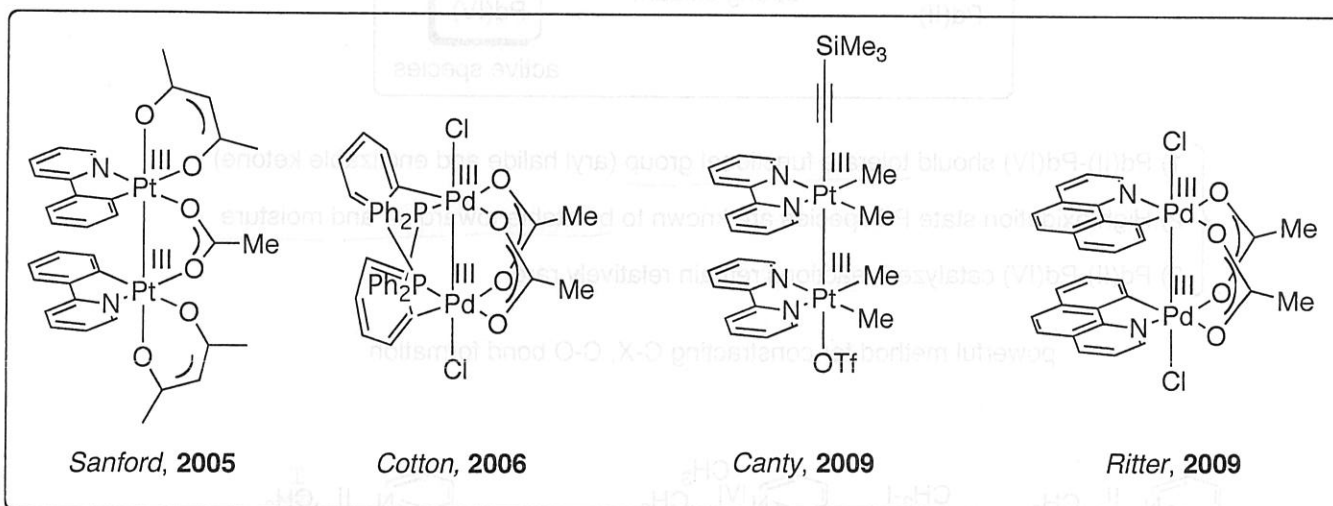


On the Mechanism of Higher Order Oxidation States of Palladium



Contents

0. Introduction (P. 2)
1. Mechanical study on reductive elimination of Pd(IV) complex (P. 3) (Sanford)
2. Pd(III)-Pd(III) in C-X bond formation (P. 7) (Ritter)
3. a) C-H arylation (P. 15) (Sanford)
- b) C-H chlorination (P. 17) (Sanford)
- c) C-H acetoxylation (P. 17) (Sanford)
4. Summary (P. 18)

ref) Dr. Itano's D1 lit.



Tobias Ritter was born in 1975 in Lubeck, Germany.

He received his master of science from Braunschweig University, Germany in 1999 after studying in Braunschweig, Bordeaux, and Lausanne and a one year tenure at Stanford University with Professor Barry M. Trost.

At Stanford Tobias' research dealt with palladium-catalyzed allylic alkylations and the synthesis of iridium and rhodium catalysts for olefin-isomerization. Subsequently, he moved to ETH Zurich for his doctoral studies in the group of Professor Erick M. Carreira on the total synthesis of the natural product Resiniferatoxin and new cholesterol absorption inhibitors.

After obtaining his Ph.D. in 2004 Tobias started as a postdoctoral fellow at the California Institute of Technology with Professor Robert H. Grubbs.

Tobias began as an Assistant Professor in the Department of Chemistry and Chemical Biology at Harvard University in July 2006.



Melanie Sanford grew up in Providence, RI.

She received her undergraduate degree in chemistry from Yale University in 1996 where she worked with Professor Bob Crabtree studying C-F bond functionalization.

She then moved to Caltech where she worked with Professor Bob Grubbs investigating the mechanism of ruthenium-catalyzed olefin metathesis reactions.

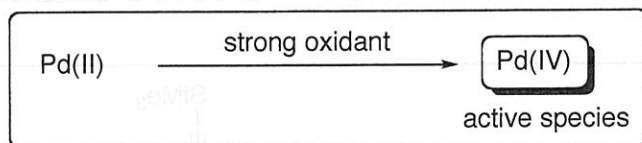
After receiving her PhD in 2001, she worked with Professor Jay Groves at Princeton University as an NIH post-doctoral fellow studying metalloporphyrin-catalyzed functionalization of olefins. Melanie has been a professor at the University of Michigan since the summer of 2003.

0. Introduction

recent review : Muniz. *Angew. Chem. Int. Ed.* **2009**, *48*, 9412.
Canty . *Dalton Trans.* **2009**, 10409.

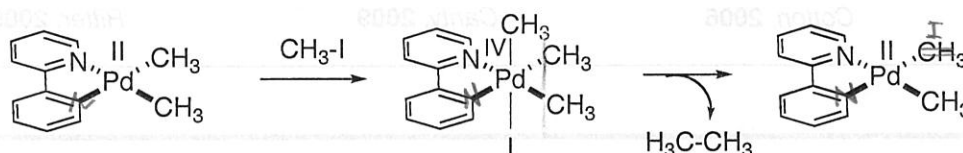
0-1. Palladium (IV)

general method



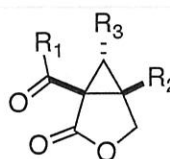
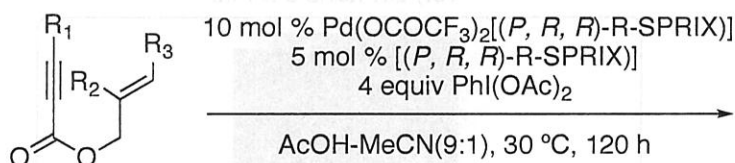
- 1) Pd(II)-Pd(IV) should tolerate functional group (aryl halide and enolizable ketone)
- 2) High oxidation state Pd species are known to be stable toward air and moisture
- 3) Pd(II)-Pd(IV) catalyzed reactions remain relatively rare

powerful method for constructing C-X, C-O bond formation

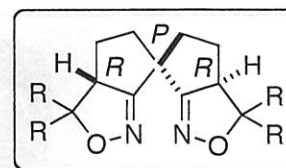


Canty *et. al.*, *Chem. Commun.* **1986**, 1722

0-2. First catalytic asymmetric synthesis via Pd(IV)-Pd(II)



up to 92%, up to 95% ee
11 examples



(*P, R, R*)-R-SPRIX

Sasai, *et. al.*, *J. Am. Chem. Soc.* **2009**, *131*, 3452.

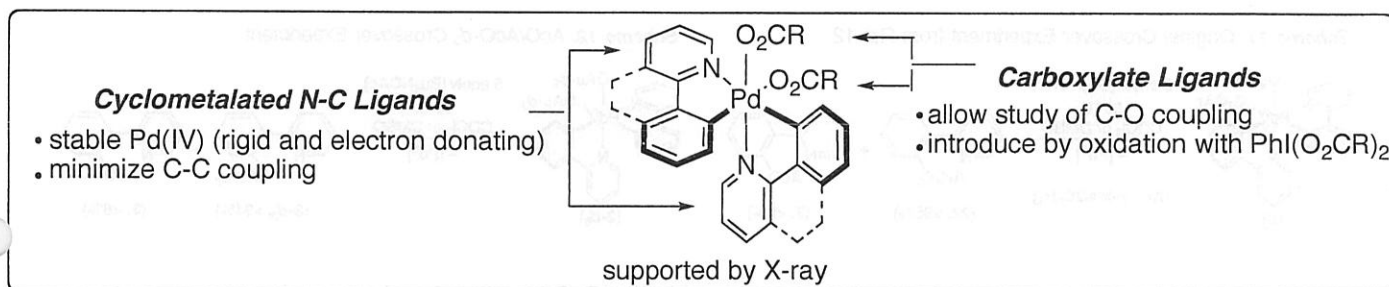
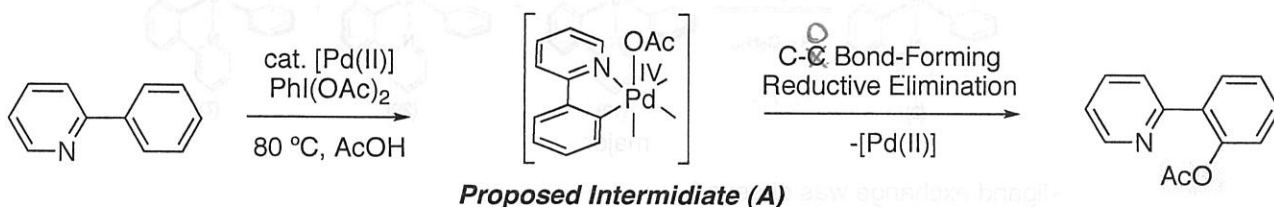
popular belief of Pd(IV) is basis on

- X-ray crystallographic analysis
- Study on reductive elimination

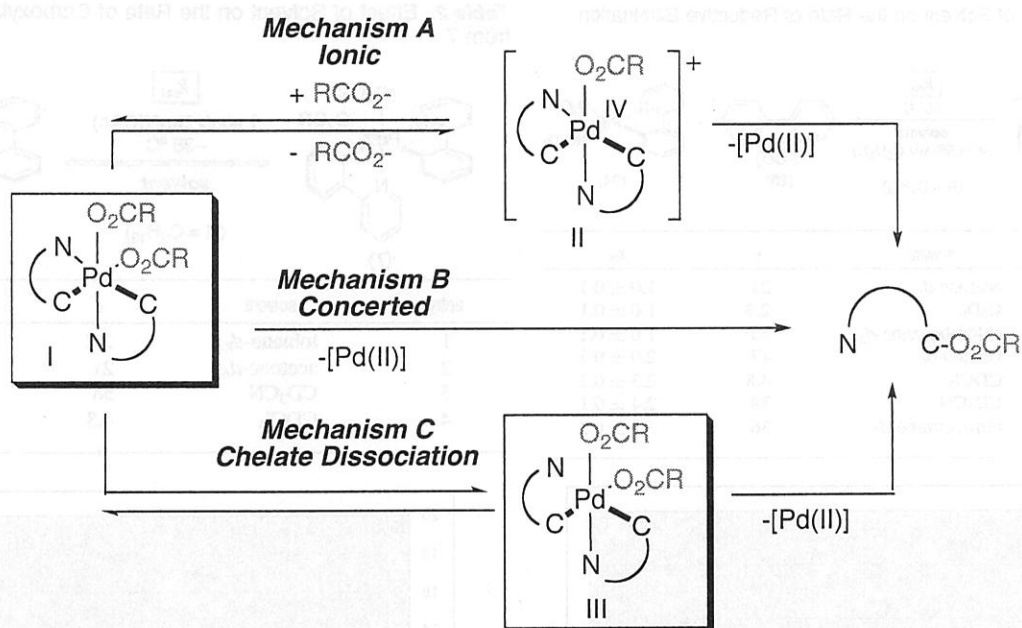
No evidence for Pd(IV) intermediate in catalysis

Detailed Study of C-O and C-C Bond-Forming Reductive Elimination from Stable C₂N₂O₂-Ligated Palladium(IV) Complexes

Joy M. Racowski, Allison R. Dick, and Melanie S. Sanford*



Possible Mechanisms for C-O Bond Forming Reductive Elimination From I



Sanford initial investigations in this area provided preliminary evidence in support of **mechanism C**.

- (i) the absence of a clear correlation between k_{obs} and solvent polarity
 - (ii) the lack of crossover between free and bound carboxylate
 - (iii) the small entropy of activation
 - (iv) the negative ρ value obtained upon substitution of the carboxylate ligand
 - (v) the decreased reaction rate with more rigid N~C ligands.

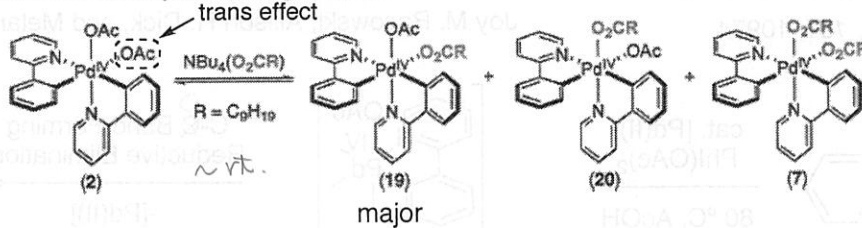
Sanford *et. al.* *J. Am. Chem. Soc.* **2005**, 127, 12790.

In 2008 **mechanism B** was suggested by computational study

mechanism	$\Delta G + \Delta G_{solv}$ (kcal/mol)	
A	31.4	Liu <i>et. al.</i> <i>Organometallics</i> 2008 , 27, 3736. reevaluation these mechanism ⇒ mechanism A is favorable
B	26.4	
C	44.3	

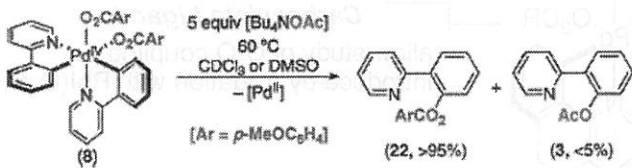
Ligand exchange

Scheme 8. Potential Products of Carboxylate Exchange Reaction

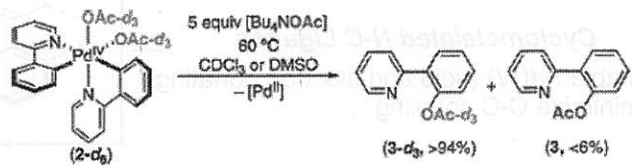


• ligand exchange was observed

Scheme 11. Original Crossover Experiment from Ref 12



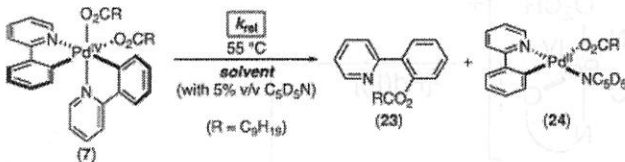
Scheme 12. AcO/AcO-d3 Crossover Experiment



• nonexchangeable carboxylate ligand in the C-O bonding forming reaction

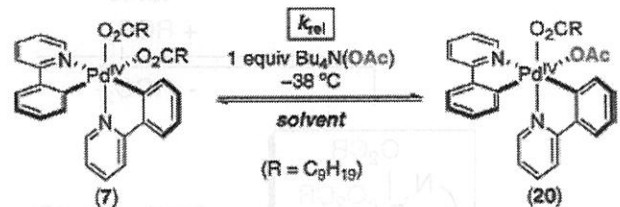
Solvent effect

Table 1. Effect of Solvent on the Rate of Reductive Elimination from 7

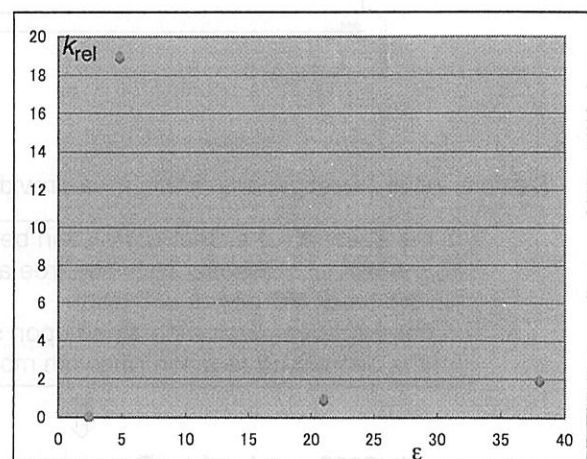
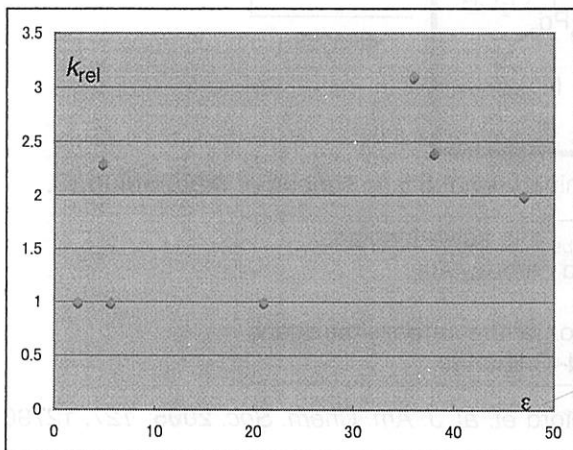


entry	solvent	ϵ	k_{rel}
1	acetone- d_6	21	1.0 ± 0.1
2	C_6D_6	2.3	1.0 ± 0.1
3	chlorobenzene- d_5	5.6	1.0 ± 0.1
4	DMSO- d_6	47	2.0 ± 0.3
5	$CDCl_3$	4.8	2.3 ± 0.2
6	CD_3CN	38	2.4 ± 0.1
7	nitrobenzene- d_5	36	3.1 ± 0.3

Table 2. Effect of Solvent on the Rate of Carboxylate Exchange from 7



entry	solvent	ϵ	k_{rel}
1	toluene- d_8	2.4	<0.1
2	acetone- d_6	21	1.0 ± 0.1
3	CD_3CN	38	2.0 ± 0.2
4	$CDCl_3$	4.8	19 ± 1



low correlation between ϵ and k_{obs} \Rightarrow initially interpreted as a strong evidence against mechanism A

Entropy of Activation

$$\Delta S^\ddagger = -1.4 \pm 1.9 \text{ eu (CDCl}_3\text{)}$$

$$4.2 \pm 1.4 \text{ eu (DMSO-}d_6\text{)}$$

C-Se bond forming reductive elimination from Pd(IV)

$$\Delta S^\ddagger -40 \text{ to } -49 \text{ eu}$$

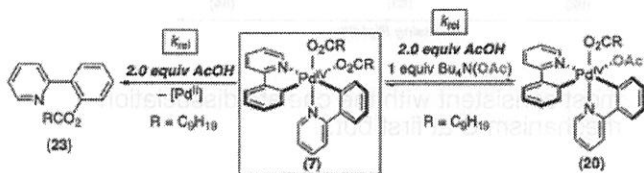
\Rightarrow evidence against mechanism A

Acidic Additives

Both Brønsted and Lewis acid accelerate C-O and C-C bond forming reductive elimination from Pt(IV)

mechanism A

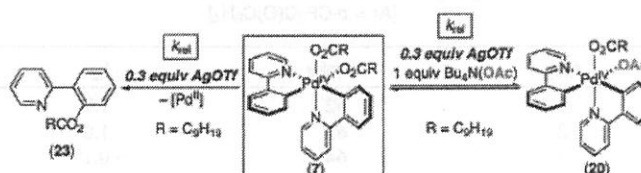
Table 3. Effect of AcOH on C–O Bond-Forming Reductive Elimination and Carboxylate Exchange at 7



entry	acid	k_{rel} C–O coupling	k_{ex} exchange
1	none	1.0 ± 0.0^a	1.0 ± 0.0^b
2	HOAc	3.6 ± 0.2^a	4.5 ± 0.5^b

^a 40 °C in acetone-*d*₆. ^b –35 °C in acetone-*d*₆.

Table 4. Effect of AgOTf on C–O Bond-Forming Reductive Elimination and Carboxylate Exchange at 7



entry	acid	k_{rel} C–O coupling	k_{ex} exchange
1	none	1.0 ± 0.2^a	1.0 ± 0.1^b
2	AgOTf	16 ± 0.8^a	8.7 ± 0.0^b

^a 23 °C in CDCl₃. ^b –53 °C in CDCl₃.

⇒ Carboxylate exchange and C-O bond forming reductive elimination are mechanistically linked as Pt(IV)

Carboxylate Electronic Effects

Scheme 14. C–O Bond-Forming Reductive Elimination from 8–18

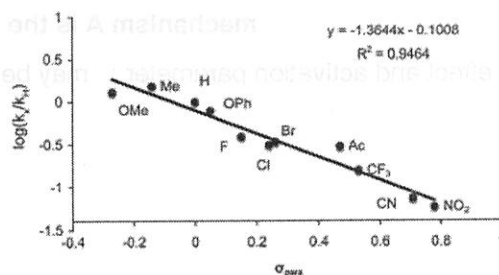
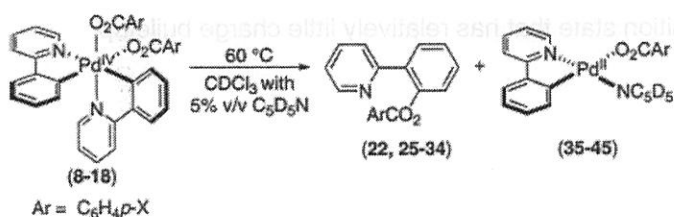


Figure 2. Hammett plot for C–O bond-forming reductive elimination from 8–18.

$\rho \sim -1.36$

ref $\rho = +1.44$ for C-O bond forming reductive elimination from (dppbz)PtMe₃(OAr) (proceeds by mechanism A)

exclude mechanism A at first but...

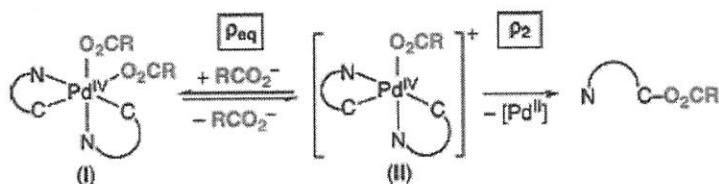


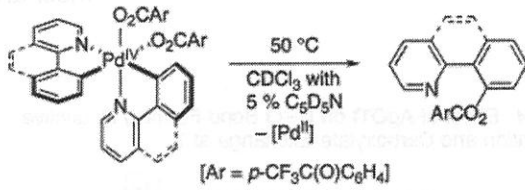
Figure 3. Values of ρ for each step of mechanism A.

$$\rho_{tot} = \rho_{eq} + \rho_2$$

the observed negative value is potentially consistent with any of these pathway (A, B, C)

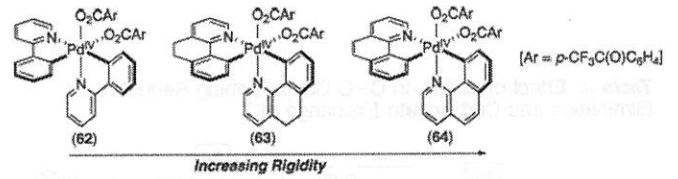
Ligand Rigidity

Table 6. Rate of C–O Bond-Forming Reductive Elimination as a Function of Ligand Rigidity



entry	complex	k_{rel}
1	62	1.9
2	63	1.0
3	64	$\sim 0.1^a$

^a The slow reaction rate along with competing C–C bond-formation prevented quantitative rate measurement in this system.



most consistent with the chelate dissociation mechanism C at first but...

rigid ligands stabilize Pd(IV) complexes



not definitively establish or rule out any of the three mechanistic manifolds

Summary

- the exchange of free and bound carboxylate free and carboxylate at (Phpy)₂Pd^{IV}(O₂CR)₂
- the rate of carboxylate exchange and of C–O coupling are increased to very similar extents upon addition of AcOH and AgOTf



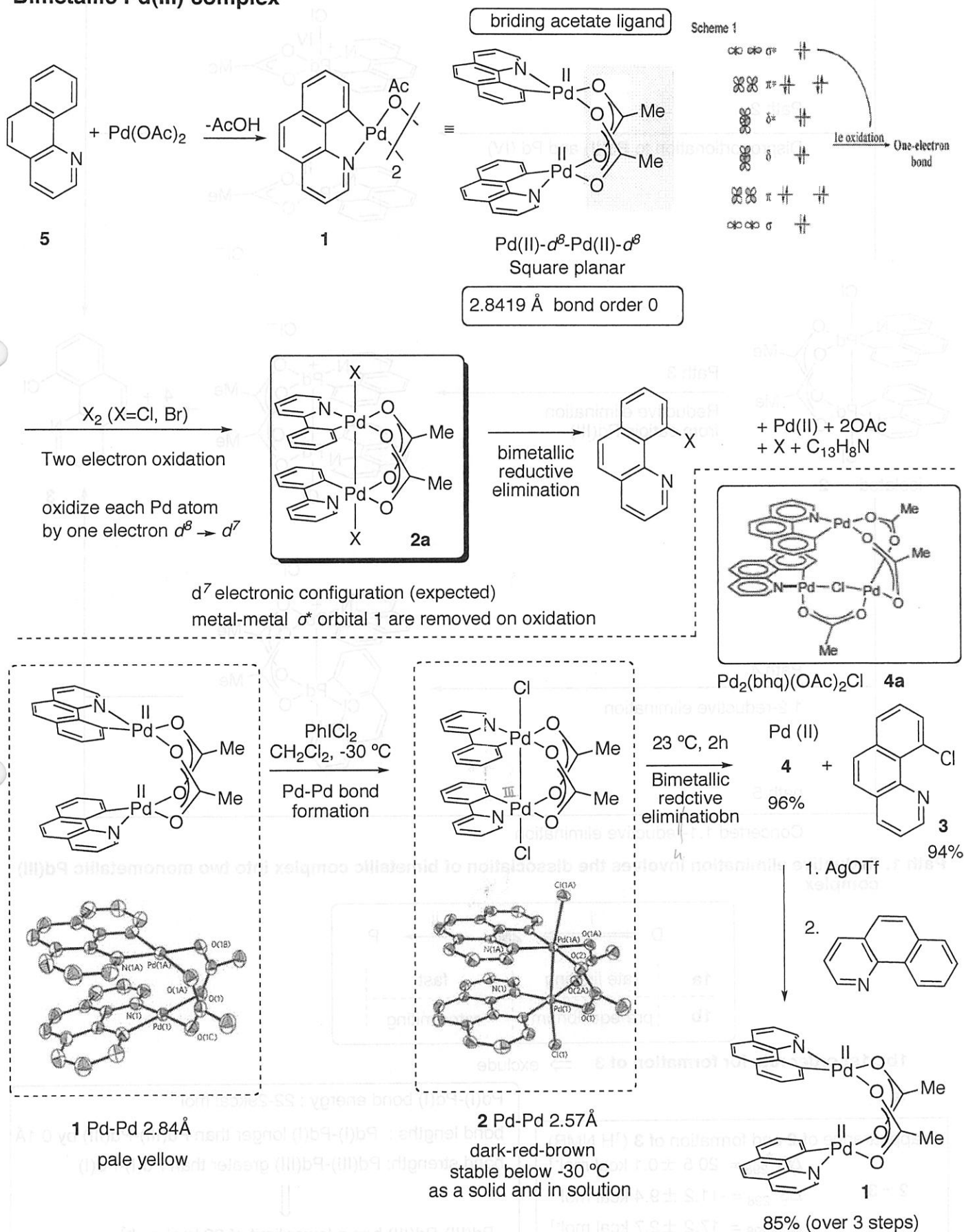
mechanism A is the most favorable

solvent effect and activation parameter : may be transition state that has relatively little charge buildup

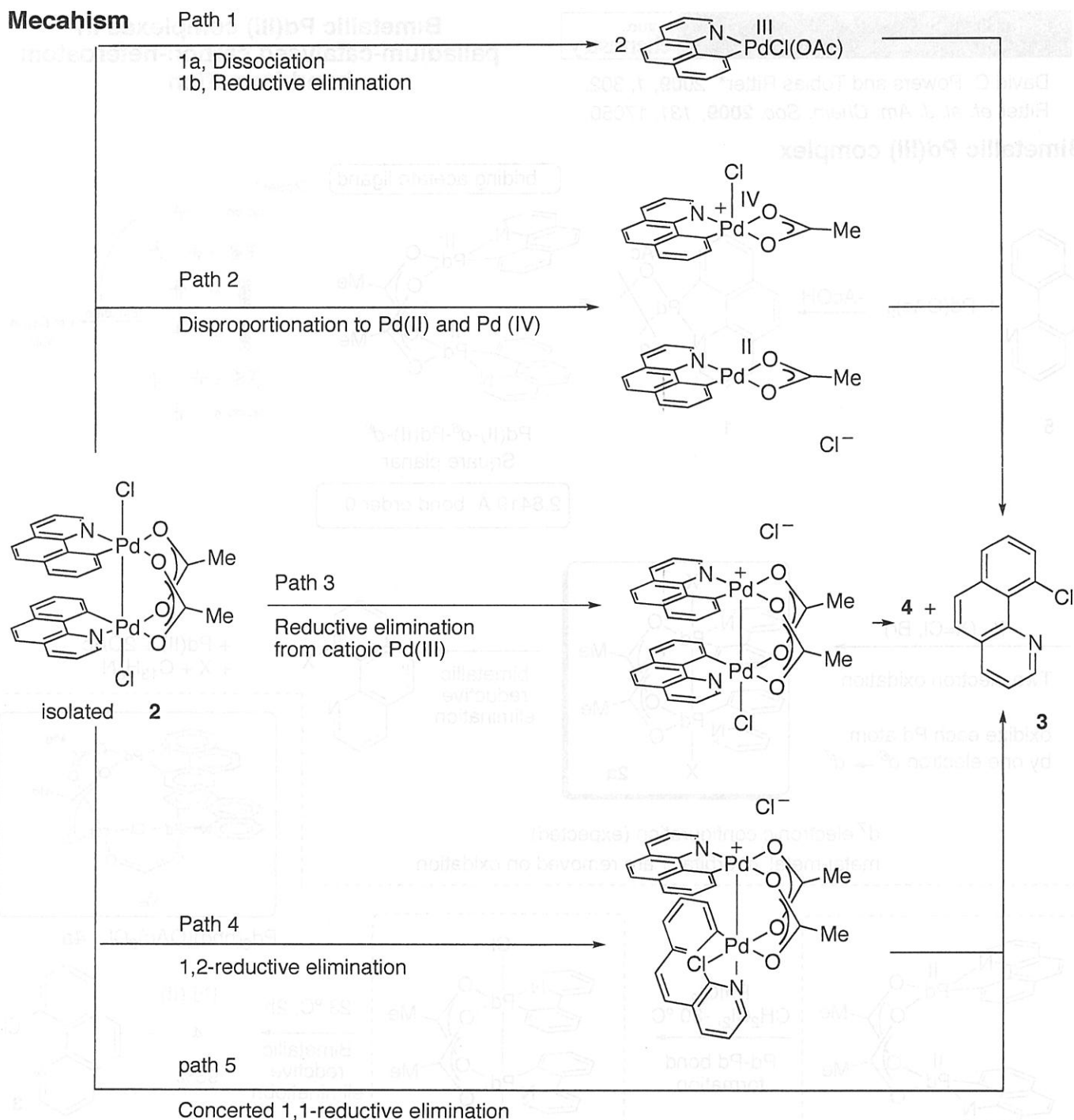
David C. Powers and Tobias Ritter* 2009, 1, 302.

Ritter et al. *J. Am. Chem. Soc.* 2009, 131, 17050.Bimetallic Pd(III) complexes in
palladium-catalysed carbon-heteroatom
bond formation

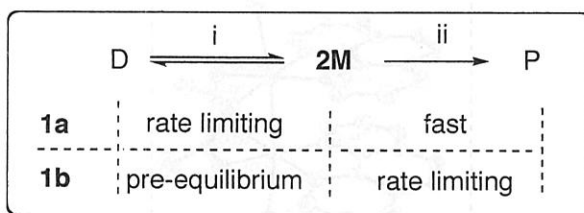
Bimetallic Pd(III) complex



Mechanism



Path 1. Reductive elimination involves the dissociation of bimetallic complex into two monometallic Pd(III) complex



1b : 1st order rate for formation of 3 ⇒ exclude

1a :

disappearance of **2** and formation of **3** (¹H NMR)

2 → 3

$$\Delta G^\ddagger_{298} = 20.5 \pm 0.1 \text{ kcal mol}^{-1}$$

$$\Delta S^\ddagger_{298} = -11.2 \pm 9.4 \text{ kcal mol}^{-1}$$

$$\Delta H^\ddagger_{298} = 17.2 \pm 2.7 \text{ kcal mol}^{-1}$$

Pd(I)-Pd(I) bond energy : 22-29 kcal mol⁻¹

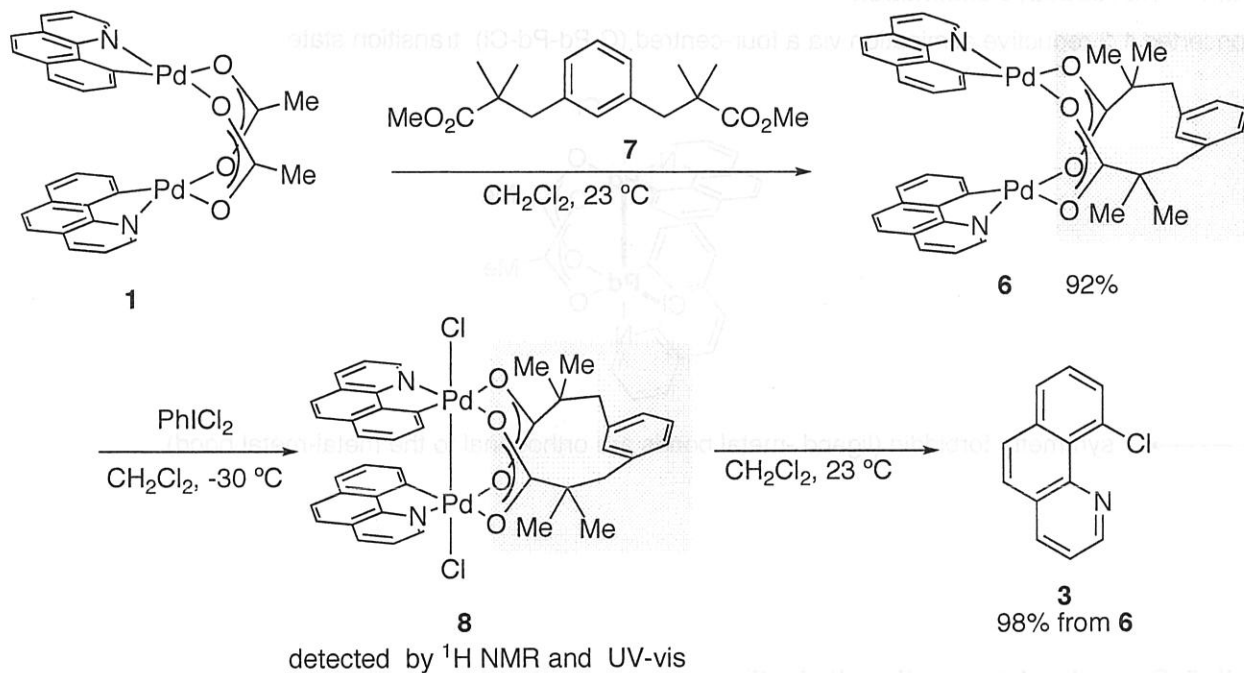
bond lengths : Pd(I)-Pd(I) longer than Pd(III)-Pd(III) by 0.1 Å

bond strength: Pd(III)-Pd(III) greater than Pd(I)-Pd(I)



Pd(III)-Pd(III) has a lower limit of 22 kcal mol⁻¹

stabilization of Pd(III)-Pd(III) with the esp ligand (Du Bis to stabilize bimetallic Rh(II) d^7 complex)



If dissociation of **2** into two monometallic Pd(III) was rds the chelating effect of the esp ligand would result in decreased reaction rate for reductive elimination

equilibrium constant $K = 1.2 \times 10^5$ ($1 + 7 \rightarrow 6 + 2\text{HOAc}$)

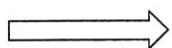
agreement with equilibrium constants determined for isoelectronic bimetallic rhodium complex

If dissociation into two monometallic palladium complex are rds

the rate of the reductive elimination would be at least 12,000 times slower because of chelating effect

↓

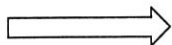
16 times slower (compared with reductive elimination step) inconsistent with the rds dissociation of bimetallic core



Dissociation of **2** into two monometallic Pd(III) complex can therefore be excluded.

Path 2 Disproportionation to Pd(II) and Pd(IV)

bimetallic core of **2** is stable on time scale reductive elimination from **2**

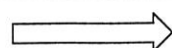


cannot be considered disproportionation into discrete Pd(II) and Pd(IV) complex

Path 3 Reductive elimination from cationic Pd(III)

If either acetate or chloride dissociation from **2** was rds, an inverse rate dependence with increasing ion concentration would be expected.

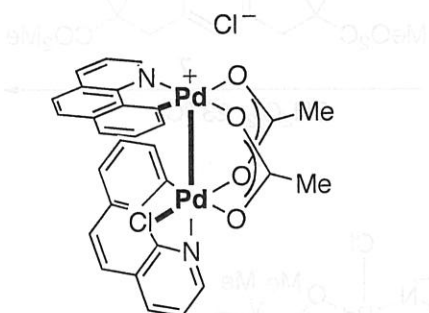
rate of reductive elimination from **2** is independent of chloride concentration ($n\text{-Bu}_4\text{NCl}$ up to 17 mM)
acetate concentration ($n\text{-Bu}_4\text{NOAc}$ up to 12 mM)



rds chloride acetate dissociation followed by reductive elimination from cationic bimetallic palladium intermediate therefore be excluded.

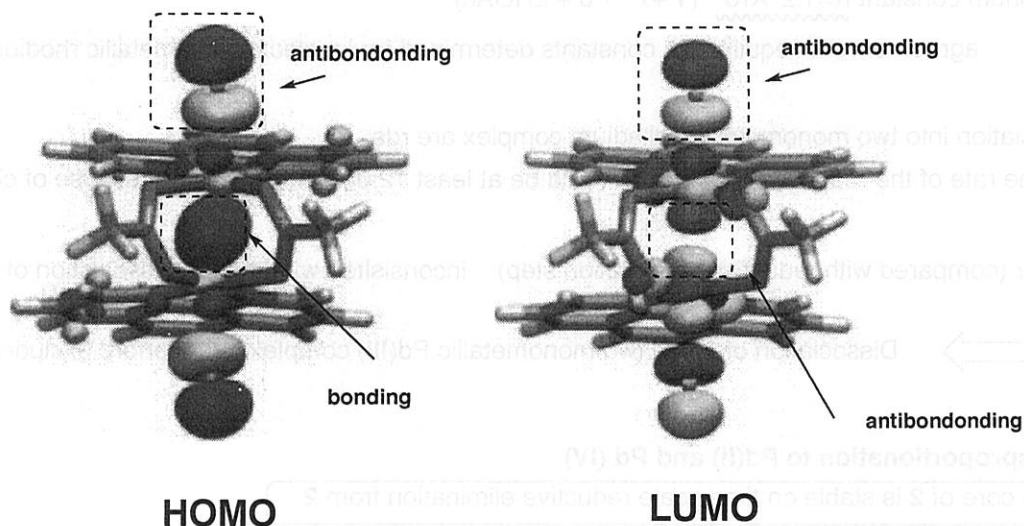
Path 4 1,2-reductive elimination

A concerted 1,2 reductive elimination via a four-centred (C-Pd-Pd-Cl) transition state



→ symmetry forbiddin (ligand -metal bonds are orthogonal to the metal-metal bond)

path 5 Concerted 1,1-reductive elimination



⇒ the obtained mechanistic evidence consistent with a concerted reductive elimination from either a hexa- or penta coordinate palladium of the bimetallic Pd(II) complex

Catalysis

5 is excess with respect to palladium, which could alter the path of reductive elimination from bimetallic complex **2**

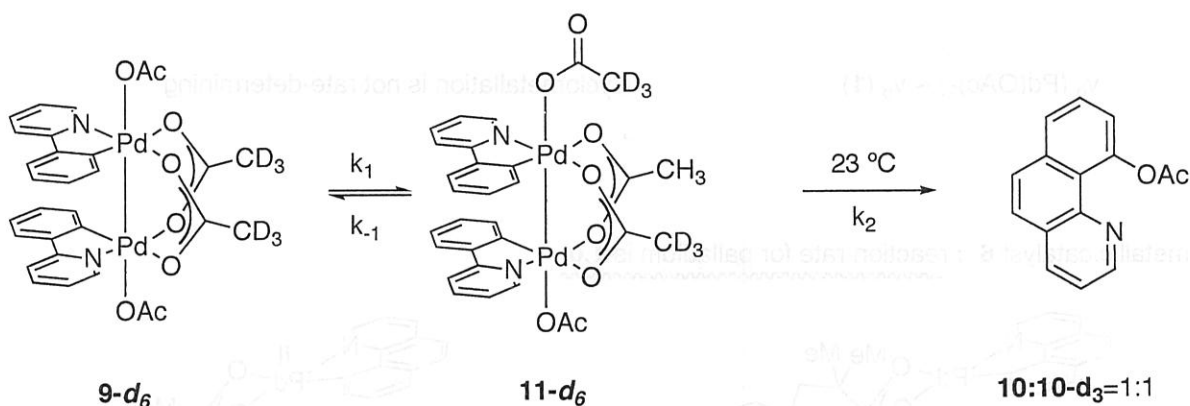
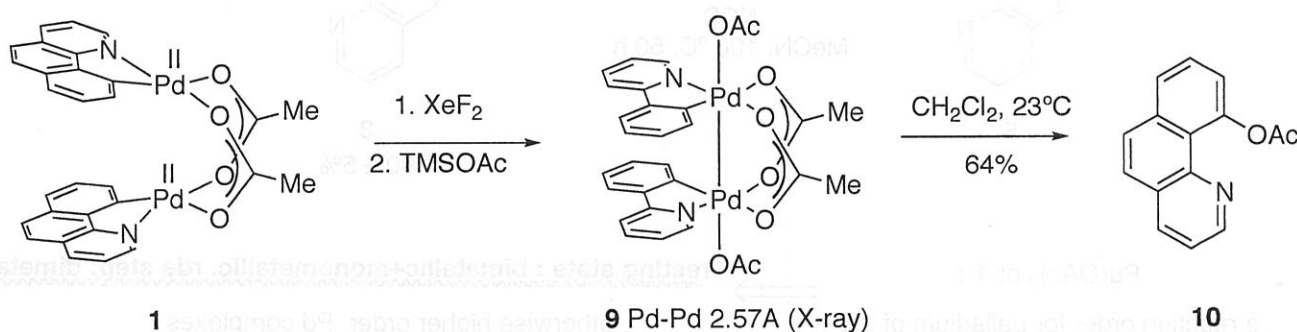
2 is stable towards **5** at -30°C but 1 eq. addition exogenous **5** to **2** have a mark on effect on the activation parameters for reductive elimination to form **3**

$$\begin{aligned} \Delta G^{\ddagger}_{298} &= 20.3 \pm 0.1 \text{ kcal mol}^{-1} \\ \Delta S^{\ddagger}_{298} &= 10.2 \pm 11.4 \text{ kcal mol}^{-1} \\ \Delta H^{\ddagger}_{298} &= 23.4 \pm 3.4 \text{ kcal mol}^{-1} \end{aligned}$$

⇒ { • ligand dissociation from **2** before reductive elimination
• involvement of exogenous **5** in the rds

activation parameter reductive elimination to form **3**

To investigate whether pre-equilibrium dissociation of ligands is operative in bimetallic Pd(III) complexes such as **2**



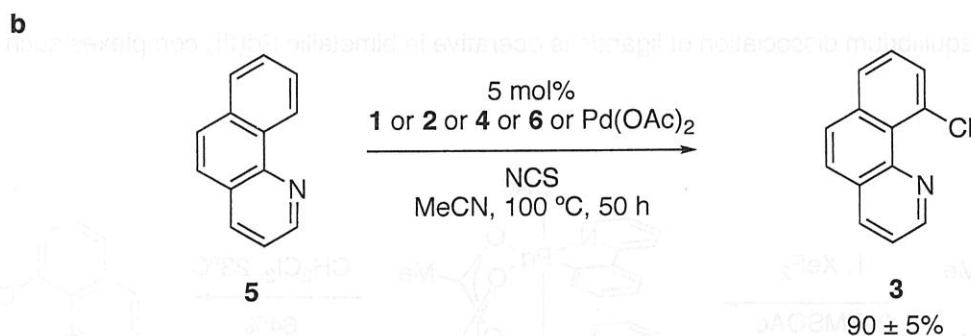
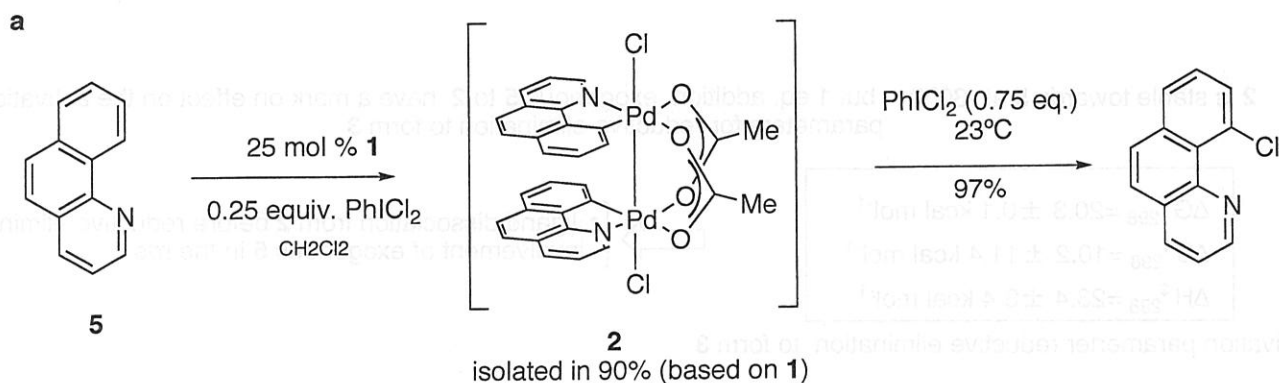
- v (ligand exchange) $>$ v (reductive elimination)
- temp.

 -50°C stable
 -10°C isomerization
 23°C reductive elimination

⇒ (Fast pre-equilibrium ligand dissociation in **2**
The involvement of exogenous **5** in the rate-determining step

⇒ from a bimetallic Pd(III) complex that exhibits one pentacoordinated palladium atom.

To establish whether bimetallic Pd(III)-IPd(III) complex 2 could be formed during catalysis

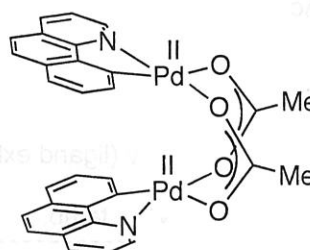
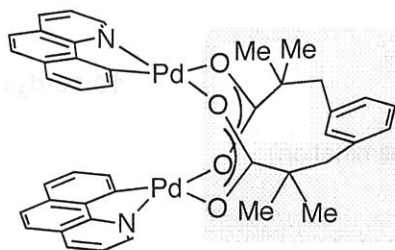


- Pd(OAc)₂ or 1 : \implies resting state : bimetallic+monometallic, rds step: dimetallic
a reaction order for palladium of 1.5 otherwise higher order Pd complexes exclude monometallic Pd(IV) complex

$v_0 (\text{Pd(OAc)}_2) \sim v_0 (1)$

Cyclometallation is not rate-determining

- bimetallic catalyst 6 : reaction rate for palladium is 1.0



¹NMR : no line broadening (80 °C)

The equilibrium constant $K = 1.2 \cdot 10^5$

line broadening

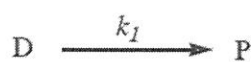
resting state : bimetallic, rds step:bimetallic

-Appendix-

Derivation of Rate Laws (Moore, J.W.; Pearson, R. G. Kinetics and Mechanism. (John Wiley & Sons, Inc., New York 1981))

Resting State	Rate Determining Step	Measured Pd order
D	D	1
M	D	2
D	M	0.5
M	M	1
D+M	M	0.5 - 1
D+M	D	1 - 2

Case #1 Resting State and Rate Determining Step Dimeric:



$$\frac{d[P]}{dt} = k_1[D]$$

If the resting state is dimeric and the rate-determining step is dimeric, the reaction is first-order dependent on palladium concentration. This condition is equivalent to a classic first-order reaction.

Case #2 Resting State Monomeric and Rate Determining Step Dimeric:



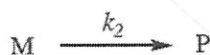
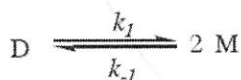
$$\frac{d[P]}{dt} = k_2[D]$$

$$\frac{k_1}{k_{-1}} = K_{eq} = \frac{[D]}{[M]^2}; [D] = K_{eq}[M]^2$$

$$\frac{d[P]}{dt} = k_2 K_{eq} [M]^2 = k[M]^2$$

If the resting state is monomeric and the rate-determining step is dimeric, the reaction is second-order dependent on palladium concentration. This condition is equivalent to a second order reaction in which the two reactants are identical.

Case #3 Resting State Dimeric and Rate Determining Step Monomeric



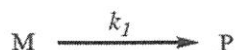
$$\frac{d[P]}{dt} = k_2[M]$$

$$\frac{k_1}{k_{-1}} = K_{eq} = \frac{[M]^2}{[D]}; [M] = \sqrt{K_{eq}[D]}$$

$$\frac{d[P]}{dt} = k_2 \sqrt{K_{eq}[D]} = k\sqrt{[D]}$$

If the resting state is dimeric and the rate-determining step is monomeric, the reaction is half-order dependent on palladium concentration.

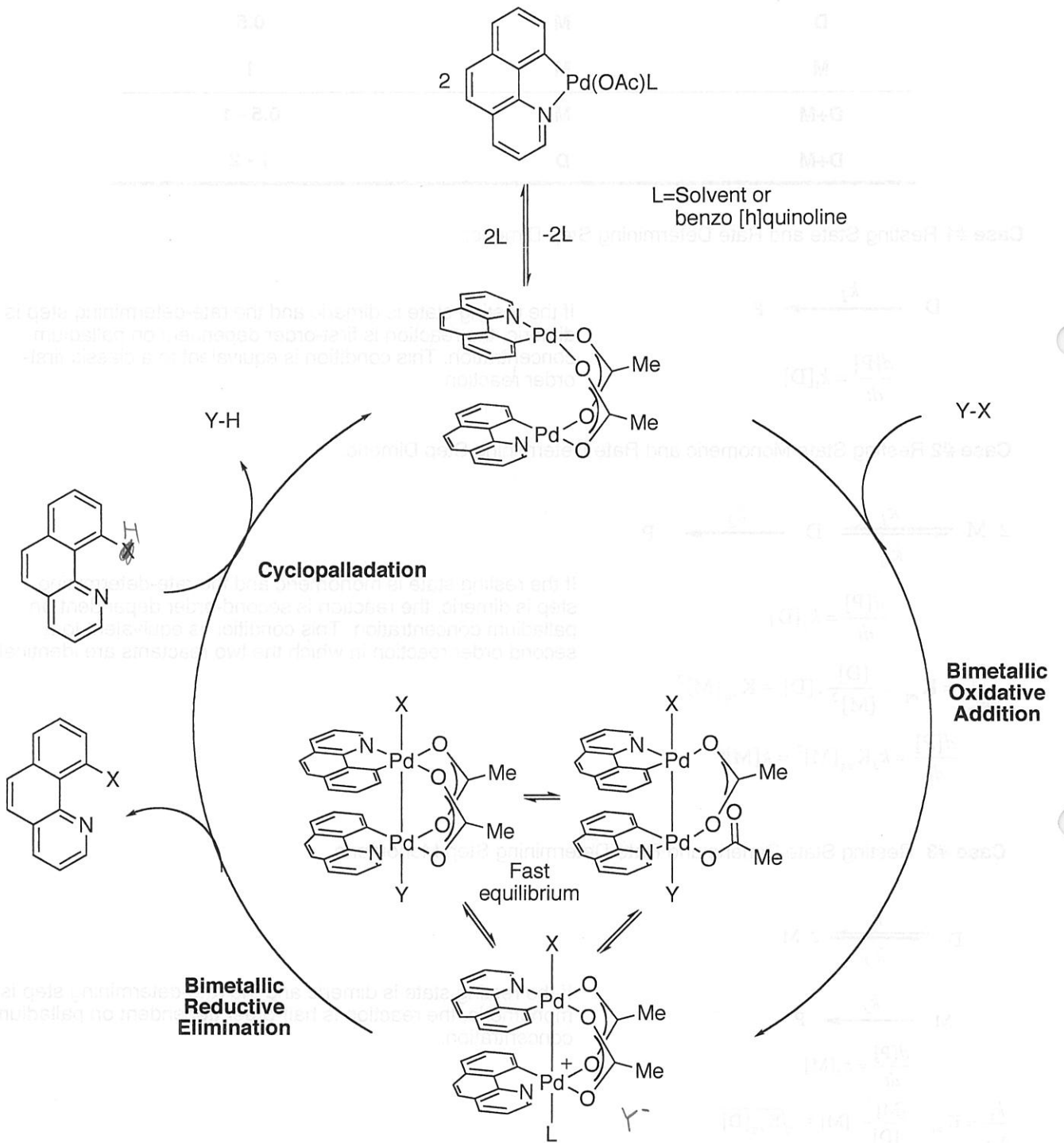
Case #4 Resting State is Monomeric and Rate Determining Step is Monomeric

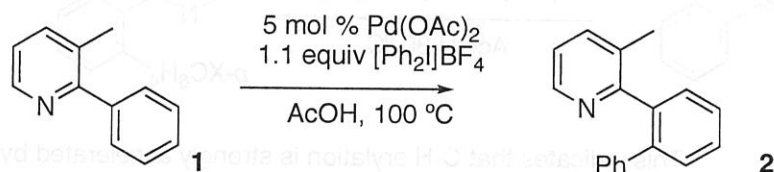


$$\frac{d[P]}{dt} = k_1[M]$$

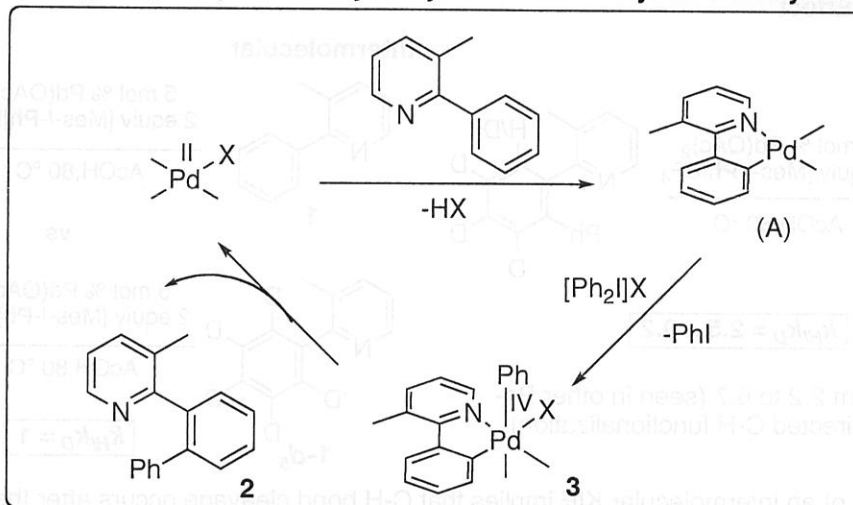
If the resting state is monomeric and the rate-determining step is monomeric, the reaction is first-order dependent on palladium concentration. This condition is equivalent to a classic first-order reaction.

Proposed Mechanism





Scheme 1 Originally Proposed Catalytic Cycle for Pd Catalyzed C-H Arylation



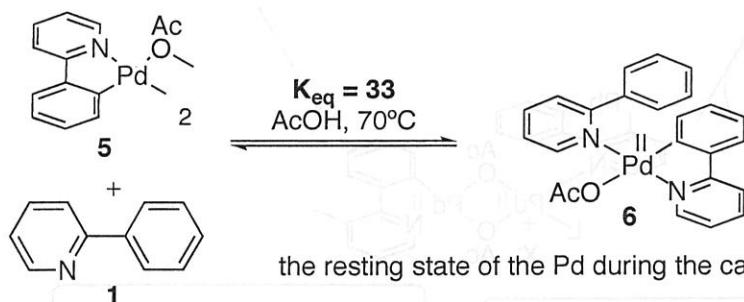
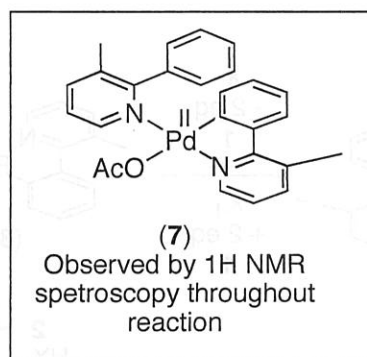
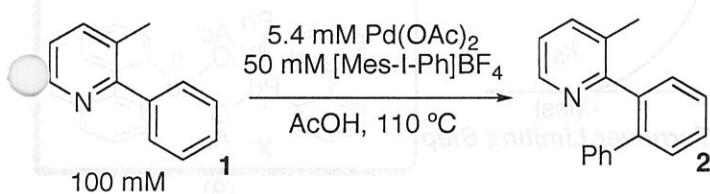
1) Kinetic order

1st order on [I(III)],
2nd order on [Pd],
inverse 3rd on [1]



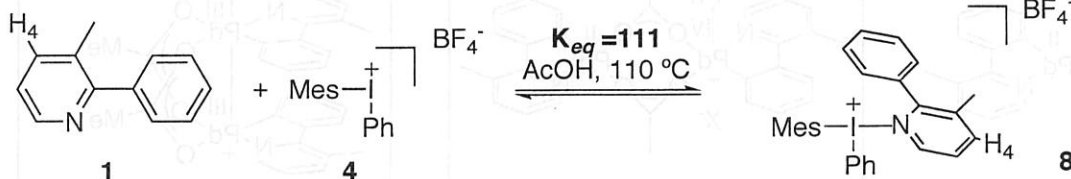
I(III) involved in the turnover-limiting step
involved in the turnover-limiting step
3 equiv of **1** must be lost in order to progress from the resting state to the transition state

2-1) Resting state of the catalyst

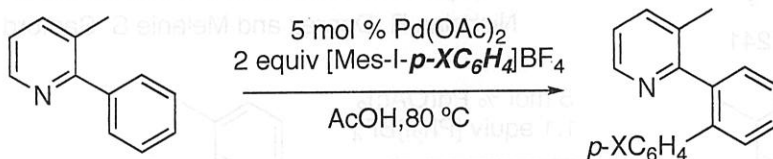


(Ryabov, A. D. *Inorg. Chem.* **1987**, 26, 1252)

2-2) Resting state of iodonium



3) Hammett Study

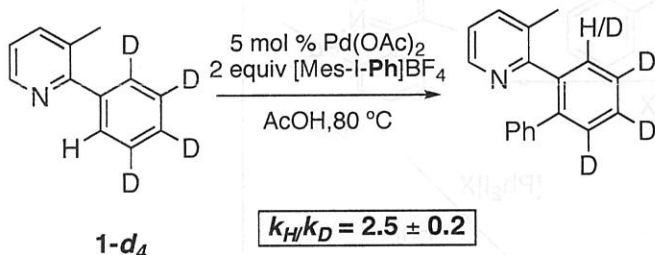


value of $+1.7 \pm 0.2$

This indicates that C-H arylation is strongly accelerated by electronwithdrawing groups on the iodine(III) reagent

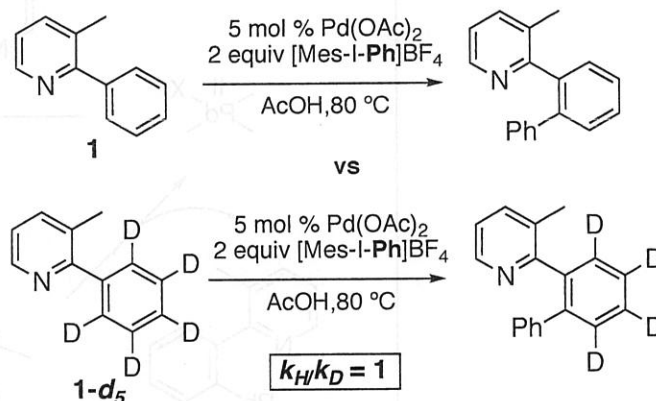
4) Kinetic Isotope Effect

Intramolecular



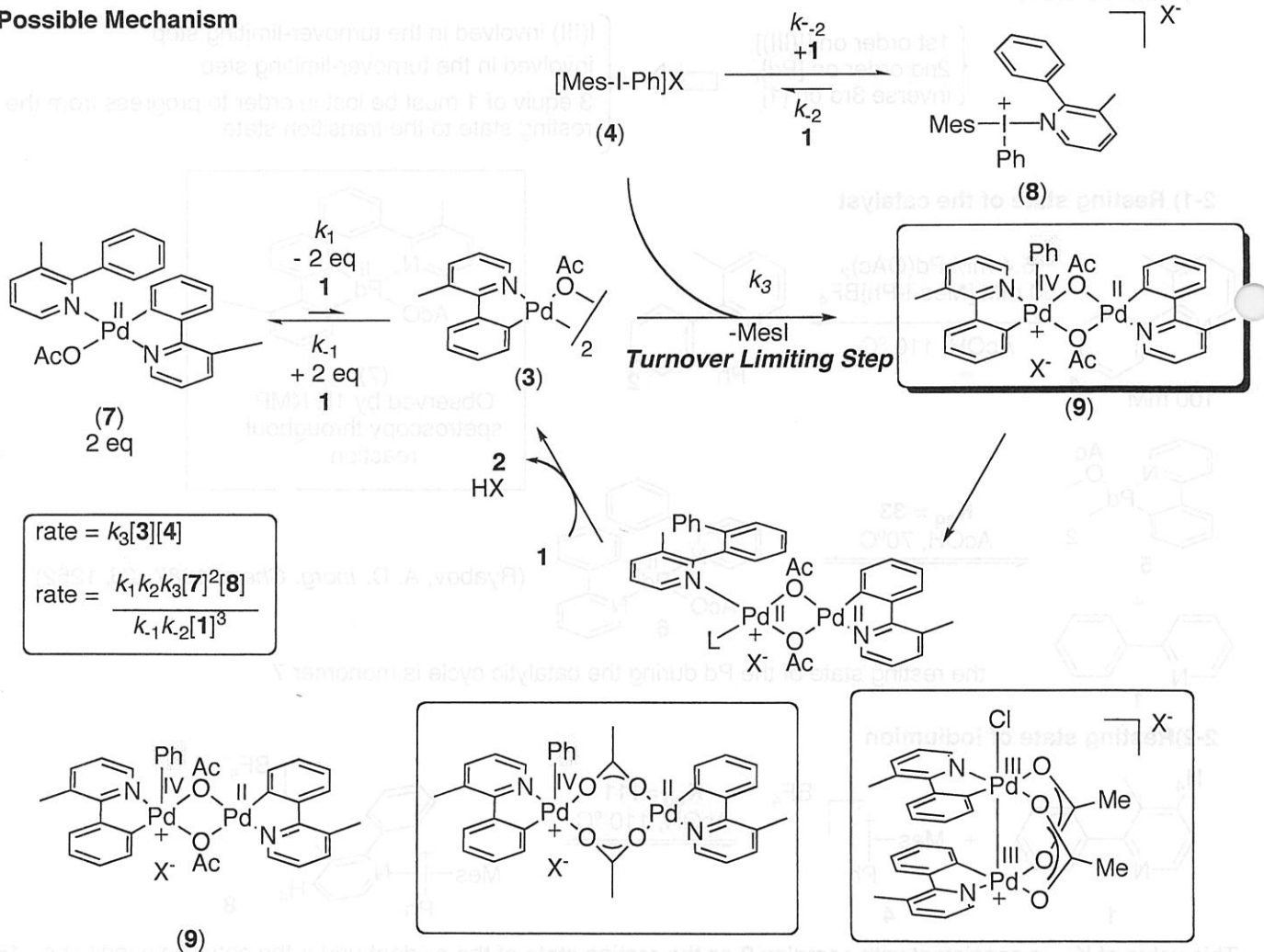
values ranging from 2.2 to 6.7 (seen in other Pd-catalyzed ligand-directed C-H functionalization)

Intermolecular



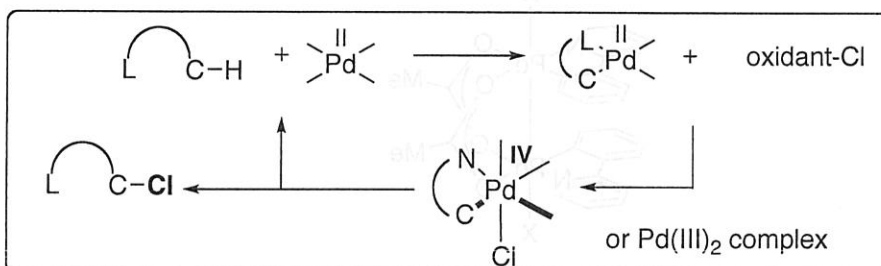
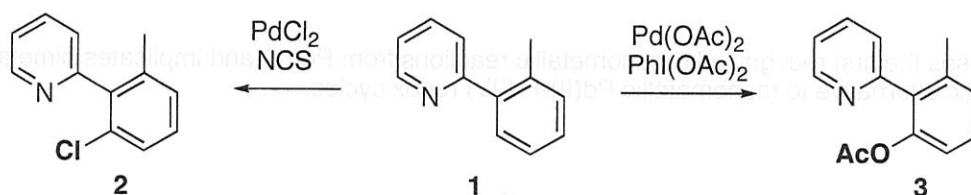
The observed lack of an intermolecular KIE implies that C-H bond cleavage occurs after the rate-determining step of the reaction.

Possible Mechanism



Mechanistic Comparison between Pd-Catalyzed Ligand-Directed C-H Chlorination and C-H Acetoxylation

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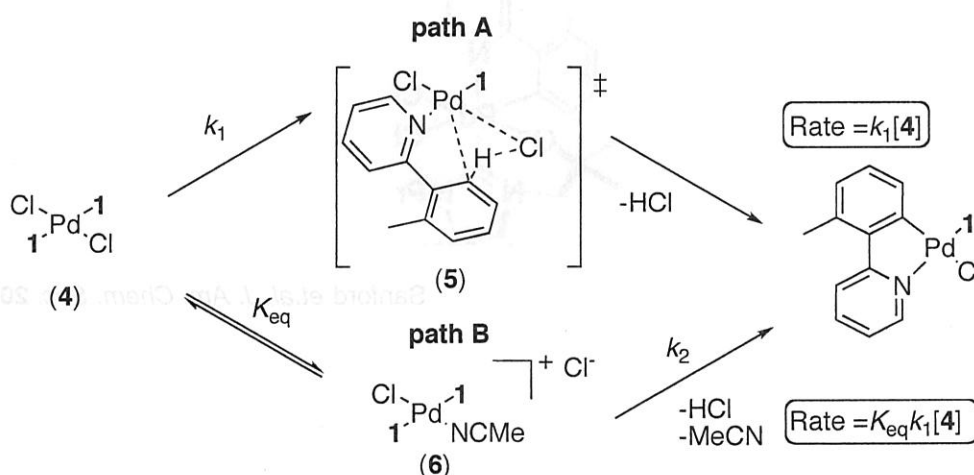


C-H Chlorination

$k_H/k_D = 4.4 \pm 0.2$ (Intermolecular)

0 order on [oxidant] 1st order on [Pd] 0 order on [1]
hammett -0.43

turnover-limiting cyclopalladation

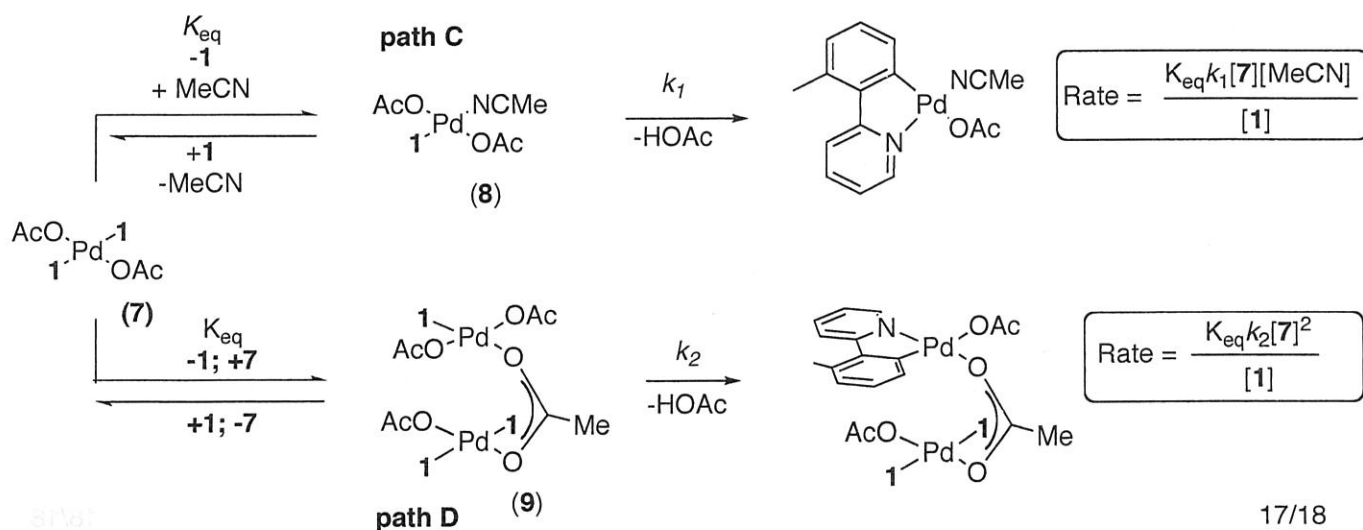


C-H Acetoxylation

$k_H/k_D = 4.3 \pm 0.5$ (Intermolecular)

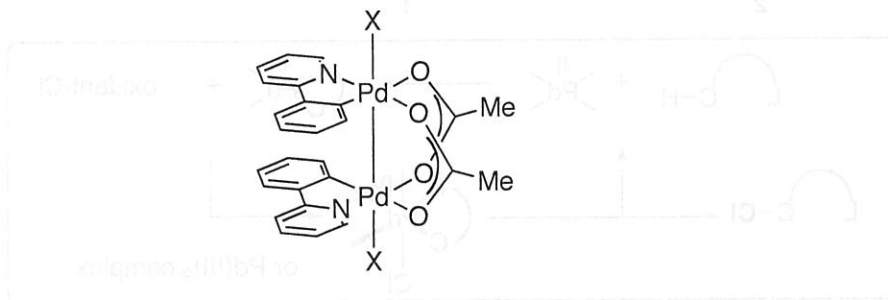
0 order on [oxidant] 1.5 ± 0.2 order on [Pd] inverse 1st order on [1]
hammett +0.89

turnover-limiting cyclopalladation

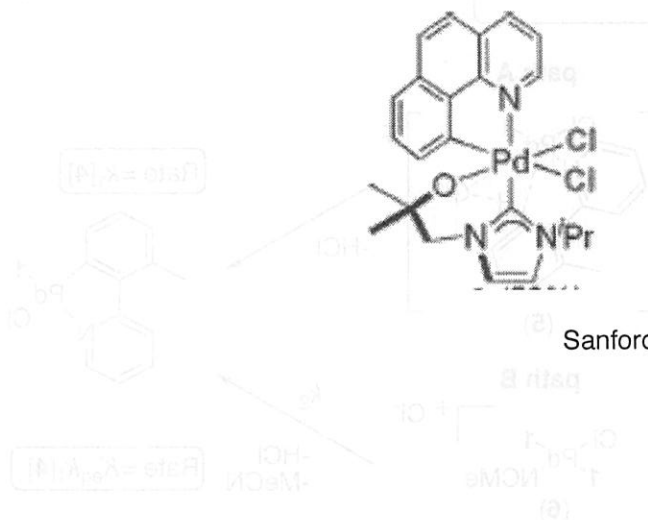


Summary

Ritter discloses the first recognized organometallic reactions from Pd(III) and implicates bimetallic Pd(III) catalysis as a mechanistic alternative to monometallic Pd(II)-Pd(IV) redox cycles.



Pd(IV) : Recently stable Pd(IV) complexes have been synthesized and isolated. Mechanistic analysis allow further mechanical investigation.



Sanford et.al. *J. Am. Chem. Soc.* **2009**, *131*, 13912.

