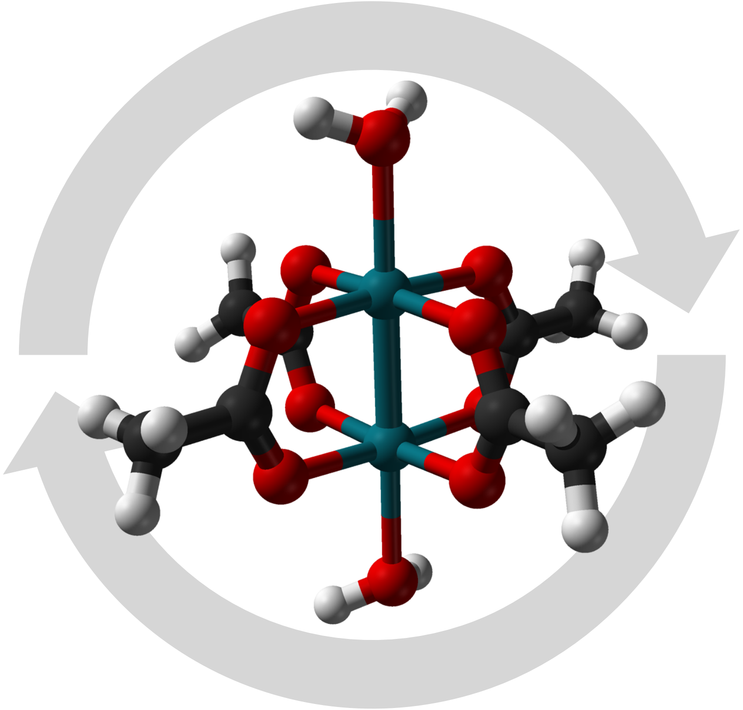
Metal-Metal Bonds in Organic Catalysis



Artem V. Tsymbal

MacMillan Group Literature Talk

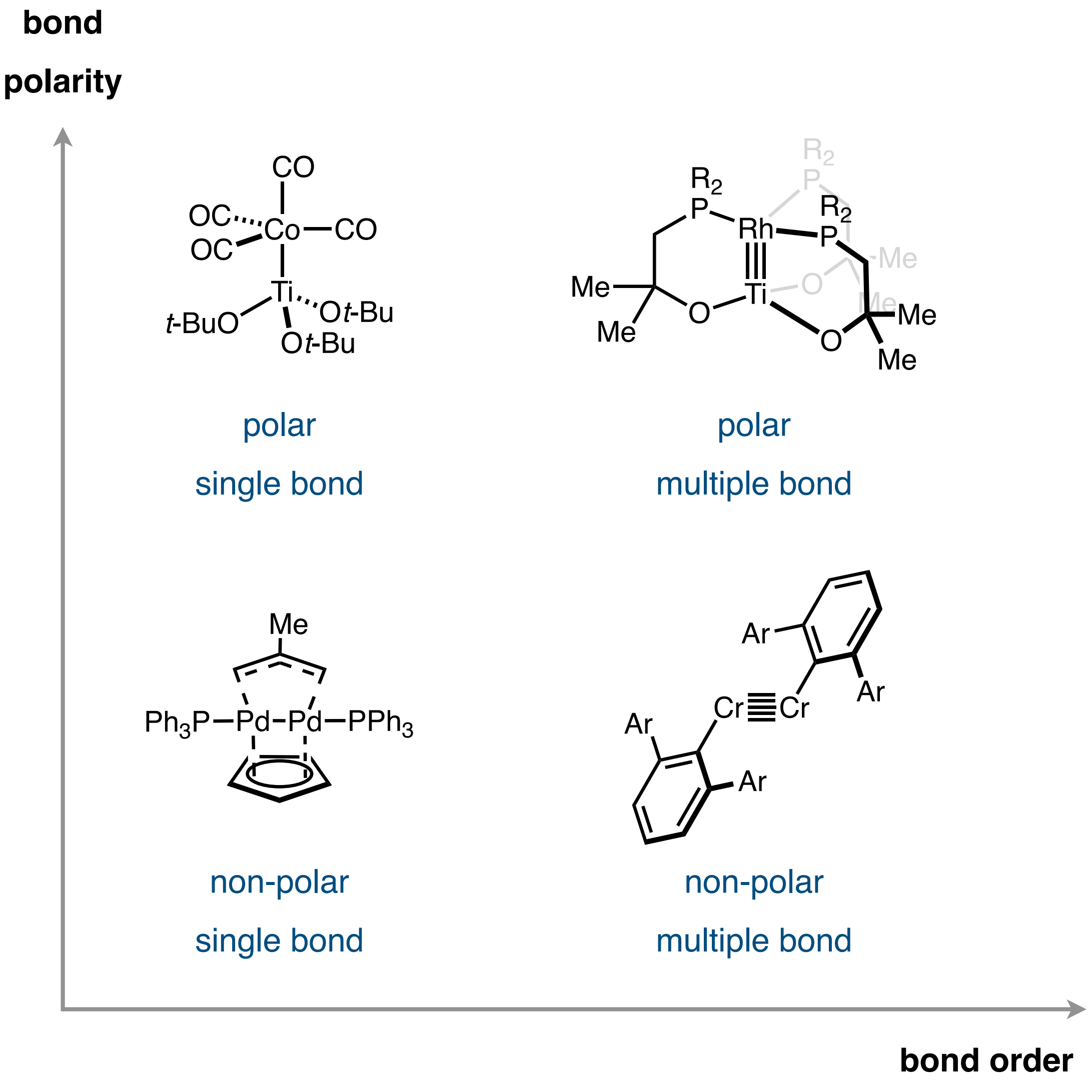
May 3, 2022

Metal-Metal Bonds — Diversity of the Phenomenon

- > 40 000 multinuclear complexes in CSD
- few catalytic platforms feature M–M bonds

Why so?

- challenging to outperform single-center catalysis platforms
- challenging to establish the role of M–M bonded species
- challenging to design ligands that simultaneously protect M–M bonds and still provide access for a substrate binding



polar single bond

polar multiple bond

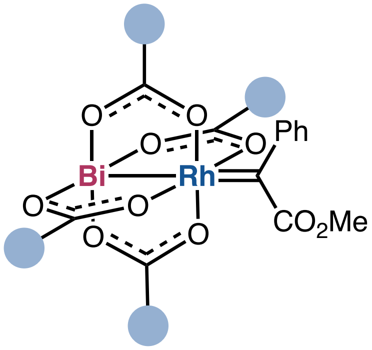
non-polar single bond

non-polar multiple bond

Powers, I. G.; Uyeda, C. *ACS Catal.* **2017**, *7*, 936–958.

Metal-Metal Bonds Play Multiple Roles in Catalysis

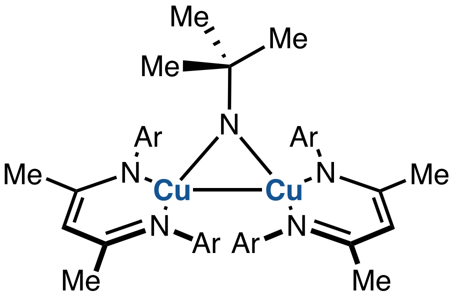
single-site reactivity



the second metal acts as

a metalloligand

off-cycle species

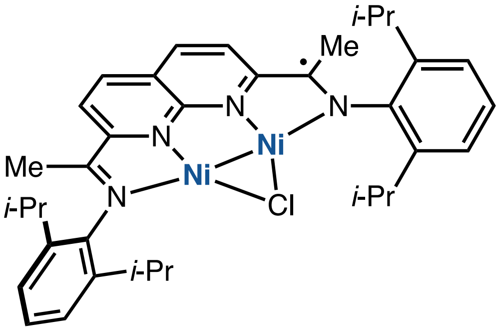


metal-metal bonding

stabilizes low-coördination

metal centers

multi-site reactivity

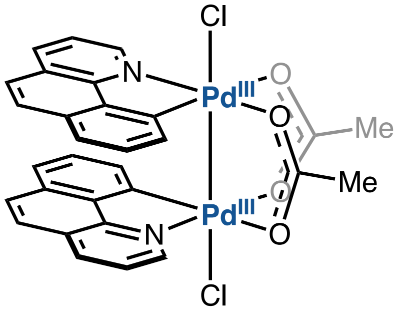


both centers are engaged in

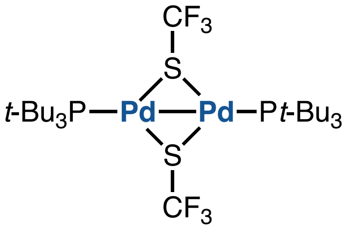
bond forming/breaking

Metal-Metal Bonds in Catalysis — Outline of the Talk

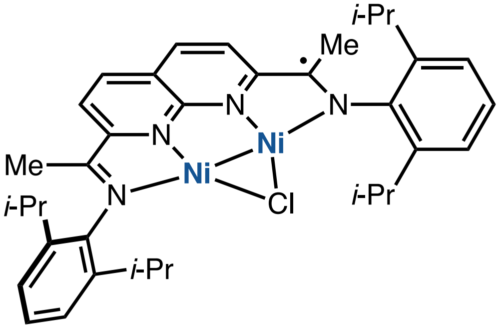
Pd(III)–Pd(III) dimers



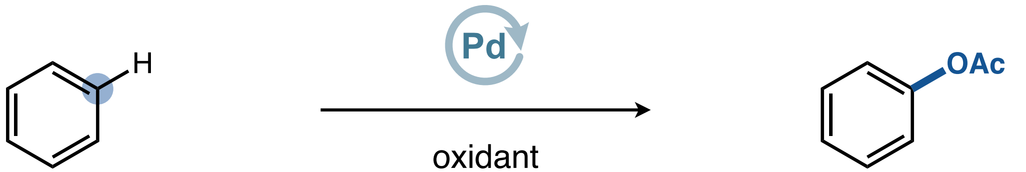
Pd(I)–Pd(I) dimers



Ni$_2$ NDI complexes



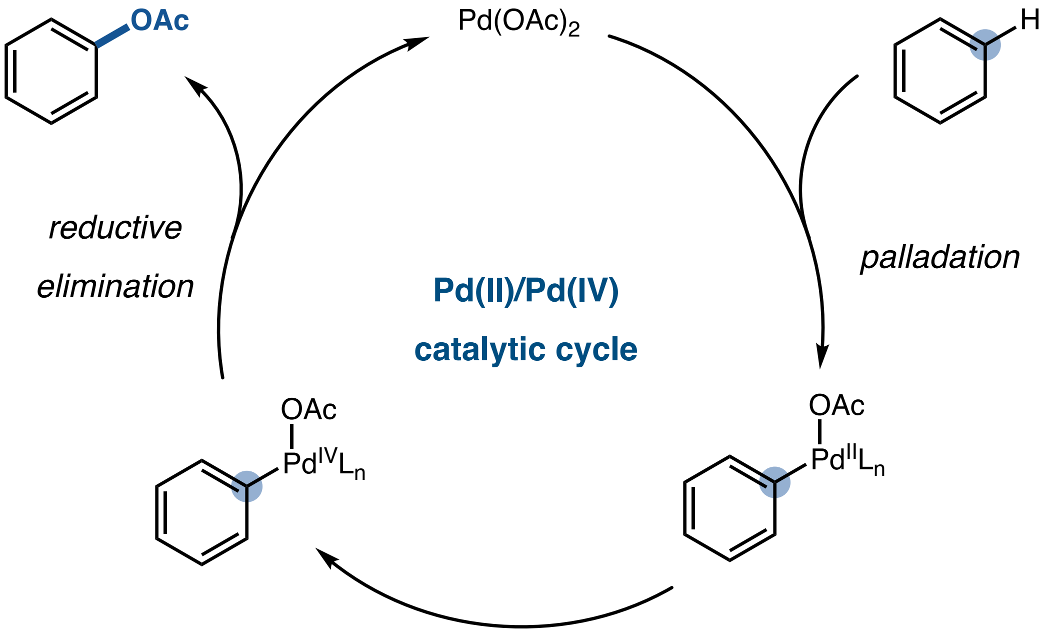
Palladium-Catalyzed C–H Bond Acetoxylation — Historical Perspective



oxidant

simple arene

phenol acetate



reductive elimination

palladation

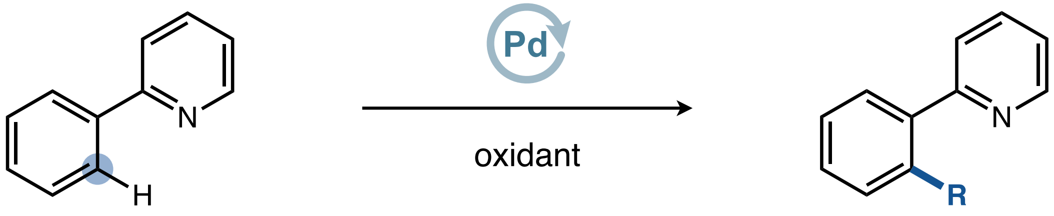
Pd(II)/Pd(IV) catalytic cycle

oxidation

Henry, P. M. *J. Org. Chem.* **1971**, *36,* 1886–1890.

Stock, L. M., Tse, K. T., Vorvick, L. J.; Walstrum, S. A. *J. Org. Chem.* **1981**, *46*, 1757–1759.

Substrate Directed Palladium-Catalyzed C–H Bond Functionalization



C–H nucleophile

oxidized product

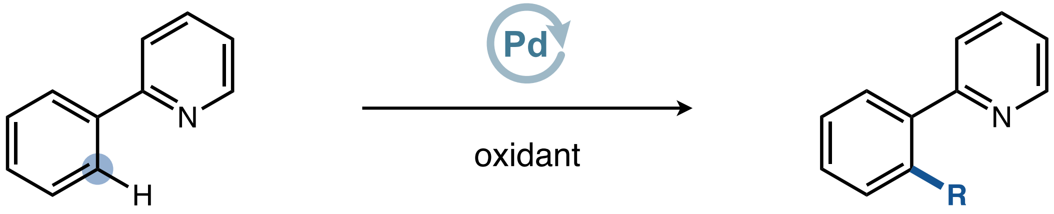
simple donors dictate positional selectivity

Melanie S. Sanford

University of Michigan

Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936–946.

Substrate Directed Palladium-Catalyzed C–H Bond Functionalization



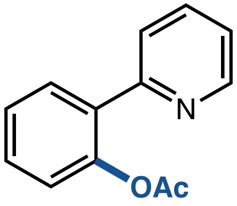
C–H nucleophile

oxidized product

simple donors dictate

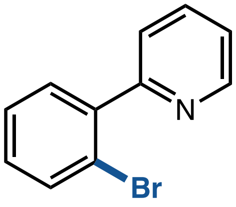
positional selectivity

Acetoxylation



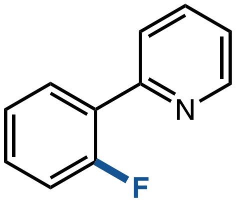
with $PhI(OAc)_2$

Halogenation



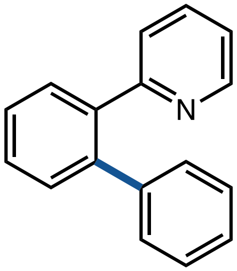
with NBS

Fluorination



with N-fluoropyridinium

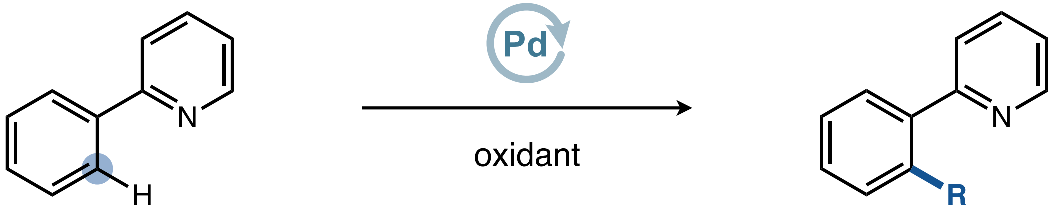
Arylation



with Ar_2I^+

Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936–946.

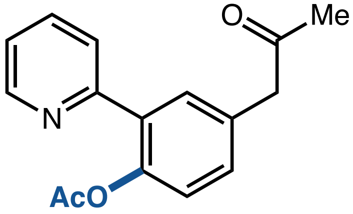
Substrate Directed Palladium-Catalyzed C–H Bond Functionalization



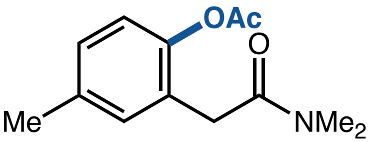
C–H nucleophile

oxidized product

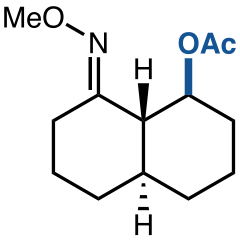
simple donors dictate positional selectivity



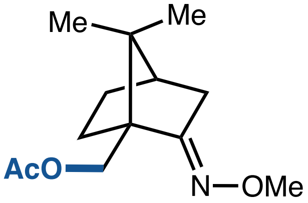
83% yield



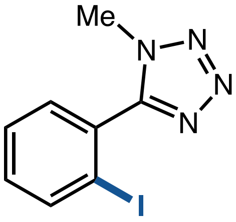
77% yield



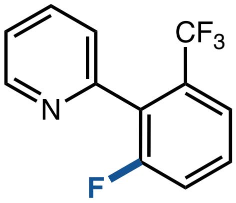
81% yield



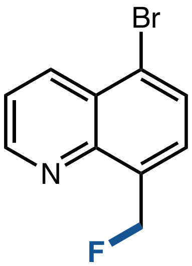
75% yield



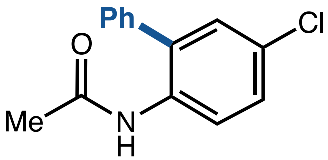
41% yield



59% yield



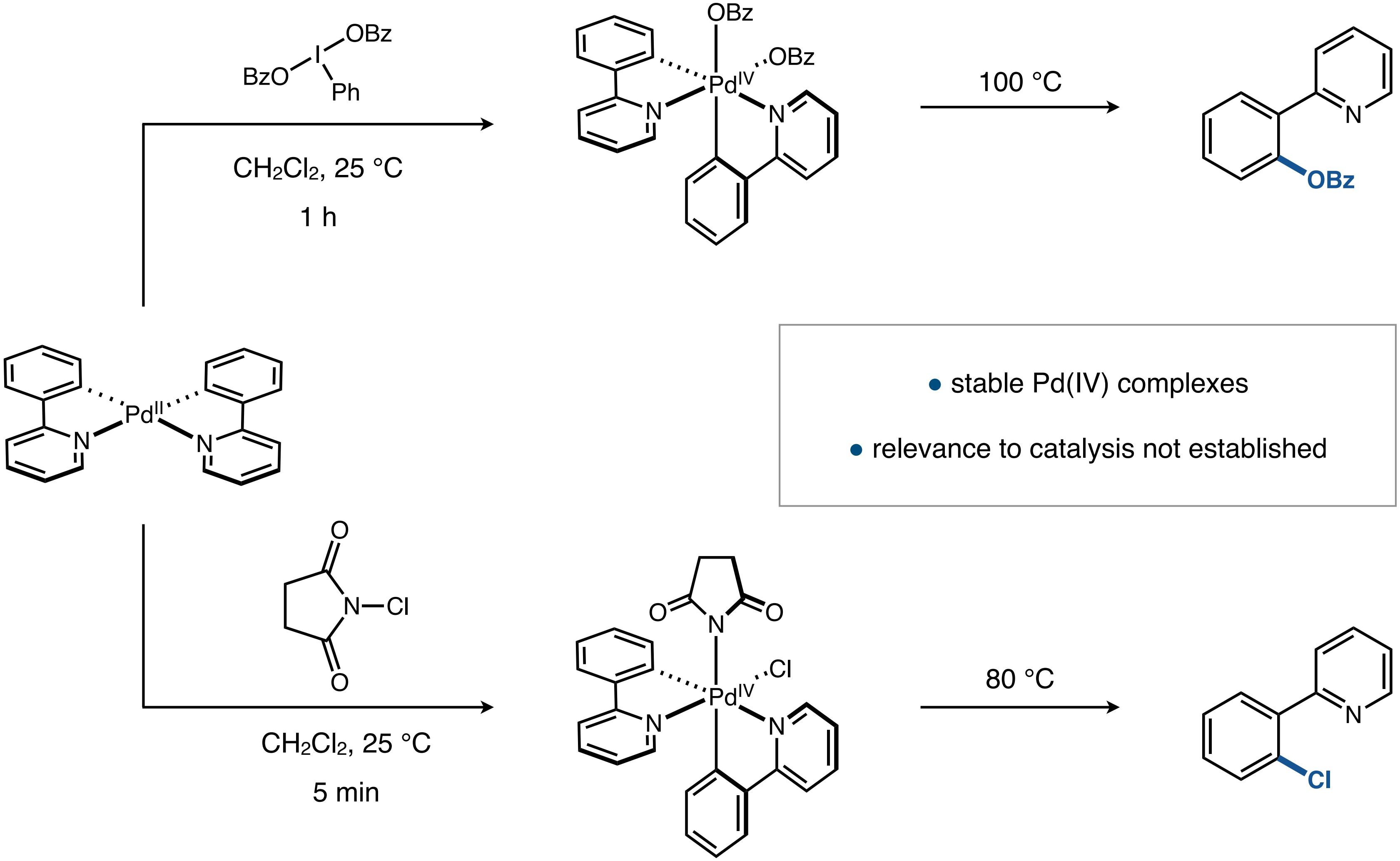
53% yield



67% yield

Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936–946.

Discrete Pd(IV) Complexes as Putative Intermediates

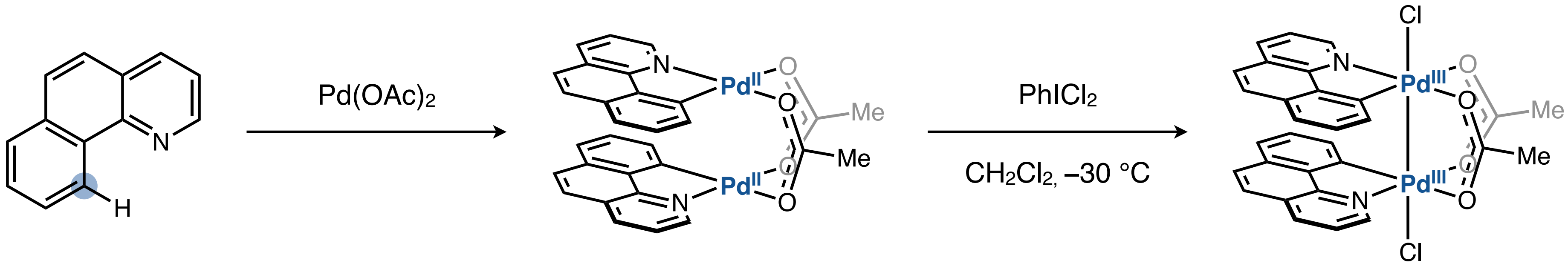


- stable Pd(IV) complexes
- relevance to catalysis not established

Dick, A. R.; Kampf, J. W.; Sanford, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 12790–12791.

Whitfield, S. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 15142–15143.

Bimetallic Pd(III) Complexes in Carbon–Heteroatom Bond Formation



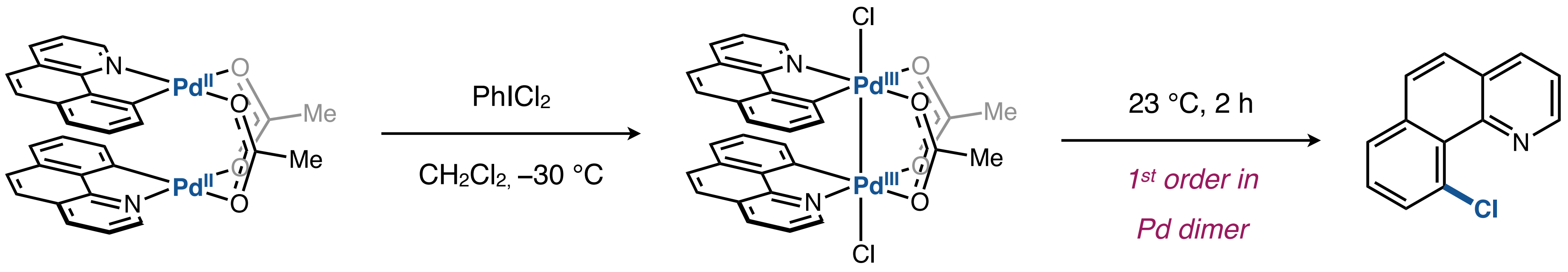
stable below –30 °C

Tobias Ritter

Max Planck Institute

Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302–309.

Bimetallic Pd(III) Complexes in Carbon–Heteroatom Bond Formation



$PhICl_2$

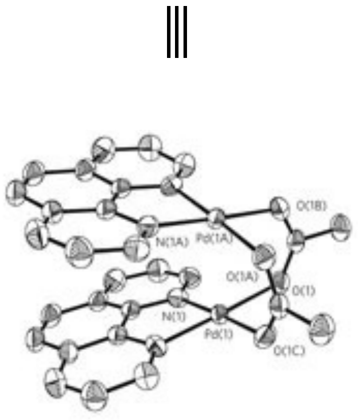
CH_2Cl_2, –30 °C

23 °C, 2 h

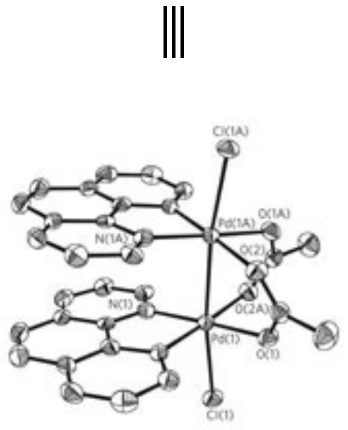
1st order in Pd dimer

stable below –30 °C

94% yield



Pd–Pd 2.84 Å



Pd–Pd 2.57 Å

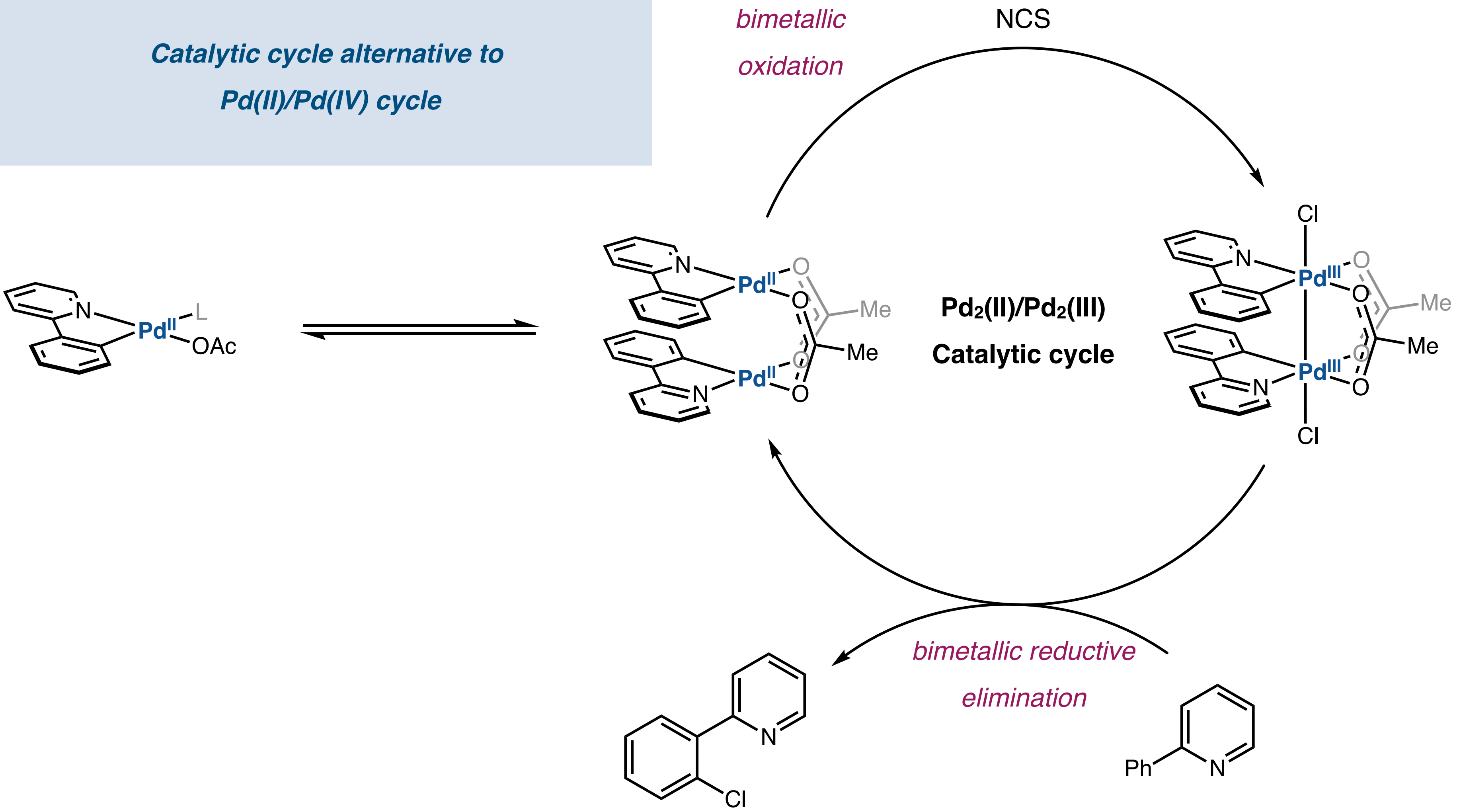
diamagnetic complex

substantial contraction of the Pd–Pd contact signifies formation of the bond

Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302–309.

Bimetallic Pd(III) Complexes in Carbon–Heteroatom Bond Formation

Catalytic cycle alternative to
Pd(II)/Pd(IV) cycle


bimetallic oxidation

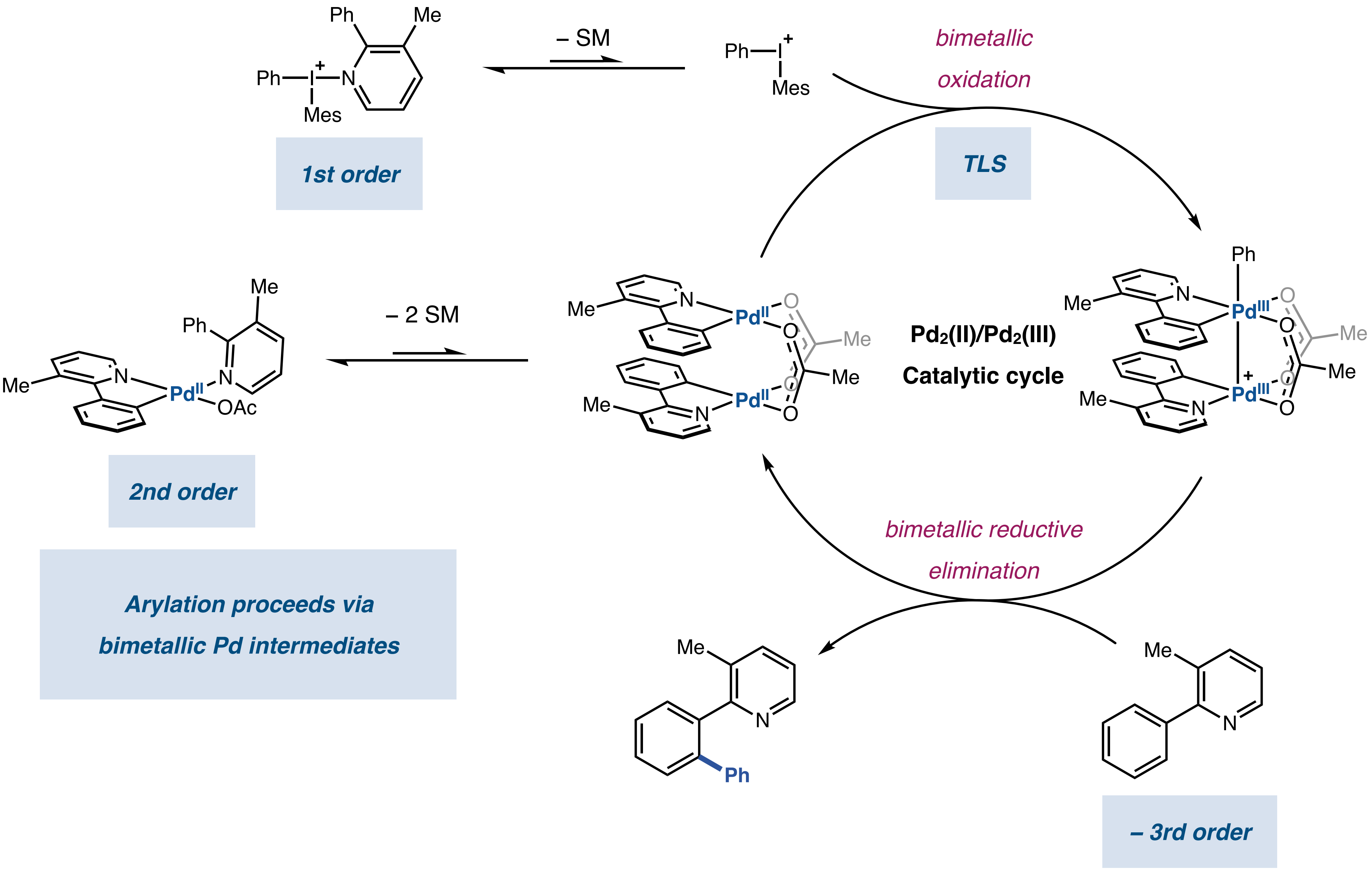
NCS

$Pd_2(II)/Pd_2(III)$ Catalytic cycle

bimetallic reductive elimination

Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302–309.

Bimetallic Pd(III) Complexes in C–H Arylation with Iodonium Salts



bimetallic oxidation

TLS

1st order

$Pd_2(II)/Pd_2(III)$

Catalytic cycle

2nd order

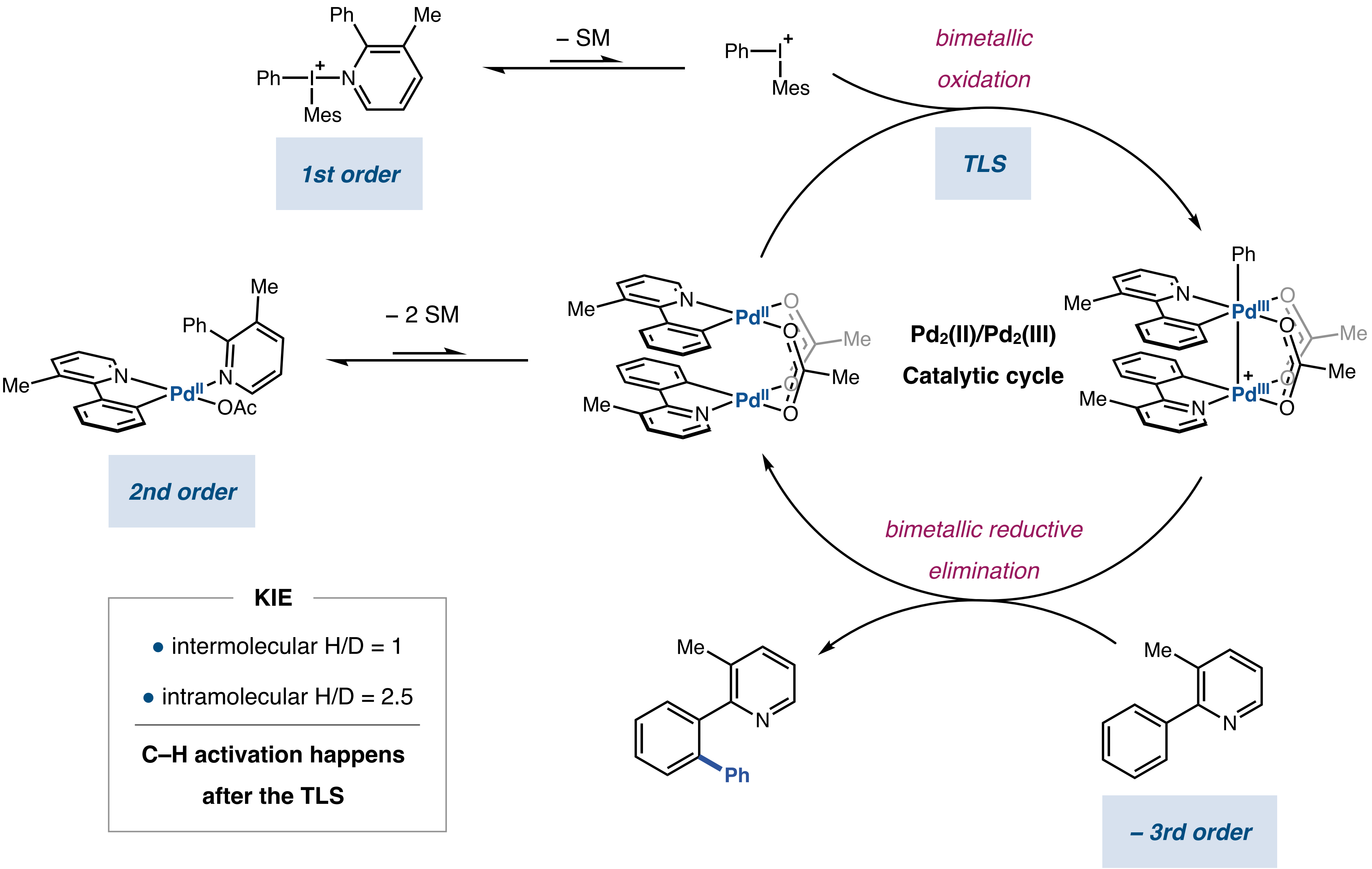
bimetallic reductive elimination

Arylation proceeds via bimetallic Pd intermediates

– 3rd order

Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234–11241.

Bimetallic Pd(III) Complexes in C–H Arylation with Iodonium Salts



– SM

bimetallic oxidation

TLS

1st order

– 2 SM

2nd order

$Pd_2(II)/Pd_2(III)$ Catalytic cycle

bimetallic reductive elimination

– 3rd order

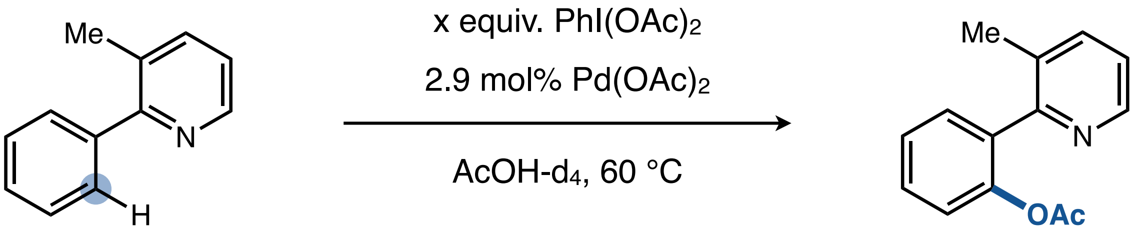
KIE

- intermolecular H/D = 1
- intramolecular H/D = 2.5

C–H activation happens after the TLS

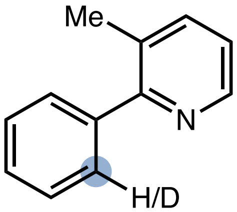
Deprez, N. R.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 11234–11241.

Bimetallic Pd(III) Complexes in Oxidative Acetoxylation Reactions



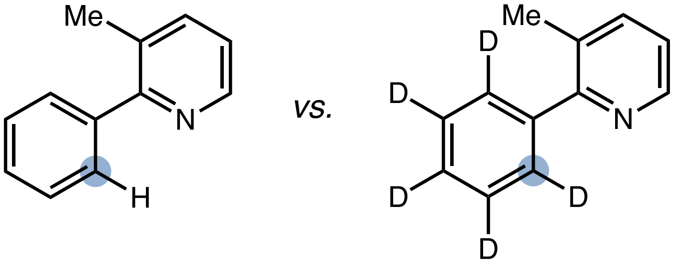
Kinetic studies

- 0^{th} order in $PhI(OAc)_2$



intramolecular

$k_H/k_D = 5.1$



intermolecular

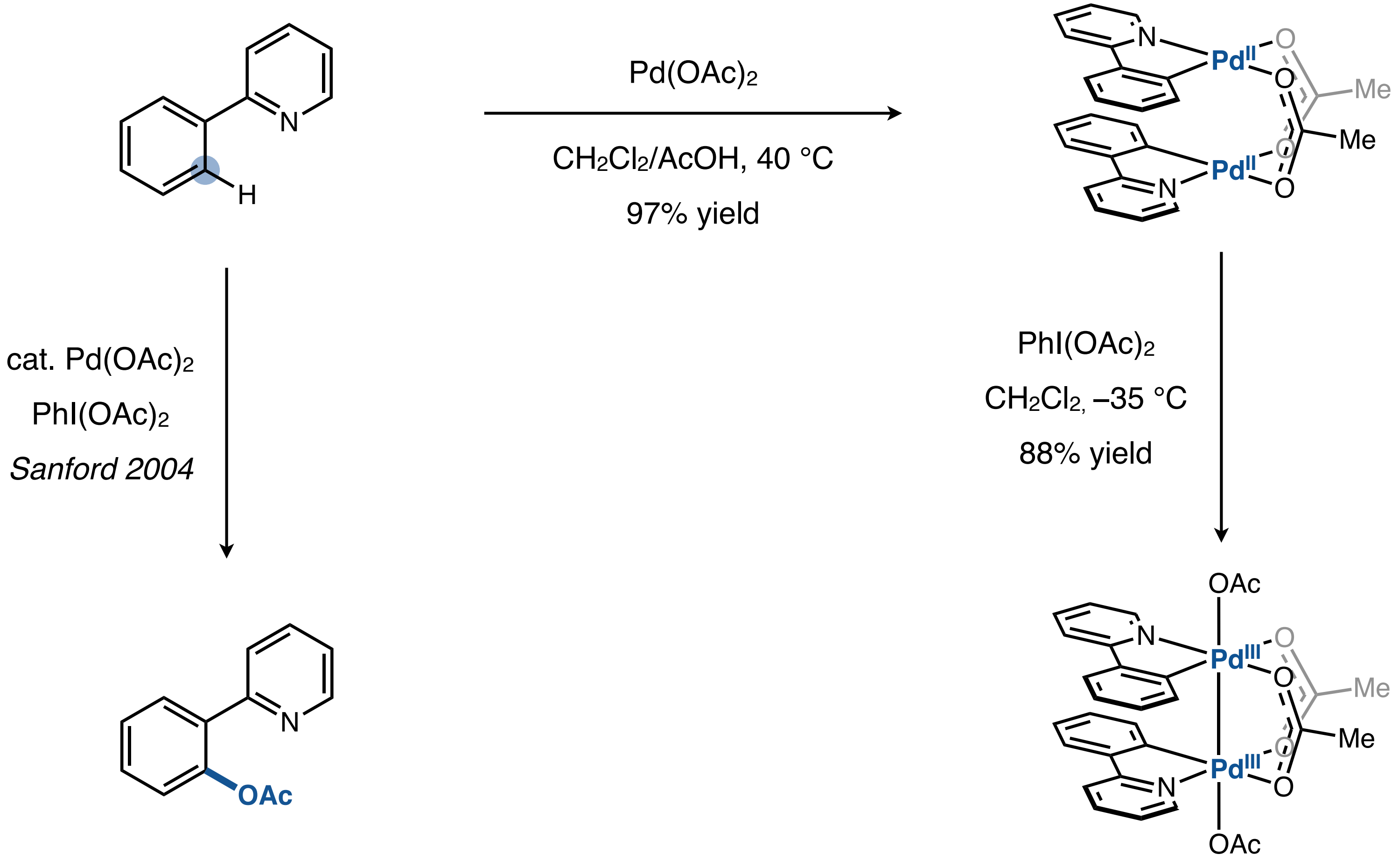
$k_H/k_D = 5.0$

cyclometalation is turnover-limiting step

Powers, D. C.; Geibel, M. A.; Klein, J. E.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050–17051.

Direct Observation of Pd(III)–Pd(III) Intermediates

Isolation of discrete intermediates



$Pd(OAc)_2$

$CH_2Cl_2/AcOH$, 40 °C

97% yield

cat. $Pd(OAc)_2$

$PhI(OAc)_2$

Sanford 2004

$PhI(OAc)_2$

CH_2Cl_2, –35 °C

88% yield

Powers, D. C.; Geibel, M. A.; Klein, J. E.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050–17051.

Direct Observation of Pd(III)–Pd(III) Intermediates

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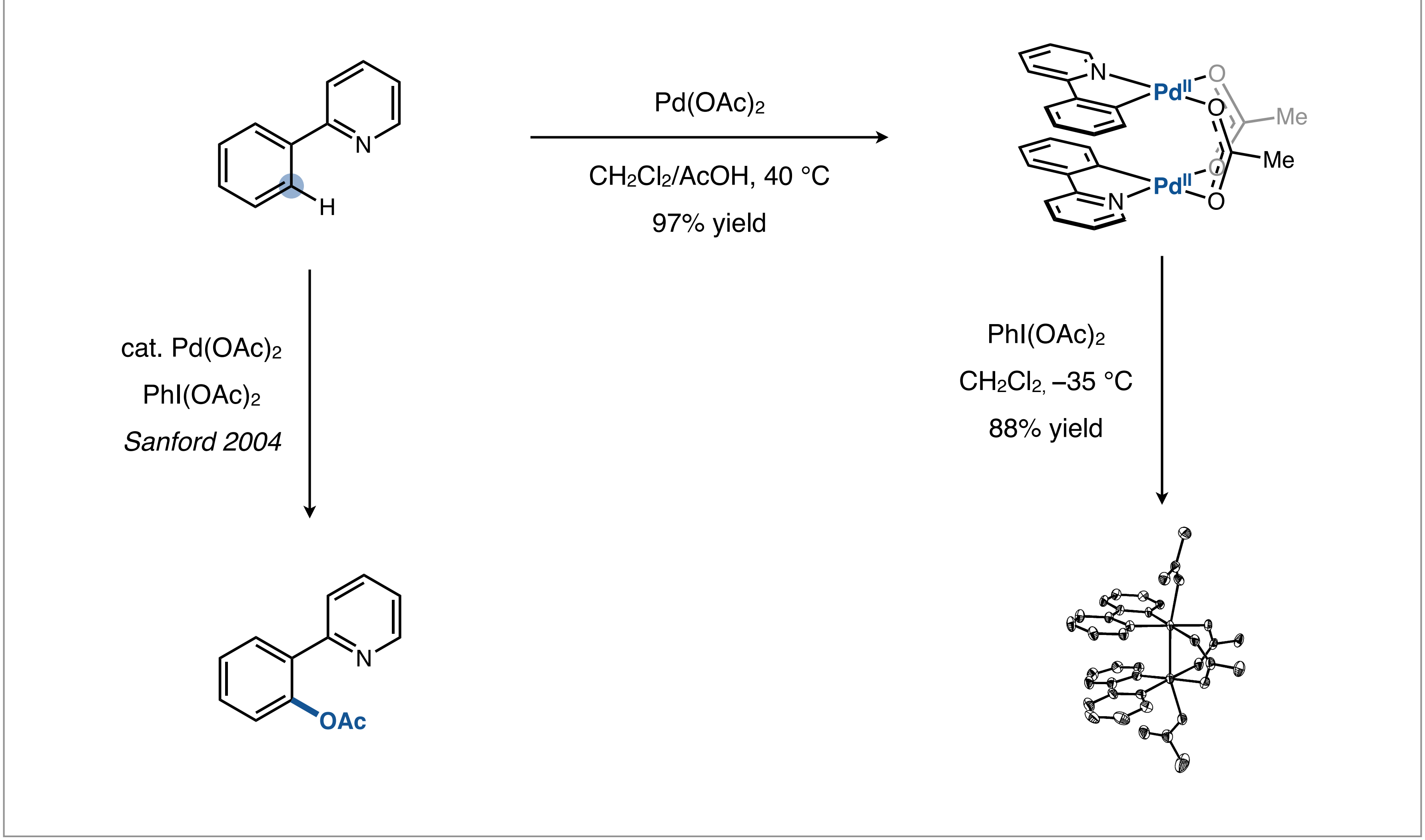

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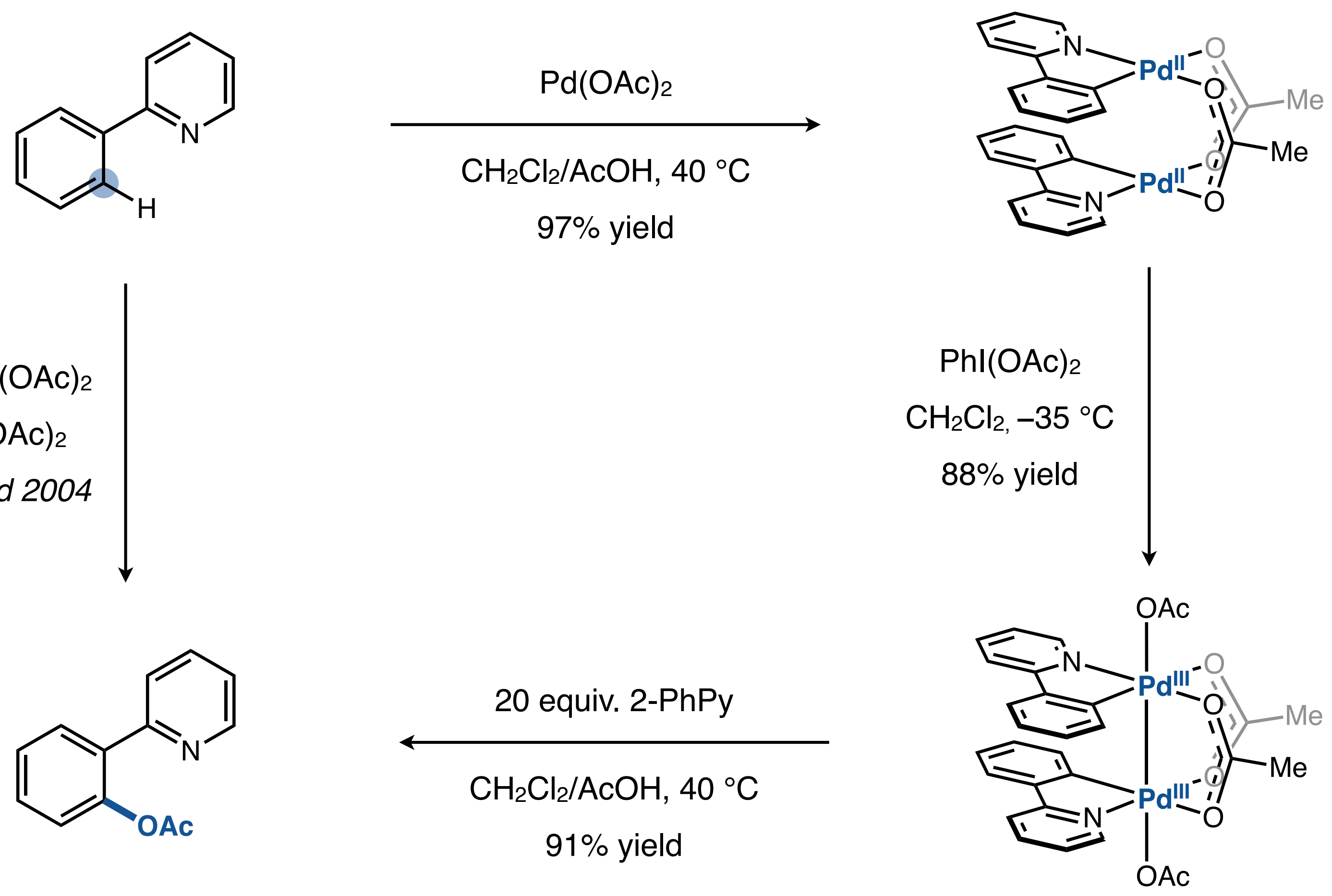


$Pd(OAc)_2$

$CH_2Cl_2/AcOH$, 40 °C

97% yield

$PhI(OAc)_2$

CH_2Cl_2, –35 °C

88% yield

20 equiv. 2-PhPy

$CH_2Cl_2/AcOH$, 40 °C

91% yield

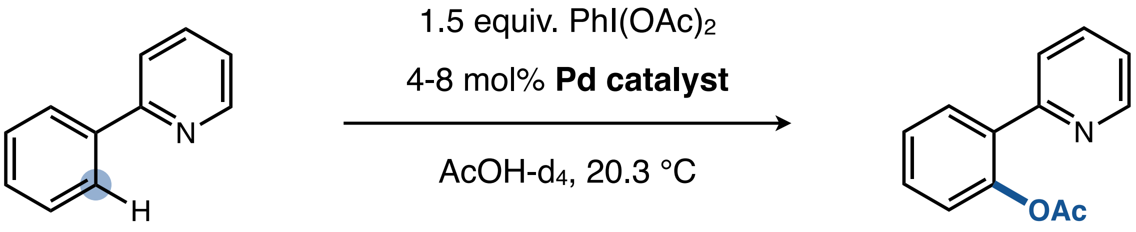
cat. $Pd(OAc)_2$

$PhI(OAc)_2$

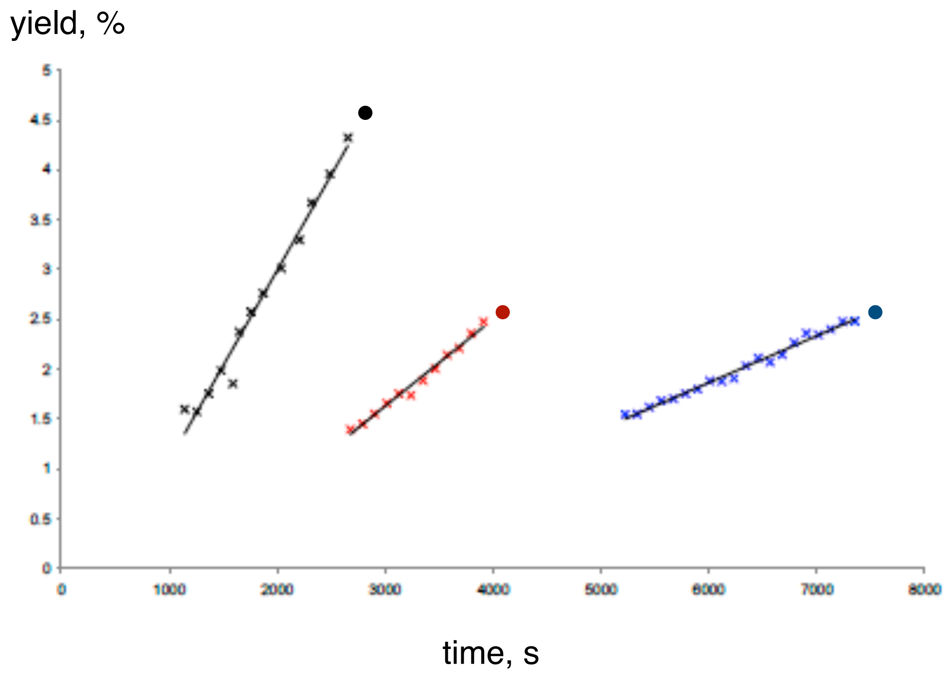
Sanford 2004

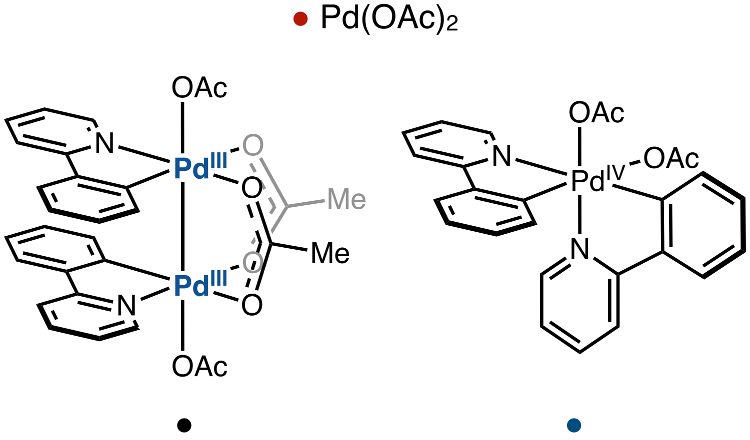
Powers, D. C.; Geibel, M. A.; Klein, J. E.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050–17051.

Bimetallic Pd(III) Complexes in Oxidative Acetoxylation Reactions



Initial rates of the product formation

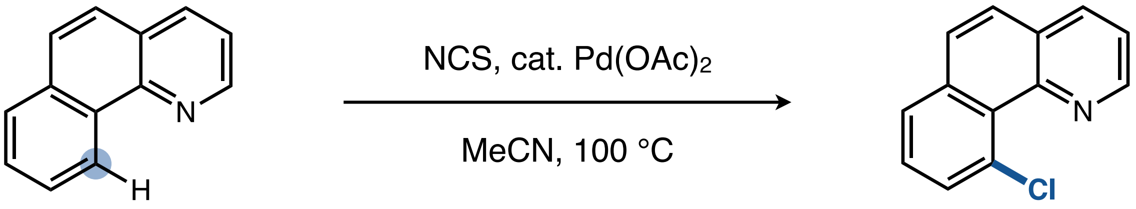


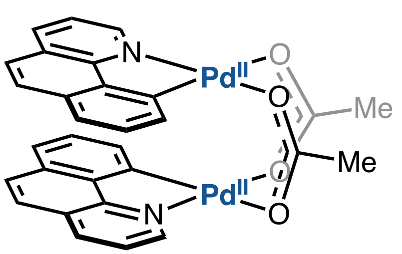


preformed Pd(III) complex is kinetically competent catalyst, but Pd(IV) complex is not

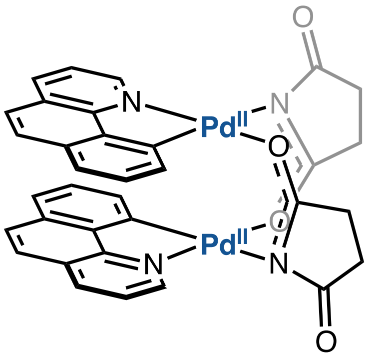
Powers, D. C.; Geibel, M. A.; Klein, J. E.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 17050–17051.

Bimetallic Pd(III) Complexes in Oxidative Acetoxylation Reactions





- not observed during catalysis



- catalyst resting state
- chemically competent catalyst
- kinetically incompetent catalyst

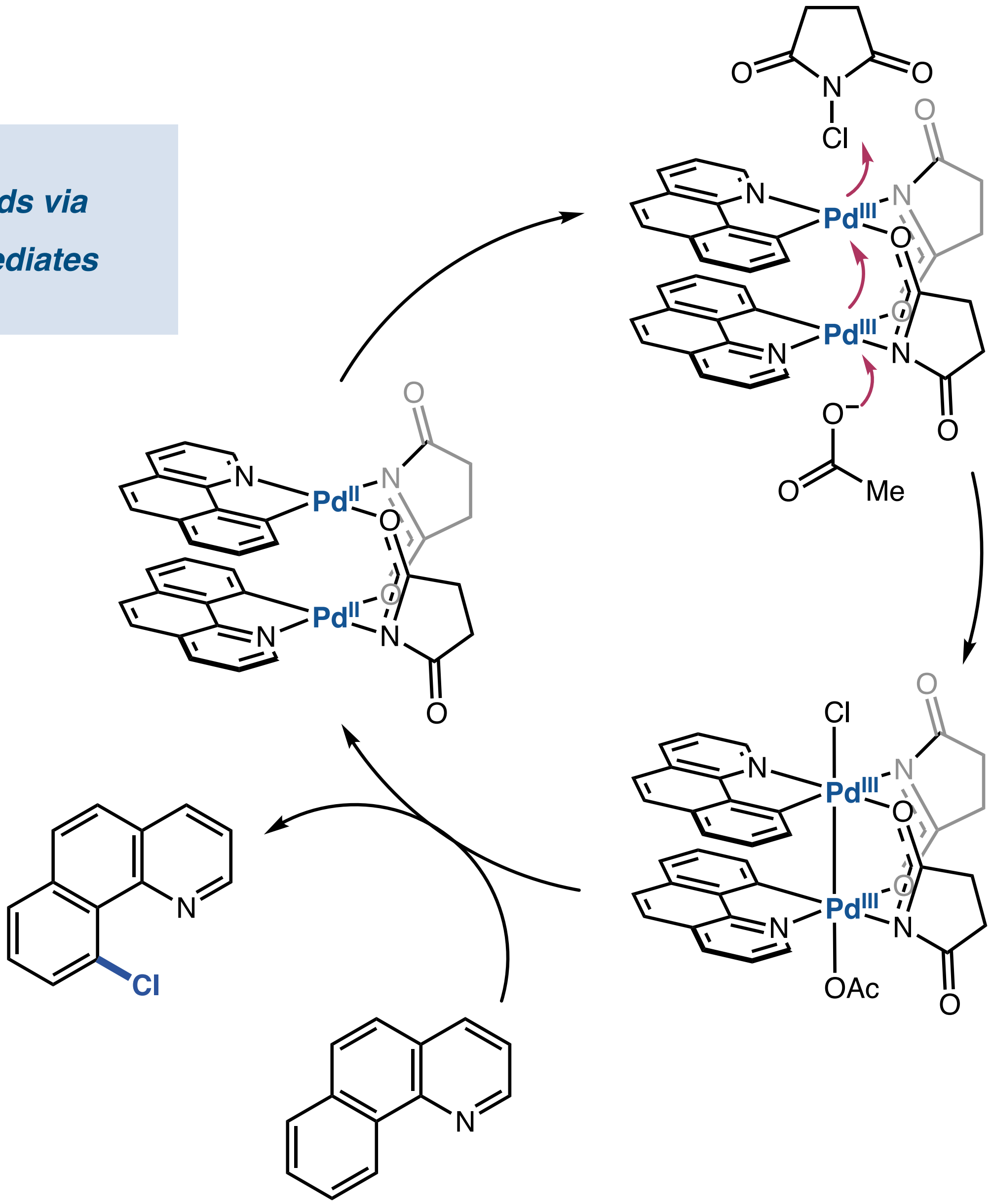
Kinetic studies

- 1st order in NCS
- 1st order in Pd dimer
- 1st order in acetate

Powers, D. C.; Xiao, D. Y.; Geibel, M. A. L; Ritter, T. *J. Am. Chem. Soc.* **2010**, *132*, 14530–14536.

Bimetallic Pd(III) Complexes in Oxidative Acetoxylation Reactions

Chlorination proceeds via bimetallic Pd intermediates



turnover-limiting

acetate-assisted

bimetallic oxidation

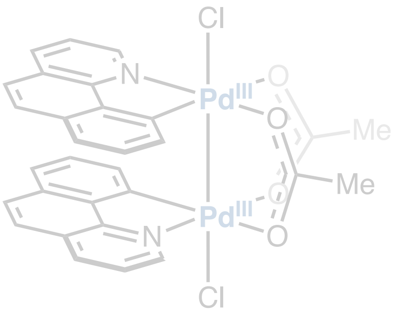
- highly selective C–Cl bond formation

- independently generated and observed by NMR

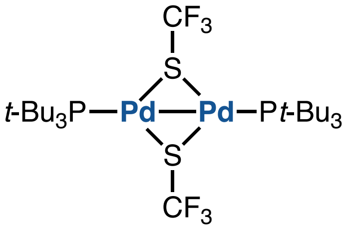
Powers, D. C.; Xiao, D. Y.; Geibel, M. A. L; Ritter, T. *J. Am. Chem. Soc.* **2010**, *132*, 14530–14536.

Metal-Metal Bonds in Catalysis — Outline of the Talk

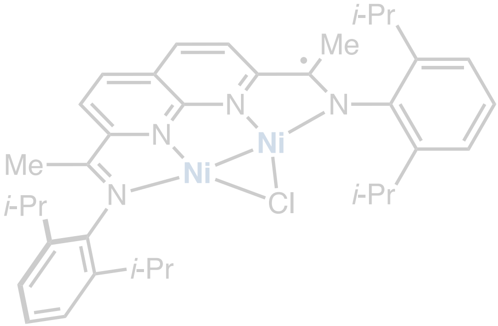
Pd(III)–Pd(III) dimers



Pd(I)–Pd(I) dimers

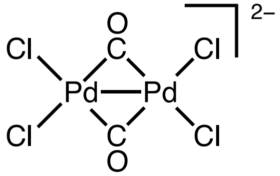


Ni_2 NDI complexes



Catalysis with Palladium(I) Dimers — Historical Development

First reported Pd(I) dimer

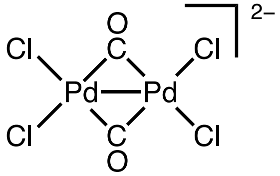


Gelman 1942

Gelman, A. D.; Meilakh, E. *Proc. USSR Acad. Sci.* **1942**, *36*, 188–195.

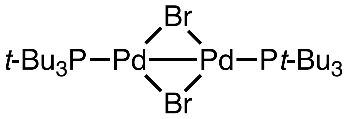
Catalysis with Palladium(I) Dimers — Historical Development

First reported Pd(I) dimer



Gelman 1942

Precatalyst for Pd(0)/Pd(II) cycle



Hartwig 2002

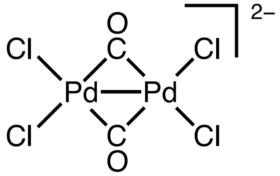
Novartis 2003

Stambuli, J. P.; Kuwano, R.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2002**, *41*, 4746–4748.

Prashad, M.; Mak, X. Y.; Liu, Y.; Repič, O. *J. Org. Chem.* **2003**, *68*, 1163–1164.

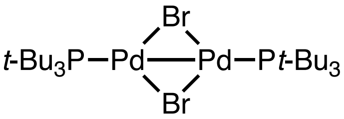
Catalysis with Palladium(I) Dimers — Historical Development

First reported Pd(I) dimer



Gelman 1942

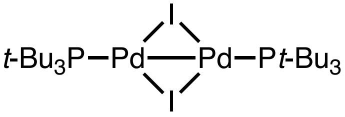
Precatalyst for Pd(0)/Pd(II) cycle



Hartwig 2002

Novartis 2003

Can Pd(I) dimers enable generic bimetallic Pd(I)/Pd(II) catalysis?



Schoenebeck 2013

Bonney, K. J.; Proutiere, F.; Schoenebeck, F. *Chem. Sci.* **2013**, *4*, 4434–4439.

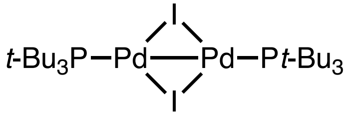
Kalvet, I.; Bonney, K. J.; Schoenebeck, F. *J. Org. Chem.* **2014**, *79*, 12041–12046.

Catalysis with Palladium(I) Dimers — Historical Development

Franziska Schoenebeck

RWTH Aachen University

Can Pd(I) dimers enable generic bimetallic Pd(I)/Pd(II) catalysis?



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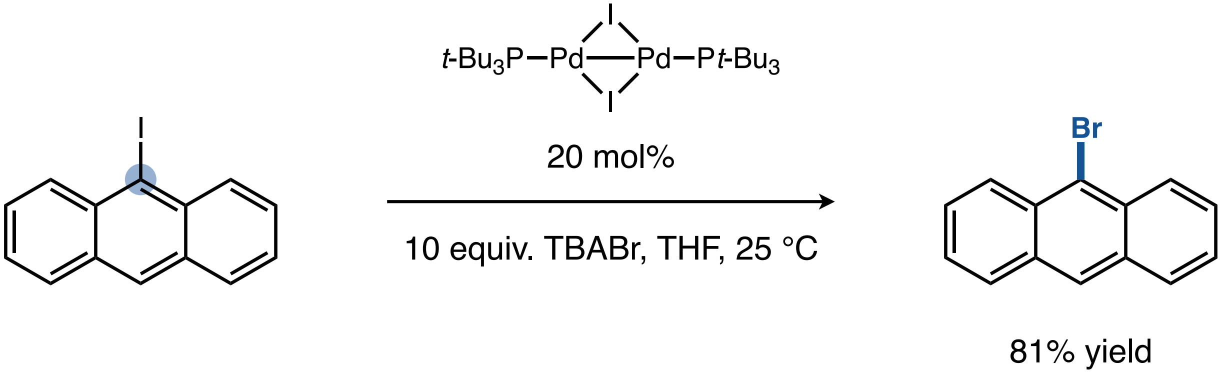
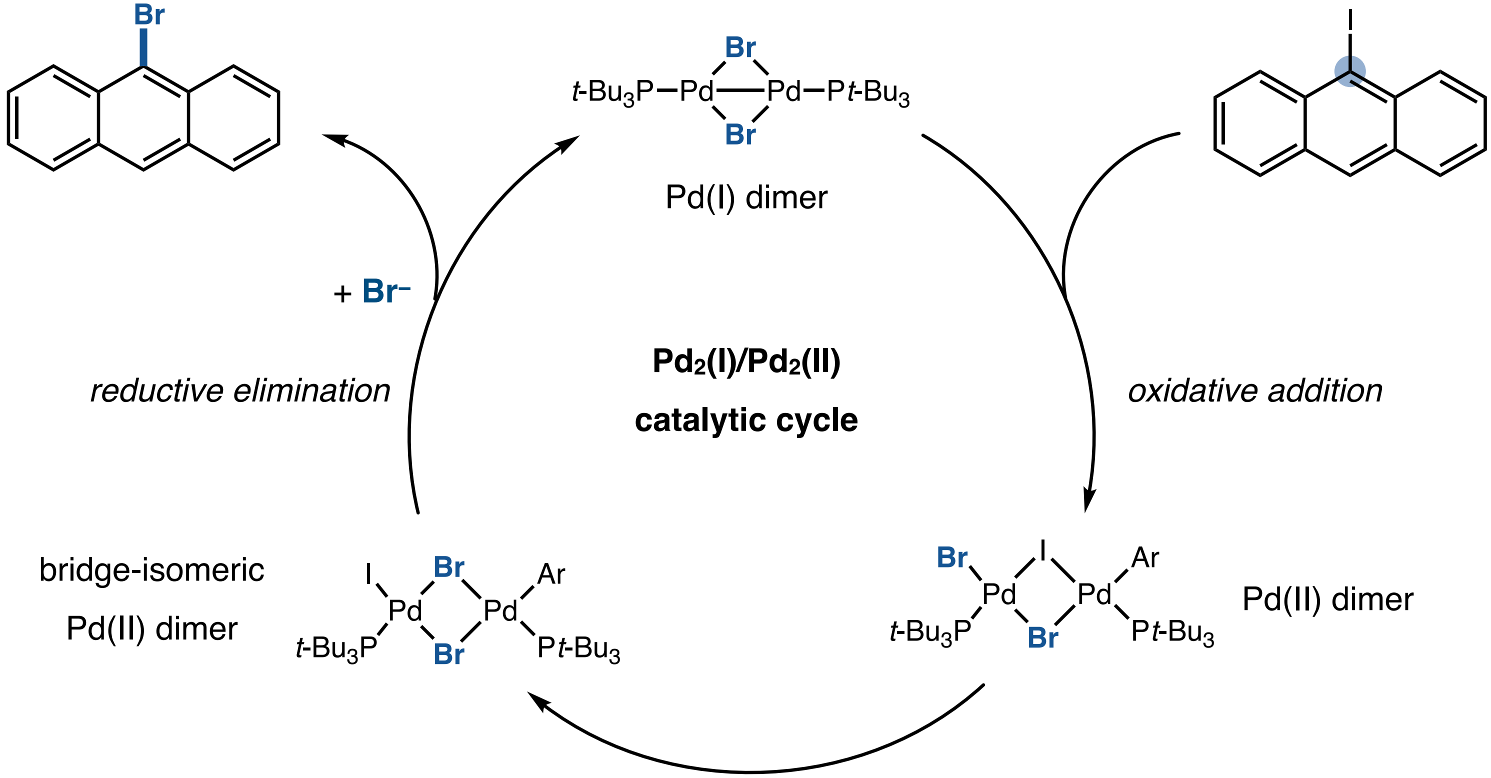
Kalvet, I.; Bonney, K. J.; Schoenebeck, F. *J. Org. Chem.* **2014**, *79*, 12041–12046.

Catalysis with Palladium(I) Dimers — Early Mechanistic Studies





Bonney, K. J.; Proutiere, F.; Schoenebeck, F. *Chem. Sci.* **2013**, *4*, 4434–4439.

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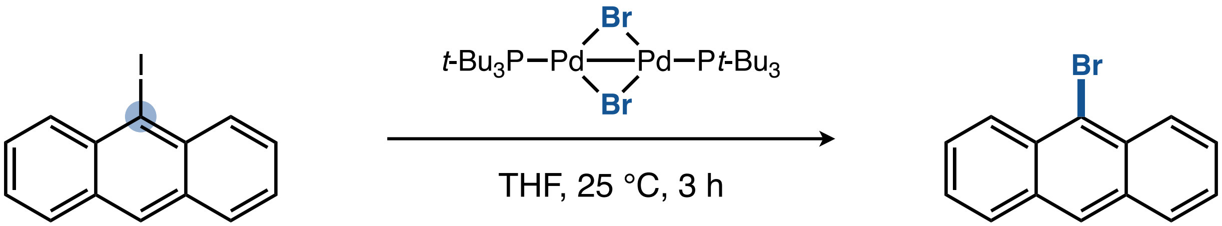


10 equiv.

92% yield

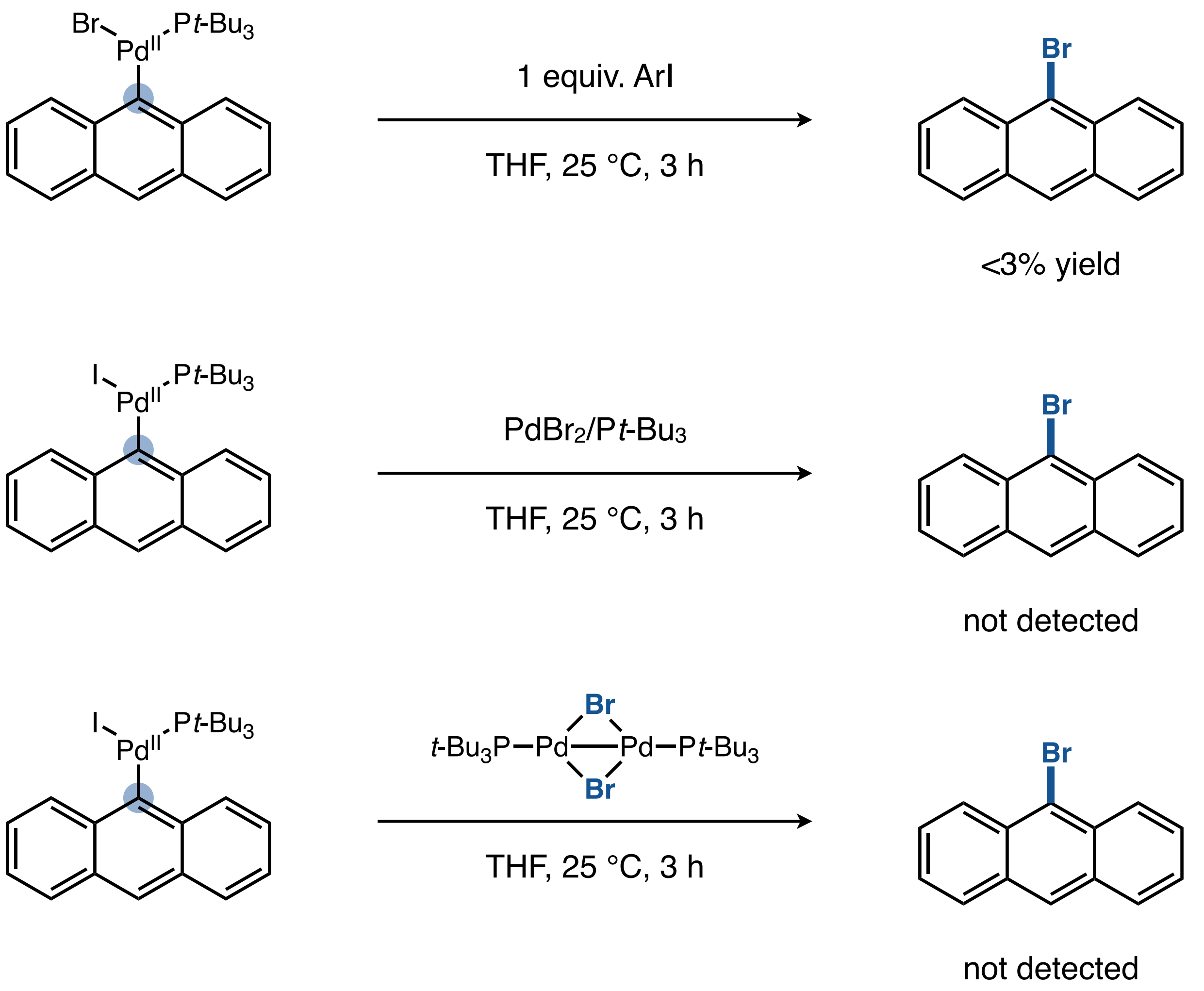
Control experiment	**ArBr yield**
$Pd_2(dba)_3$/P*t*-Bu_3 + TBABr	1%
Pd(P*t*-Bu_3)$_2$ + TBABr	3%

Pd(0) catalysis is inefficient

Bonney, K. J.; Proutiere, F.; Schoenebeck, F. *Chem. Sci.* **2013**, *4*, 4434–4439.

Kalvet, I.; Bonney, K. J.; Schoenebeck, F. *J. Org. Chem.* **2014**, *79*, 12041–12046.

Direct Reactivity of a Pd(I) Dimer with an Aryl Iodide



Reductive elimination from mononuclear Pd(II) is not viable

Bonney, K. J.; Proutiere, F.; Schoenebeck, F. *Chem. Sci.* **2013**, *4*, 4434–4439.

Kalvet, I.; Bonney, K. J.; Schoenebeck, F. *J. Org. Chem.* **2014**, *79*, 12041–12046.

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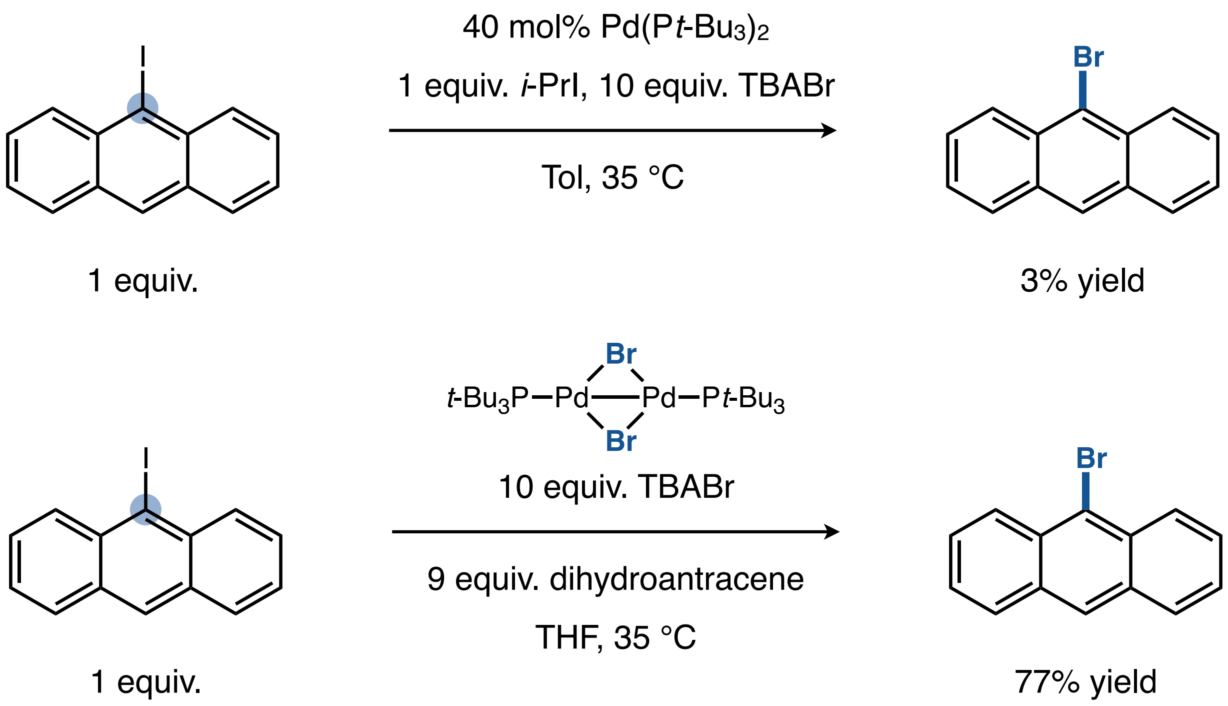
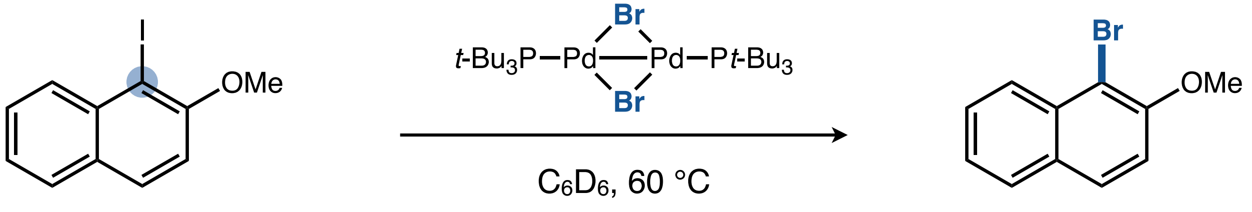


The reaction is unlikely to proceed via intermediate aryl radicals

Bonney, K. J.; Proutiere, F.; Schoenebeck, F. *Chem. Sci.* **2013**, *4*, 4434–4439.

Kalvet, I.; Bonney, K. J.; Schoenebeck, F. *J. Org. Chem.* **2014**, *79*, 12041–12046.

Direct Reactivity of a Pd(I) Dimer with an Aryl Iodide



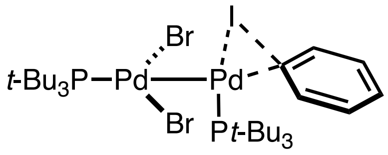
iodoarene

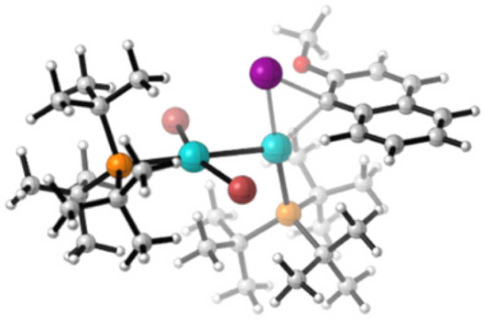
bromoarene

Kinetic studies

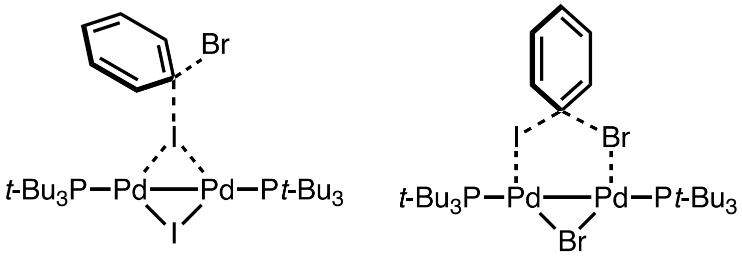
- 1st order in ArI
- 1st order in Pd dimer

Favored TS





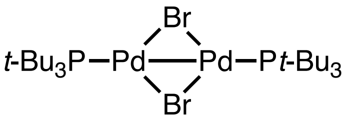
Disfavored TSs



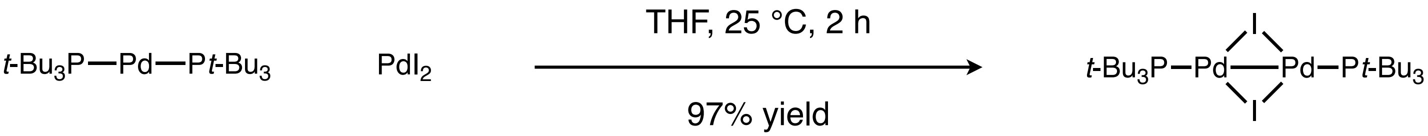
Bonney, K. J.; Proutiere, F.; Schoenebeck, F. *Chem. Sci.* **2013**, *4*, 4434–4439.

Kalvet, I.; Bonney, K. J.; Schoenebeck, F. *J. Org. Chem.* **2014**, *79*, 12041–12046.

Trifluoromethylthiolation and Trifluoromethylselenolation of Aryl Iodides and Bromides



- limited stability towards air in crystalline form
- highly air-sensitive in solution
- optimal for Pd(0) catalysis

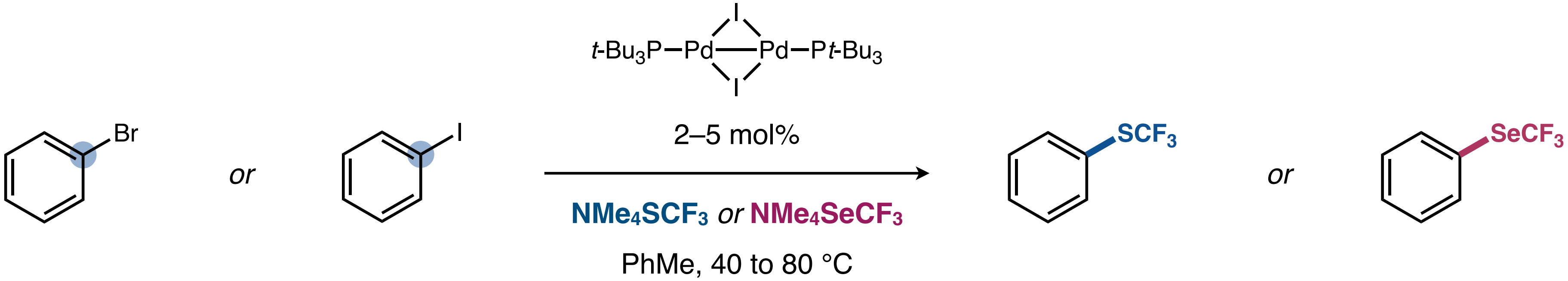


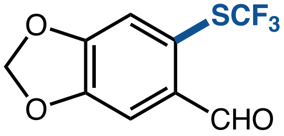
- air-stable both in crystalline form and in solutions
- optimal for Pd(I) catalysis

Yin, G.; Kalvet, I.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 6809–6813.

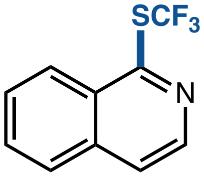
Aufiero, M.; Sperger, T.; Tsang, A. S.-K.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 10322–10326.

Trifluoromethylthiolation and Trifluoromethylselenolation of Aryl Iodides and Bromides

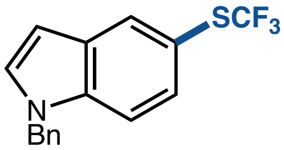




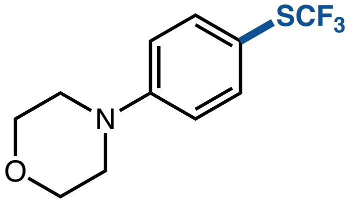
94% yield



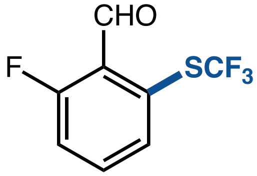
65% yield



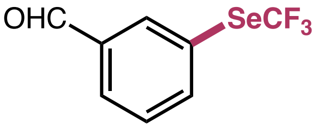
98% yield



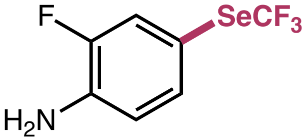
99% yield



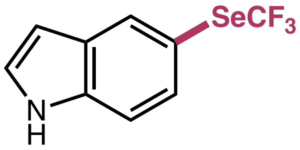
86% yield



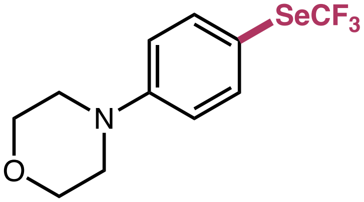
49% yield



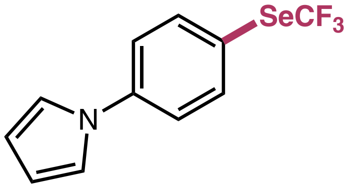
95% yield



94% yield



80% yield

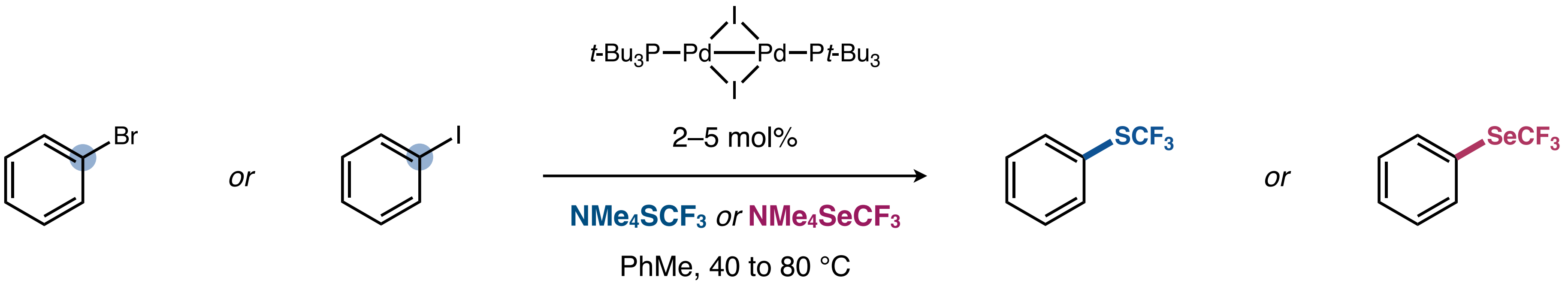


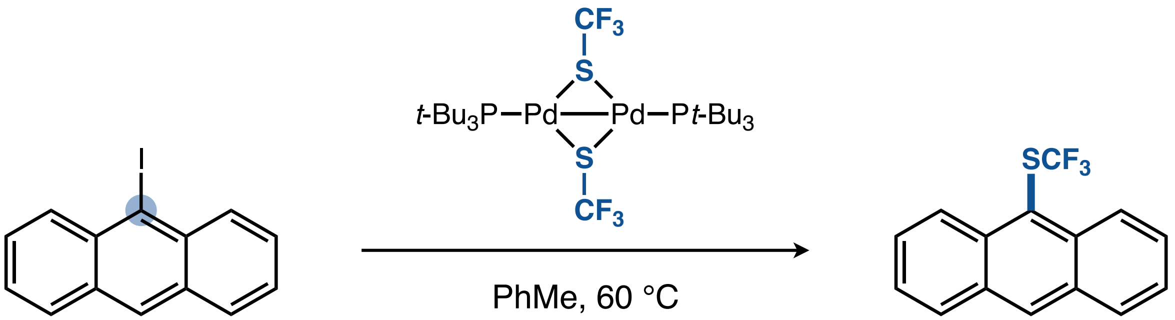
83% yield

Yin, G.; Kalvet, I.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 6809–6813.

Aufiero, M.; Sperger, T.; Tsang, A. S.-K.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 10322–10326.

Trifluoromethylthiolation and Trifluoromethylselenolation of Aryl Iodides and Bromides





Kinetic studies

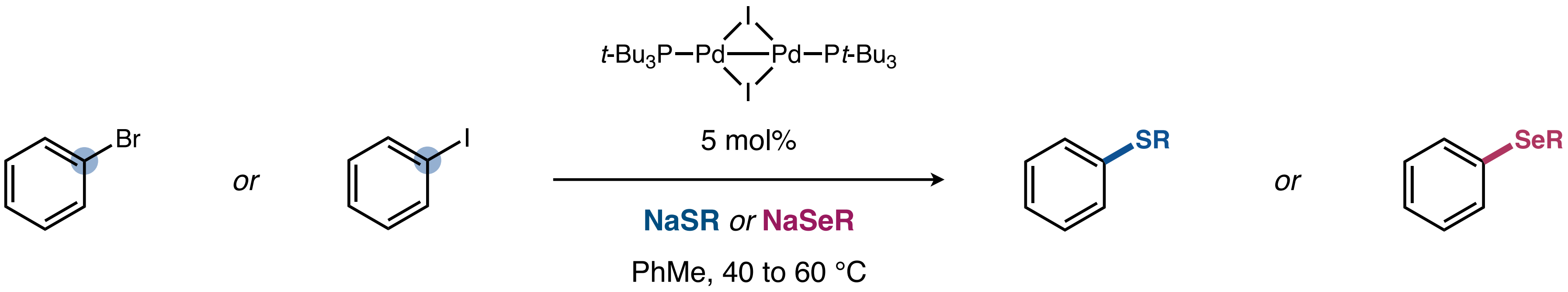
- 1st order in Pd dimer

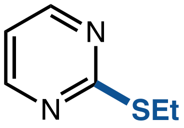
- *in situ* ^{31}P NMR did not detect any Pd(0) or Pd(II) species
- computations support proposed dimeric Pd(I)/Pd(II) cycles

Yin, G.; Kalvet, I.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 6809–6813.

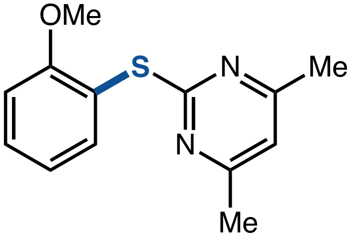
Aufiero, M.; Sperger, T.; Tsang, A. S.-K.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015**, *54*, 10322–10326.

Thiolation and Selenolation of Aryl Iodides and Bromides

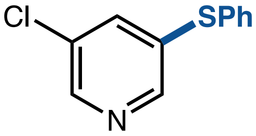




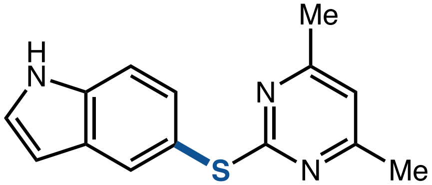
90% yield



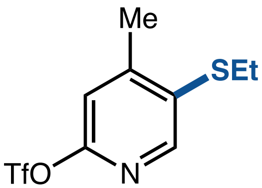
97% yield



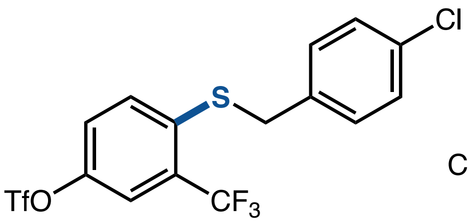
93% yield



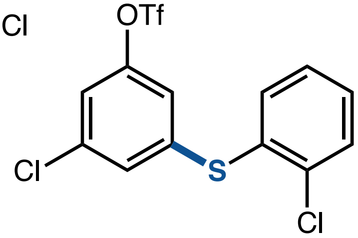
97% yield



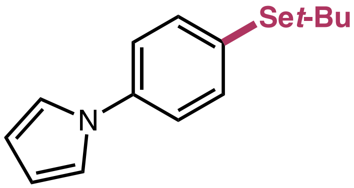
98% yield



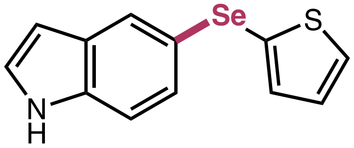
89% yield



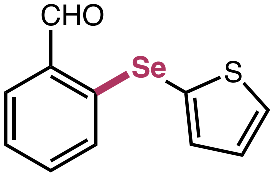
92% yield



95% yield



91% yield

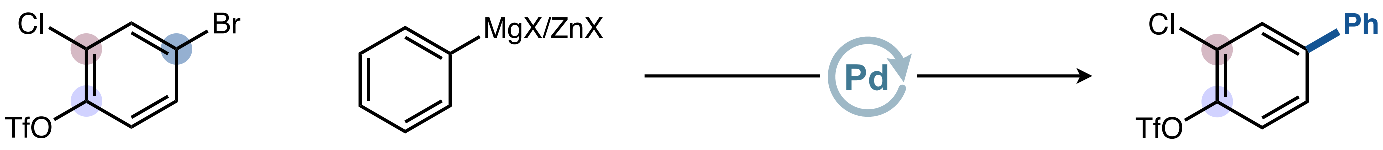


90% yield

Scattolin, T.; Senol, E.; Yin, G.; Guo, Q.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2018**, *57*, 12425–12429.

Senol, E.; Scattolin, T.; Schoenebeck, F. *Chem. Eur. J.* **2019**, *25*, 9419–9422.

Chemoselective Coupling of Polyhalogenated Arenes



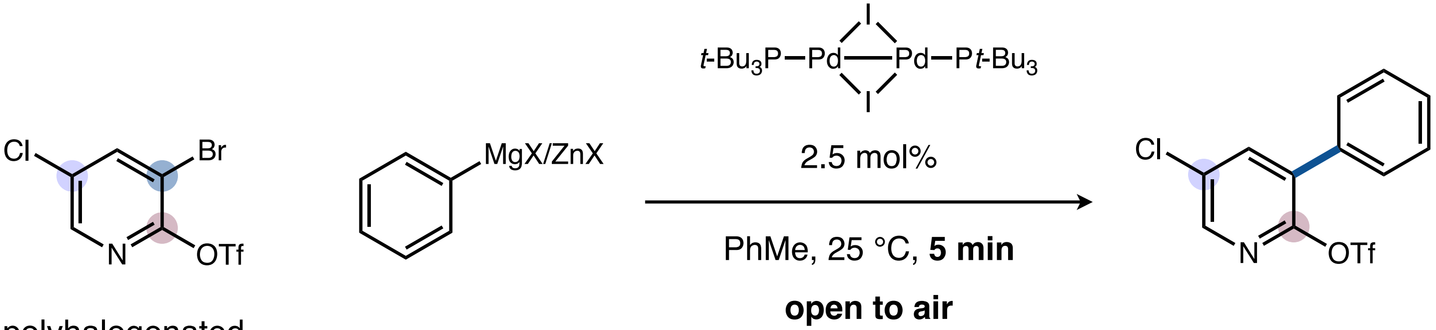
polyhalogenated arene

selectivity unpredictably depends on substrate and reaction conditions

Pd catalyst	**Yield**
Pd(OAc)$_2$/SPhos	8% yield
RuPhos-G2	2% yield
PEPPSI-IPr	13% yield
Pd(I) dimer	**93% yield**

Kalvet, I.; Magnin, G.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 1581–1585.

Chemoselective Coupling of Polyhalogenated Arenes

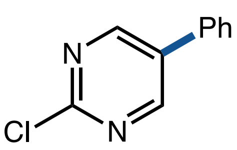


polyhalogenated

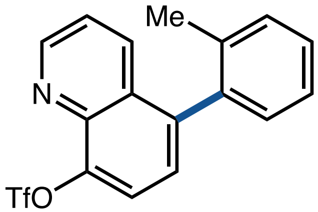
arene

exclusive coupling of

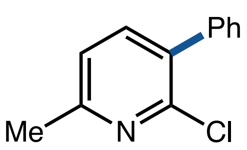
the bromide



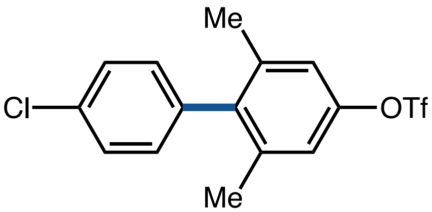
95% yield



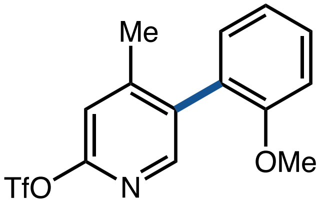
78% yield



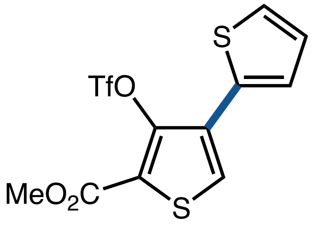
96% yield



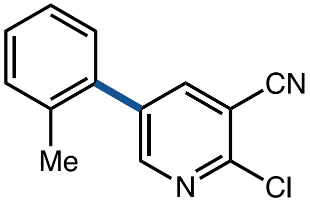
92% yield



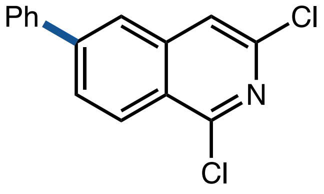
86% yield



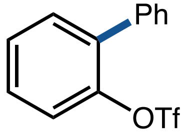
86% yield



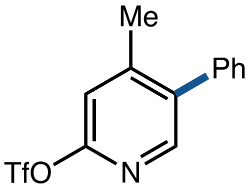
71% yield



92% yield



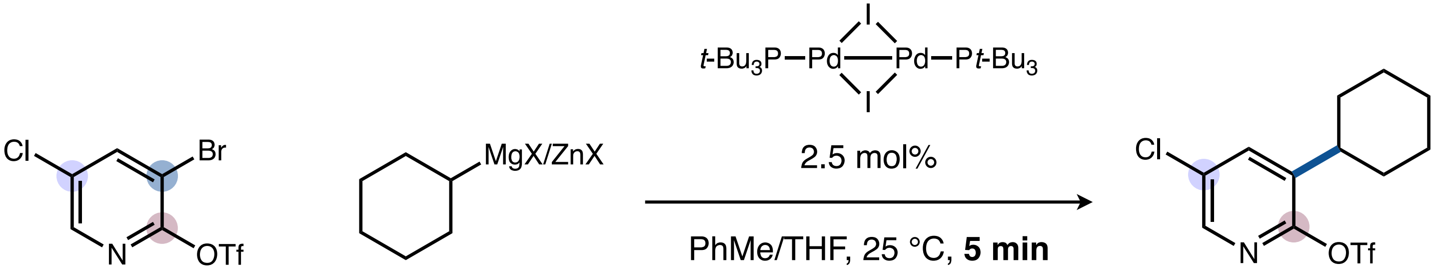
93% yield



86% yield

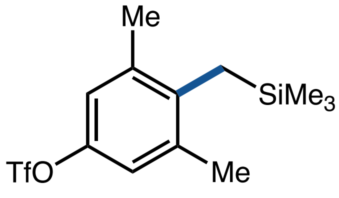
Kalvet, I.; Magnin, G.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 1581–1585.

Chemoselective Coupling of Polyhalogenated Arenes

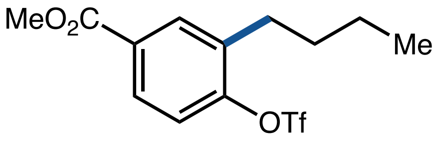


polyhalogenated arene

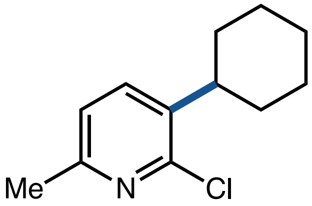
exclusive coupling of the bromide



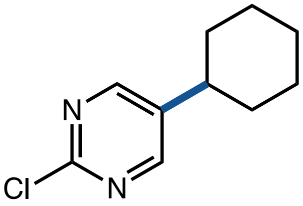
93% yield



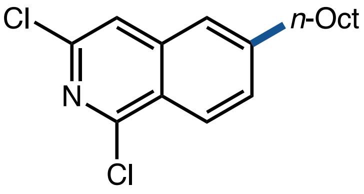
79% yield



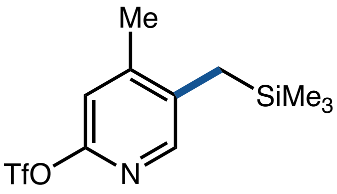
87% yield



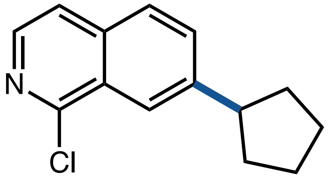
67% yield



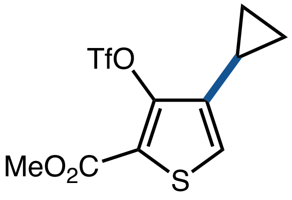
76% yield



79% yield



94% yield

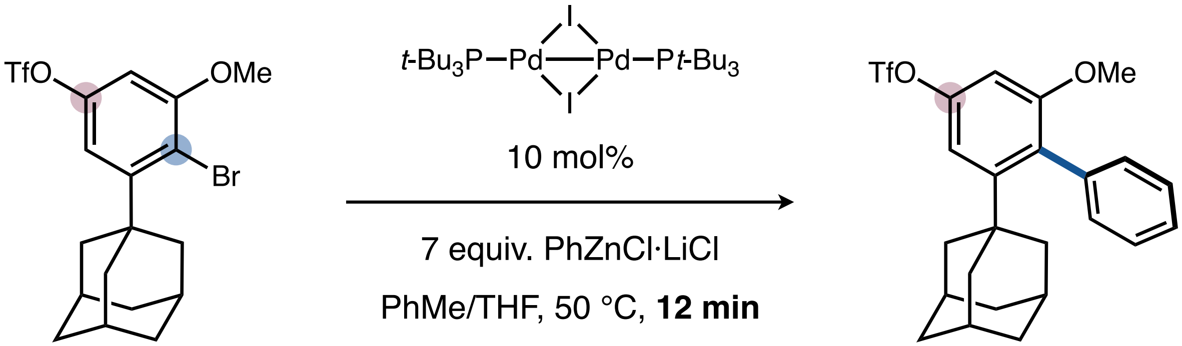


83% yield

Kalvet, I.; Sperger, T.; Scattolin, T.; Magnin, G.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 7078–7082.

Catalysis with Palladium(I) Dimers — Early Mechanistic Studies

Selectivity remains even in case of extreme steric hinderance



10 mol%

7 equiv. PhZnCl·LiCl

PhMe/THF, 50 °C, **12 min**

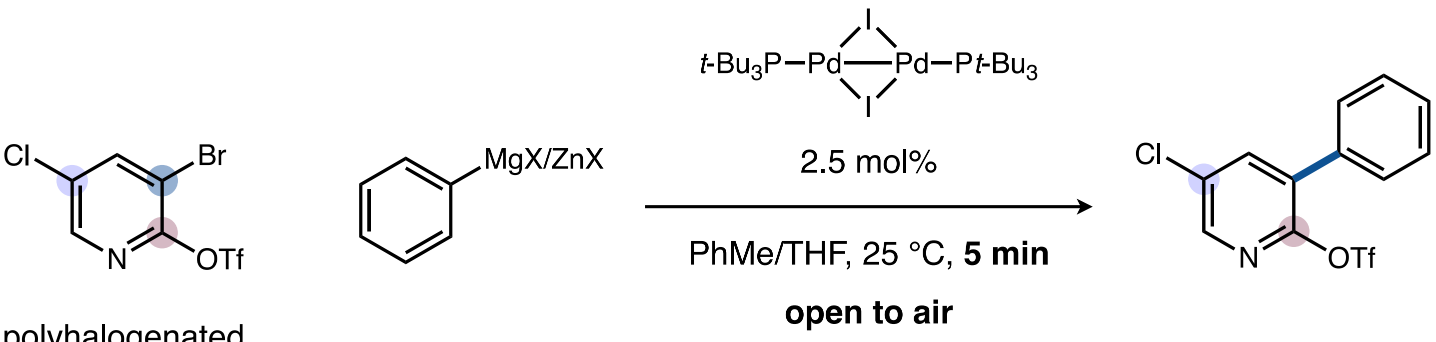
electronic and steric deactivation of ArBr

flask open to air

65% yield

Kalvet, I. et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 7721–7725.

Chemoselective Coupling of Polyhalogenated Arenes



2.5 mol%

PhMe/THF, 25 °C, **5 min**

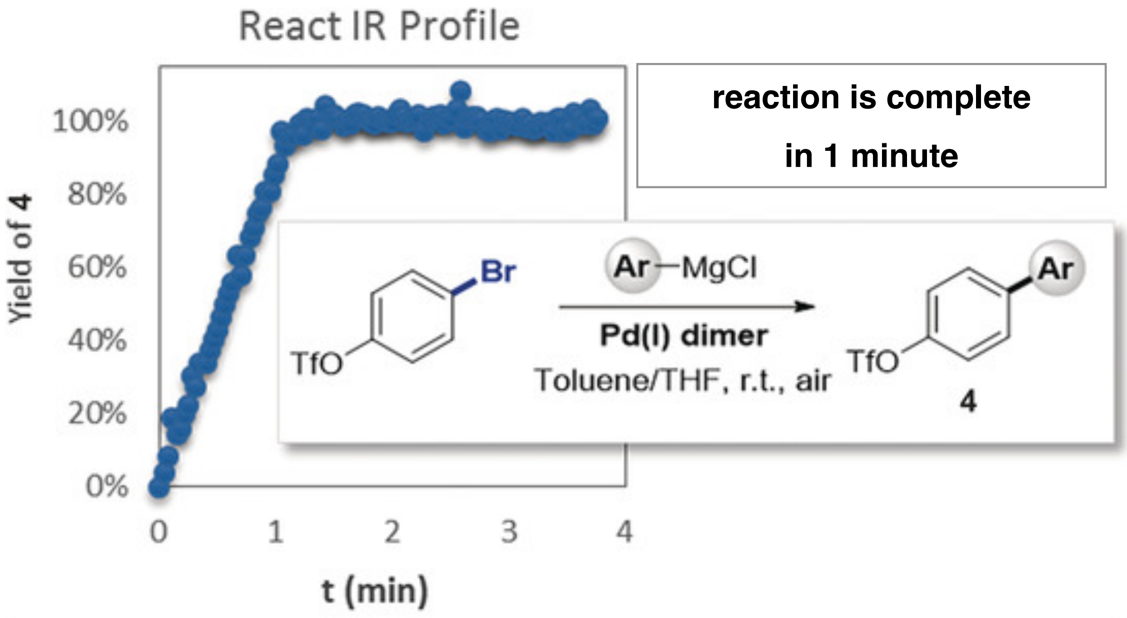
open to air

polyhalogenated

arene

exclusive coupling of

the bromide

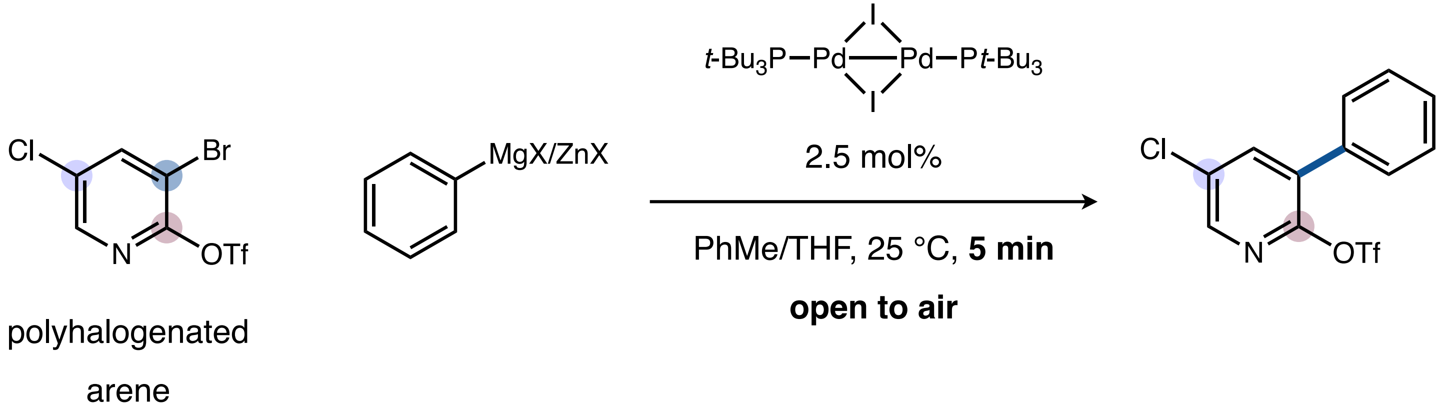


reaction is complete

in 1 minute

Kalvet, I.; Magnin, G.; Schoenebeck, F. Angew. Chem. Int. Ed. **2017**, *56*, 1581–1585.

Chemoselective Coupling of Polyhalogenated Arenes



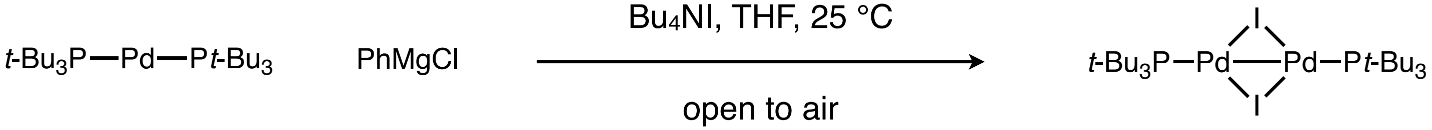
polyhalogenated arene

2.5 mol%

PhMe/THF, 25 °C, **5 min**

open to air

exclusive coupling of the bromide



Bu_4NI, THF, 25 °C

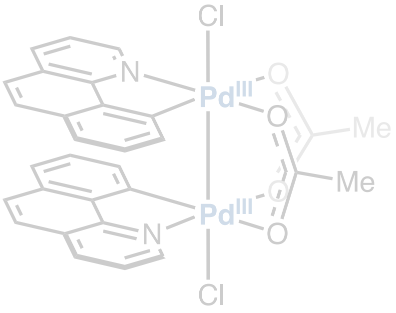
open to air

- spontaneous formation of Pd(I) dimers

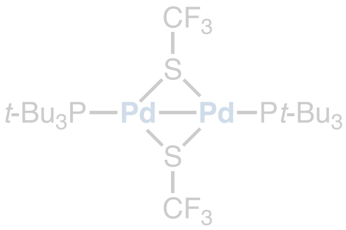
Kalvet, I.; Magnin, G.; Schoenebeck, F. Angew. Chem. Int. Ed. **2017**, *56*, 1581–1585.

Metal-Metal Bonds in Catalysis — Outline of the Talk

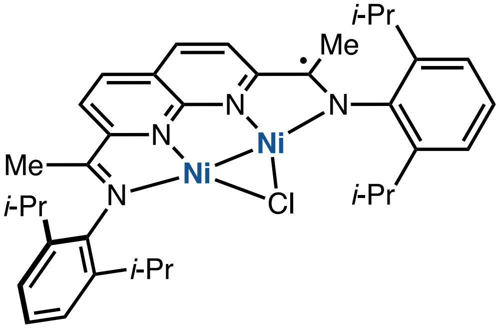
Pd(III)–Pd(III) dimers



Pd(I)–Pd(I) dimers



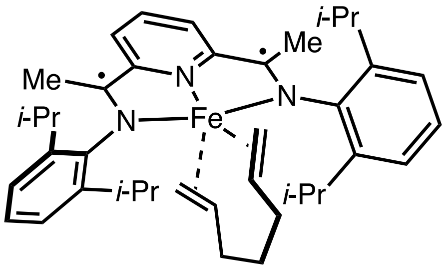
Ni$_2$ NDI complexes



Dinickel Active Sites Supported by Redox-Active Ligands

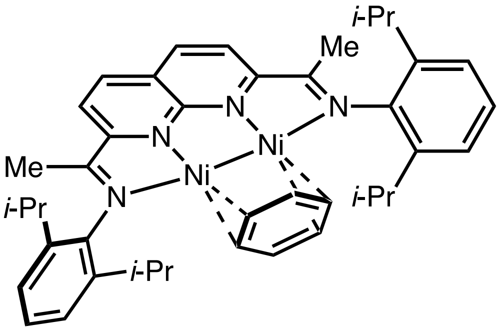
Pyridine diimine

redox-active ligand

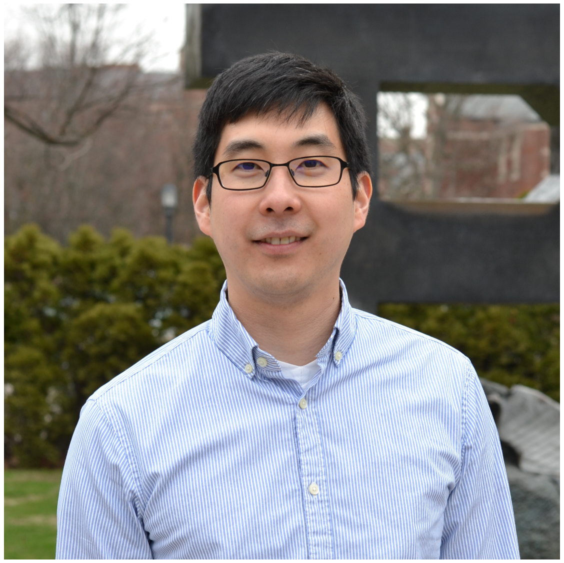


Chirik 2006

Naphthyridine diimine (NDI)



Can redox-active ligands keep a Ni–Ni bond intact throughout a catalytic cycle?

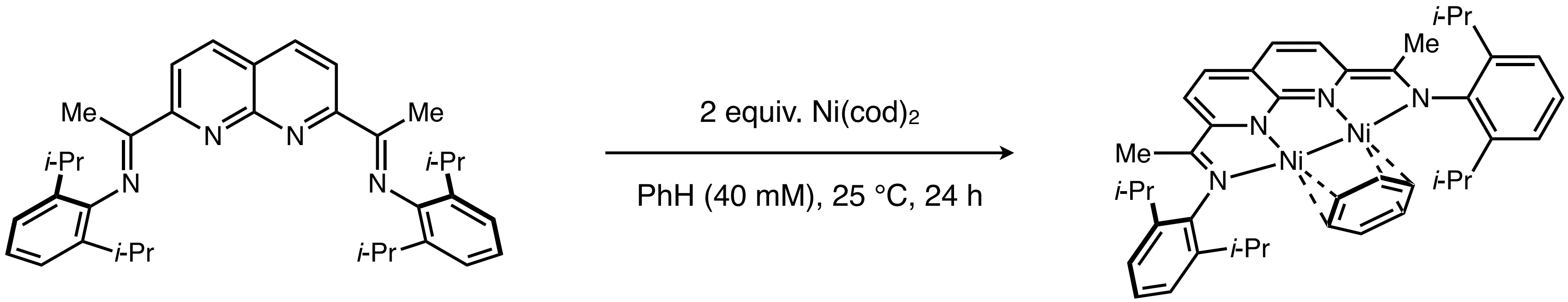


Christopher Uyeda

Purdue University

Zhou, Y. Y. et al. *Inorg. Chem.* **2014**, *53*, 11770–11777.

Dinickel Active Sites Supported by Redox-Active Ligands



2 equiv. $Ni(cod)_2$

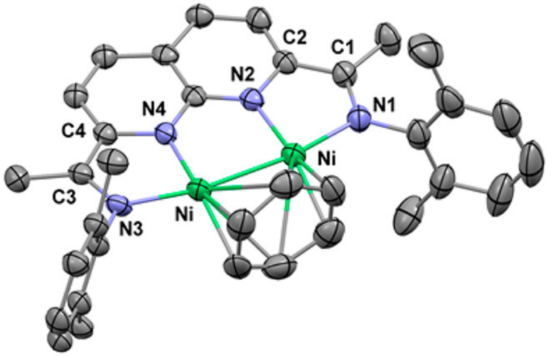
PhH (40 mM), 25 °C, 24 h

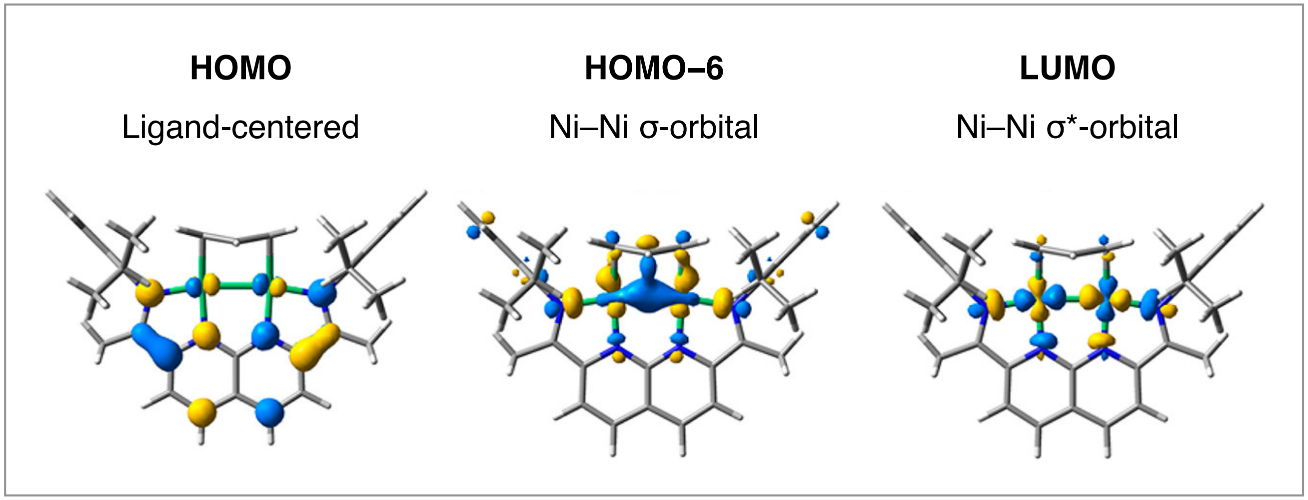
$^{i\text{-Pr}}$NDI

3 steps from commercial

($^{i\text{-Pr}}$NDI)Ni_2(PhH)

92% yield





HOMO

Ligand-centered

HOMO–6

Ni–Ni σ-orbital

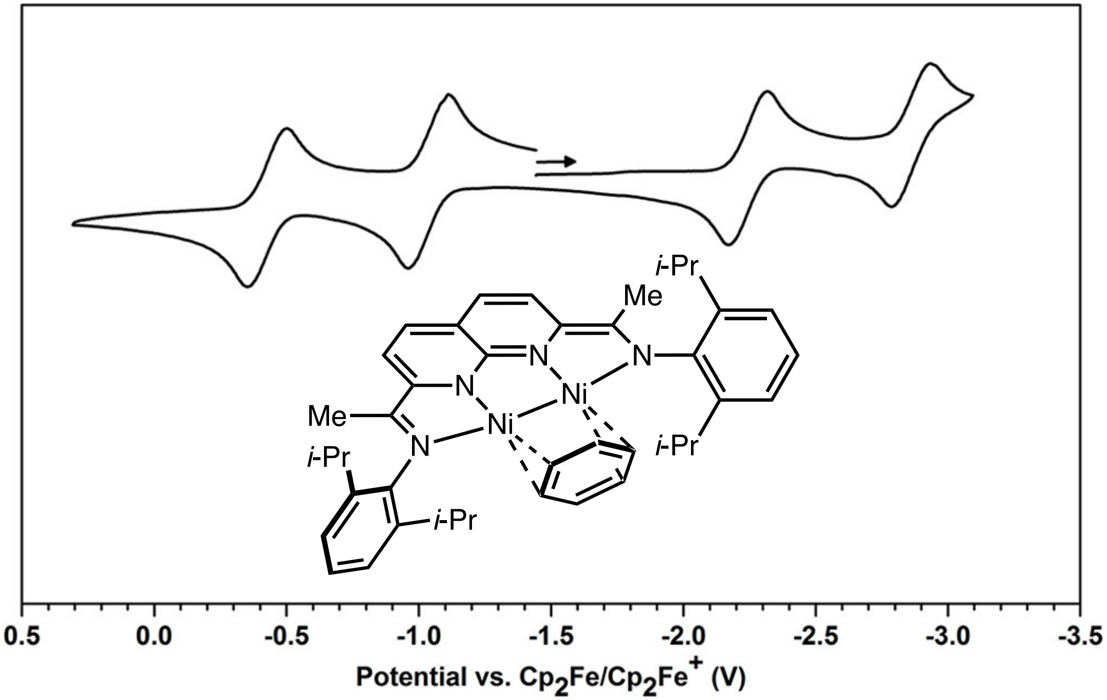
LUMO

Ni–Ni σ*-orbital

- doubly reduced NDI ligand
- single Ni(I)–Ni(I) bond
- labile PhH ligand

Zhou, Y. Y. et al. *Inorg. Chem.* **2014**, *53*, 11770–11777.

Dinickel Active Sites Supported by Redox-Active Ligands



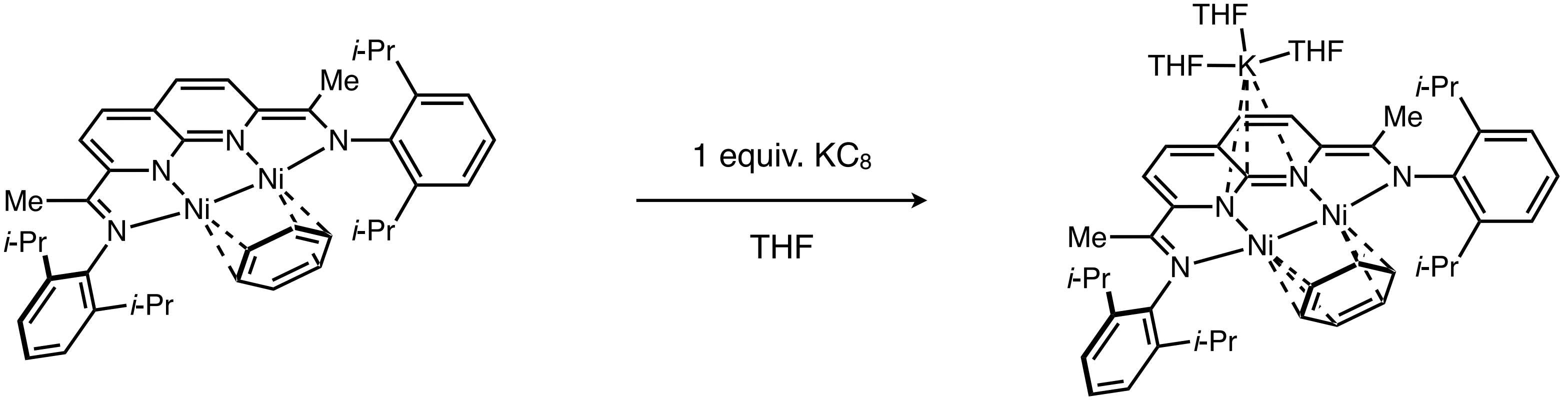
Remarkably reversible redox behavior

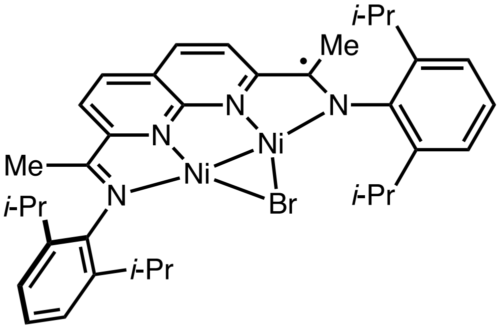
- two reductions at −2.24 and −2.86 V *vs* Fc in THF
- two oxidations at −1.04 and −0.43 V *vs* Fc in THF

Ni_2 cluster stays intact upon redox processes

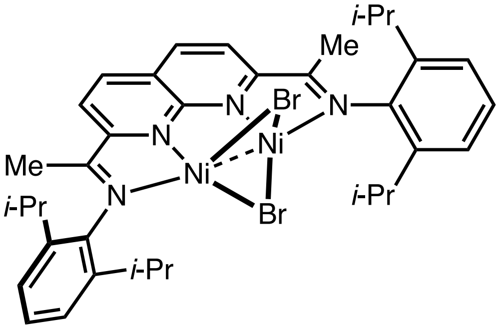
Zhou, Y. Y. et al. *Inorg. Chem.* **2014**, *53*, 11770–11777.

Dinickel Active Sites Supported by Redox-Active Ligands

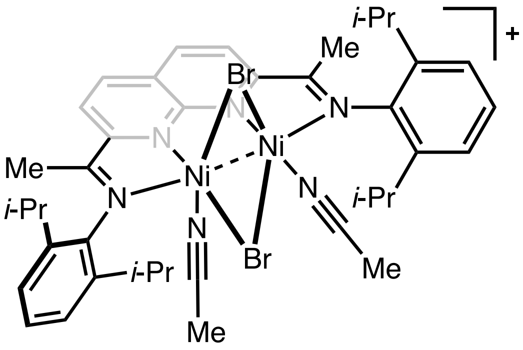




with 0.5 equiv. Bu_4NBr_3



with 1 equiv. Bu_4NBr_3

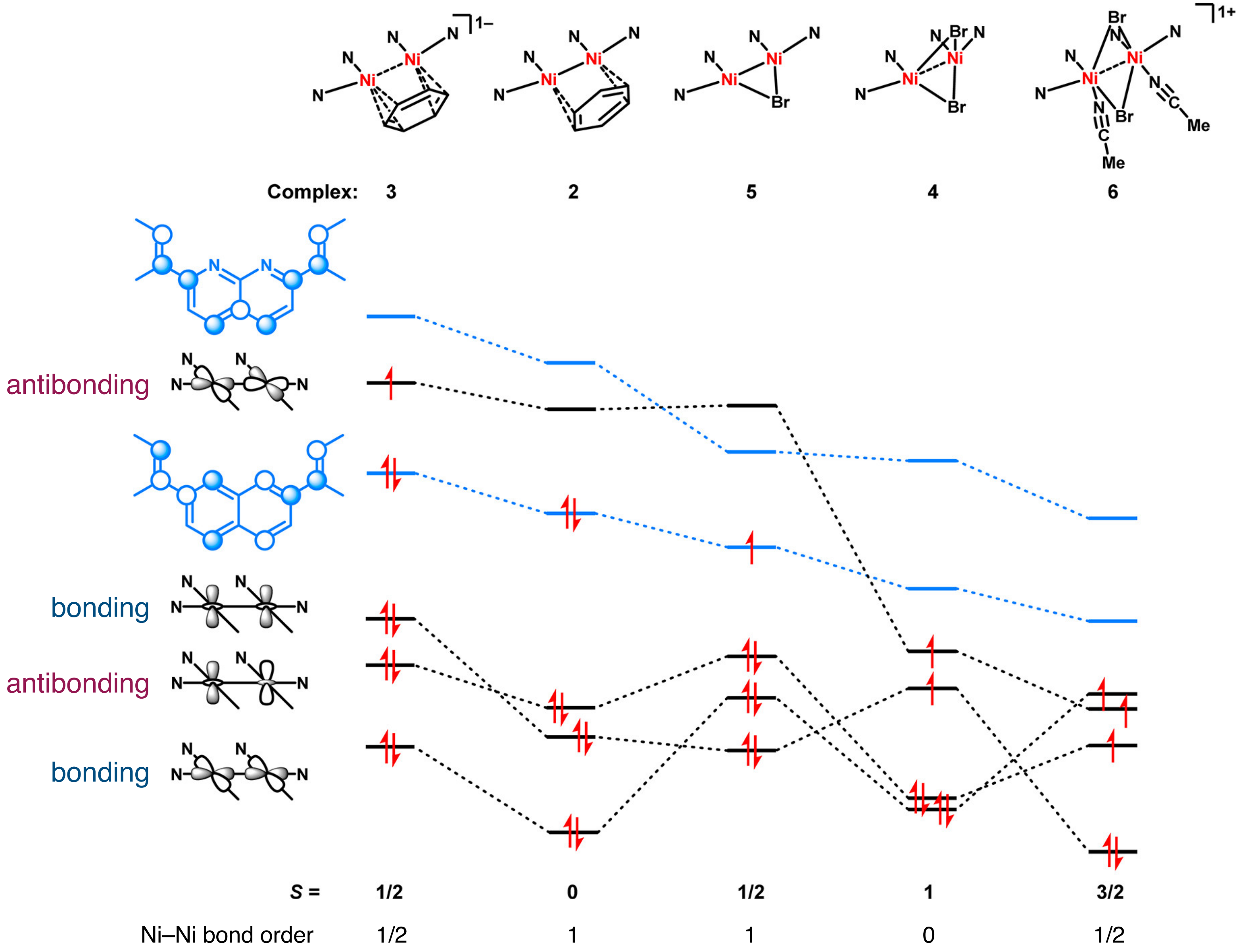


with 1 equiv. Bu_4NBr_3
then 1 equiv. $[Cp_2Fe]PF_6$

Multiple oxidation states are accessible while pertaining Ni_2 cluster

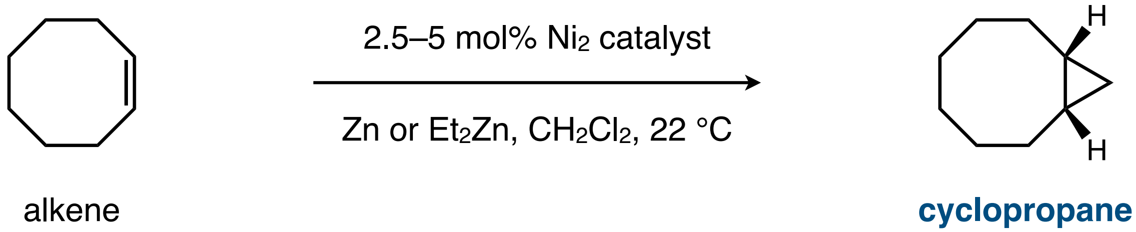
Zhou, Y. Y. et al. *Inorg. Chem.* **2014**, *53*, 11770–11777.

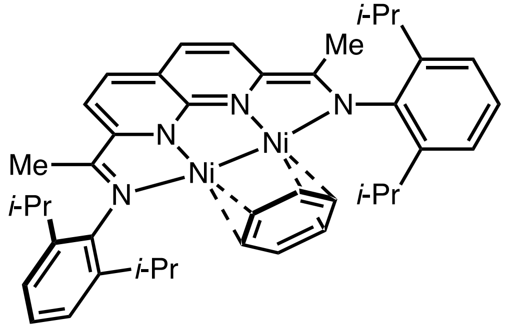
Dinickel Active Sites Supported by Redox-Active Ligands

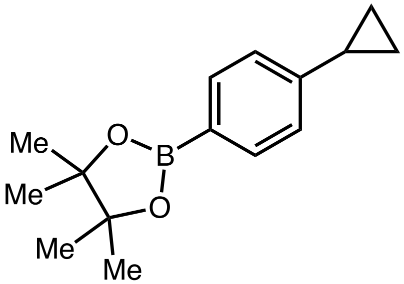


Zhou, Y. Y. et al. *Inorg. Chem.* **2014**, *53*, 11770–11777.

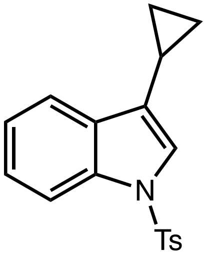
Reductive Cyclopropanations Catalyzed by Dinuclear Nickel Complexes



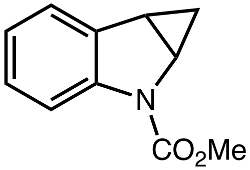




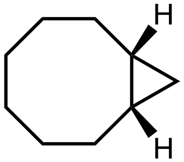
60% yield



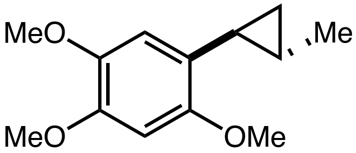
65% yield



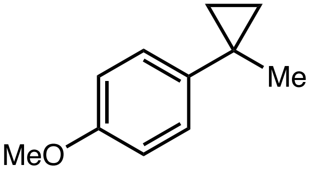
55% yield



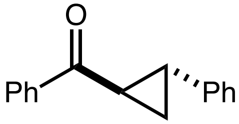
99% yield



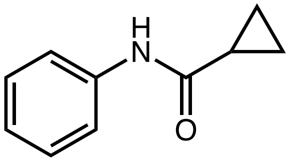
89% yield



83% yield



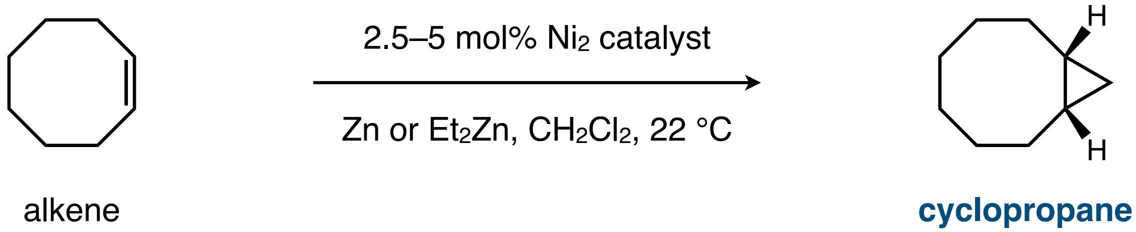
72% yield



82% yield

Zhou, Y. Y.; Uyeda, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 3171–3175.

Reductive Cyclopropanations Catalyzed by Dinuclear Nickel Complexes

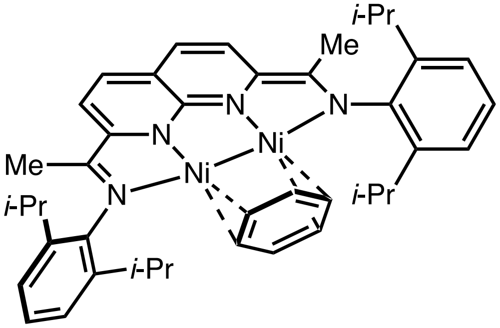


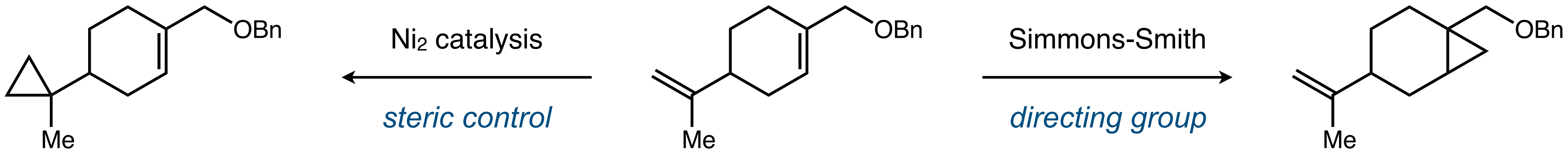
2.5–5 mol% Ni_2 catalyst

Zn or Et_2Zn, CH_2Cl_2, 22 °C

alkene

cyclopropane





Ni_2 catalysis

steric control

Simmons-Smith

directing group control

85% yield

>50:1 rr

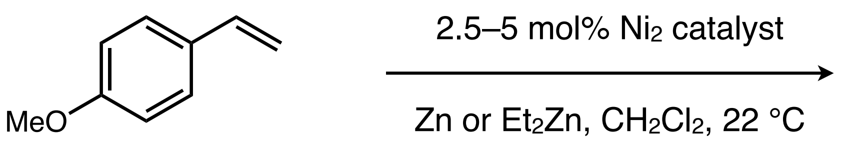
bisalkene

1:47 rr

Ni_2 catalysis alters regeoselectivity of cyclopropanation

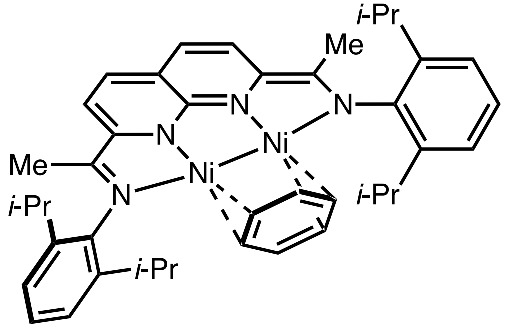
Zhou, Y. Y.; Uyeda, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 3171–3175.

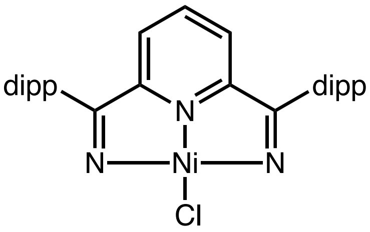
Reductive Cyclopropanations Catalyzed by Dinuclear Nickel Complexes



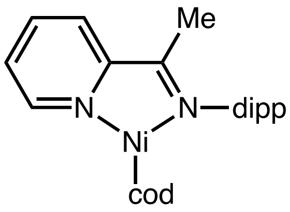
alkene

cyclopropane

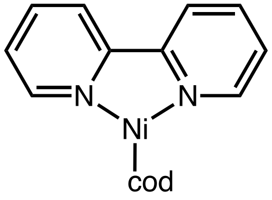




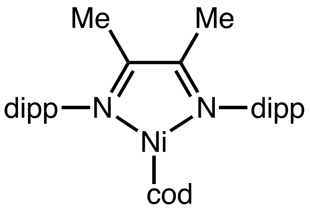
20% yield



19% yield



8% yield

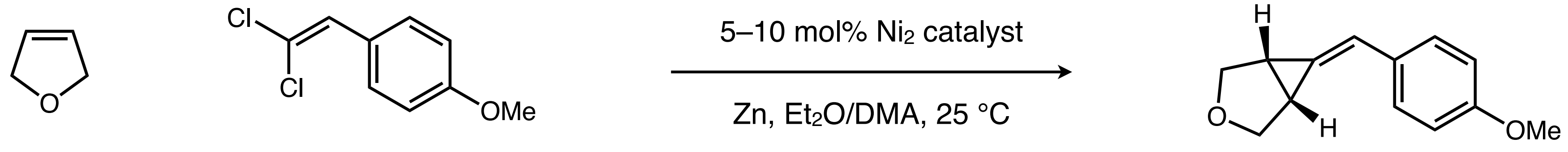


2% yield

mononuclear Ni catalysis were inefficient

Zhou, Y. Y.; Uyeda, C. *Angew. Chem. Int. Ed.* **2016**, *55*, 3171–3175.

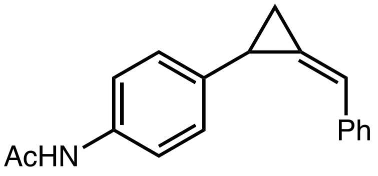
Catalytic Reductive Vinylidene Transfer Reactions



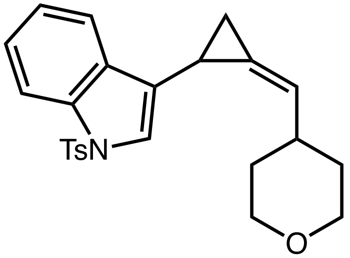
alkene

dichloroalkene

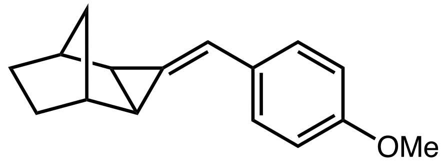
methylenecyclopropane



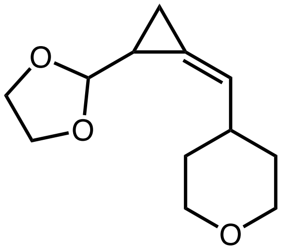
97% yield
E/Z 1:9



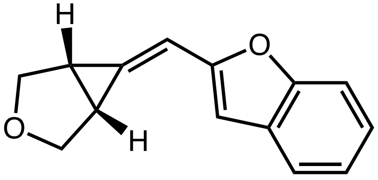
66% yield
E/Z 1:3



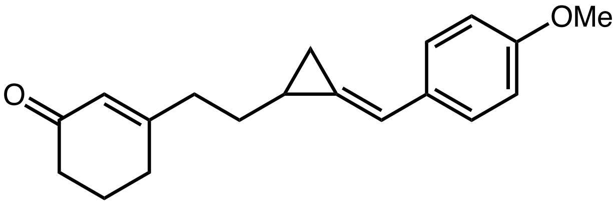
86% yield



50% yield
E/Z 8:1



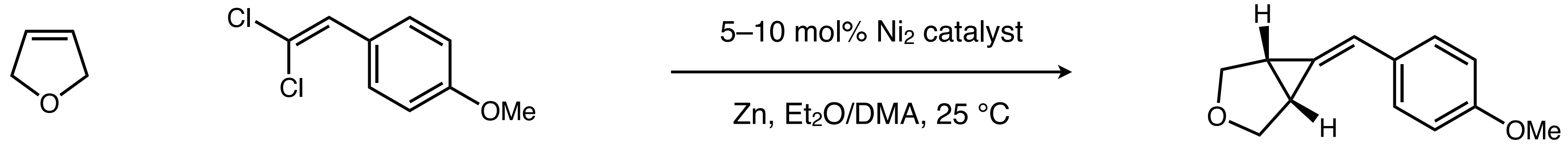
77% yield



67% yield
E/Z 1:1

Pal, S.; Zhou, Y. Y.; Uyeda, C. *J. Am. Chem. Soc.* **2017**, *139*, 11686–11689.

Catalytic Reductive Vinylidene Transfer Reactions



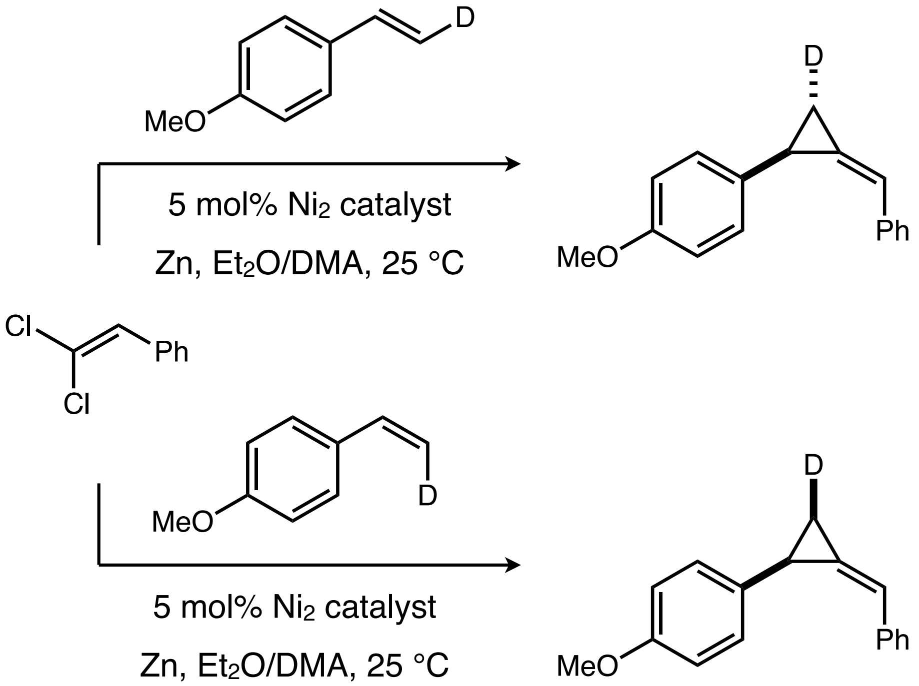
5–10 mol% Ni_2 catalyst

Zn, Et_2O/DMA, 25 °C

alkene

dichloroalkene

methylenecyclopropane



5 mol% Ni_2 catalyst

Zn, Et_2O/DMA, 25 °C

cis/trans
1:4

5 mol% Ni_2 catalyst

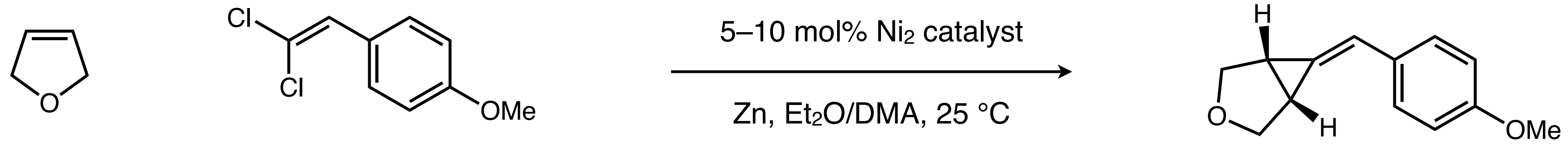
Zn, Et_2O/DMA, 25 °C

cis/trans
3.7:1

cyclopropanation step is stereoselective, but not stereospecific

Pal, S.; Zhou, Y. Y.; Uyeda, C. *J. Am. Chem. Soc.* **2017**, *139*, 11686–11689.

Catalytic Reductive Vinylidene Transfer Reactions



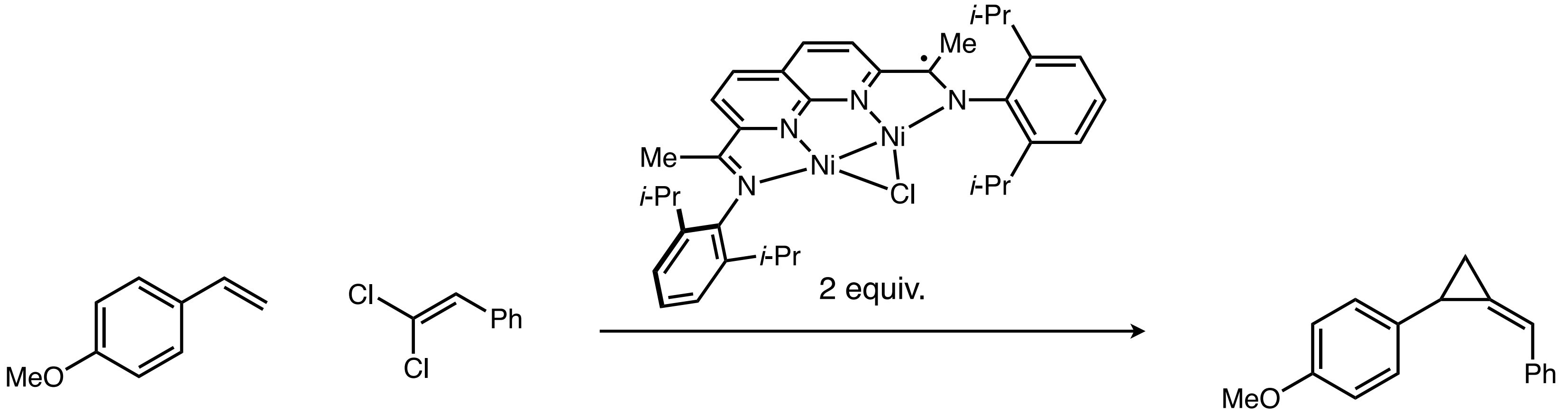
5–10 mol% Ni_2 catalyst

Zn, Et_2O/DMA, 25 °C

alkene

dichloroalkene

methylenecyclopropane



2 equiv.

1 equiv.

1 equiv.

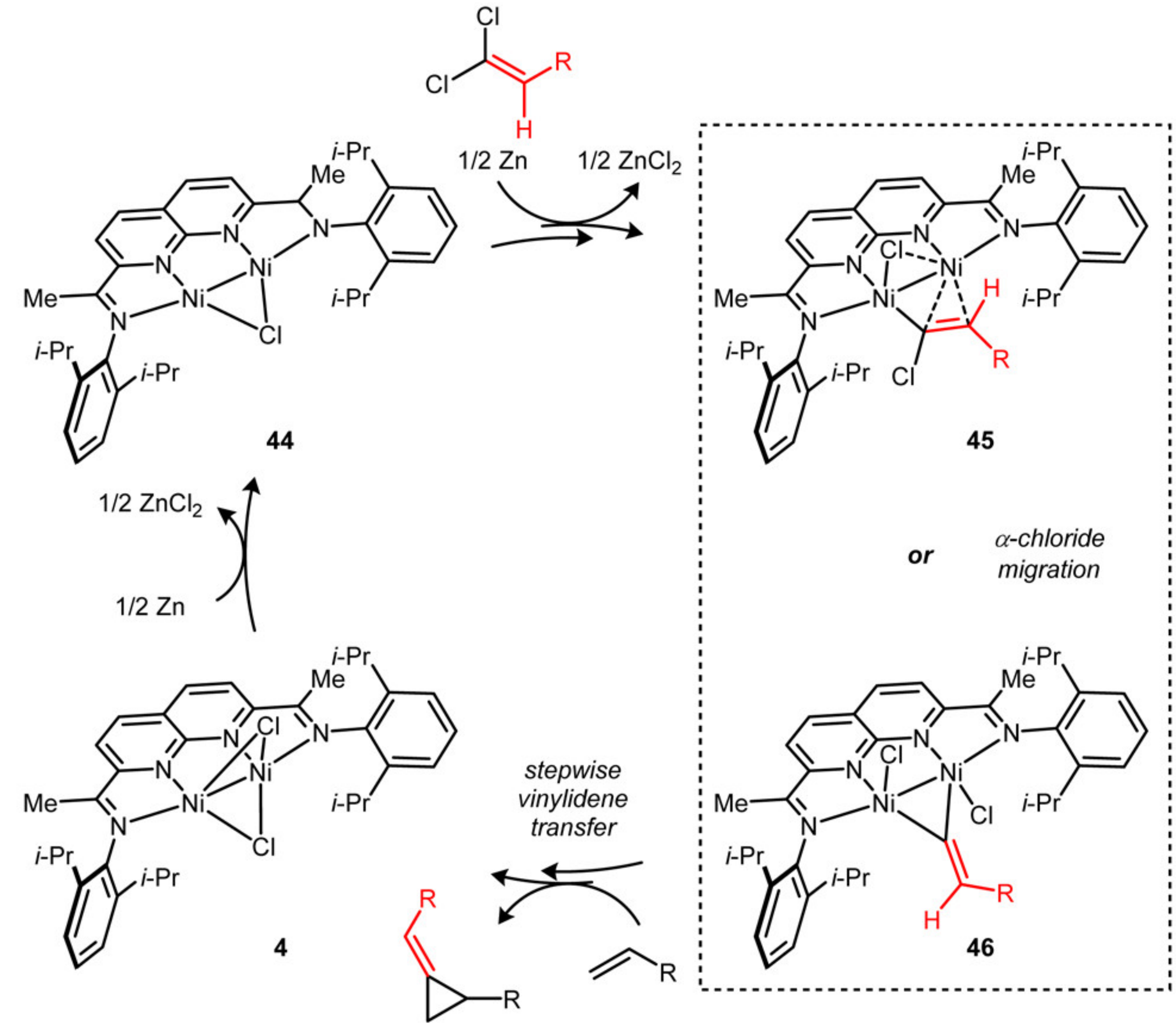
67% yield

E/Z 1:2

Zn is not required to observe the reactivity

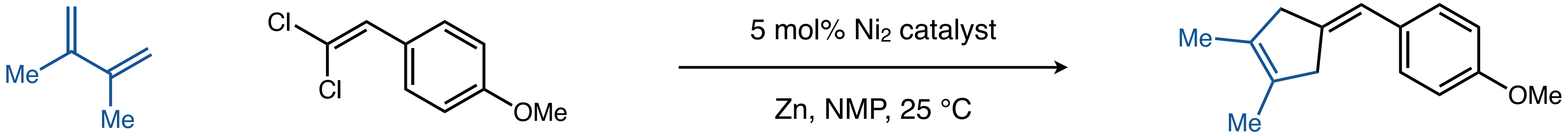
Pal, S.; Zhou, Y. Y.; Uyeda, C. *J. Am. Chem. Soc.* **2017**, *139*, 11686–11689.

Catalytic Reductive Vinylidene Transfer Reactions



Pal, S.; Zhou, Y. Y.; Uyeda, C. *J. Am. Chem. Soc.* **2017**, *139*, 11686–11689.

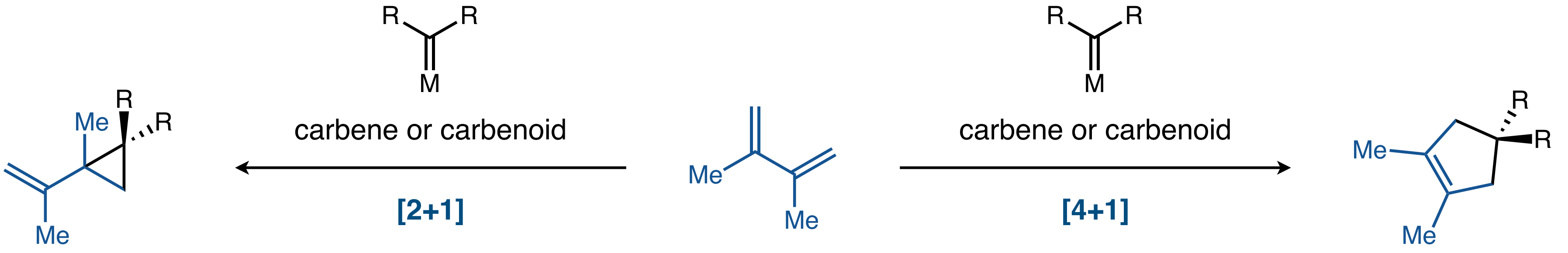
Catalytic Reductive [4 + 1]-Cycloadditions of Vinylidenes and Dienes



diene

dichloroalkene

[4+1] product



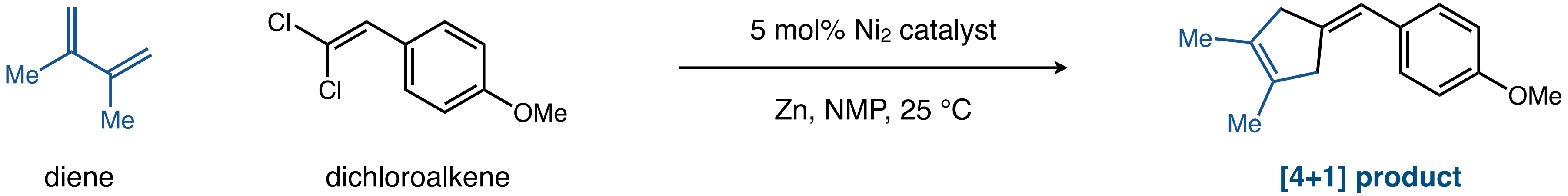
common

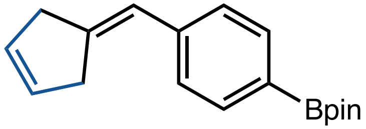
diene

exceptionally rare

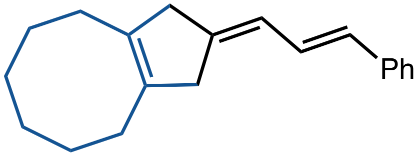
Zhou, Y. Y.; Uyeda, C. *Science* **2019**, *363*, 857–862.

Catalytic Reductive [4 + 1]-Cycloadditions of Vinylidenes and Dienes

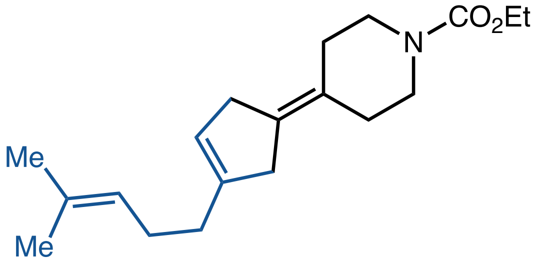




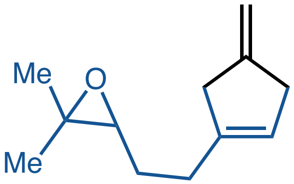
83% yield



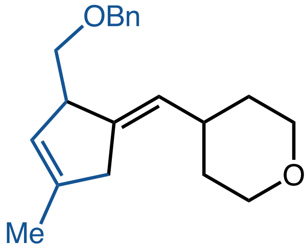
99% yield



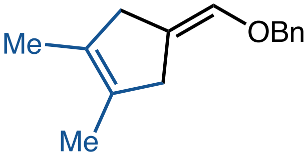
50% yield



44% yield



74% yield
E/Z 9:1



26% yield

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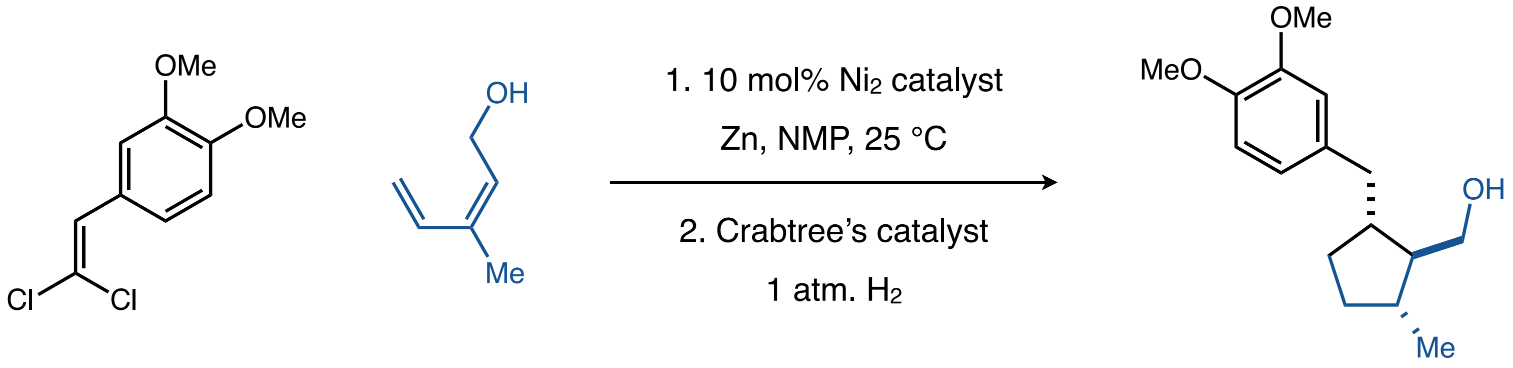
Quick access to chiral cyclopentanes



1. 10 mol% Ni_2 catalyst

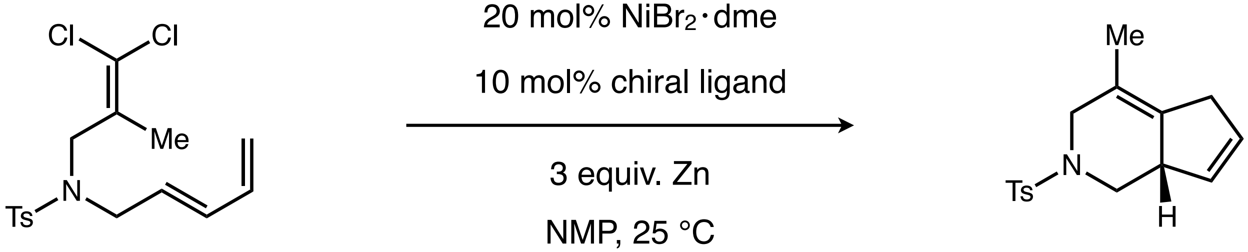
Zn, NMP, 25 °C

2. Crabtree's catalyst

1 atm. H_2

unprotected alcohol

81% yield



20 mol% $NiBr_2 \cdot dme$

10 mol% chiral ligand

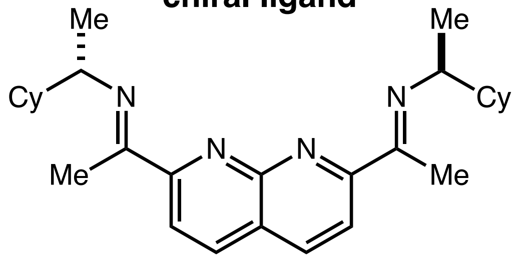
3 equiv. Zn

NMP, 25 °C

91% yield

78% ee

chiral ligand



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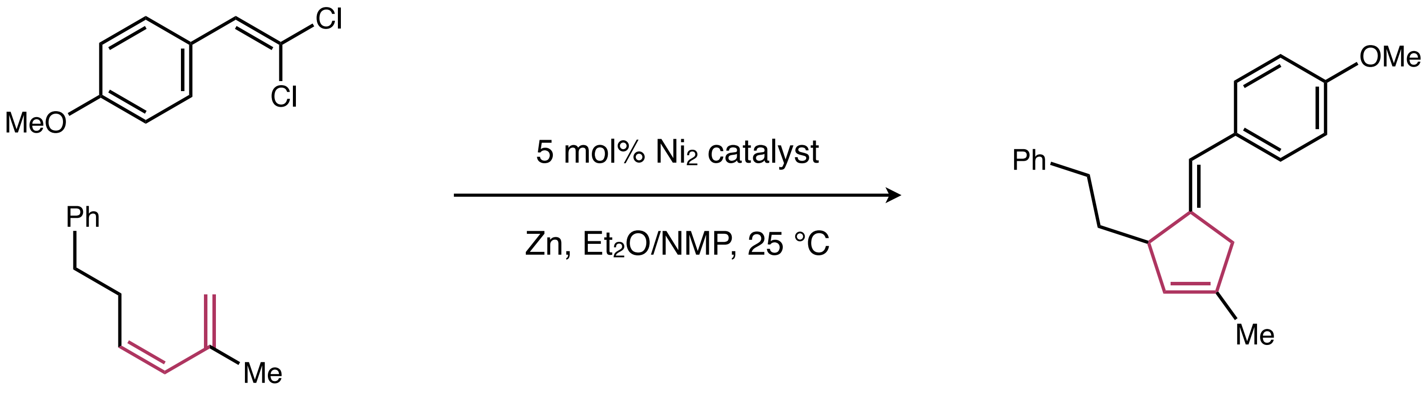
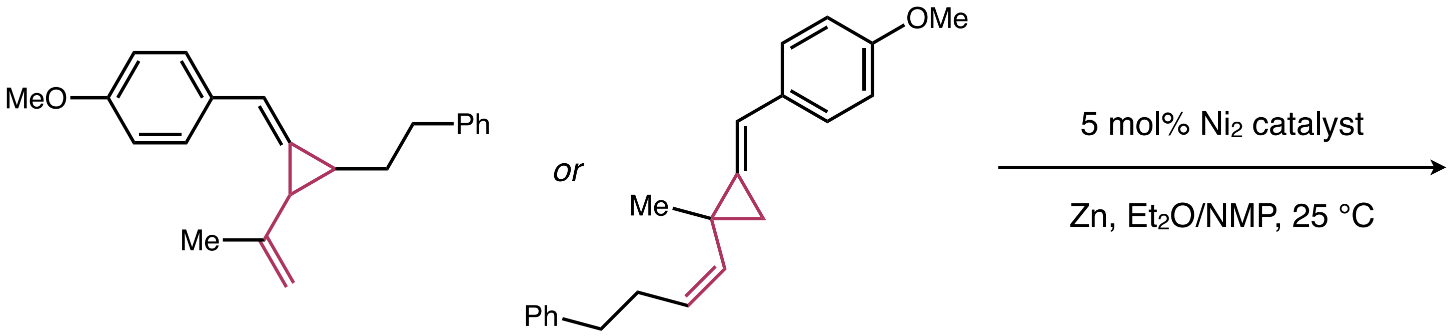
Catalytic Reductive [4 + 1]-Cycloadditions of Vinylidenes and Dienes



76% yield

E/Z >20:1



no rearranged products

The reaction does not proceed through intermediacy of vinylcyclopropane

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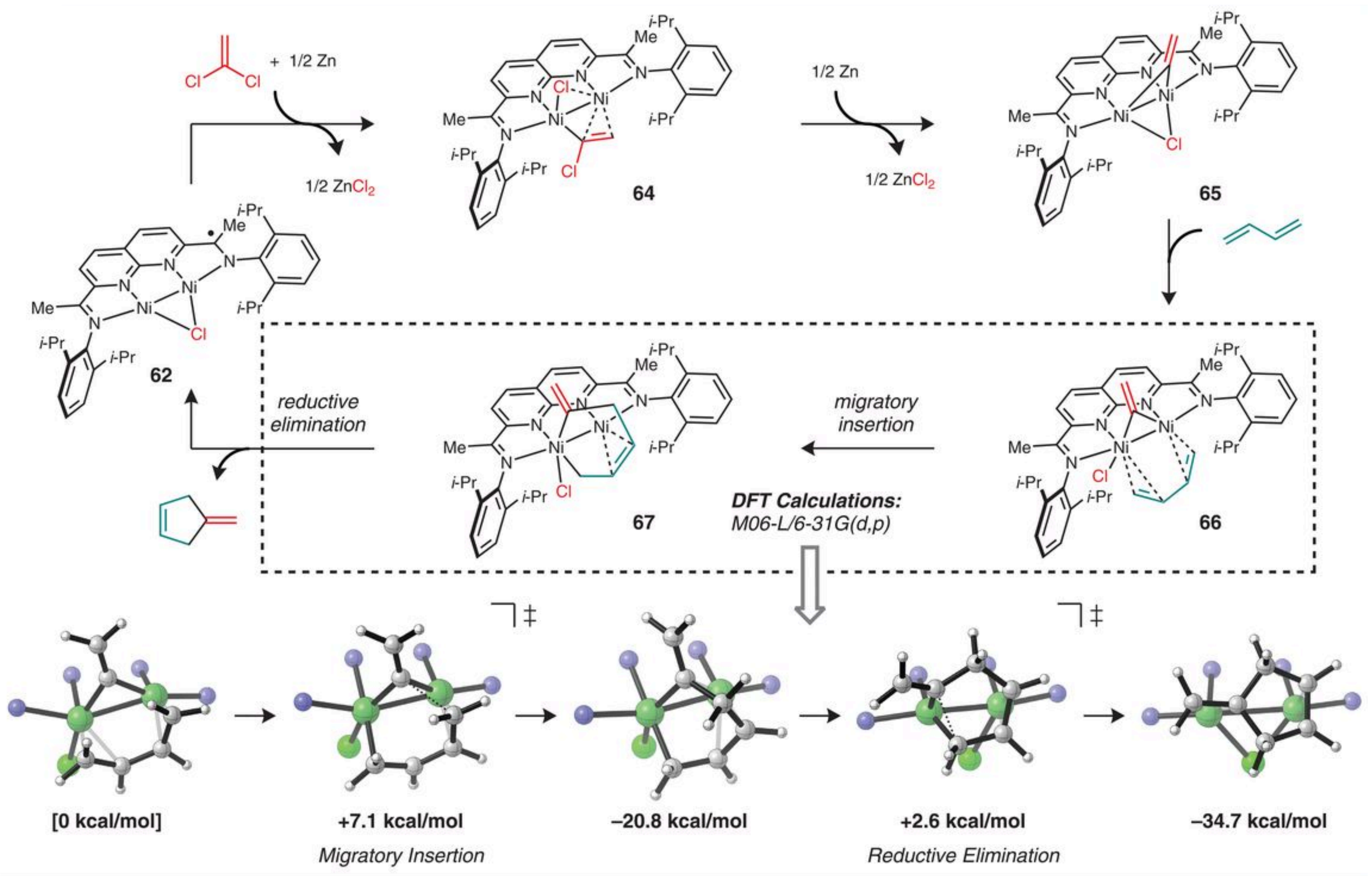

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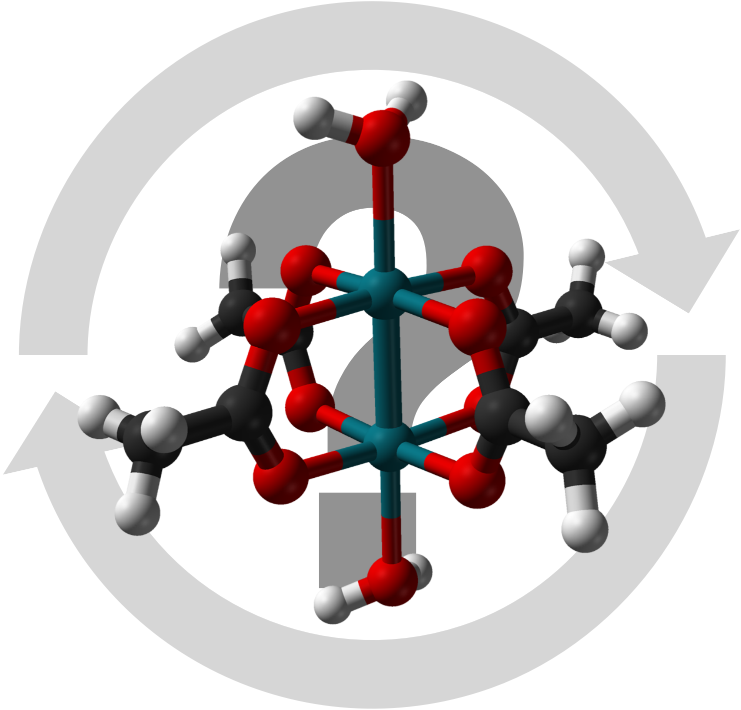
Metal-Metal Bonds in Organic Catalysis



Artem V. Tsymbal

MacMillan Group Literature Talk

May 3, 2022