

*Preparation  
and structure*

*C-C bond  
formation*

# Organopalladium(IV) Chemistry

*C-X bond  
formation*

*sp<sup>2</sup>/sp<sup>3</sup> C-H  
bond activation*

Jingyu Hu  
2014/8/18

# Contents

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**1. Background**

**2. Characterizations**

**3. Reactions**

**3.1 C-C bond construction**

**3.2 C-X bond construction**

**4. Outlooks**

# Contents

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## 1. Background

## 2. Characterizations

## 3. Reactions

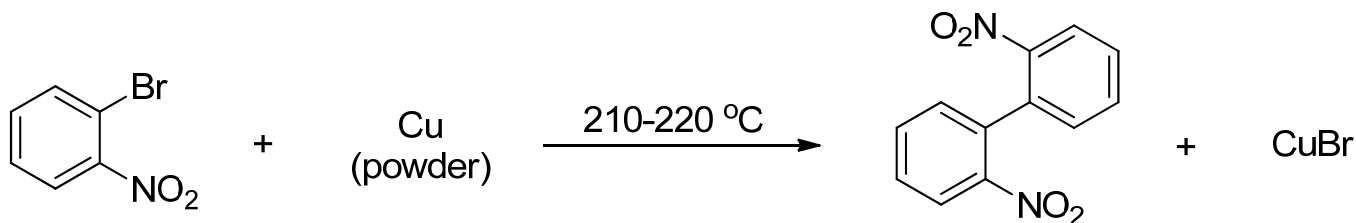
### 3.1 C-C bond construction

### 3.2 C-X bond construction

## 4. Outlooks

# Background

- Fritz Ullmann (1901), discovery of the Cu-mediated coupling reaction.



Ullmann, F. *Chem. Ges.* **1901**, 34,2174.

- Well-defined palladium-catalyzed cross-coupling reactions were first developed in the 1970s, and they quickly surpassed copper-based methods in both scope and popularity.

# Background

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“ For palladium-catalyzed cross couplings in organic synthesis.”



Akira Suzuki



Ei-ichi Negishi

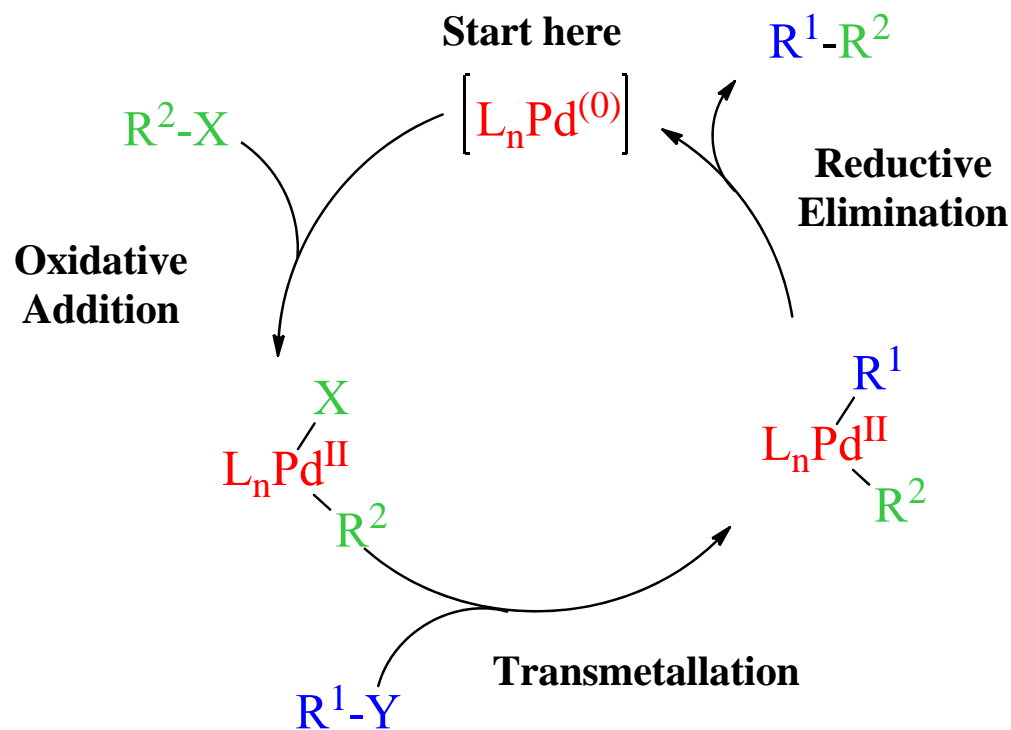


Richard F. Heck

The wide-ranging impact of the palladium-based methodology was recognized in the awarding of the Nobel Prize in Chemistry in 2010.

# Background

## Pd<sup>0/II</sup> Catalytic Cycle

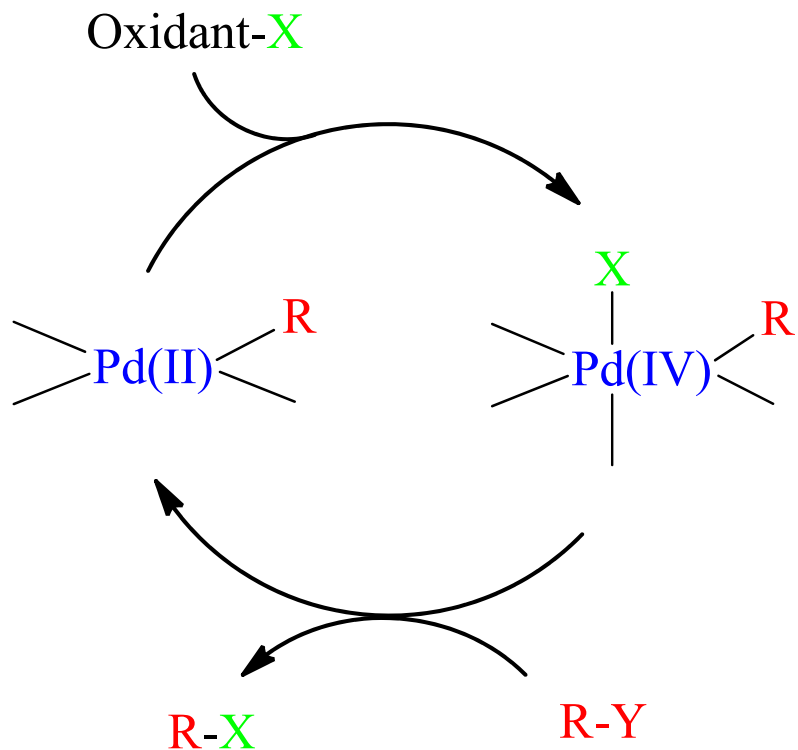


### Limitations:

1. Limited reactivity to forming certain important types of chemical bond (for example C-X and C-CF<sub>3</sub> linkages).
2. High susceptibility to decomposition pathways such as  $\beta$ -hydride elimination

# Background

## Pd(II)/Pd(IV) Catalytic Cycle



R-Y, organic substrate

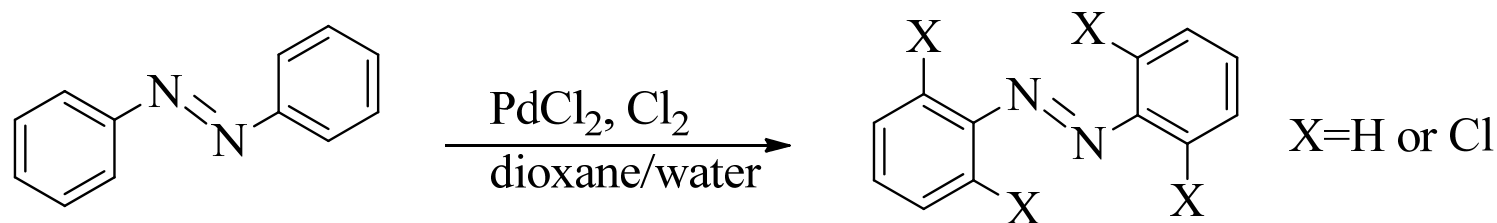
X, new functional group being introduced

Whether Pd(IV) intermediates really exist and can they overcome the limitation of low-valent palladium catalyzed cross-coupling reactions?

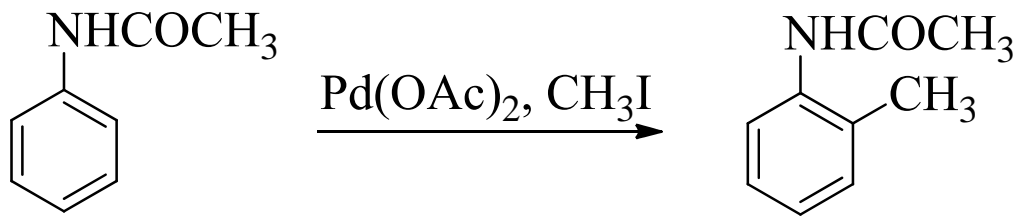


# Background

Sporadic reports over the past 50 years have proposed the intermediacy of Pd(IV) in catalysis.



Darryl R. Fahey. *J. Organometal. Chem.* **1971**, 27, 283.



Samuel J. Tremont. *J. Am. Chem. Soc.* **1984**, 106, 5759.

## Key Challenge:

Determine whether it was possible to form, detect and isolate Pd(IV) complexes from the reactions of Pd(II) precursors with oxidants.



# Contents

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**1. Background**

**2. Characterizations**

**3. Reactions**

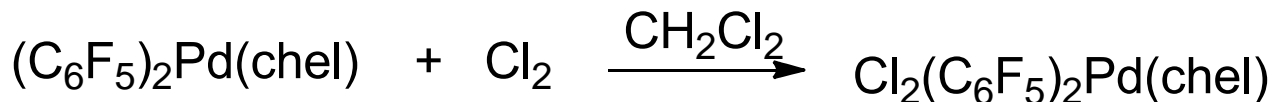
**3.1 C-C bond construction**

**3.2 C-X bond construction**

**4. Outlooks**

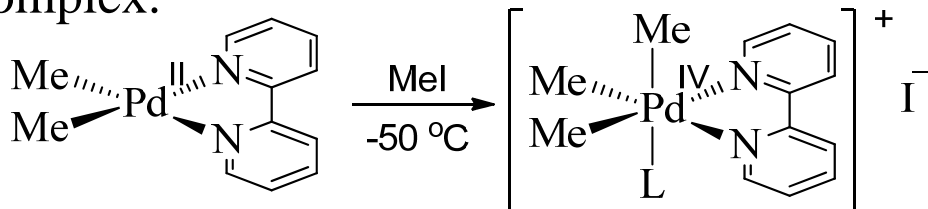
# Characterizations

- In 1975, the very first Pd<sup>IV</sup> compounds containing a Pd-C bond was synthesized, but little attention was paid to them.

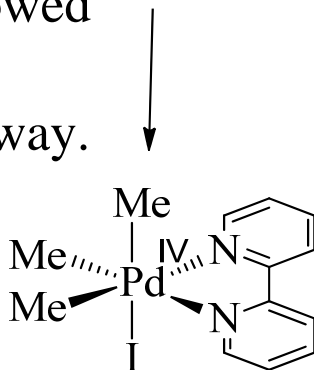


R. Uson, *J. Organomet. Chem.* **1975**, 96, 307.

- In 1986, the first single-crystal X-ray structure of a palladium(IV) complex.



- In situ <sup>1</sup>H NMR studies showed the oxidative addition went through a general S<sub>N</sub>2 pathway.

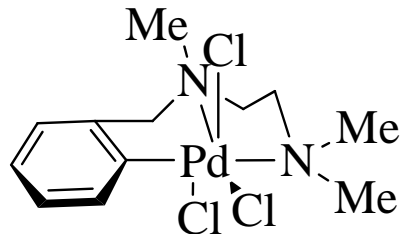


**Allan. J. Canty**  
**The pioneer**

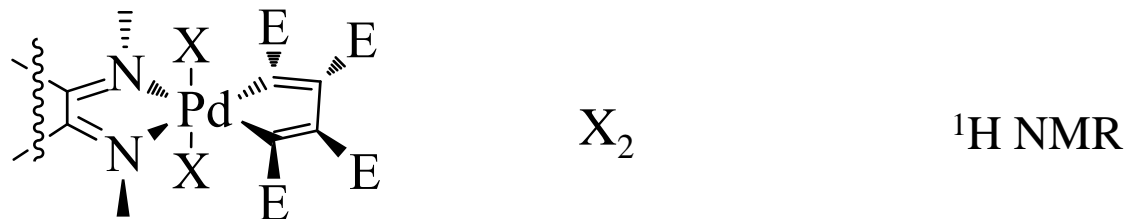
A. J. Canty, *J. Chem. Soc., Chem. Commun.*, **1986**, 1722.

# Characterizations

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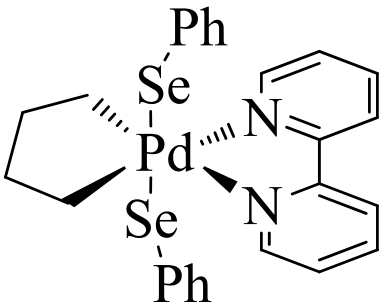
Compound	Oxidant	Characterization	Remarks
	$\text{Cl}_2$	$^1\text{H NMR}$	Too unstable to other characterization.

G. van Koten, *Organometallics*, **1993**, *12*, 1831.



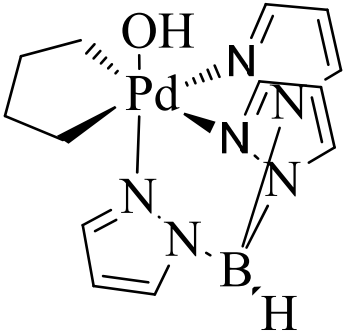
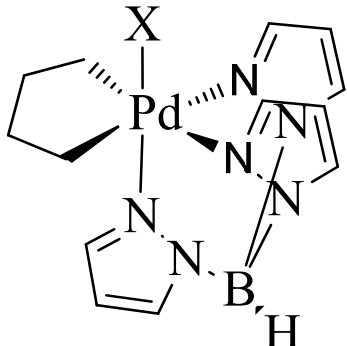
C. J. Elsevier, *Angew. Chem. Int. Ed. Engel.*, **1997**, *36*, 1743.

# Characterizations

Compound	Oxidant	Characterization	Remarks
$\text{PdMe}_2(\text{O}_2\text{CPh})_2(\text{bpy})$	$(\text{O}_2\text{CPh})_2$	$^1\text{H}$ NMR	The incorporation of heteroatoms in the Pd(IV) complexes is important since it provides opportunities for the study of C-hetero-atom formation by reductive elimination
$\text{PdMe}_2(\text{SPh})_2(\text{bpy})$	$(\text{SPh})_2$	$^1\text{H}$ NMR	
	$(\text{SePh})_2$	$^1\text{H}$ NMR X-ray Analysis	

A. J. Canty, *Inorg. Chem.*, **1998**, 3758.

# Characterizations

Compound	Oxidant	Characterization	Remarks
	$\text{H}_2\text{O}_2$ or $\text{H}_2\text{O}$	$^1\text{H}$ NMR X-ray Analysis	Low reductive potential of Pd(II) complexes, which were supported by the high electron donating alkyl and TP group.
	$\text{X}_2$	$^1\text{H}$ NMR X-ray Analysis	

A. J. Canty, *Organometallics*, **1996**, 5713.

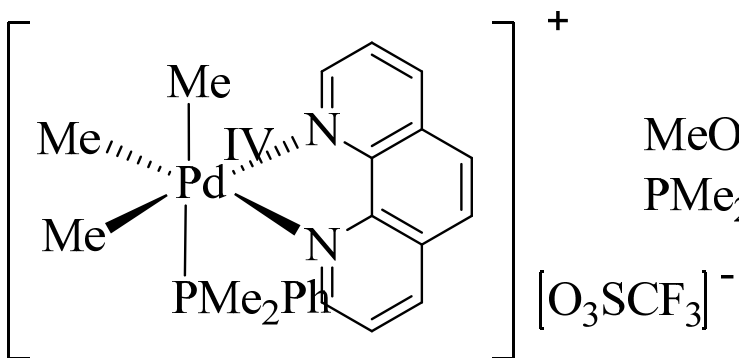
# Characterizations

**Compound**

**Oxidant**

**Characterization**

**Remarks**

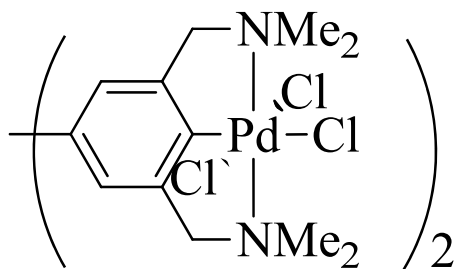


MeOTf  
PMe<sub>2</sub>Ph

<sup>1</sup>H NMR / <sup>13</sup>P NMR

The first mono-dentate phosphine supported cationic organopalladium complex was isolated and structurally determined.

A. J. Canty. *J. Organometal. Chem.* **2000**, 595, 296.



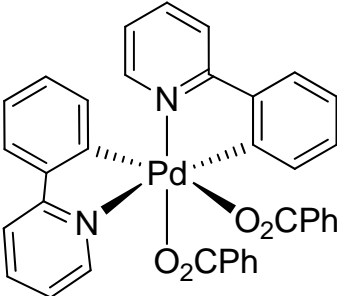
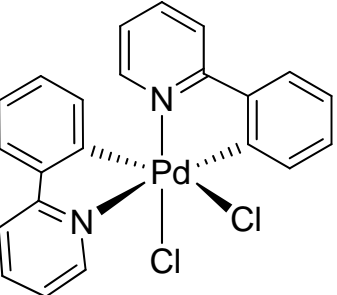
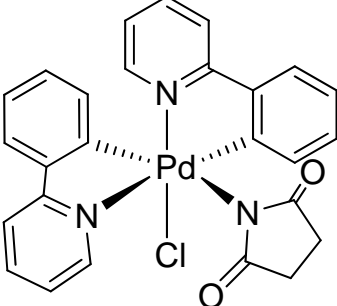
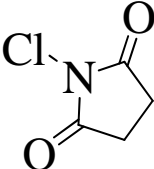
PhICl<sub>2</sub>

<sup>1</sup>H NMR

The first reported complex being oxidized by PhICl<sub>2</sub> but relatively unstable decomposed in a few minutes.

G. van Koten, *Organometallics*, **1998**, 17, 731.

# Characterizations

Compound	Oxidant	Characterization	Remarks
	PhI(O <sub>2</sub> CPh)		
	PhICl <sub>2</sub>	<sup>1</sup> H NMR X-ray analysis	Stable at room temperature.
			

M. S. Sanford, *J. Am. Chem. Soc.* **2007**, *129*, 15142.

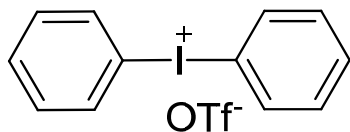
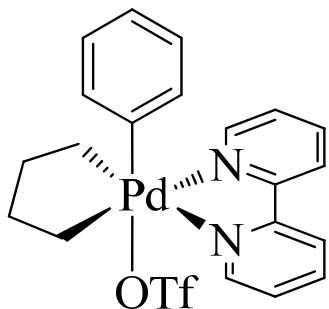
# Characterizations

Compound

Oxidant

Characterization

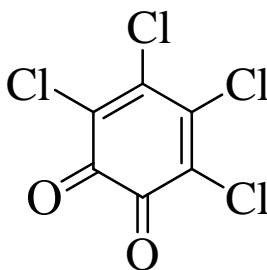
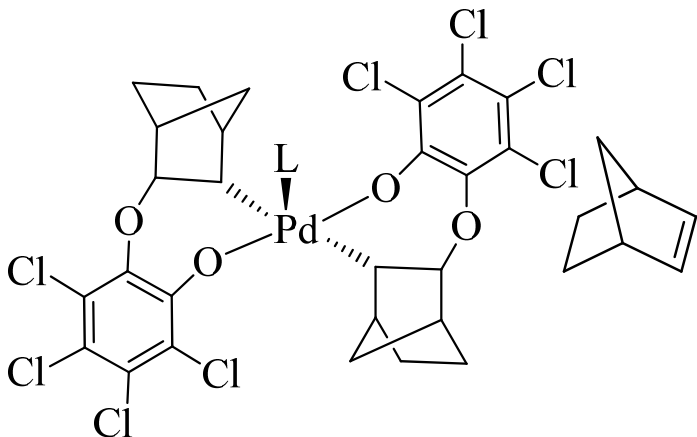
Remarks



$^1\text{H}$  NMR

First example to oxidize Pd(II) complex to Pd(IV) by diphenyliodonium(III) Triflate.

A. J. Canty, *Organometallics*, **2004**, 23, 3466.



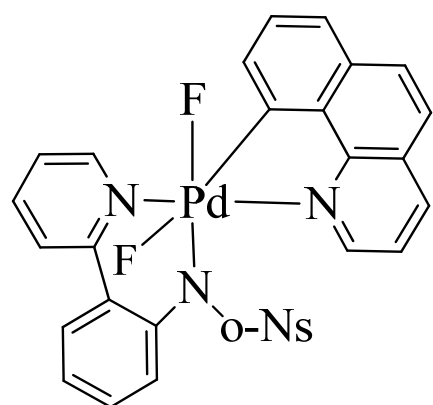
$^1\text{H}$  NMR  
XRD

First example to produce a Pd(IV) complex directly from a Pd(0) species.

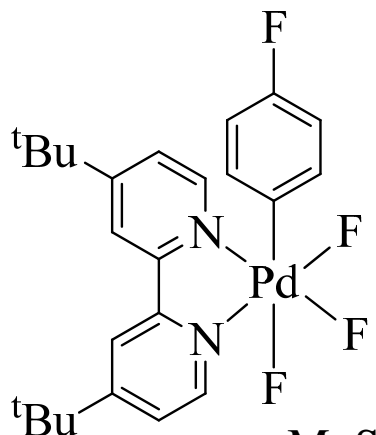
Y. Yamamoto, *Angew. Chem. Int. Ed.*, **2002**, 41, 3662.



# Characterizations

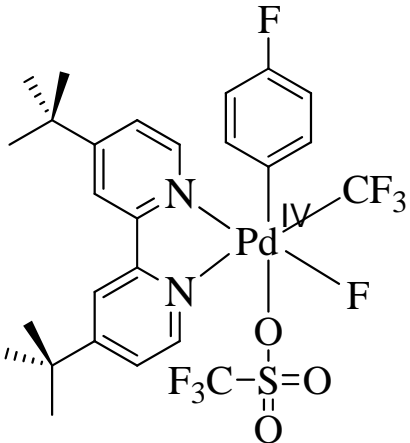
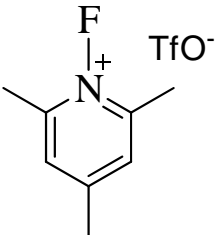
Compound	Oxidant	Characterization	Remarks
	Selectfluor then Me <sub>4</sub> NF or XeF <sub>2</sub>	<sup>1</sup> H NMR X-ray analysis	

T. Ritter. *J. Am. Chem. Soc.* **2008**, *130*, 10060.

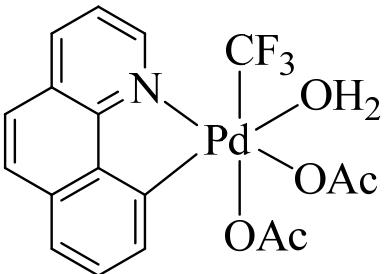
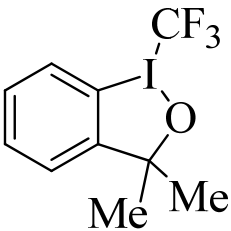
	XeF <sub>2</sub>	<sup>1</sup> H NMR ,XRD	
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M. S. Sanford, *J. Am. Chem. Soc.*, **2009**, *131*, 3796.

# Characterizations

Compound	Oxidant	Characterization	Remarks
		$^1\text{H NMR}$ , XRD	

M. S. Sanford, *J. Am. Chem. Soc.*, **2010**, *132*, 2879.

		$^1\text{H NMR}$ , XRD	
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M. S. Sanford, *J. Am. Chem. Soc.*, **2010**, *132*, 14685.

# Characterizations

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## Summary

1. Various oxidants such as dihalogens, peroxides, alkyl halides, hypervalent iodine(III), can be used to produce Pd(IV) complexes.
2. Strong  $\sigma$ -donor alkyl ligands and chelating nitrogen ligands can be used to stabilize the Pd(IV) complexes.
3. The high electron donating alkyl and other group can support the low reductive potential of the Pd(II) complexes.
4. More sterically hindered ligands will destabilize the Pd(IV) complexes, and promotes the reductive elimination process, which might be useful in its reaction applications.

# Contents

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**2. Characterizations**

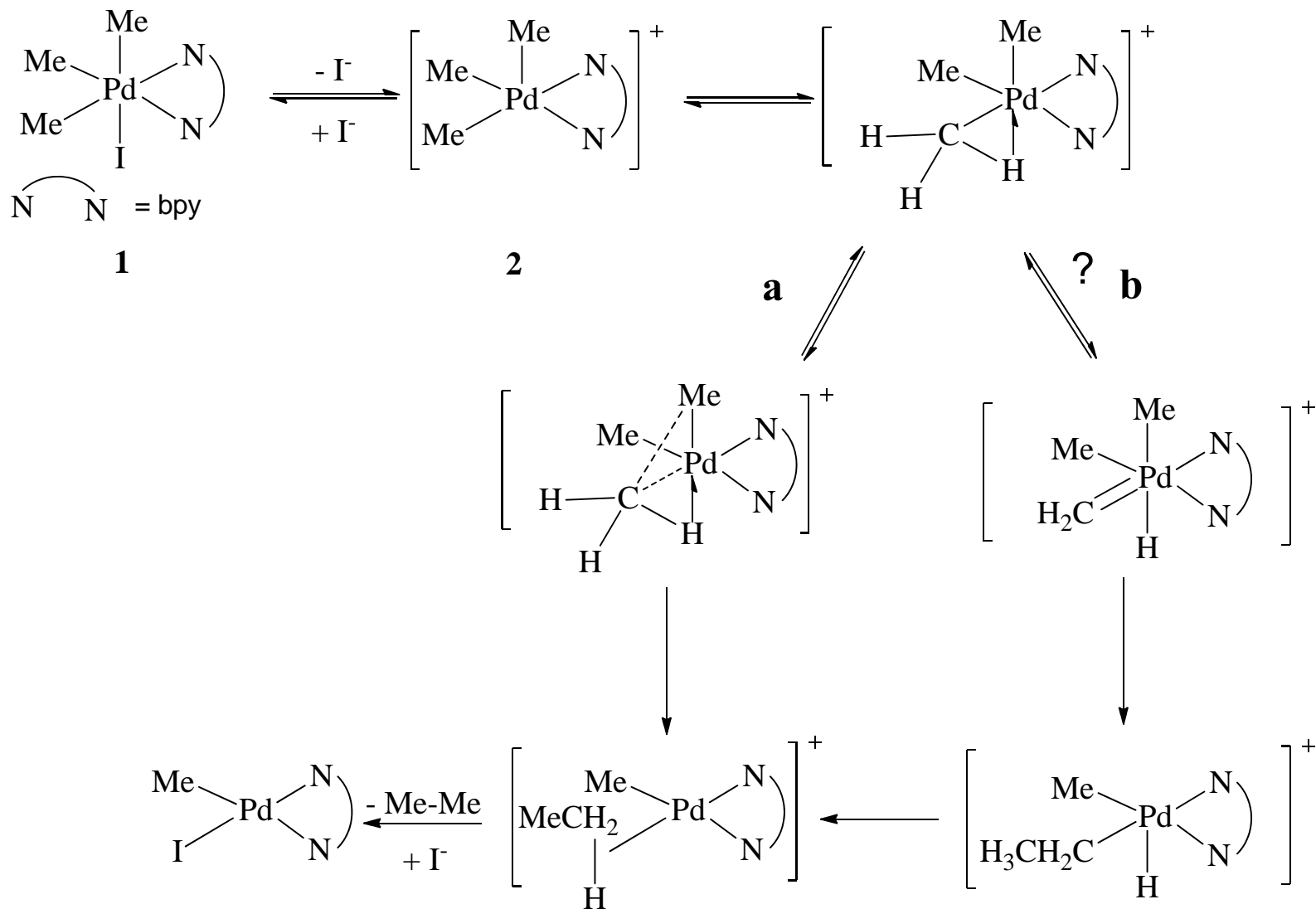
**3. Reactions**

**3.1 C-C bond construction**

**3.2 C-X bond construction**

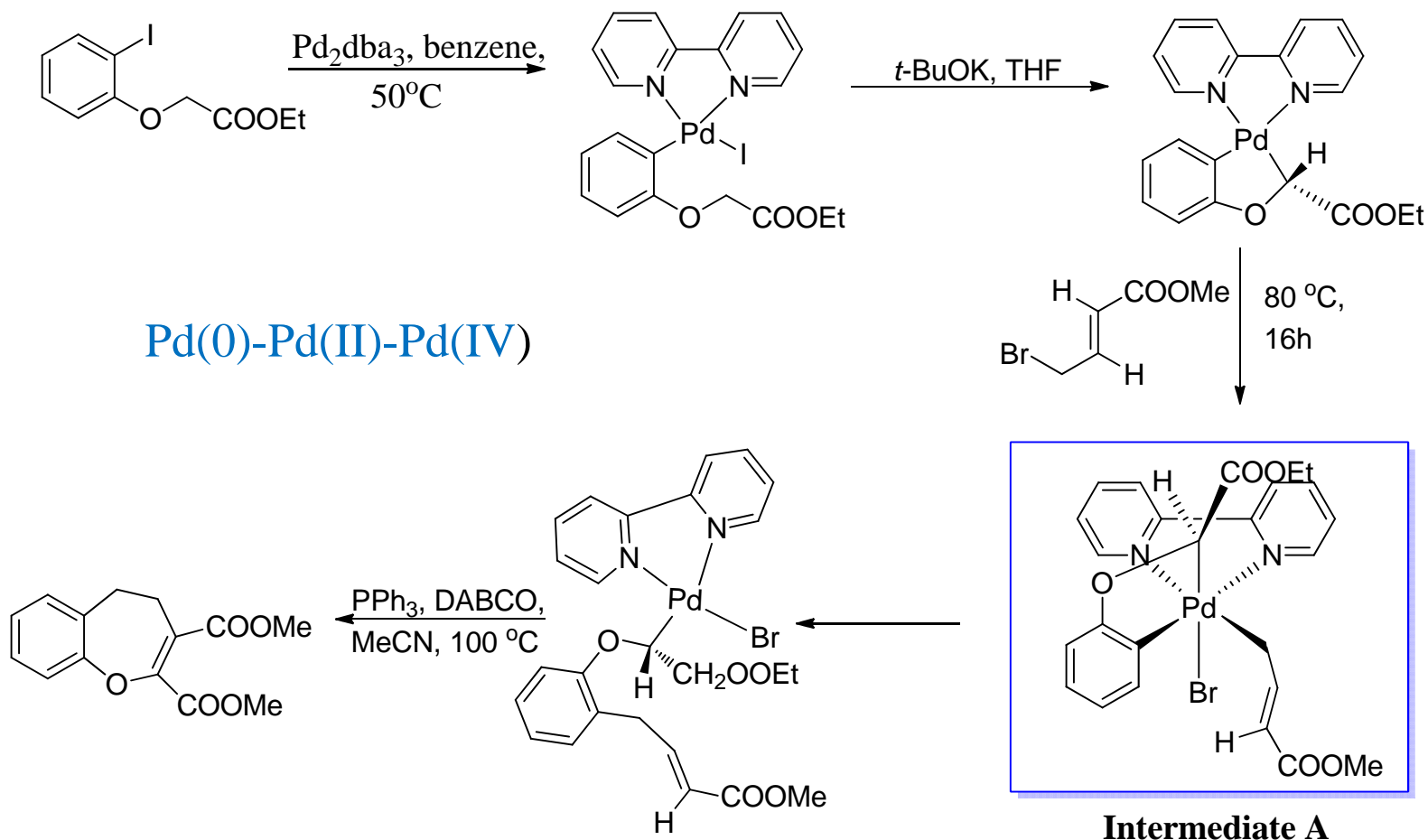
**4. Outlooks**

# C-C bond construction



A. J. Canty, *Organometallics*, **1988**, 7, 1363.

# C-C bond construction

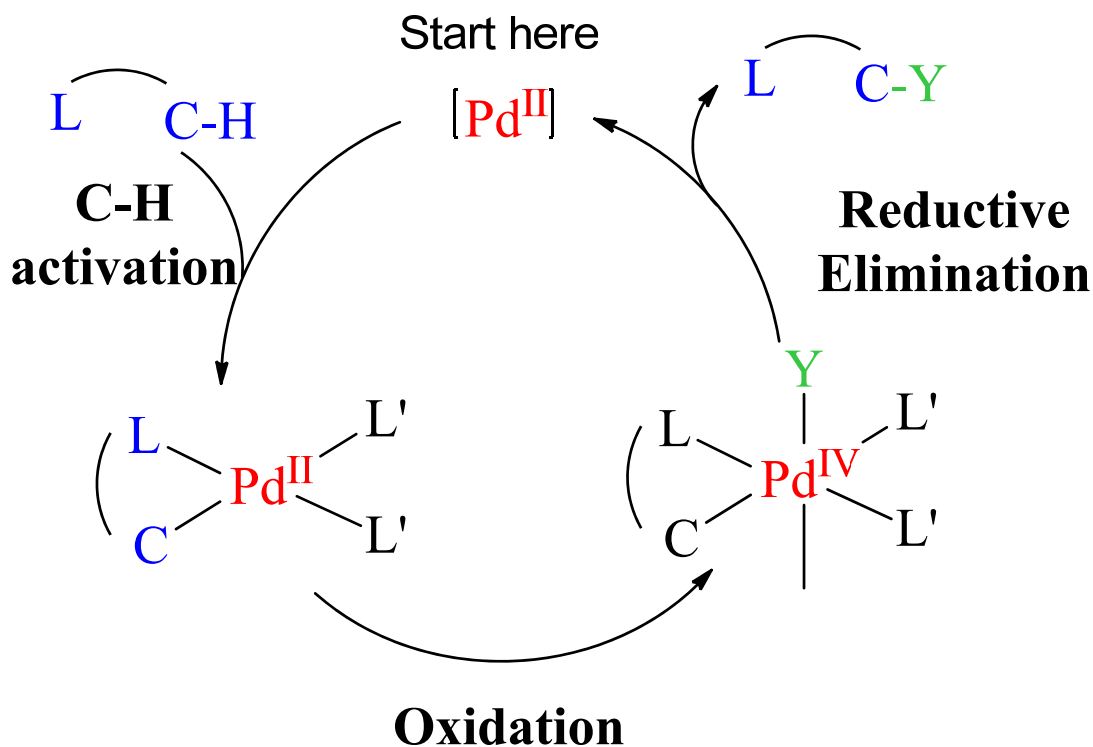


H. C. Malinakova, *Organometallics*, **2007**, *26*, 3874.

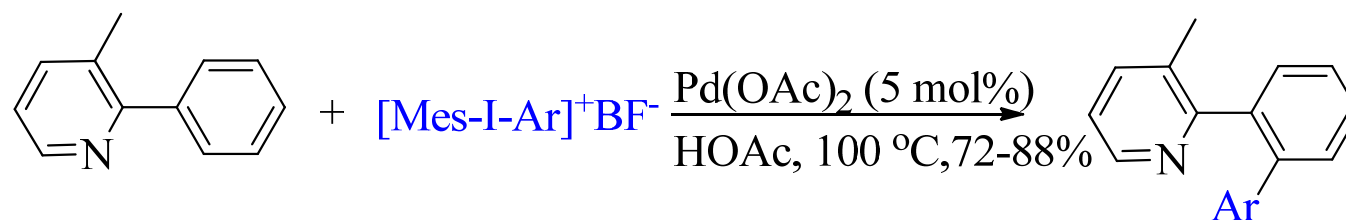
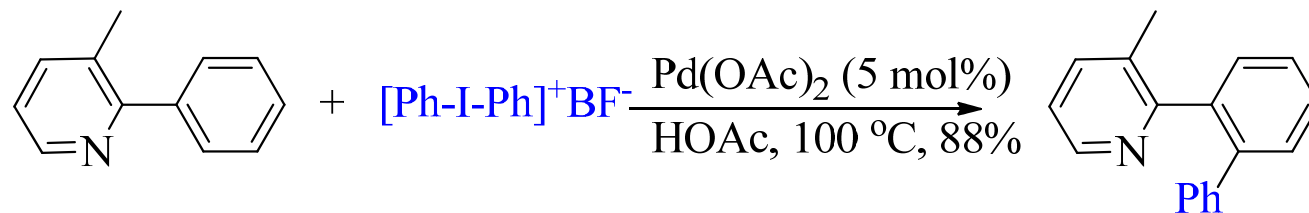
# C-C bond construction

## C-H Activation through Pd(II)/Pd(IV) mechanism

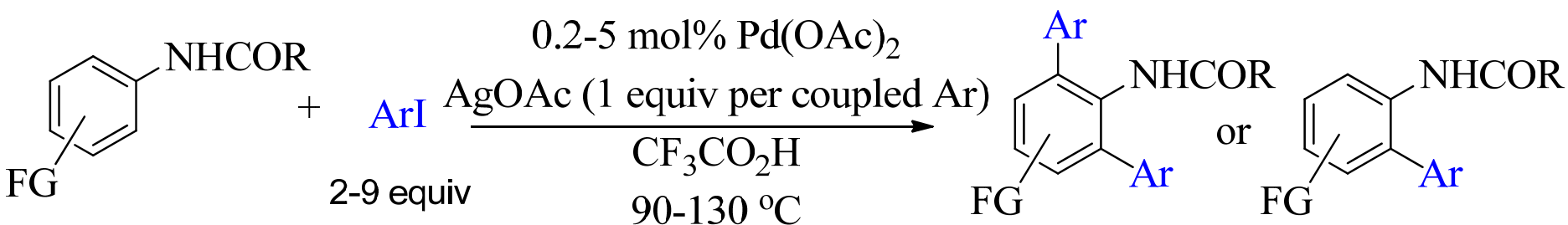
### Pd<sup>II/IV</sup> Catalytic Cycle



# C-C bond construction



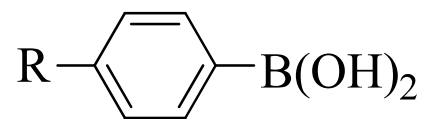
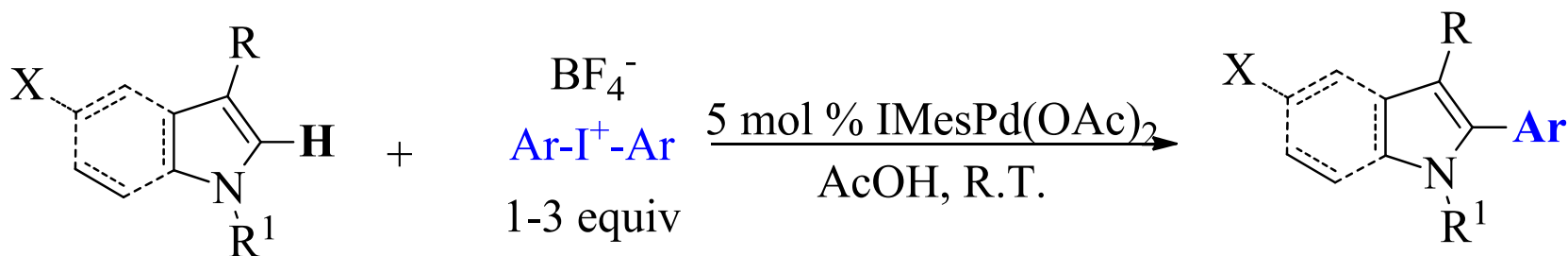
M. S. Sanford, *J. Am. Chem. Soc.*, **2005**, 127, 7330.



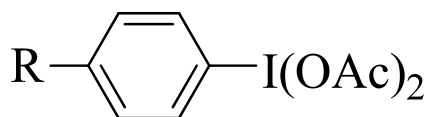
Olafs Daugulis, *Angew. Chem. Int. Ed.*, **2005**, 44, 4046.



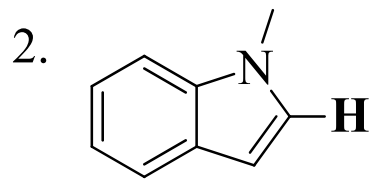
# C-C bond construction



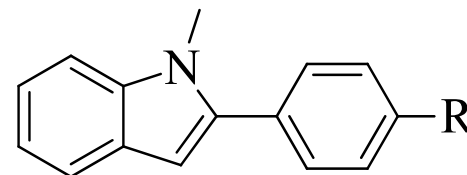
+



1.  $\text{Pd(OAc)}_2$  (5 mol%)  
HOAc, 25 °C, 15min



25 °C, 15h

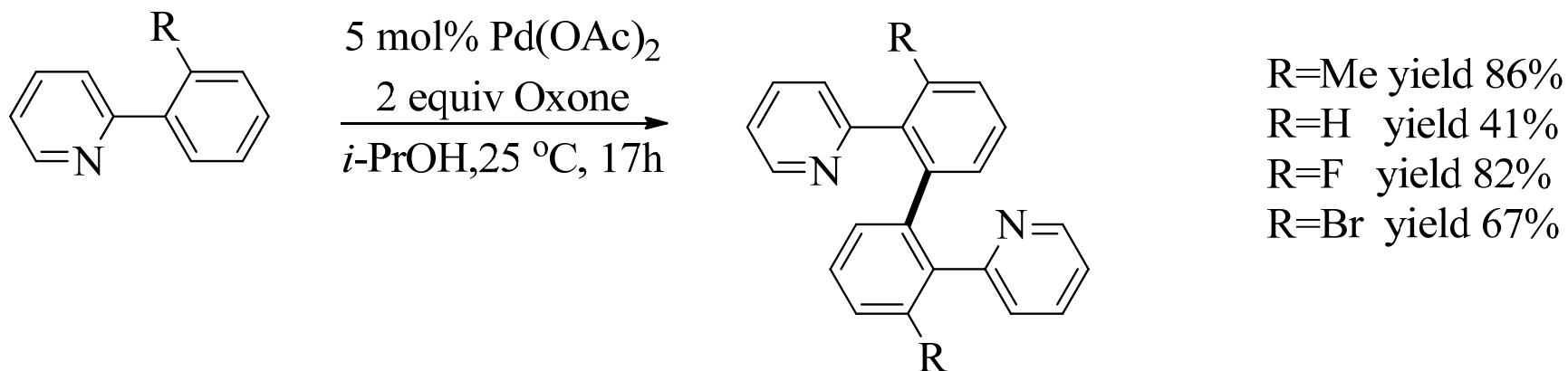


R=H; 80% yield  
R=Cl; 67% yield  
R= Me; 81% yield

M. S. Sanford, *J. Am. Chem. Soc.*, **2006**, 128, 4972.

# C-C bond construction

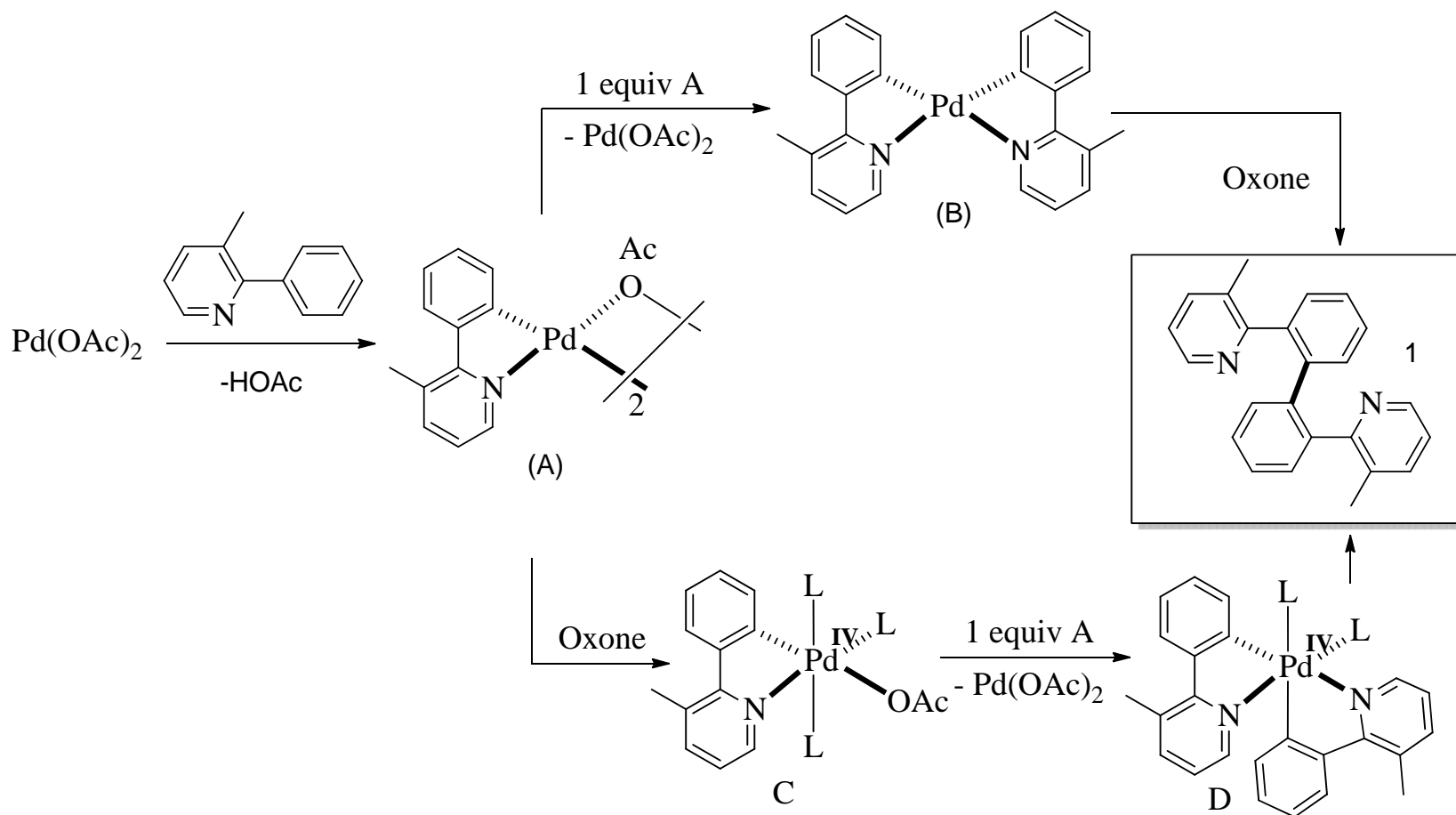
## Regioselective homocoupling:



M. S. Sanford, *J. Am. Chem. Soc.*, **2006**, *128*, 14047.

# C-C bond construction

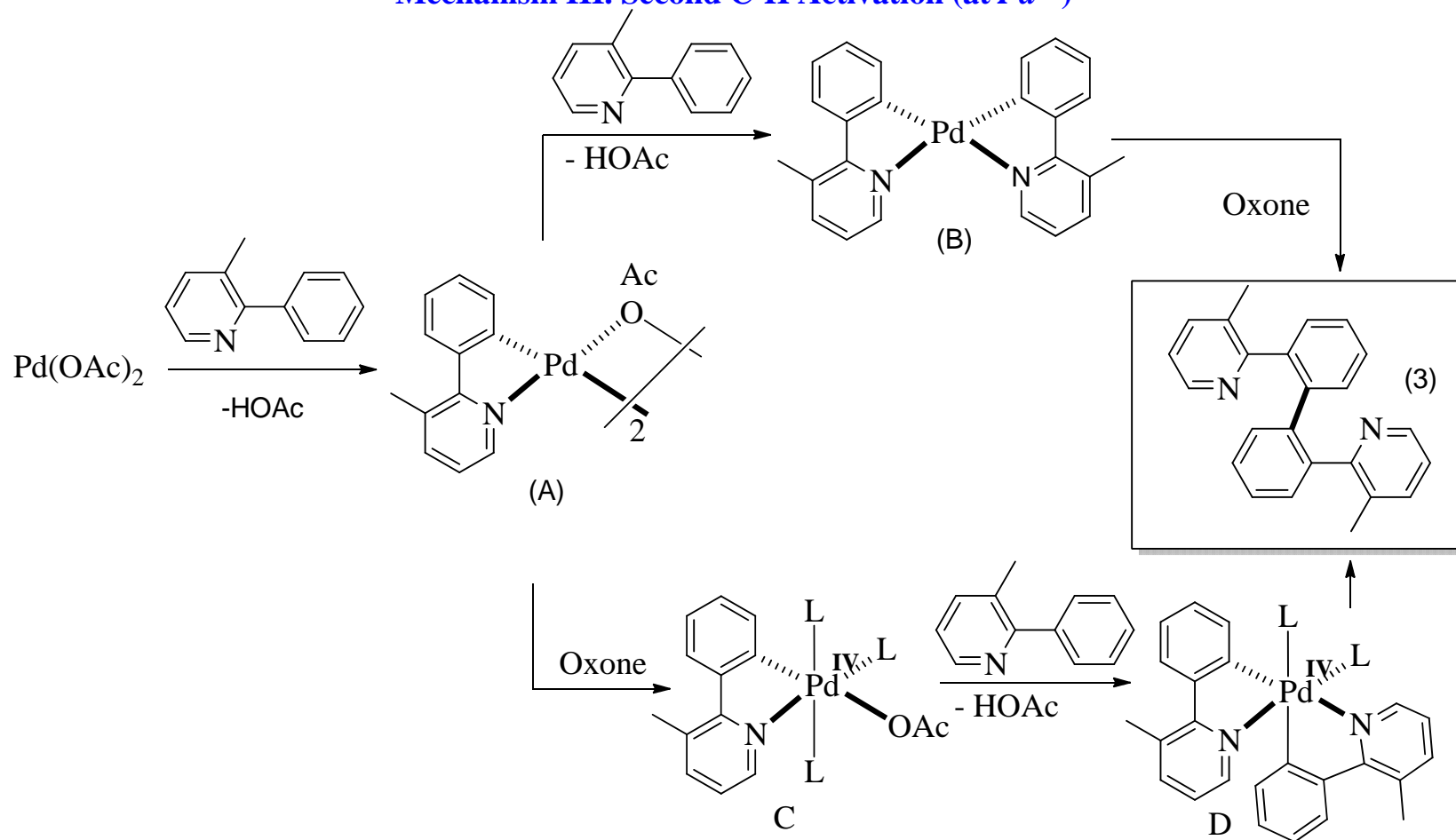
## Mechanism I. Transmetalation(at $Pd^{II}$ )



## Mechanism II. Transmetalation(at $Pd^{IV}$ )

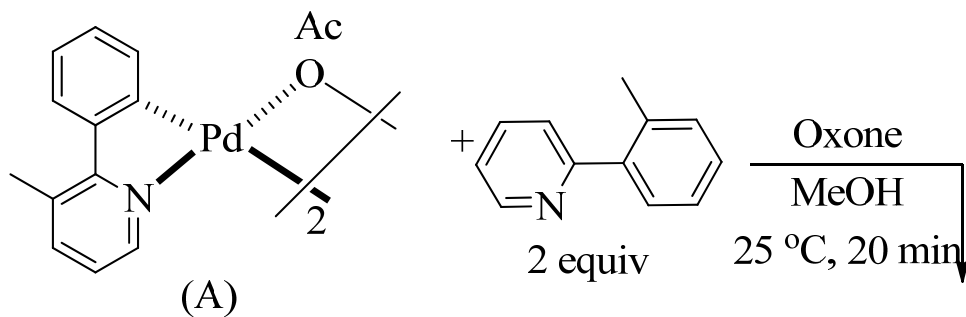
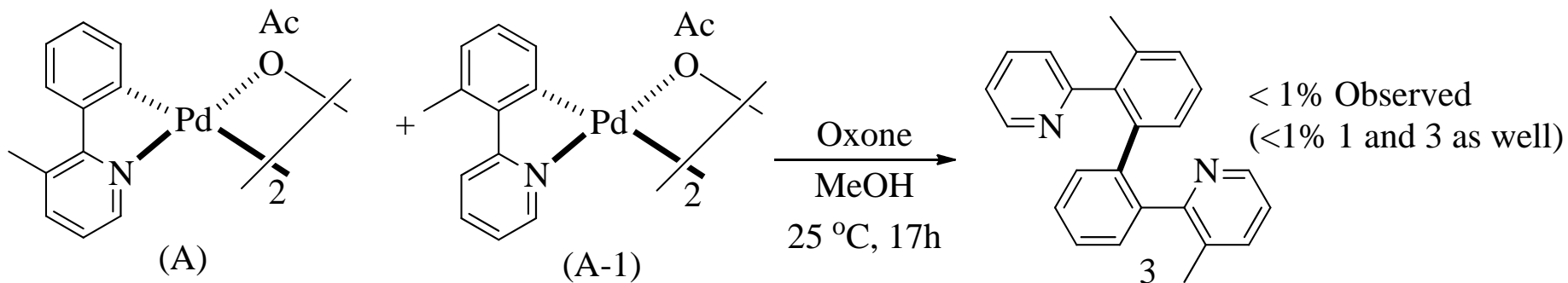
# C-C bond construction

## Mechanism III. Second C-H Activation (at Pd<sup>II</sup>)

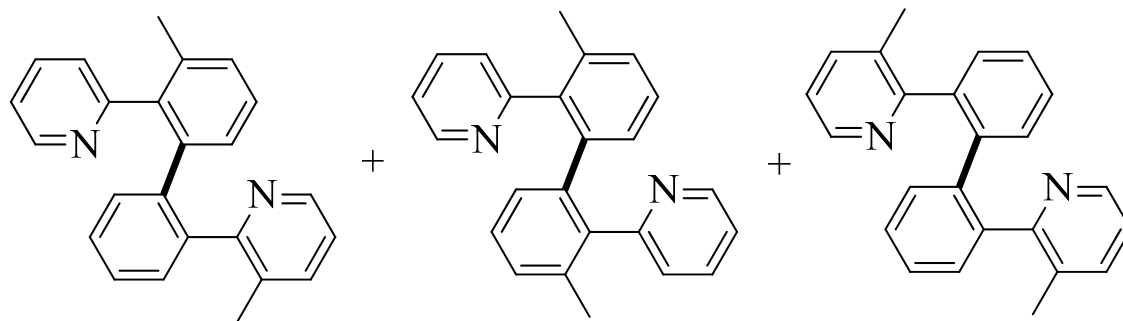


## Mechanism IV. Second C-H Activation (at Pd<sup>IV</sup>)

# C-C bond construction



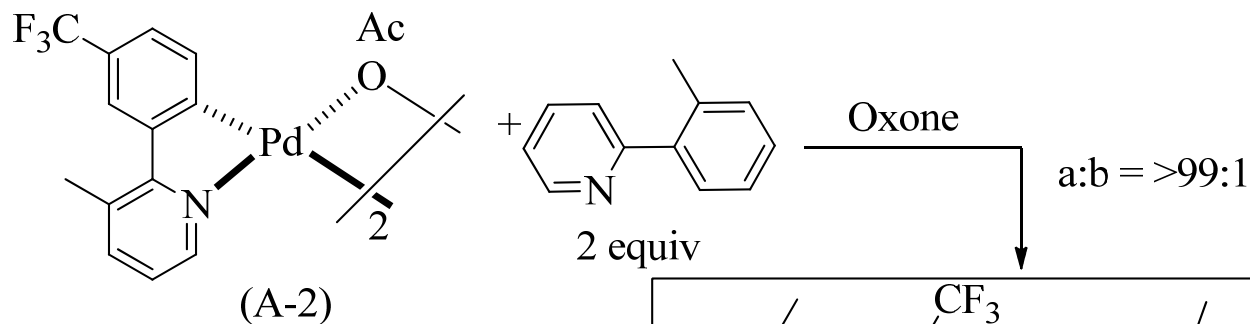
Against mechanism I and II !



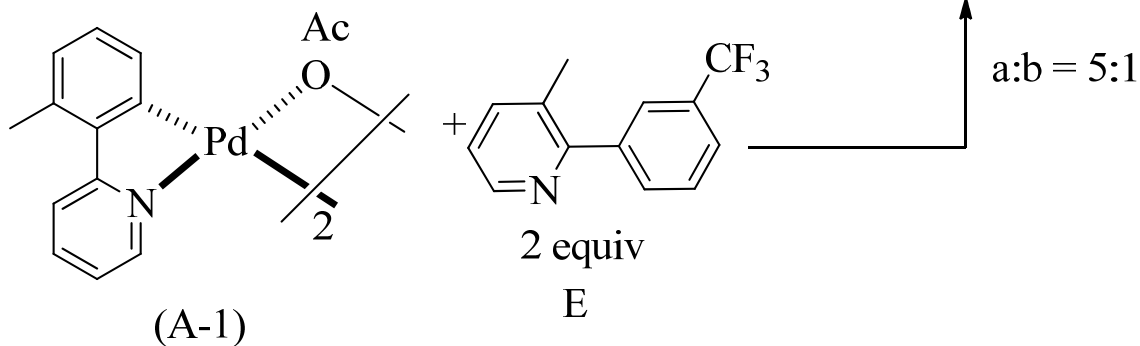
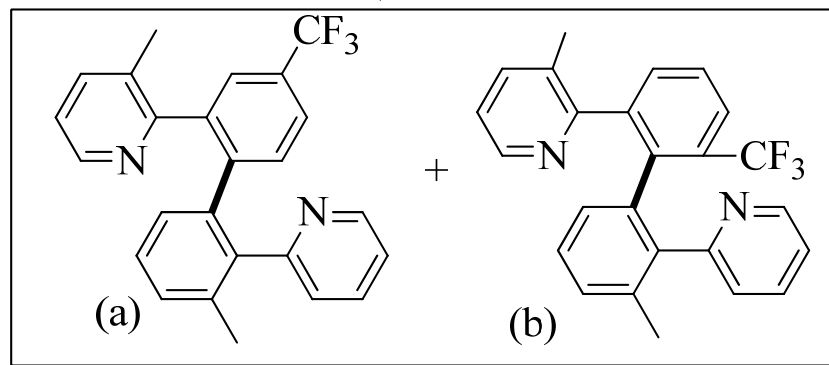
<math>< 1\%</math> Observed

Against mechanism I and II !

# C-C bond construction



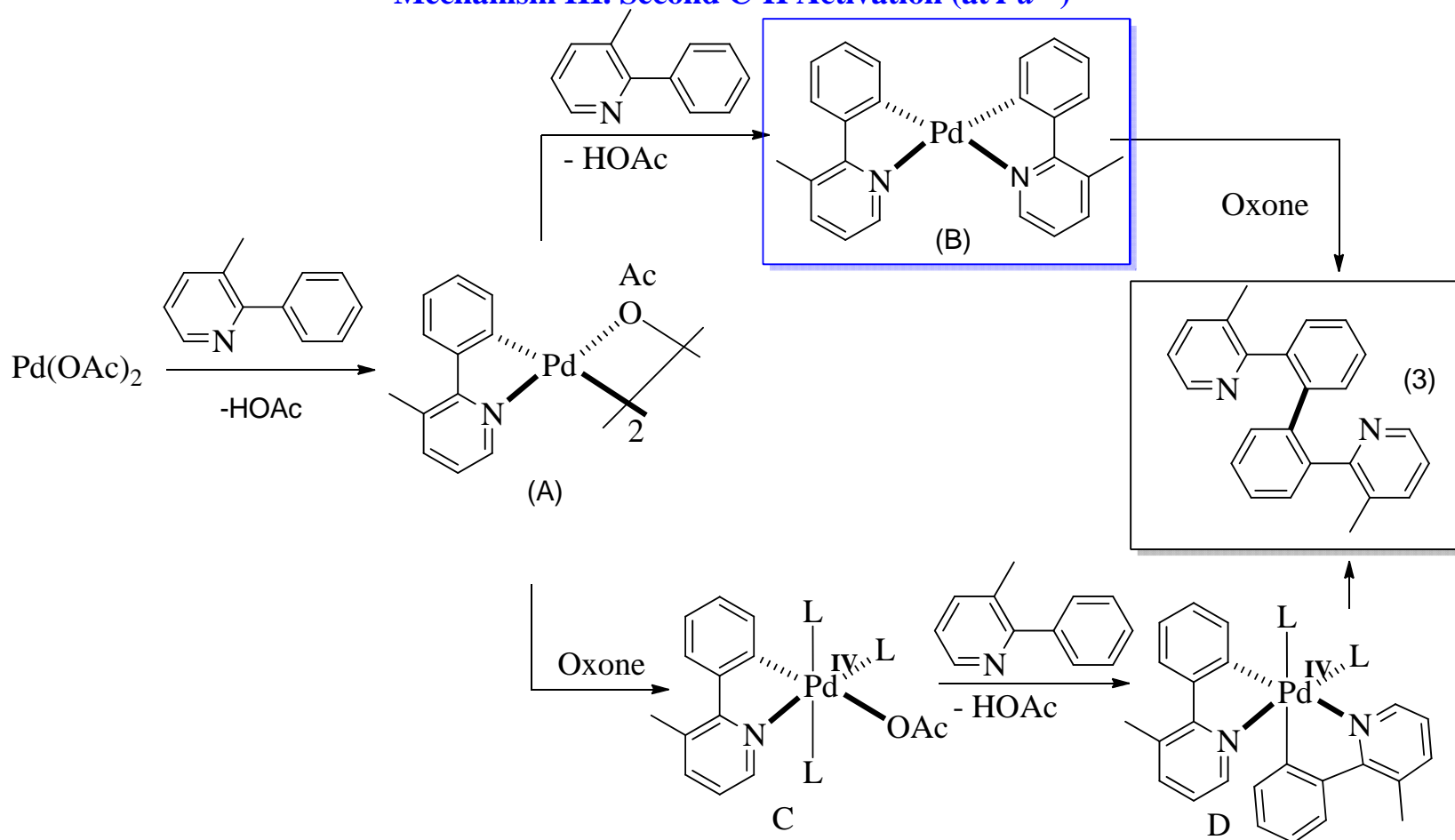
**Palladated with >20:1 selectivity  
at the less hindered ortho-position**



Against mechanism I and II !

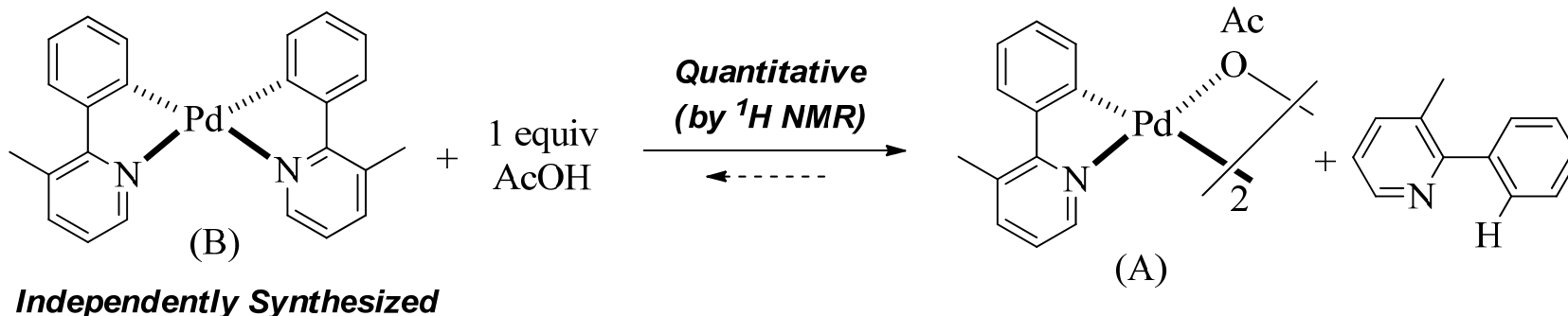
# C-C bond construction

## Mechanism III. Second C-H Activation (at Pd<sup>II</sup>)

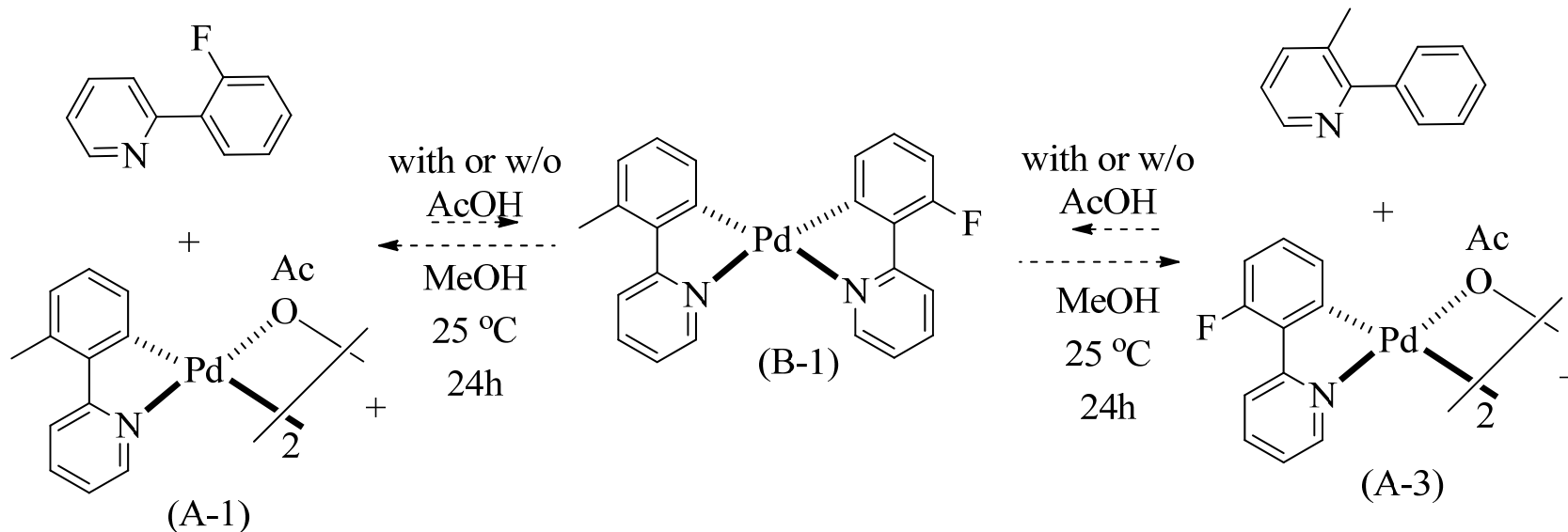


## Mechanism IV. Second C-H Activation (at Pd<sup>IV</sup>)

# C-C bond construction



Unfavorable for mechanism III !



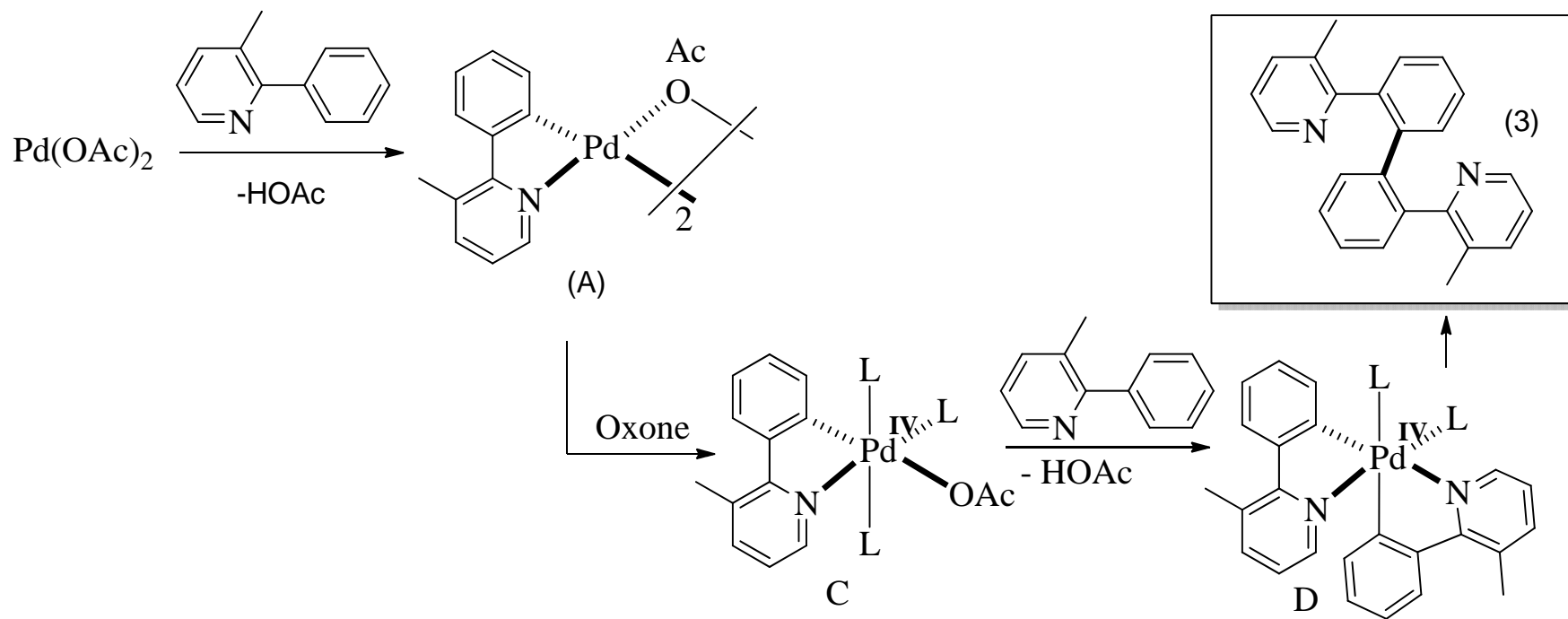
*No change in either direction by  $^{19}\text{F}$  NMR*  
*No equilibration between A-1 and A-3*

Against mechanism III!



# C-C bond construction

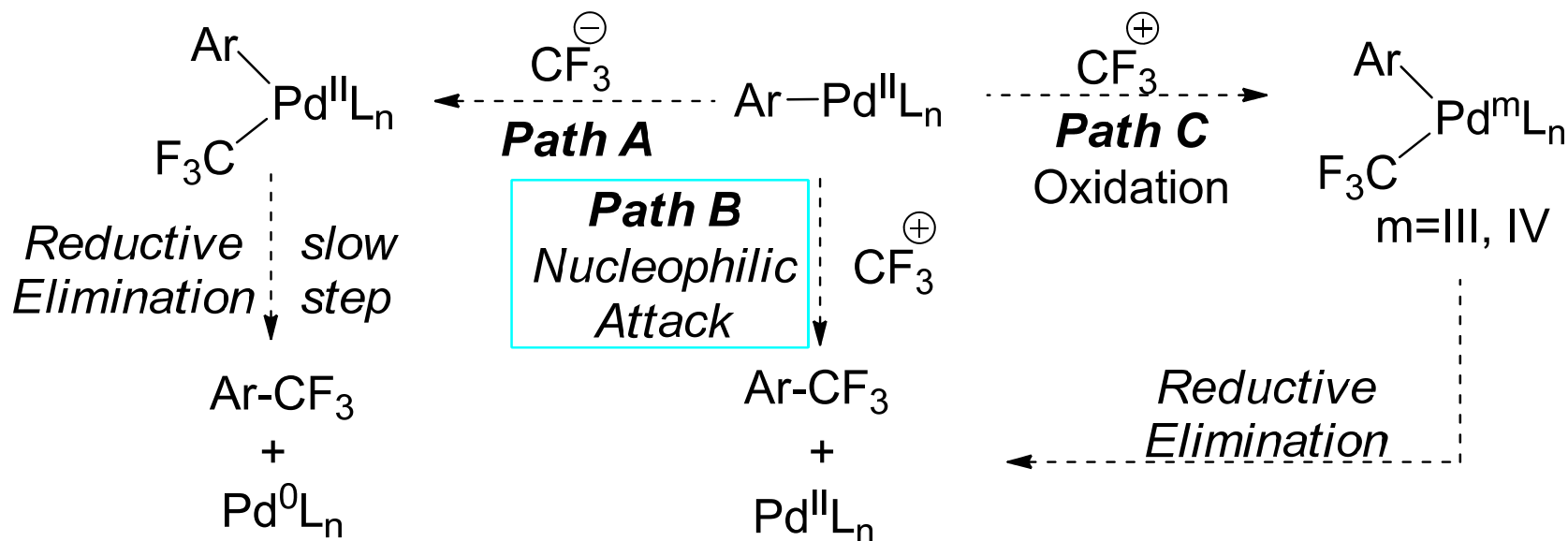
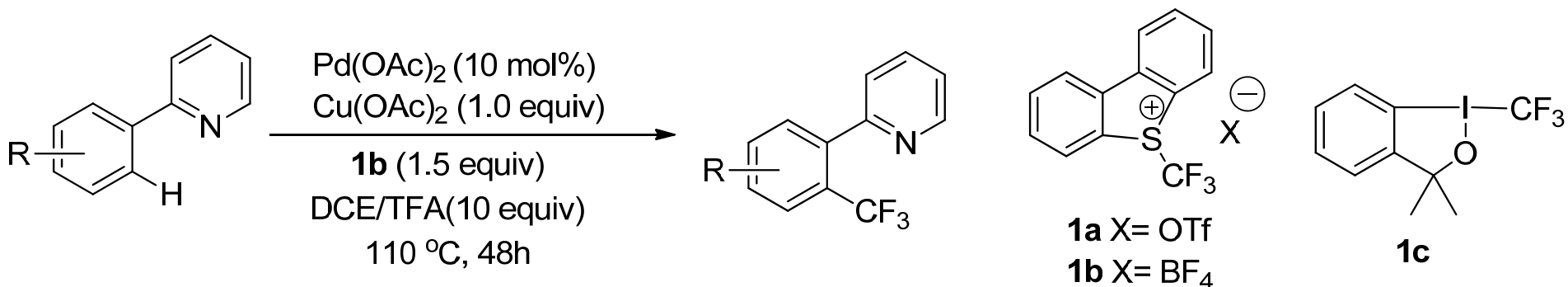
Strongly suggested mechanism:



This mechanism also provides a rationale for the low regioselectivity of the second C-H activation step:

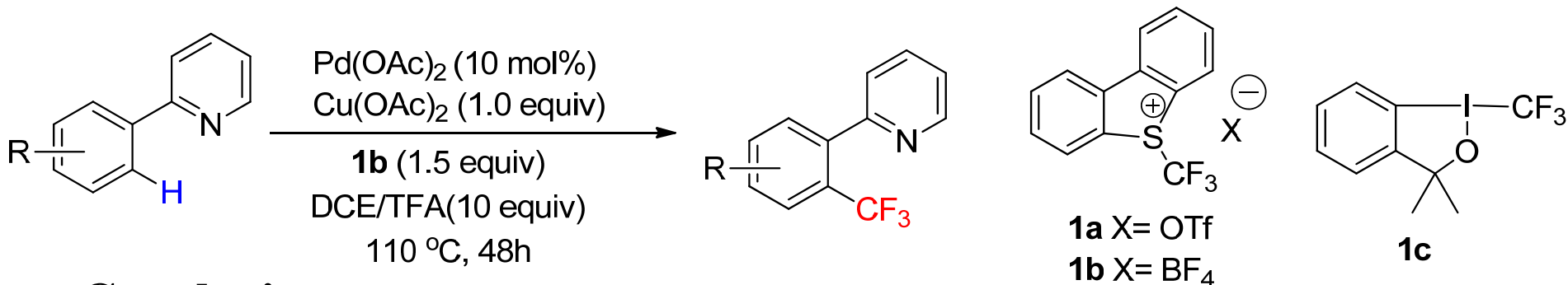
Highly electrophilic  $\text{Pd}^{\text{IV}}$  center is likely to be more reactive and therefore less selective in C-H activation reactions.

# C-C bond construction



Jin-Quan Yu, *J. Am. Chem. Soc.*, **2010**, *132*, 3648.

# C-C bond construction

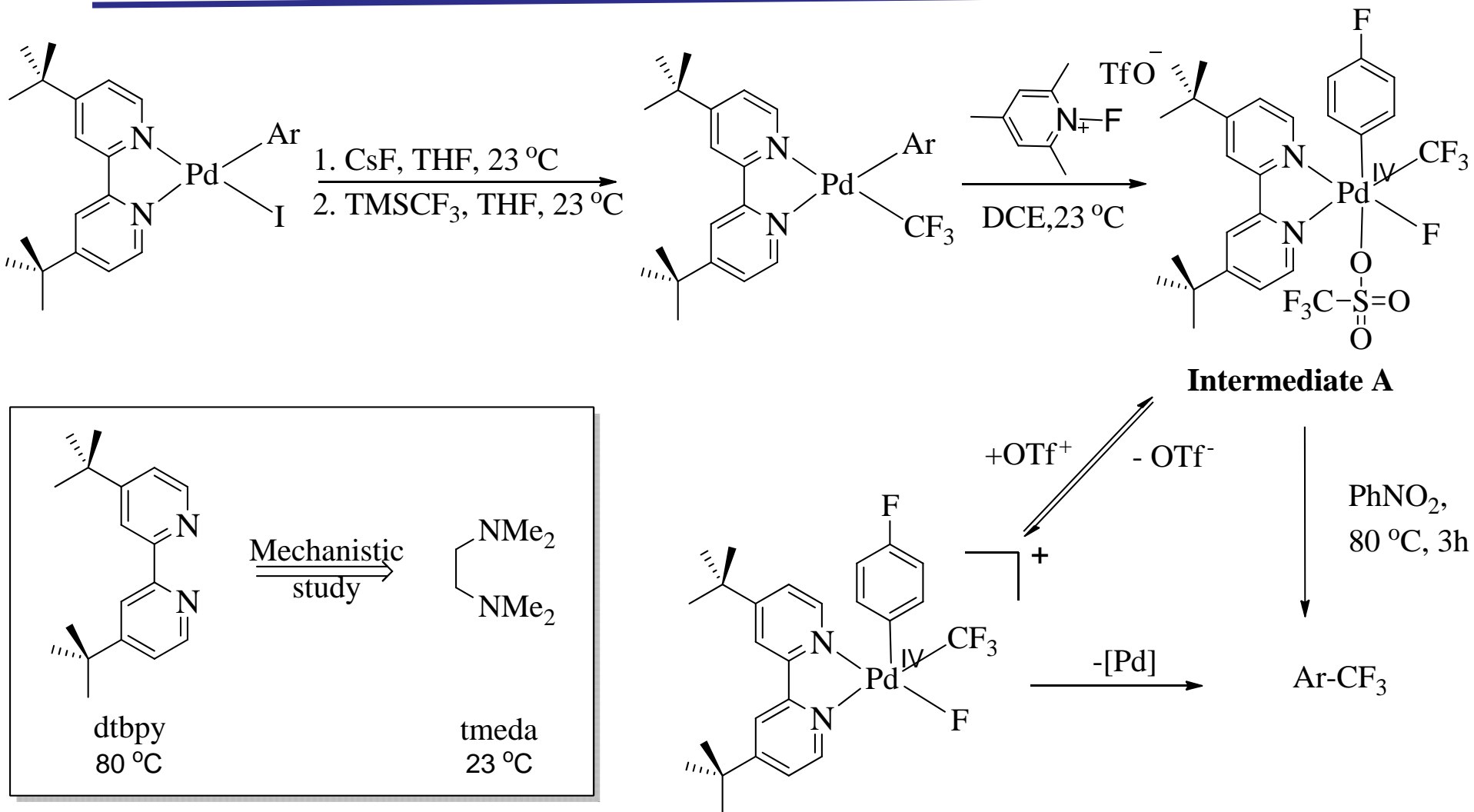


## Conclusions:

1. TFA is essential for the observed trifluoromethylation reaction instead of Pd(OTFA)<sub>2</sub> or other acid
2. The presence of copper(II) acetate significantly improved the yield, might act as both Lewis acids for sulfur and oxidants for Pd(0)
3. **1b** exhibits stronger electrophilicity than **1a**, while **1c** give low yield

Jin-Quan Yu, *J. Am. Chem. Soc.*, **2010**, *132*, 3648.

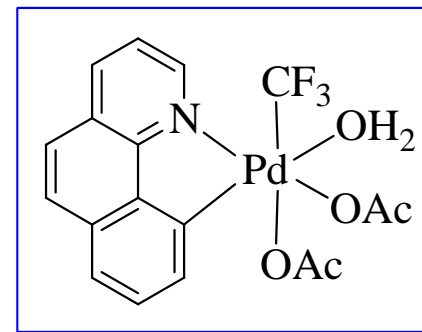
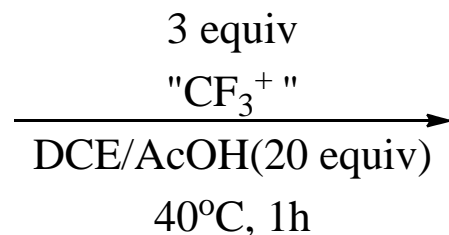
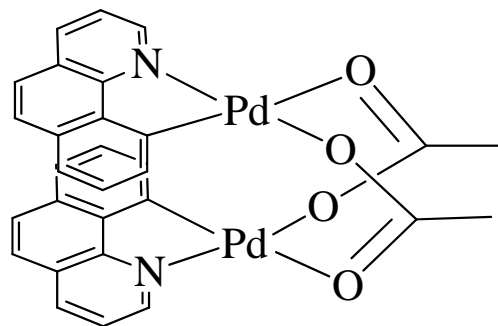
# C-C bond construction



M. S. Sanford, *J. Am. Chem. Soc.*, **2010**, *132*, 2878.

M. S. Sanford, *J. Am. Chem. Soc.*, **2011**, *133*, 7577.

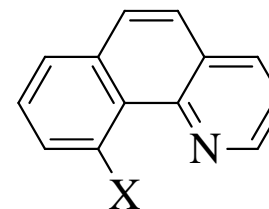
# C-C bond construction



XRD,  
<sup>1</sup>H NMR  
<sup>19</sup>F NMR

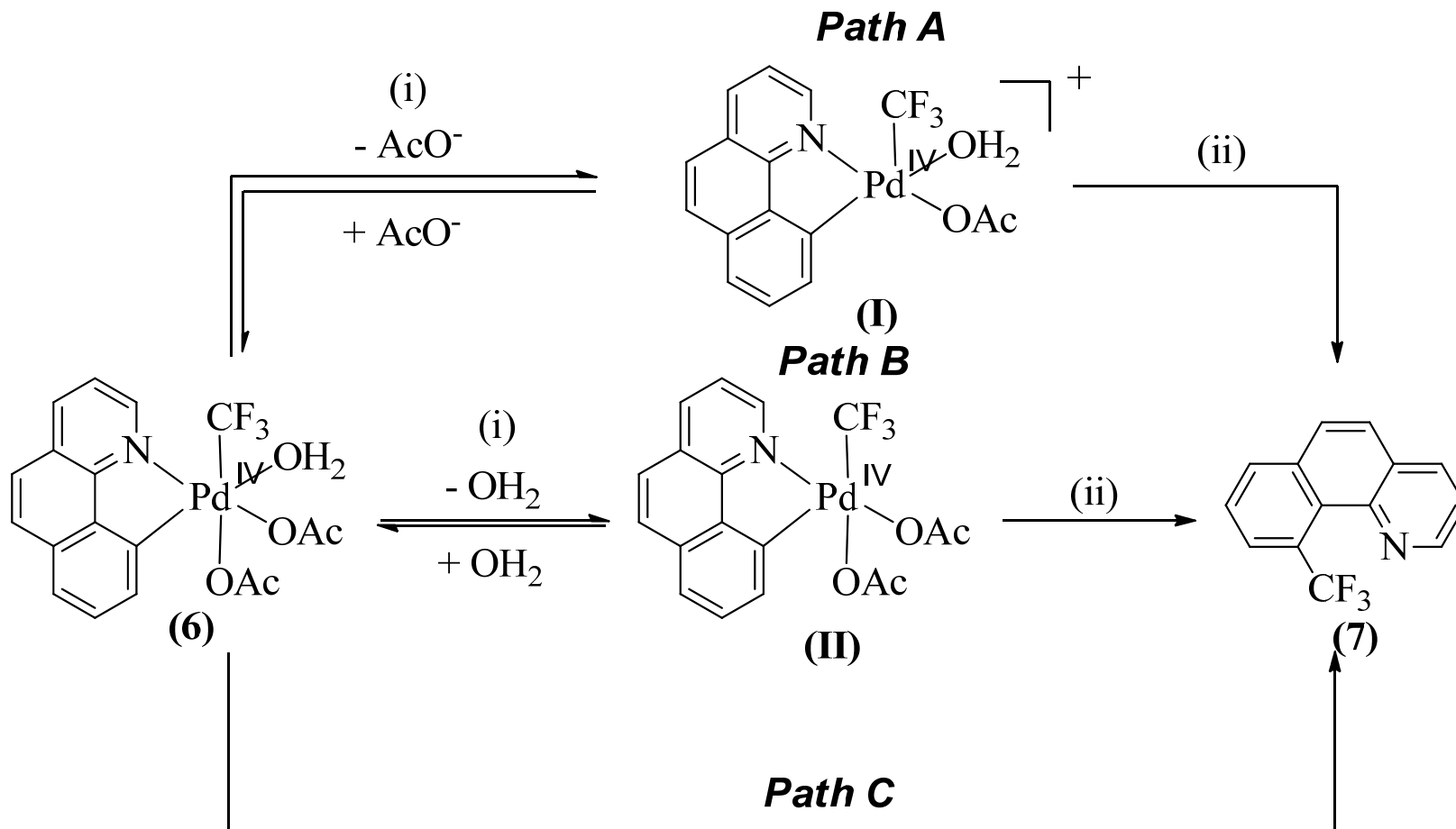
entry	solvent	yield 1	yield 2	yield 3
1	AcOH	56%	<2%	<2%
2	DCE	54%	<2%	<2%
3	CHCl <sub>3</sub>	62%	<2%	<2%
4	NO <sub>2</sub> Ph	57%	<2%	<2%
5	DCE/50 equiv of pyridine	<2%	<2%	84%

60 °C, 12 h  
solvent

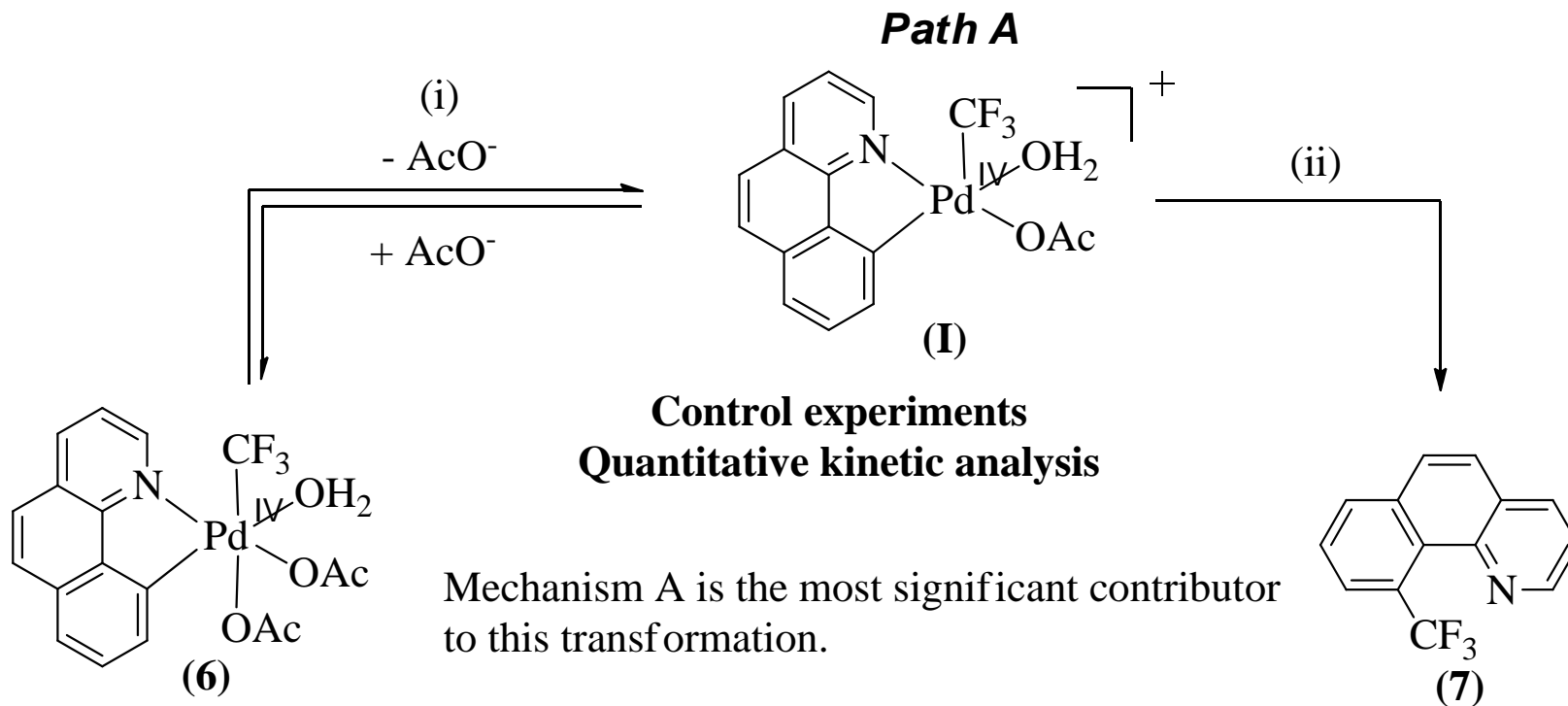


X=CF<sub>3</sub> (1)  
X=OAc(2)  
X=OH (3)

# C-C bond construction



# C-C bond construction



The roles of promoters in the catalytic transformations:



1. Serve as a source of AcOH (which is critical for oxidation addition process)
2. Accelerate and enhance mass balance in C-CF<sub>3</sub> coupling from **6**.

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**2. Characterizations**

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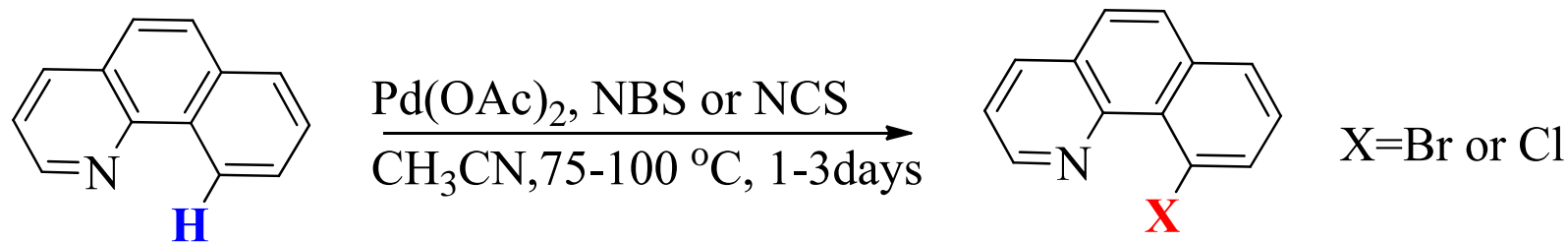
**3.1 C-C bond construction**

**3.2 C-X bond construction**

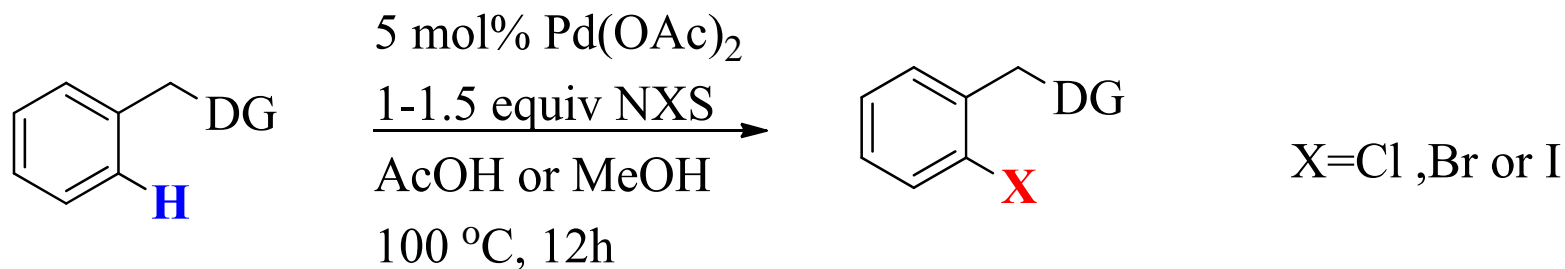
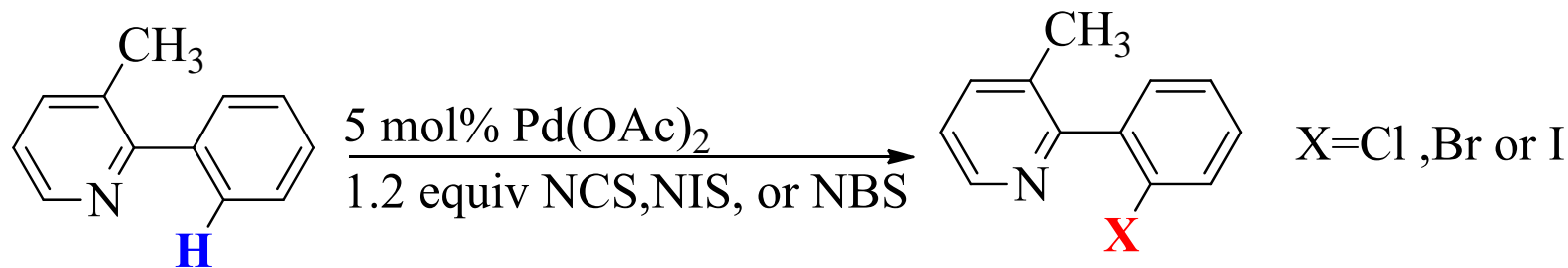
**4. Outlooks**



# C-X bond construction

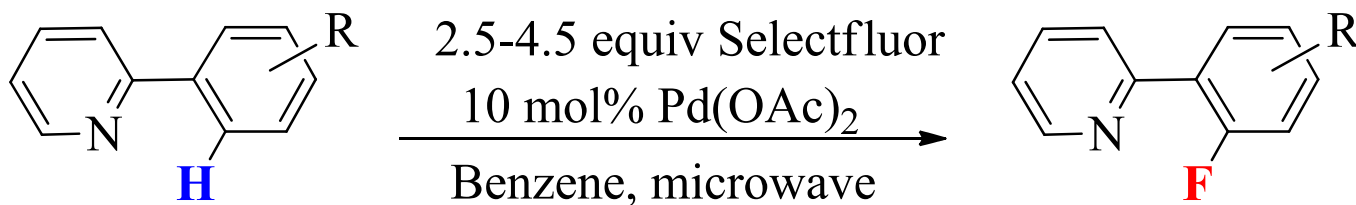
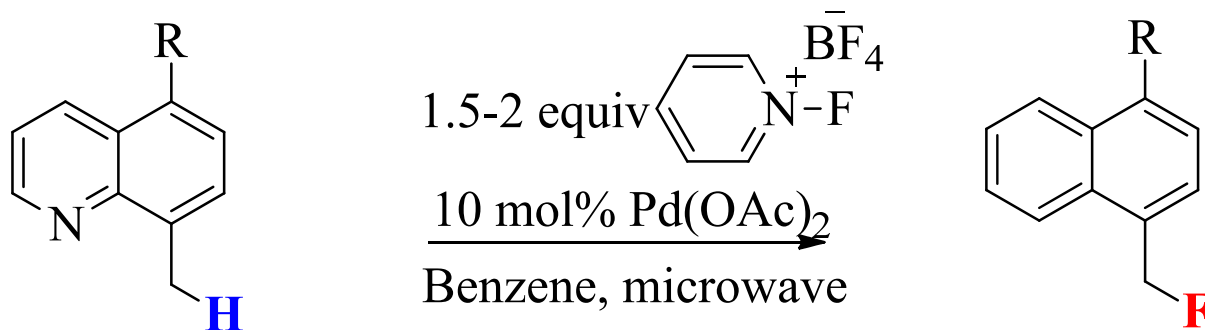


M. S. Sanford, *J. Am. Chem. Soc.*, **2004**, *126*, 2300.



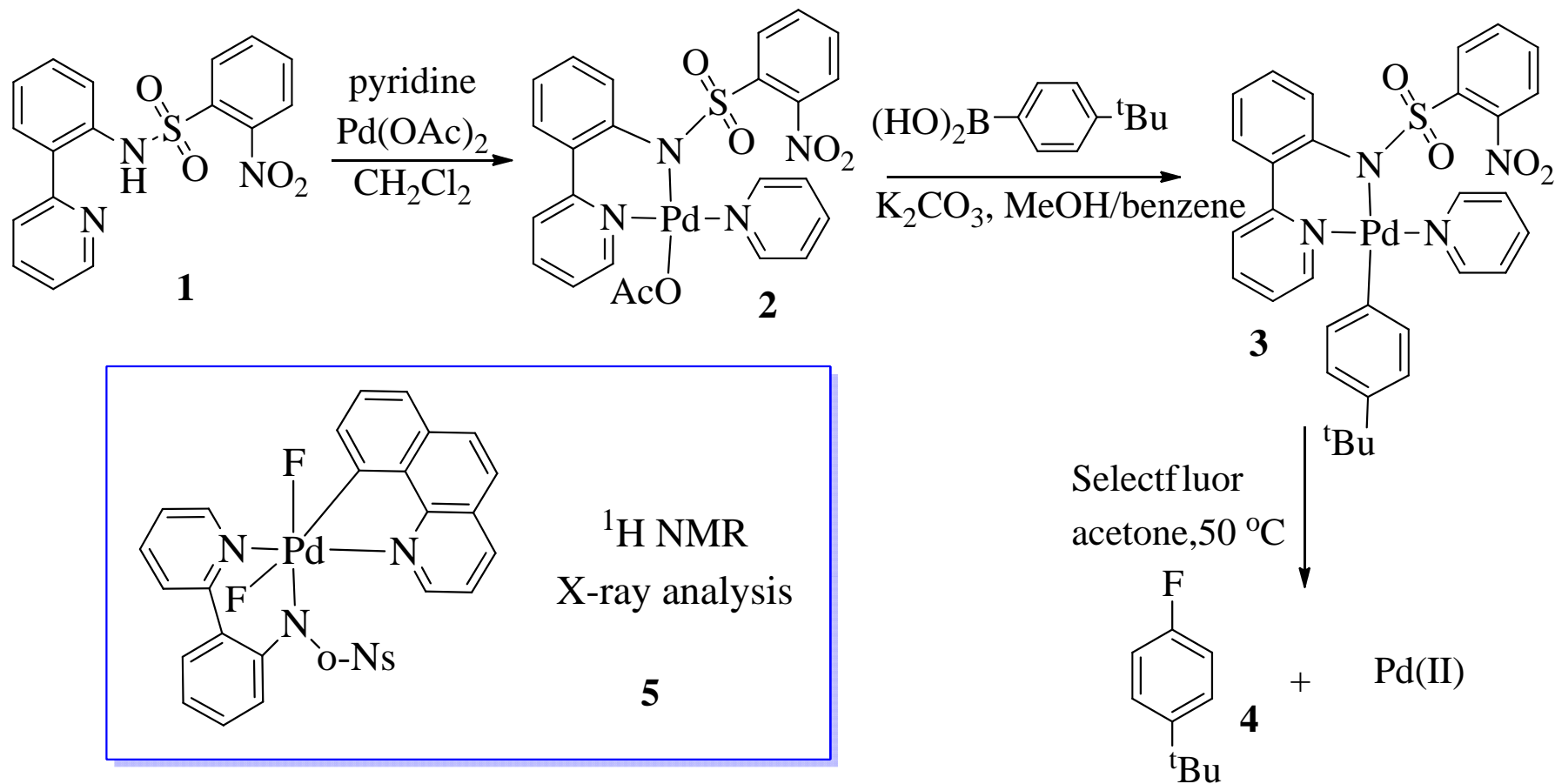
M. S. Sanford, *Org. Lett.*, **2006**, *8*, 2523.

# C-X bond construction



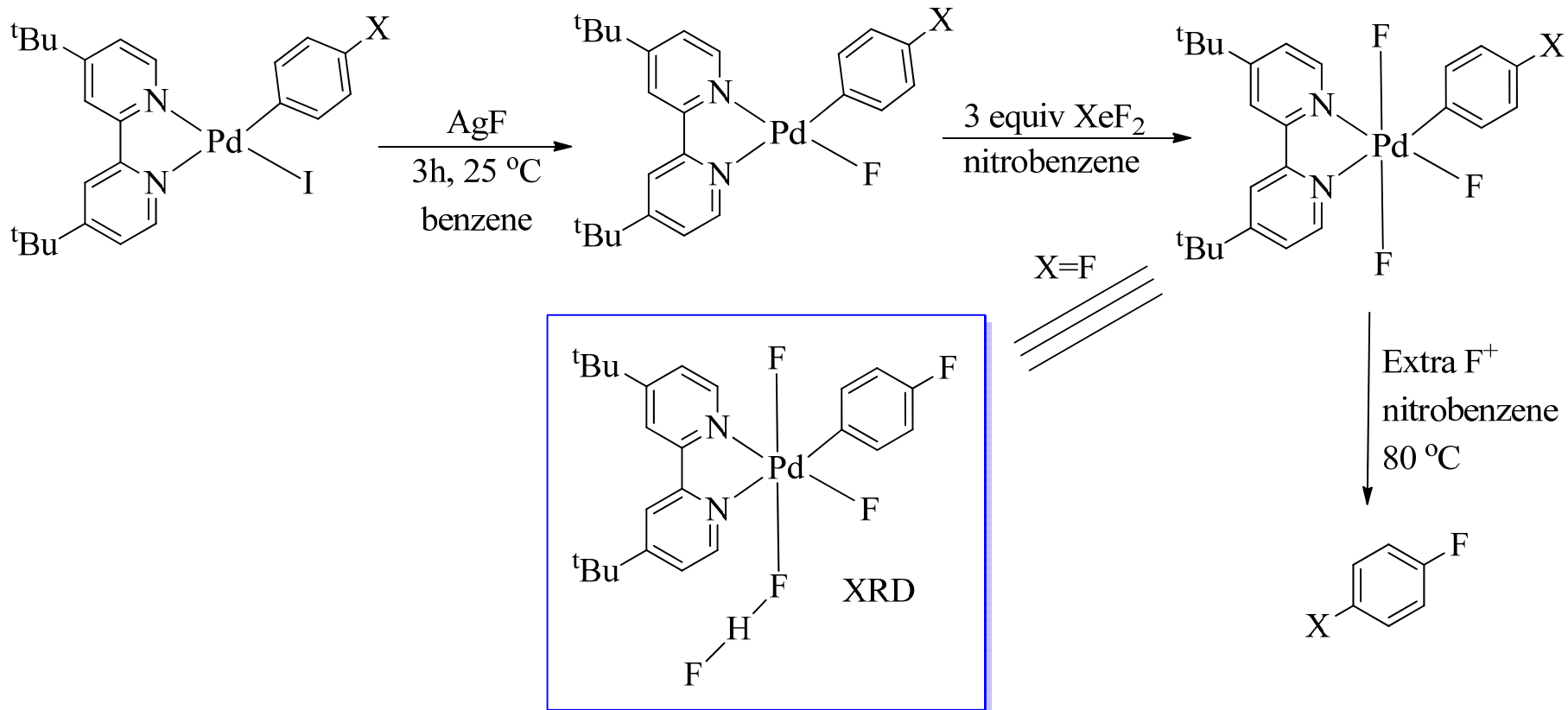
M. S. Sanford, *J. Am. Chem. Soc.*, **2006**, *128*, 7134.

# C-X bond construction



Tobias Ritter, *J. Am. Chem. Soc.*, **2008**, *130*, 10060.

# C-X bond construction



M. S. Sanford, *J. Am. Chem. Soc.*, **2009**, *131*, 3796.

# Reactions

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## Summary

1. Pd(IV) species are often resistant to  $\beta$ -H elimination process.
2. Usually, Pd(IV) species undergo facile reductive elimination.
3. Pd(II)/Pd(IV) catalyzed reactions exhibit complementary functional group tolerance to Pd(0)/Pd(II) catalyzed transformations.
4. Pd(II)/Pd(IV) catalyzed reactions are operationally simple and do not require the careful exclusion of air (especially O<sub>2</sub>) and moisture.
5. In some cases, Pd(II)/Pd(IV) catalysis can realize transformations that are hardly accessible by Pd(0)/Pd(II) catalyzed reactions.

# Contents

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# Outlooks

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Although organopalladium(IV) chemistry has attracted much attention from the chemical community in recent years, much limitation still remain.

Future attention should be paid on these aspects:

1. Enhancing the chemo-, regio- and stereoselectivity of catalytic processes involving high-valent palladium intermediates.
2. Expanding the scope of the fundamental organometallic reactions that are possible at high-valent palladium centers, such as carbon-hydrogen activation,  $\sigma$ -bond metathesis, migratory insertion and nucleopalladation reactions.

Undoubtedly, the fields of palladium(IV) chemistry are sure to have a bright and rapidly expanding future.



**THANKS**