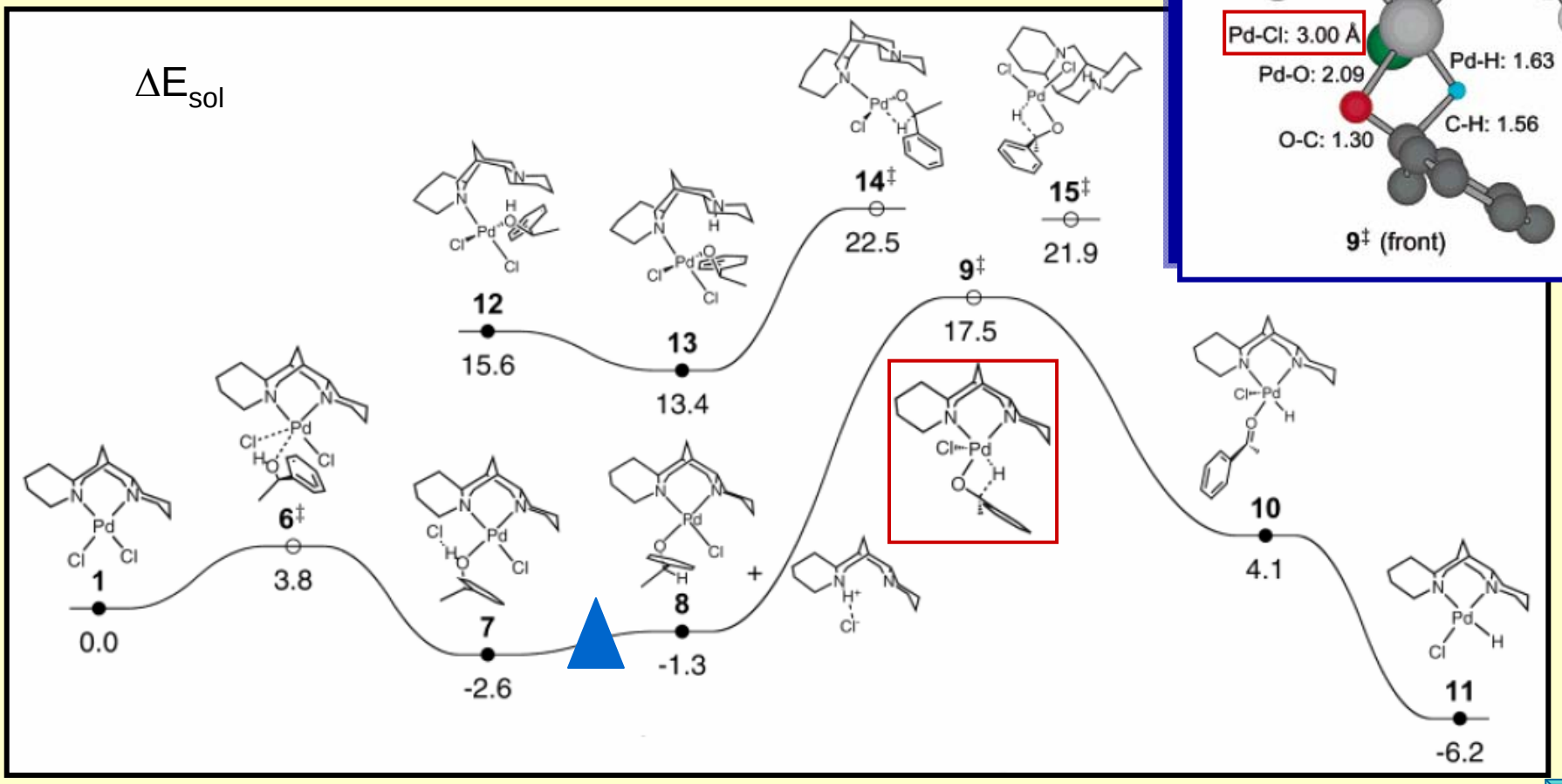




Mueller, J. A.; Jensen, D. R.; Sigman, M. S. *JACS*, **2002**, *124*, 8202

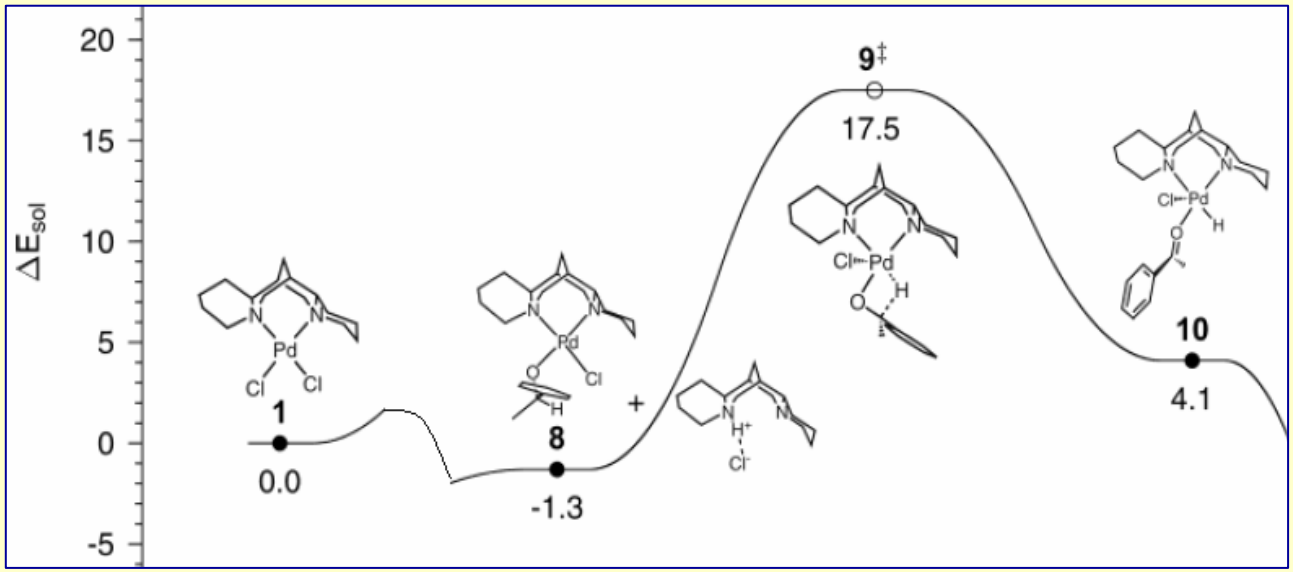
Computational Studies of System 5

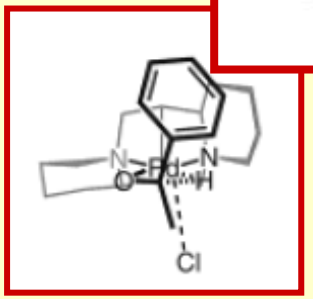
General Mechanism

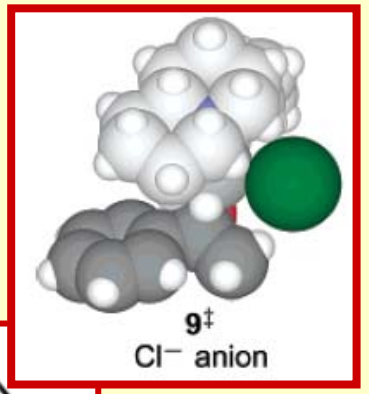


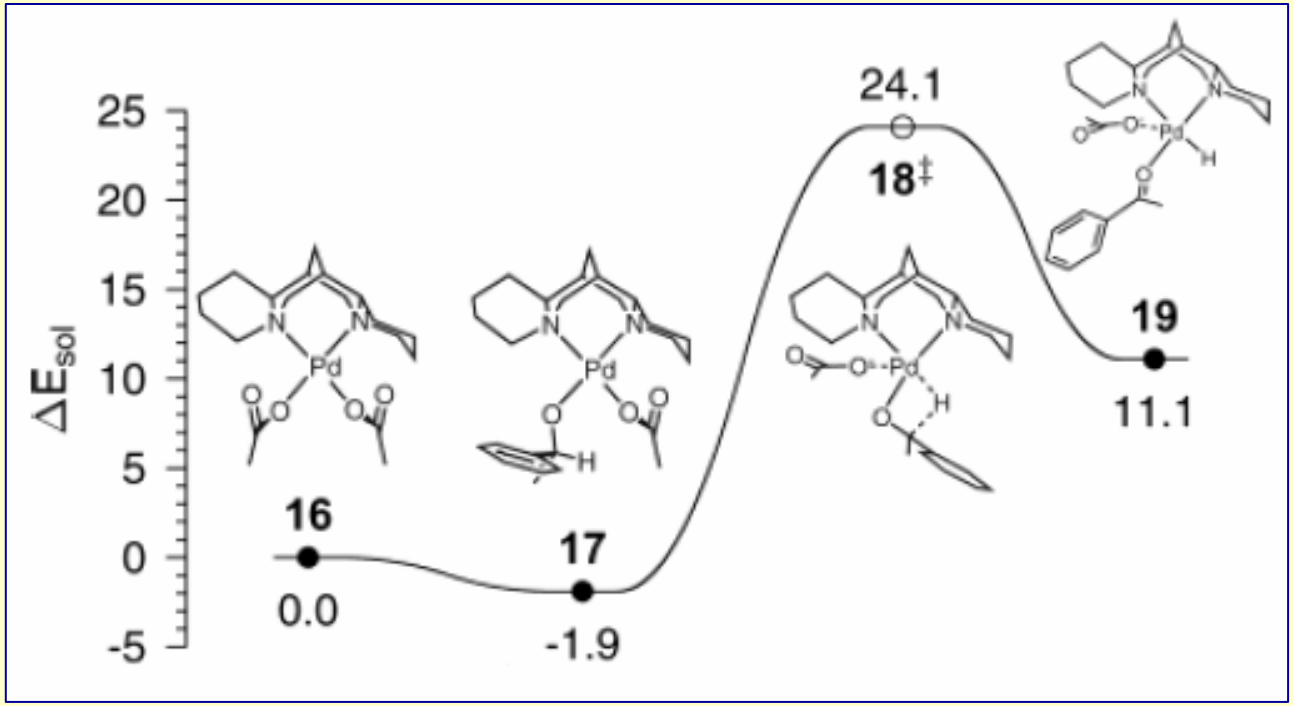
Nielsen, R. J.; Keith, J. M.; Stoltz, B. M.; Goddard, W. A., III. *JACS*, **2004**, *126*, 7967

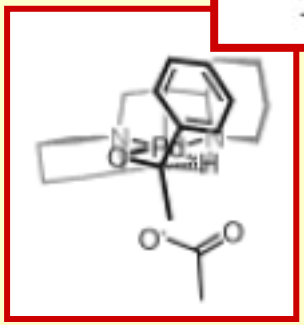
Cloride vs Acetate

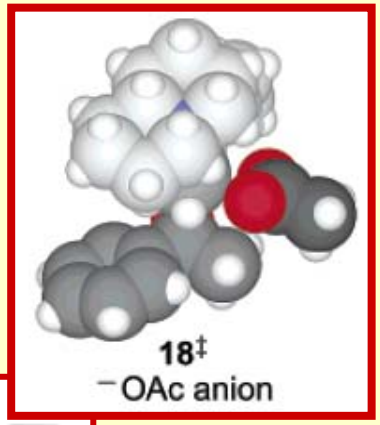






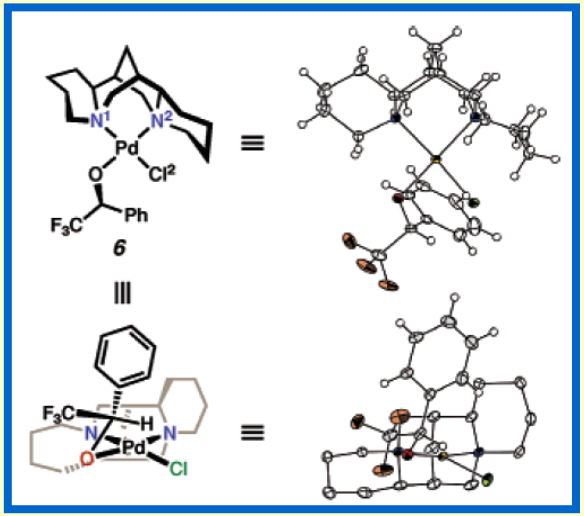


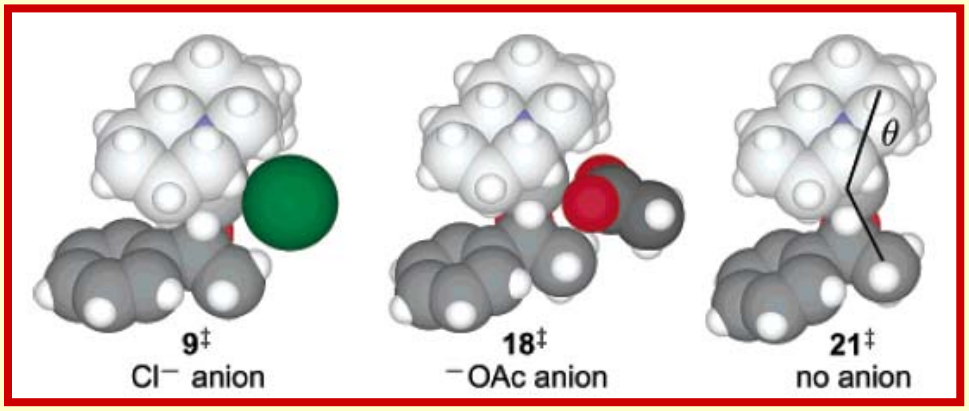


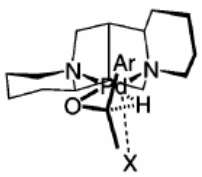
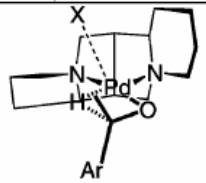
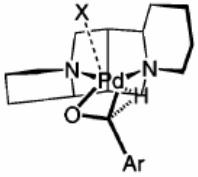
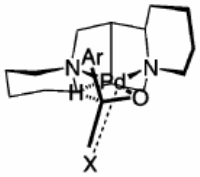


Nielsen, R. J.; Keith, J. M.; Stoltz, B. M.; Goddard, W. A., III. *JACS*, **2004**, *126*, 7967

Selectivity



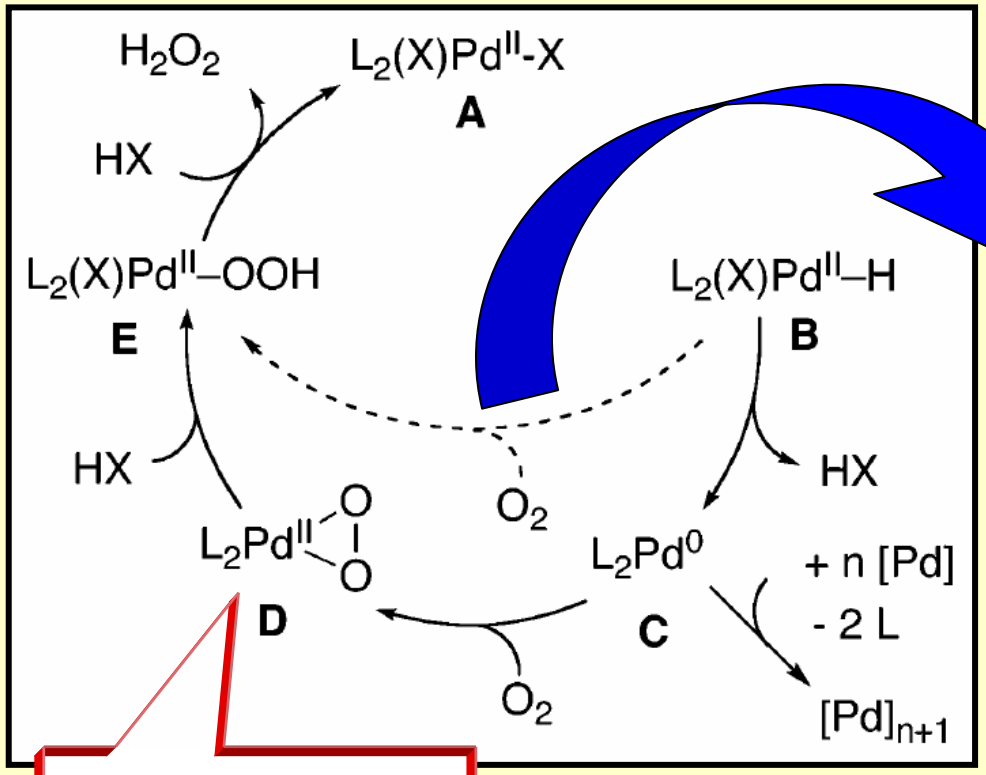


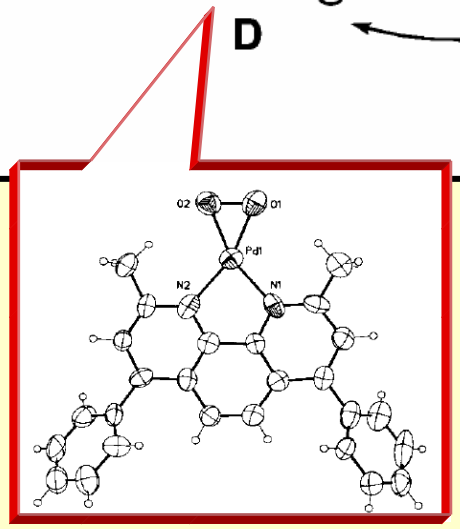
Entry	Substrate Anion	Solvent Temp	E_{sol}[a] ($\Delta E^{\ddagger}_{sol}$[b]), kcal/mol C–H$_\beta$ (Å) Pd···X[d] (Å)	E_{sol} C–H$_\beta$ Pd···X	E_{sol} C–H$_\beta$ Pd···X	E_{sol} C–H$_\beta$ Pd···X	s_{calc}[c] s_{exp}[e]	$\Delta\Delta G_{eff,calc}$ $\Delta\Delta G_{eff,exp}$
	bidentate sparteine		 R1	 R2	 S1	 S2		
1	Ar = C_6H_5 X = Cl^-	toluene 60°C	0.0 (17.5) 1.61 3.11	1.73 1.64 3.23	2.82 1.52 3.11	2.03 1.62 3.28	17.7 20.0[f]	1.9 2.0
2	Ar = *p*-$MeOC_6H_4$ X = Cl^-	toluene 60°C	0.0 (16.6) 1.58 3.25	1.21 1.61 3.28	2.65 1.48 3.12	1.82 1.59 3.31	14.1 14.9[f]	1.8 1.8
3	Ar = *p*-FC_6H_4 X = Cl^-	toluene 60°C	0.0 (17.8) 1.61 3.24	1.18 1.64 3.23	2.36 1.53 3.11	1.63 1.62 3.31	10.3 12.1[f]	1.5 1.6
4	Ar = 2-Naphthyl X = Cl^-	toluene 60°C	0.0 (15.7) 1.59 3.11	2.28 1.64 3.23	2.87 1.52 3.11	2.13 1.62 3.29	19.5 15.8[f]	2.0 1.8

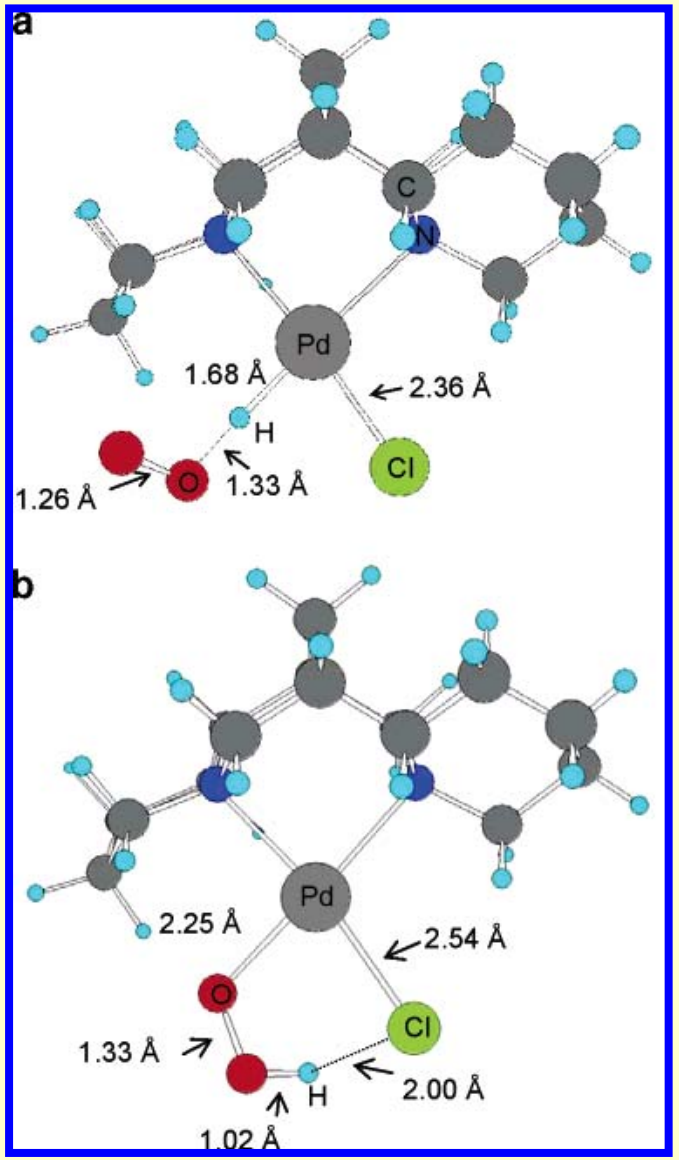
Trend, R. M.; Stoltz, B. M. *JACS*, **2004**, *126*, 4482

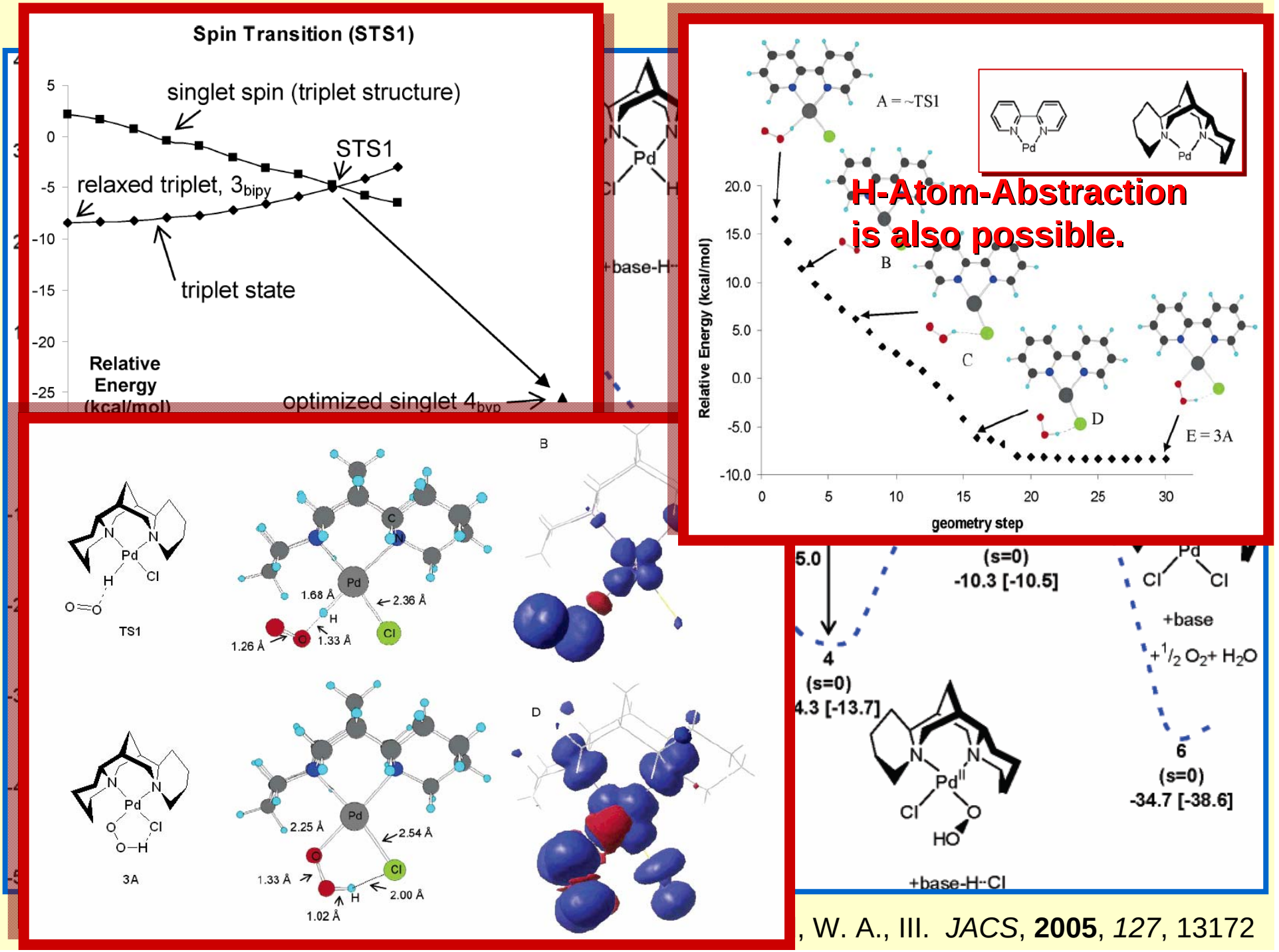
Nielsen, R. J.; Keith, J. M.; Stoltz, B. M.; Goddard, W. A., III. *JACS*, **2004**, *126*, 7967

The Regeneration of the Pd Catalyst



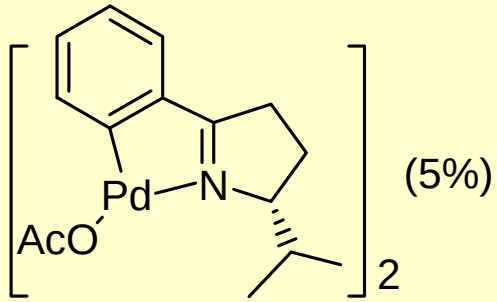






, W. A., III. *JACS*, **2005**, *127*, 13172

6. Palladacycle 6 Catalyst System



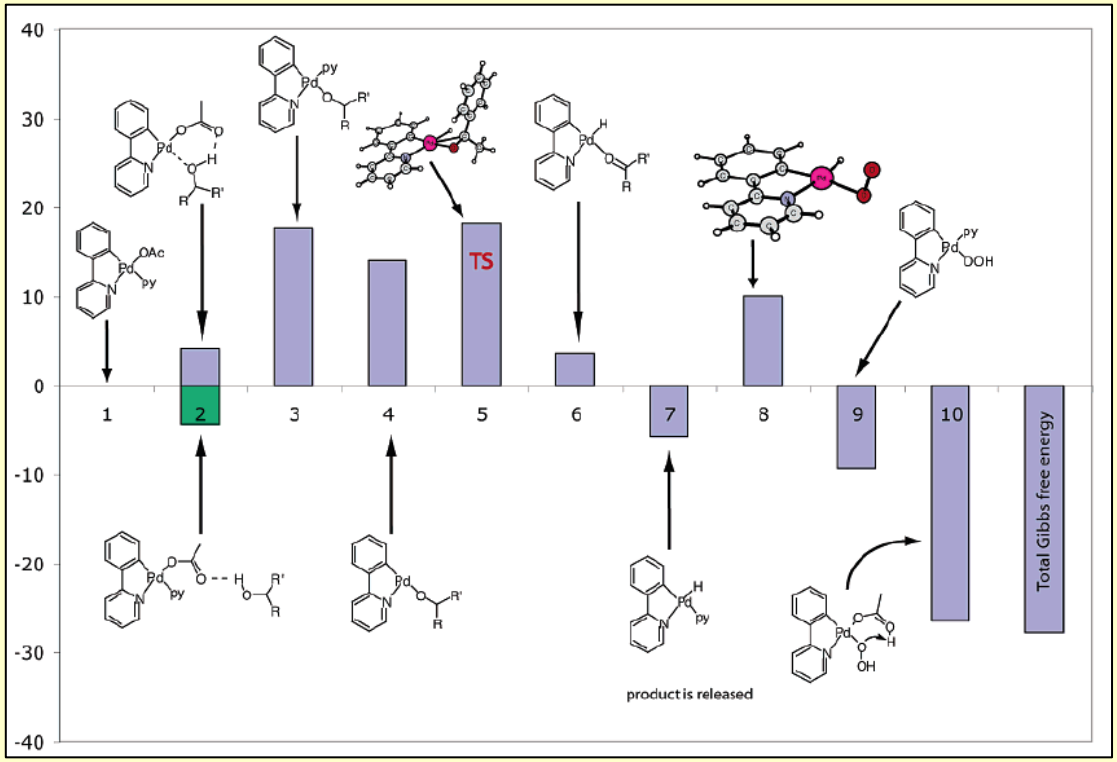
(5%)

+ pyridine (20%) /toluene

No very special

Hallman, K.; Moberg, C.
Adv. Synth. Catal. **2001**, *343*, 260

6



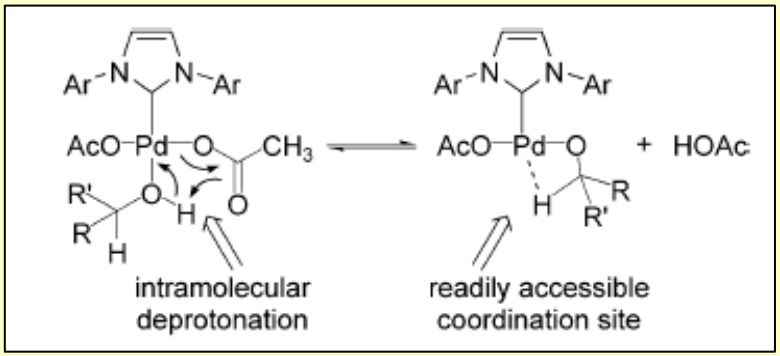
Privalov, T.; Linde, C.; Zetterberg, K.; Moberg, C.
Organometallics. **2005**, *24*, 885

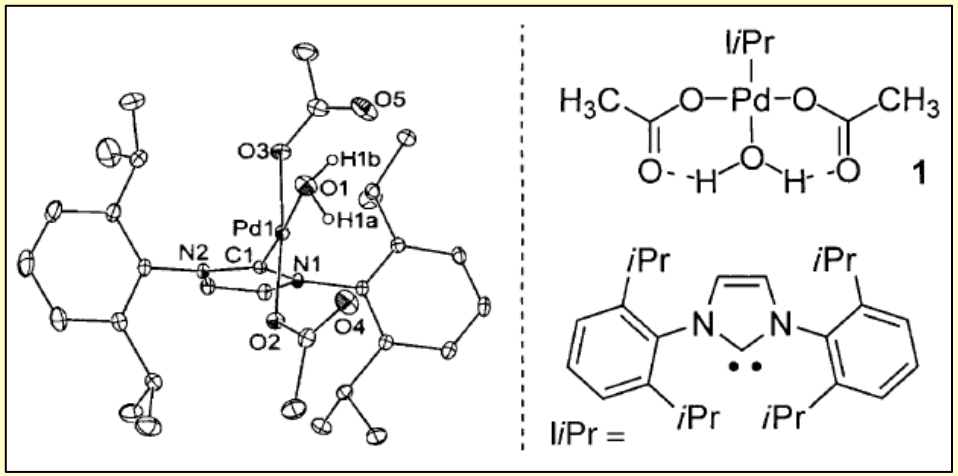
7. $Pd(OAc)_2$ / NHC Catalyst System

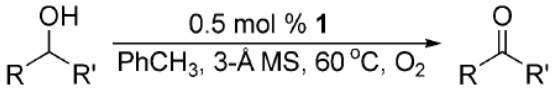
Low cat. loading, large sub. scope, potential asymmetric!

Aerobic Oxidation of Alcohols

A Well-Defined Complex for Palladium-Catalyzed Aerobic Oxidation of Alcohols: Design, Synthesis, and Mechanistic Considerations**





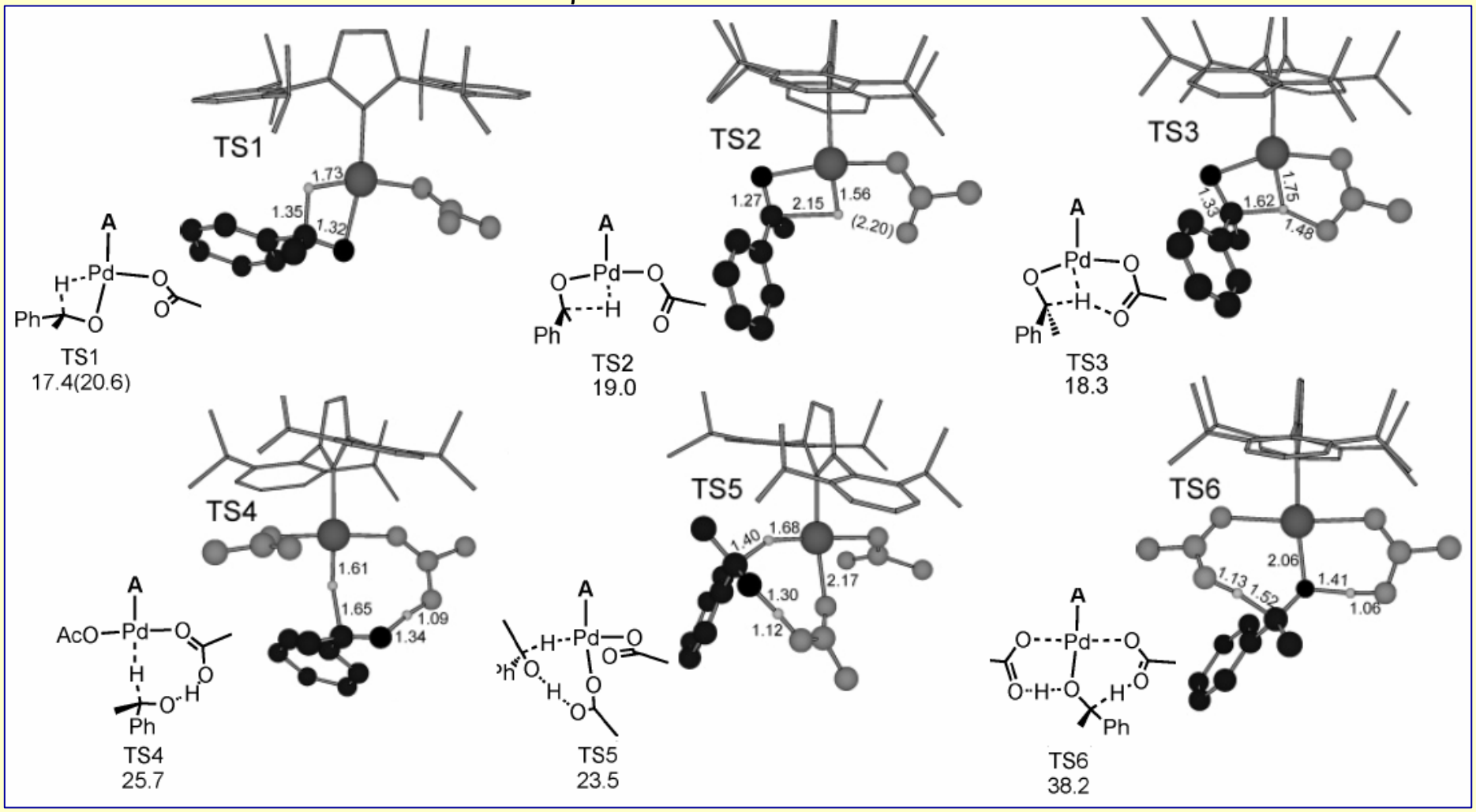


Entry[a]	Substrate	R	R′	*t* [h]	Yield [%][b,c]
1[d]	**2a**	Ph	CH_3	5	>99 (98)
2[e]	**2a**			13	>99
3[d]	**2b**	4-$MeOC_6H_4$	H	3.5	>99 (99)
4[d],[f]	**2b**			20	>99
5[d]	**2c**	3-$CF_3C_6H_4$	CH_3	12	>99 (99)
6[d],[g]	**2d**	Ph	*t*Bu	14	91
7[d]	**2e**	1-cyclohexenyl	CH_3	12	91 (84)
8[h]	**2f**	$CH_3(CH_2)_7$	CH_3	13	99 (93)
9[d]	**2g**	3-Me-cyclohexenol		12	92
10[h]	**2h**	*cis*-4-Me-cyclohexanol		13	>99
11[i]	**2i**	myrtenol		20	97
12[i],[j]	**2j**	$CH_3(CH_2)_{10}$	H	10	85 (76)
13[i],[j]	**2k**	$CH_3(CH_2)_{16}$	H	10	(85)

Jensen, D. R.; Schultz, M. J.; Mueller, J. A.; Sigman, M. S. *Angew. Chem. Int. Ed.*, **2003**, *42*, 3810

Computational Studies of System 7

Possible C-H_β Bond Scission Transition States



Nielsen, R. J.; Goddard, W. A., III. *JACS*, **2006**, *128*, 9651

Computational Studies of System 7

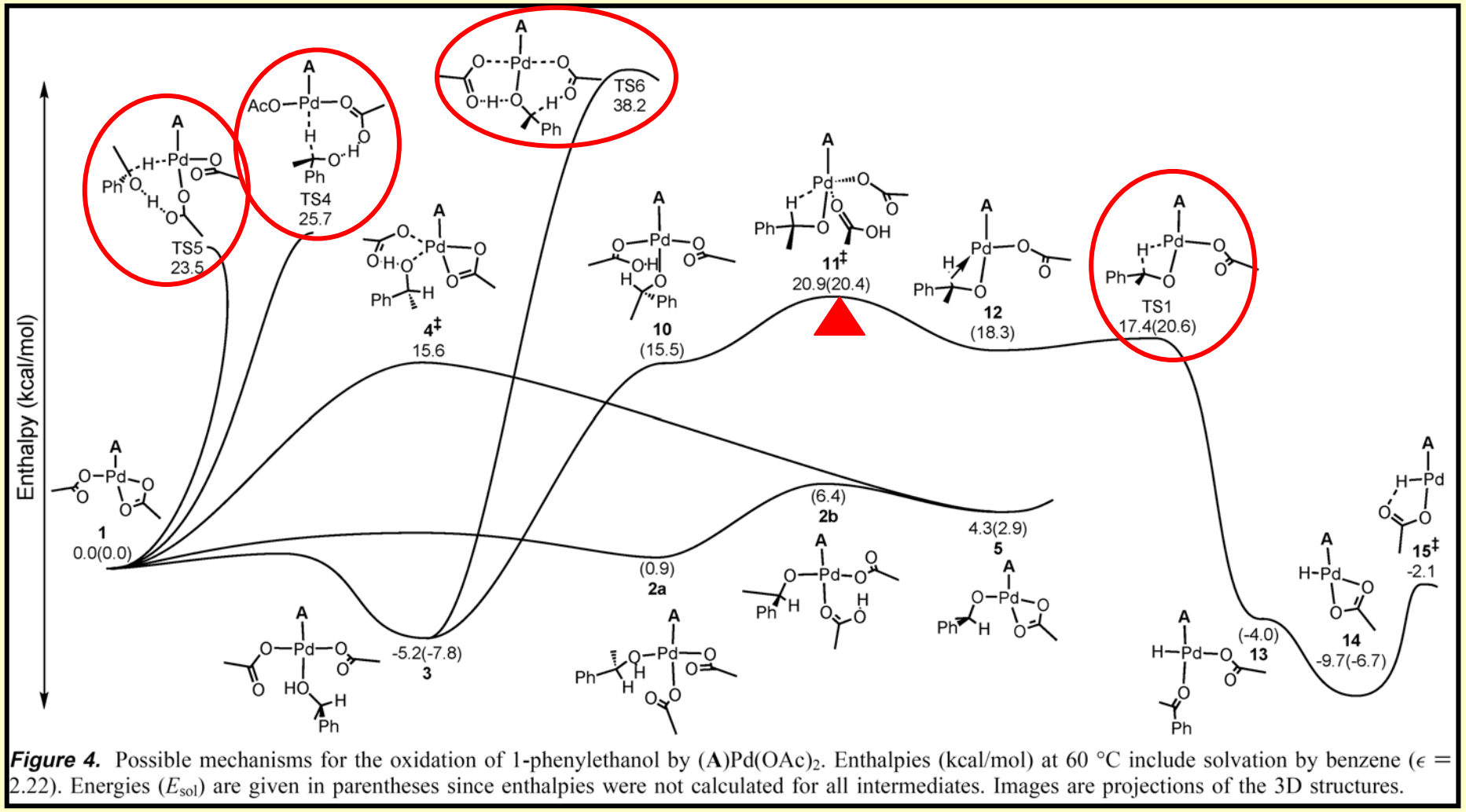


Figure 4. Possible mechanisms for the oxidation of 1-phenylethanol by (**A**)Pd(OAc)$_2$. Enthalpies (kcal/mol) at 60 °C include solvation by benzene (ϵ = 2.22). Energies (E_{sol}) are given in parentheses since enthalpies were not calculated for all intermediates. Images are projections of the 3D structures.

Nielsen, R. J.; Goddard, W. A., III. *JACS*, **2006**, *128*, 9651

Computational Studies of System 7

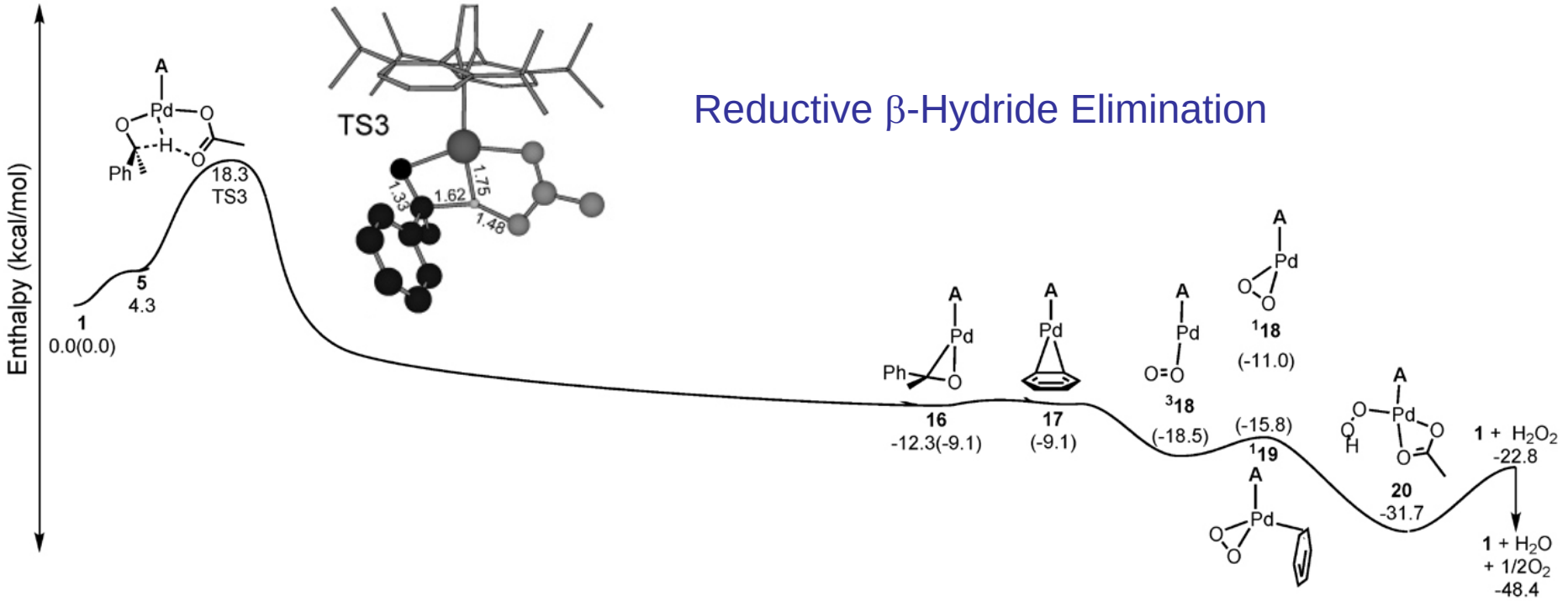
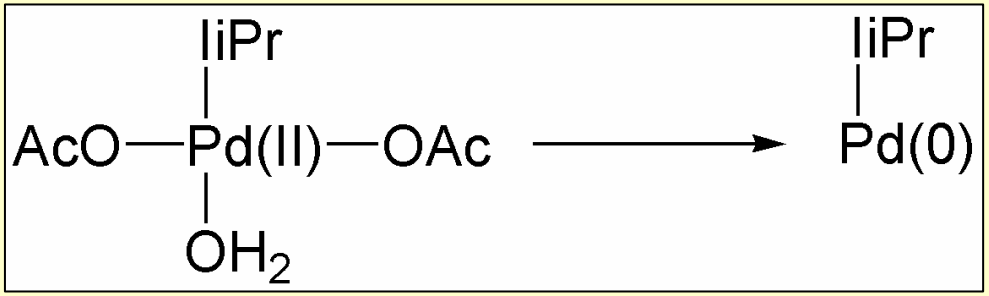


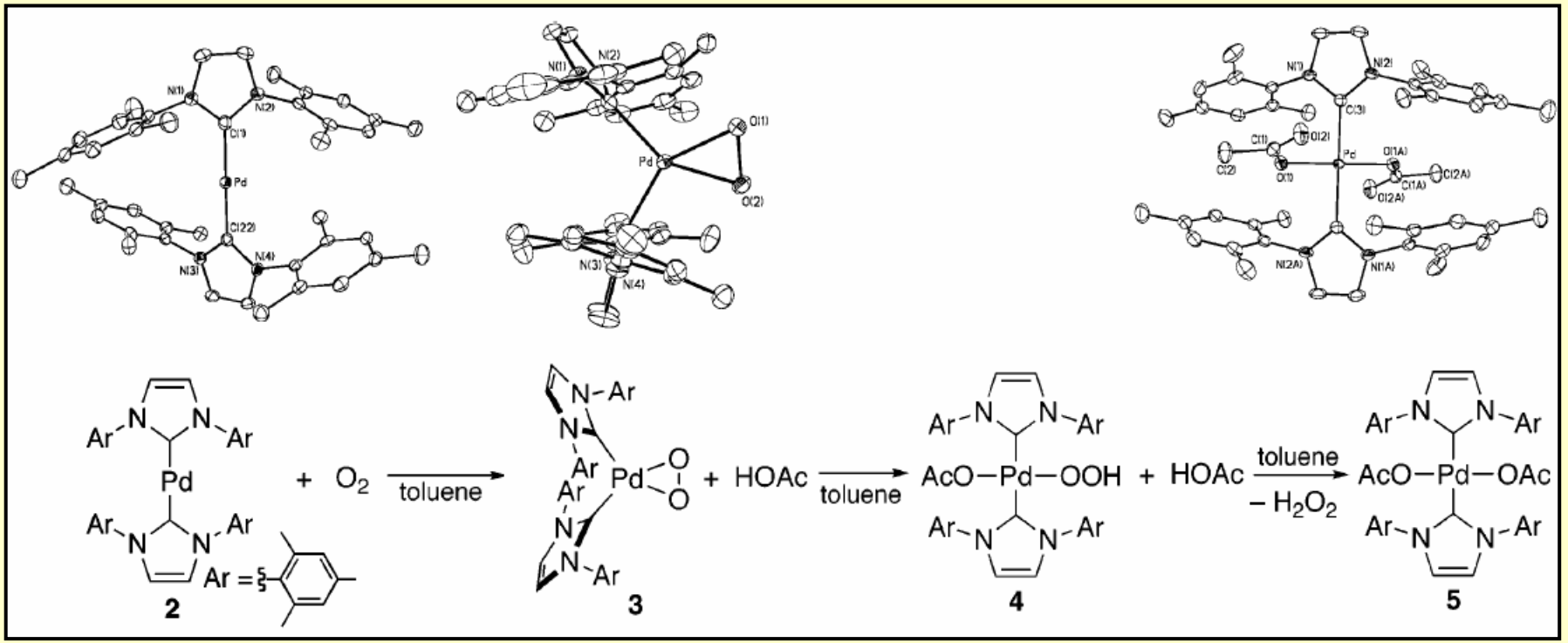
Figure 5. Possible mechanisms for the oxidation of 1-phenylethanol by (**A**)Pd(OAc)$_2$. Enthalpies (kcal/mol) at 60 °C include solvation by benzene (ϵ = 2.22). Energies (E_{sol}) are given in parentheses. Images are projections of the 3D structures.

The reactivity of the (NHC)Pd(OAc)$_2$ complex is distinguished from related palladium complexes of N-donor ligands by the strong trans influence of the carbene ligand. The formation of covalent bonds trans to the carbene is thermodynamically discouraged, leading to an alternative mechanism: **Reductive β-Hydride Elimination**.

Nielsen, R. J.; Goddard, W. A., III. *JACS*, **2006**, *128*, 9651

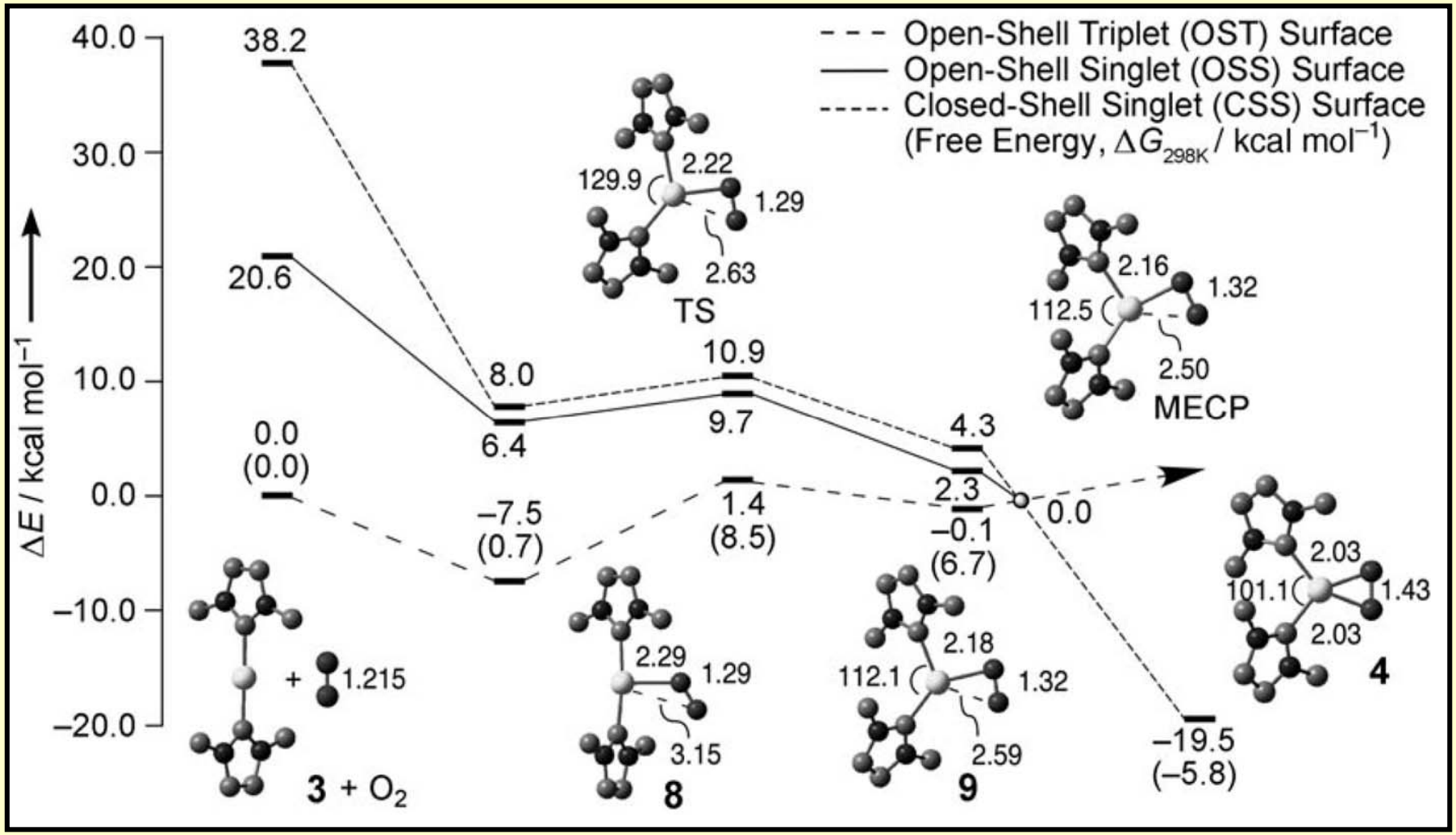
Regeneration of Pd catalyst





Konnick, M. M.; Guzei, I. A.; Stahl, S. S. *JACS*, **2004**, *126*, 10212

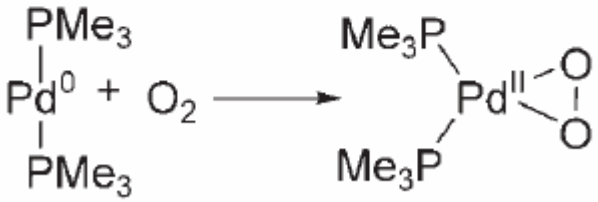
Computational Studies of System 7



Popp, B. V; Wendlandt, J. E.; Landis, C. R.; Stahl, S. S. *Angew. Chem. Int. Ed.*, **2007**, *46*, 601

Computational Studies of System 7

medium	ε	ΔG^0 [kcal/mol]
gas phase	1.0	+3.6
toluene	2.379	–5.7
tetrahydrofuran	7.58	–12.0
acetonitrile	36.64	–14.9

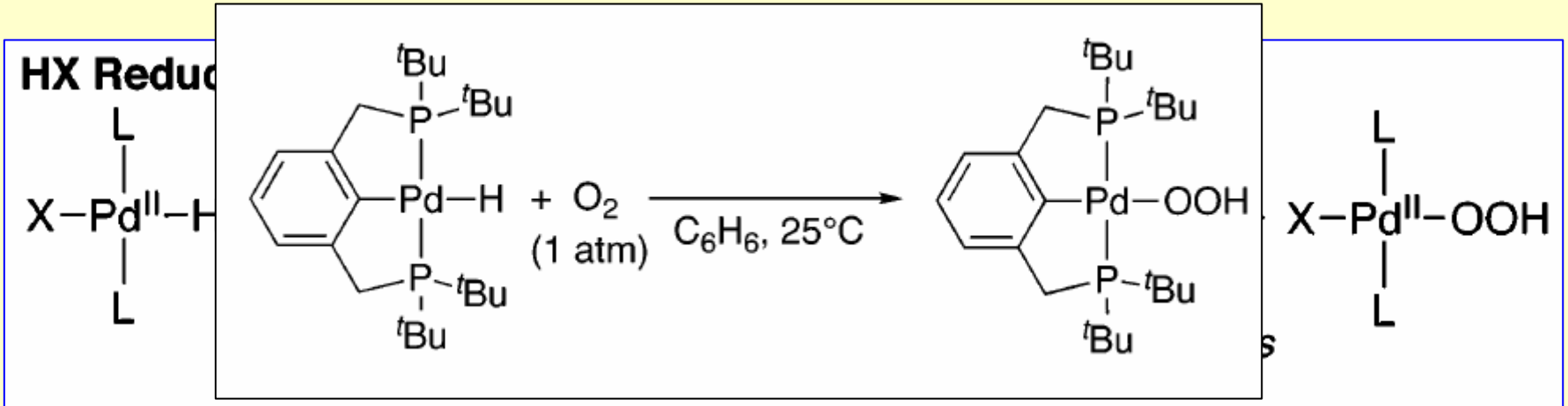


medium	ε	ΔG^0 [kcal/mol]
gas phase	1.0	+10.3
toluene	2.379	+2.3
tetrahydrofuran	7.58	–3.1
acetonitrile	36.64	–2.8

The stronger s-donor character of NHC ligands relative to phosphines promote increased charge transfer into the O_2 fragment and tighter binding

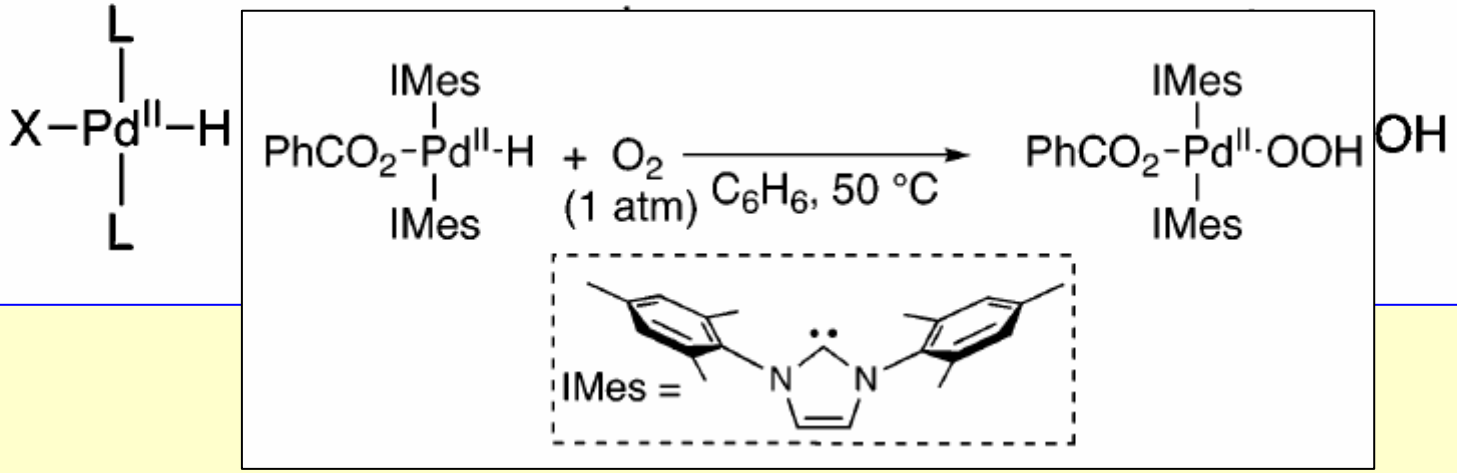
Popp, B. V; Wendlandt, J. E.; Landis, C. R.; Stahl, S. S. *Angew. Chem. Int. Ed.*, **2007**, *46*, 601

HX Reduc



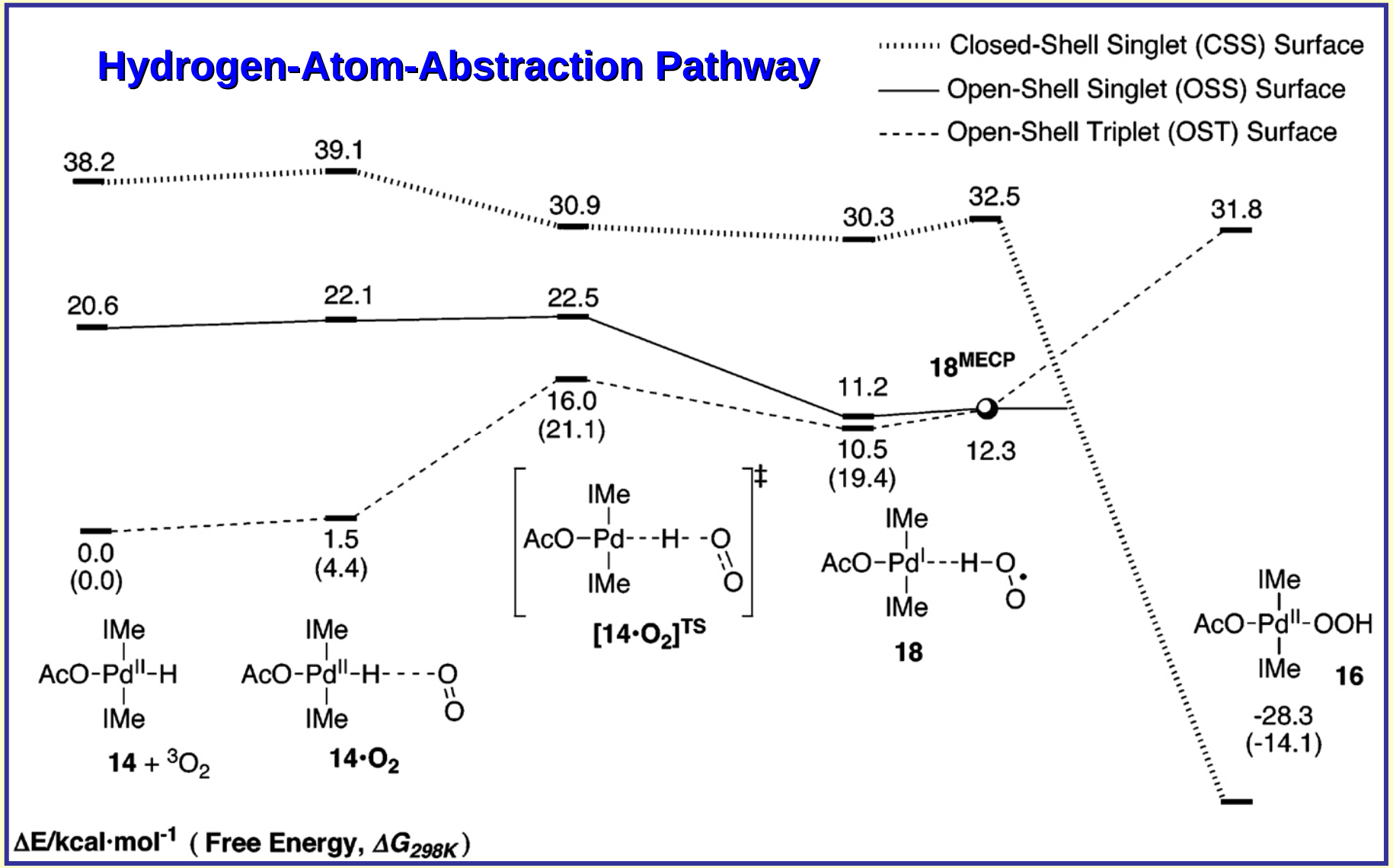
Denney, M. C.; Smythe, N. A.; Cetto, K. L.; Kemp, R. A.; Goldberg, K. I. *JACS*, **2006**, *128*, 2508

Hydrogen-Atom-Abstraction Pathway

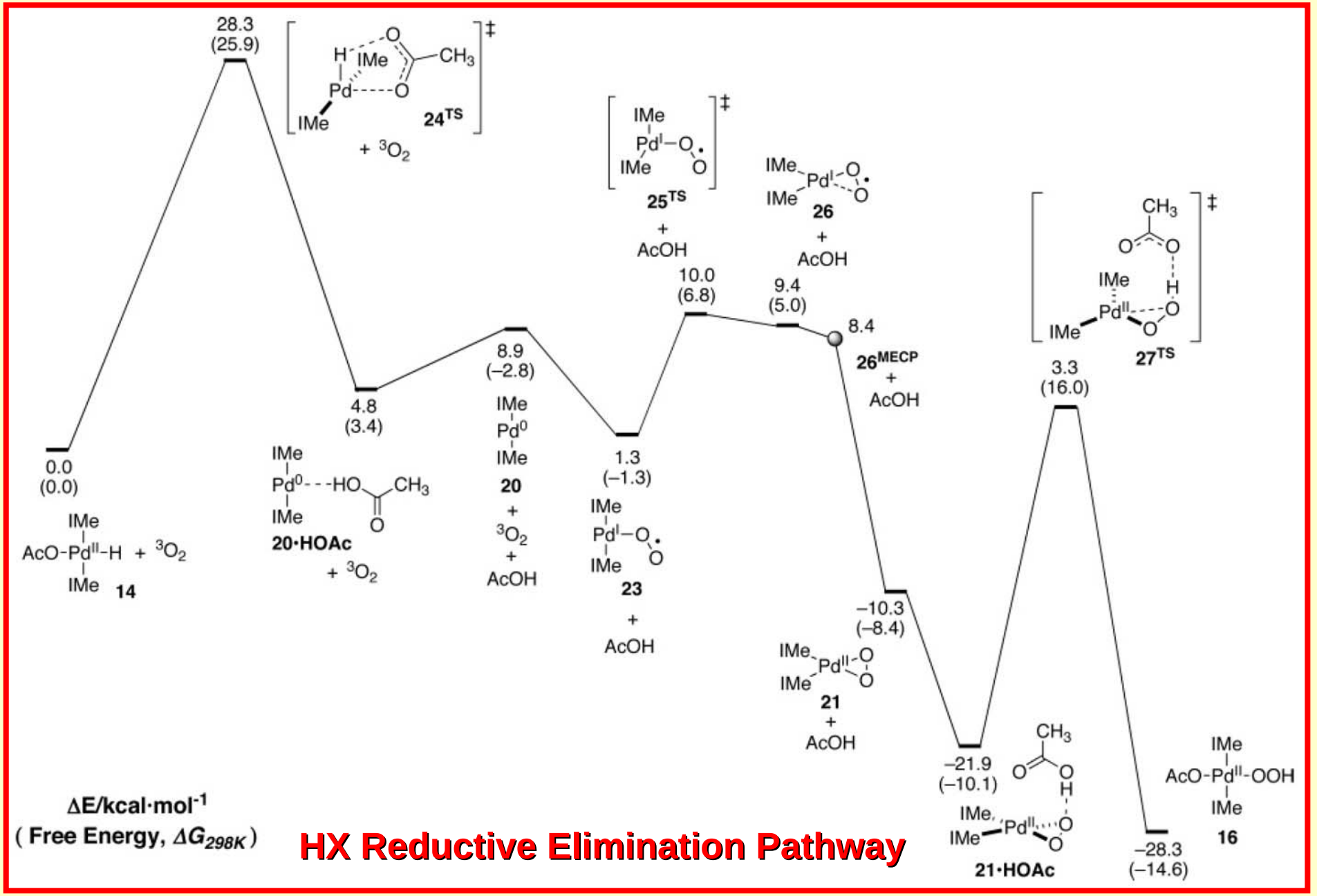


Konnick, M. M.; Gandhi, B. A.; Guzei, I. A.; Stahl, S. S. *Angew. Chem. Int. Ed.*, **2006**, *45*, 601

Computational Studies of System 7

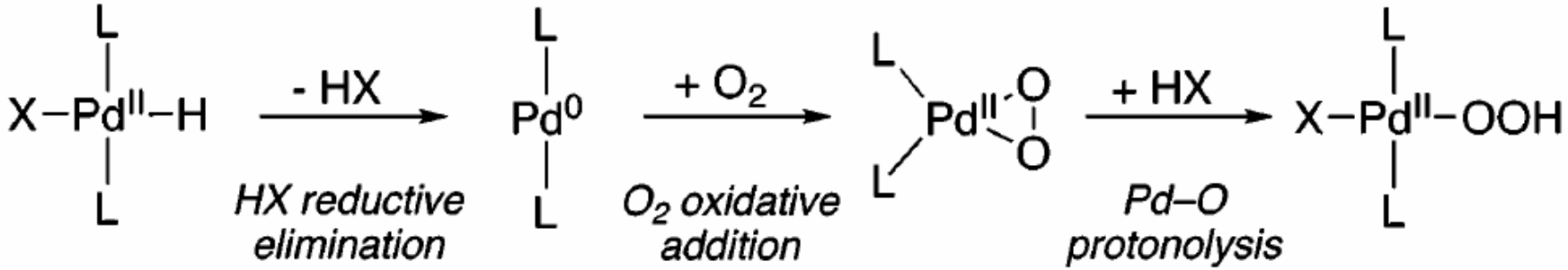


Popp, B. V.; Stahl, S. S. *JACS*, **2007**, *129*, 4410

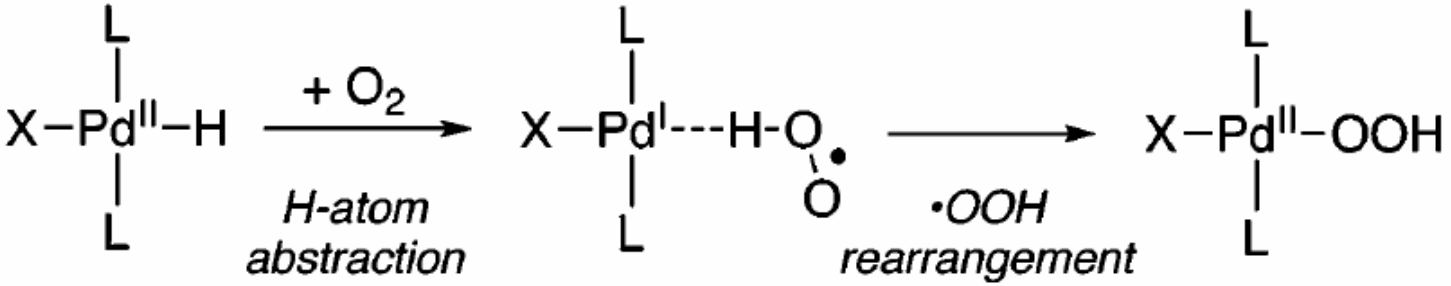

28.3
(25.9)
24TS
+ 3O2
4.8
(3.4)
20·HOAc
+ 3O2
0.0
(0.0)
14
8.9
(–2.8)
20
+
3O2
+
AcOH
25TS
+
AcOH
10.0
(6.8)
1.3
(–1.3)
23
+
AcOH
26
+
AcOH
9.4
(5.0)
8.4
26MECP
+
AcOH
21
+
AcOH
–10.3
(–8.4)
–21.9
(–10.1)
21·HOAc
27TS
3.3
(16.0)
–28.3
(–14.6)
16
ΔE/kcal·mol-1
(Free Energy, ΔG298K)
HX Reductive Elimination Pathway

Computational Studies of System 7

HX Reductive Elimination Pathway



Hydrogen-Atom-Abstraction Pathway



These two pathways are similar in energy. The preferred pathway will depend on the reaction conditions and the ancillary ligands coordinated to Pd

Summary

In conjunction with the experimental work, the recent computational studies demonstrated that the selection of the ligand on Pd is crucial in developing robust and active aerobic alcohol oxidation catalysts:

1. Base is necessary for deprotonation of the Pd-bound alcohol
2. Strong donor ligand on Pd facilitates β-Hydride Elimination
3. A ligand must dissociate to allow alcohol binding and β-HE
4. Excess ligand is needed to prevent Pd decomposition