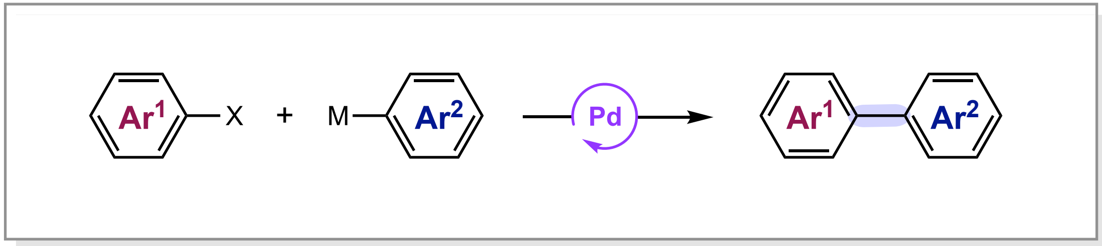
Transmetalation of Boron reagents

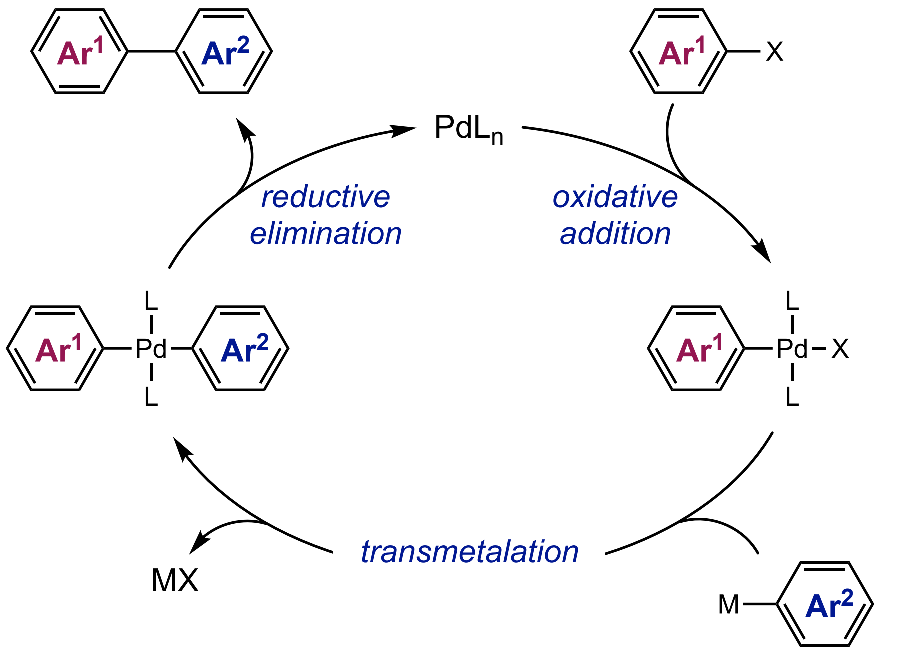
Boran Lee

Topical Seminar

02/15/2022

General mechanism of Pd-catalyzed cross-coupling



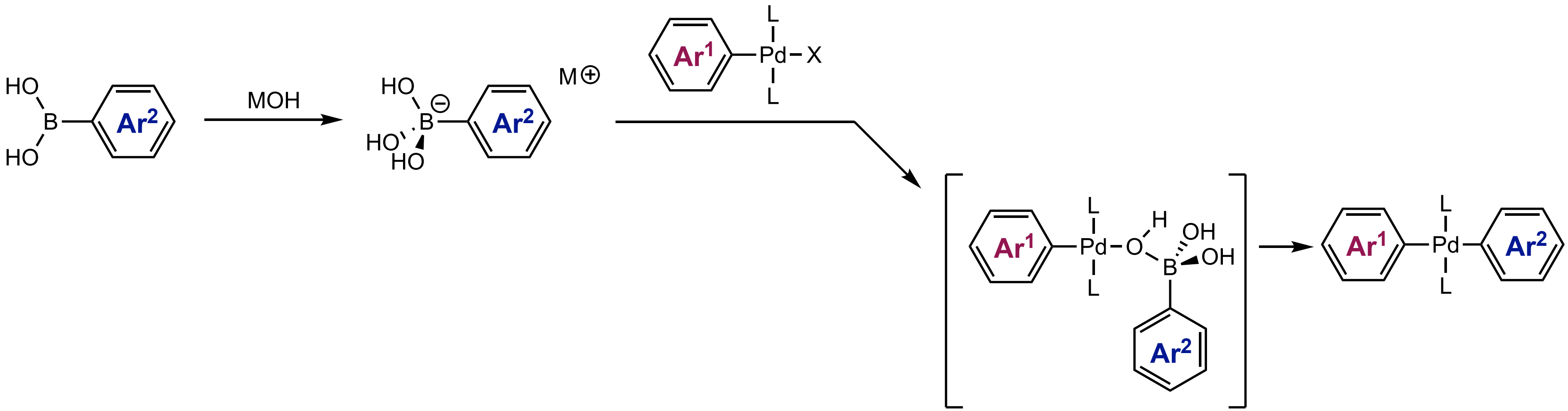


- Less is known about TM step
- Transmetalation in Suzuki-Miyaura coupling?

Minireview on SMC: Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362

Transmetalation pathways in SMC

■ *Path A: "Boronate" pathway*



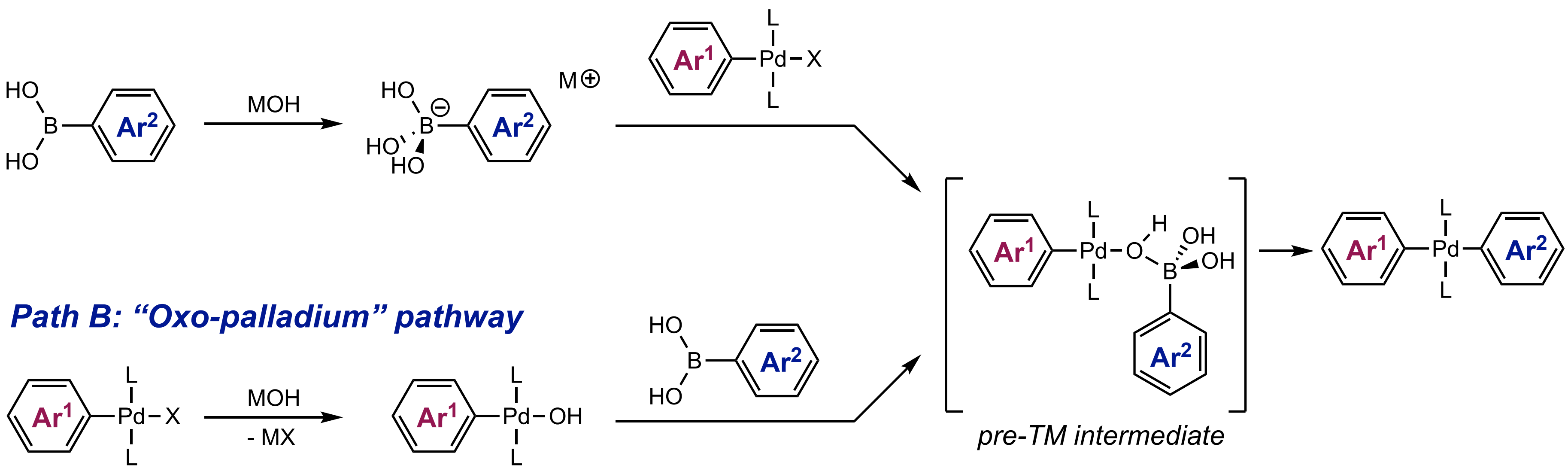
pre-TM intermediate

Minireview on SMC: Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362

Transmetalation pathways in SMC

■ *Path A: "Boronate" pathway*

■ *Path B: "Oxo-palladium" pathway*



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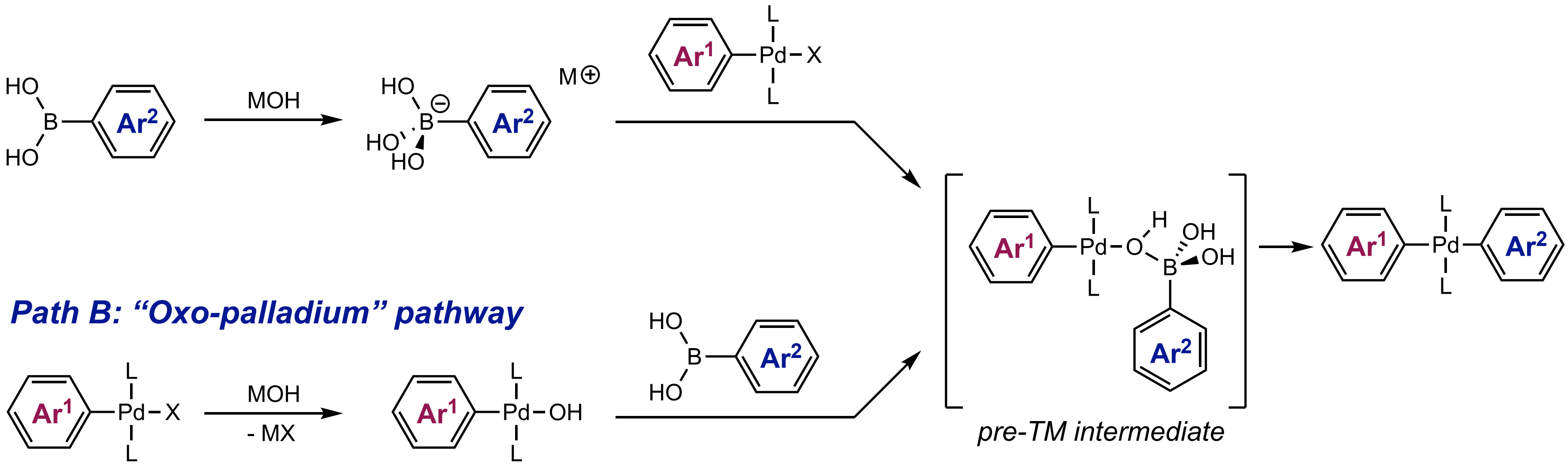
Transmetalation pathways in SMC

■ *Path A: "Boronate" pathway*



■ *Path B: "Oxo-palladium" pathway*

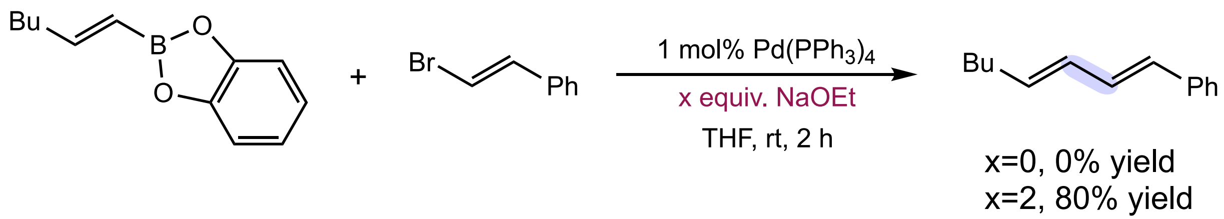
■ Palladium system	■ Other metal complexes containing M–O–B linkage	■ Nickel system
Early experimental observations	Pt, Rh	Proposed mechanism
Kinetic studies	TM of Ar from B to M	Role of hydroxide (base) ions
Attempts to observe pre-TM intermediate(s)		

Minireview on SMC: Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362

Early experimental evidence

Role of alkoxide bases

Miyaura and Suzuki (1979)



- Poor transmetalation w/o alkoxide bases
- Upon addition of NaOEt, 80% cross-coupling product obtained, high stereospecificity
- Base was proposed to react with a 3-coordinate boron center to give a more nucleophilic boronate (“Boronate” pathway proposed)

Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrahedron Lett.* **1979**, *20*, 3437.
Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107,* 972.

Early experimental evidence

Role of alkoxide bases

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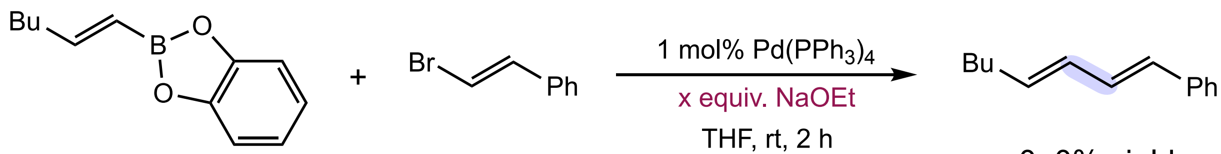
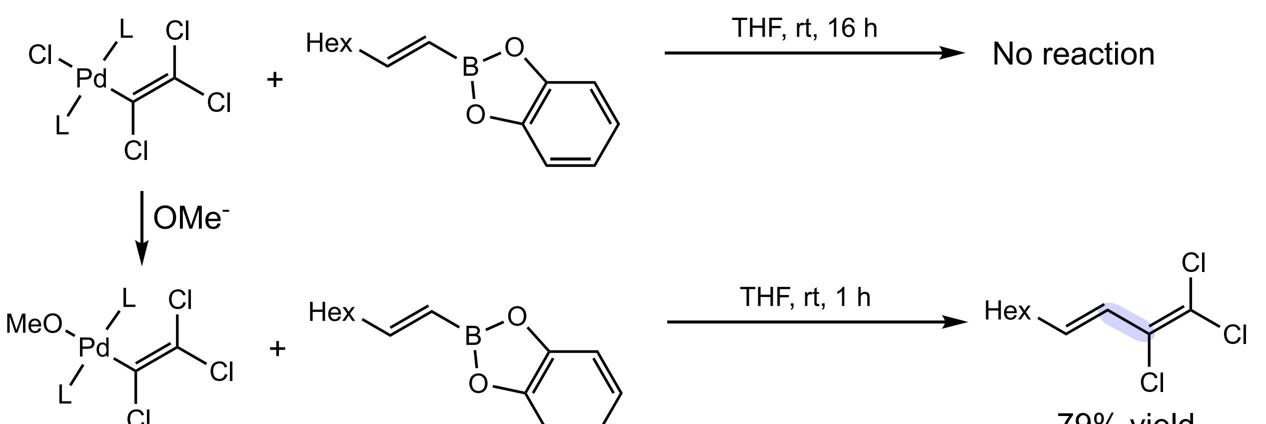


x=0, 0% yield
x=2, 80% yield

- Poor transmetalation w/o alkoxide bases
- Upon addition of NaOEt, 80% cross-coupling product obtained, high stereospecificity
- Base was proposed to react with a 3-coordinate boron center to give a more nucleophilic boronate ("Boronate" pathway proposed)

Miyaura and Suzuki (1985)



79% yield

- activation of Pd center prior to TM ("Oxo-palladium" pathway proposed)

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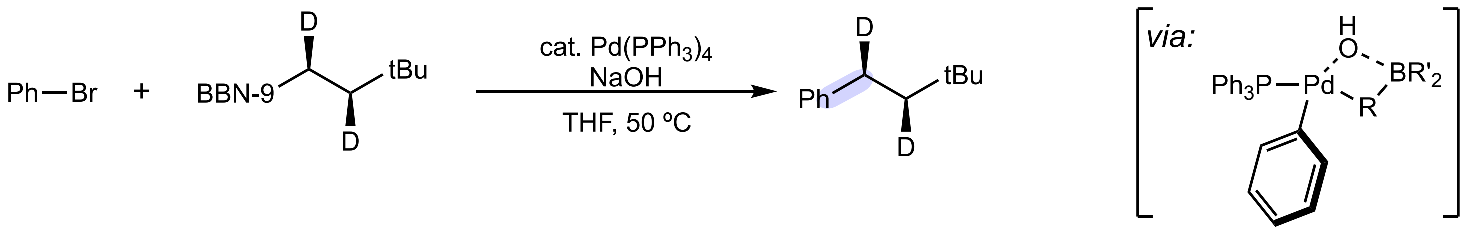
Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107,* 972.

Early experimental evidence

Soderquist (1998)

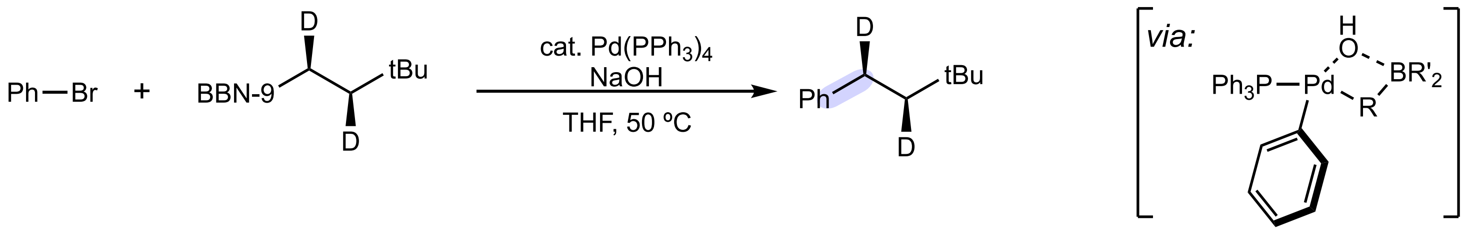


- Stereochemistry: complete retention (w.r.t. carbon)
- Pre-transmetalation intermediate containing a Pd–O–B linkage was proposed.

Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461.

Early experimental evidence

Soderquist (1998)



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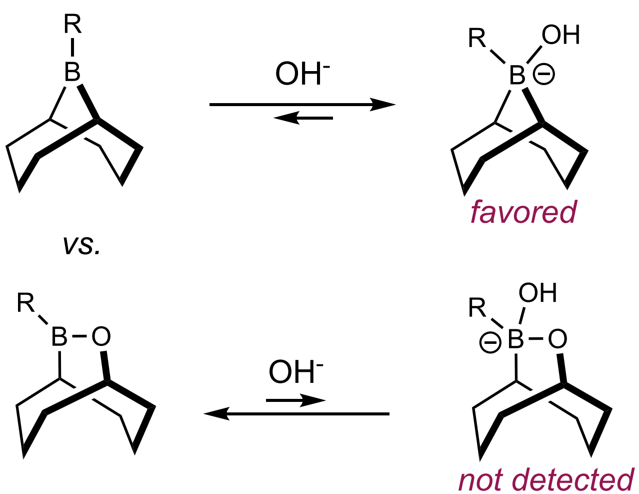

- Borane is more Lewis-acidic
  (less Lewis-acidic borinic ester)

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Early experimental evidence

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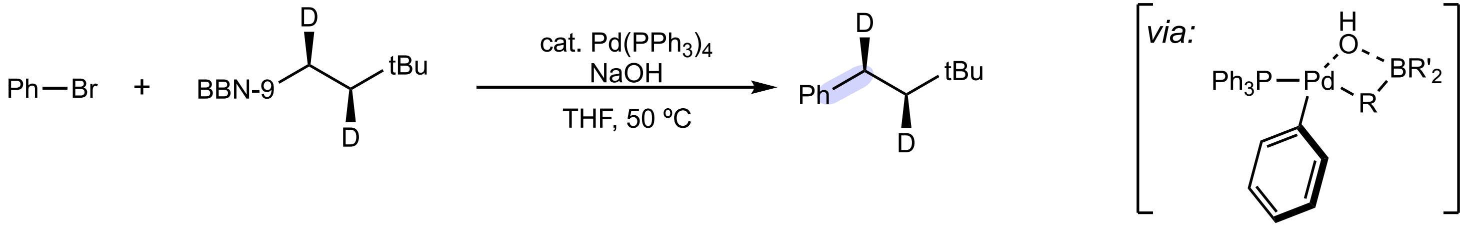

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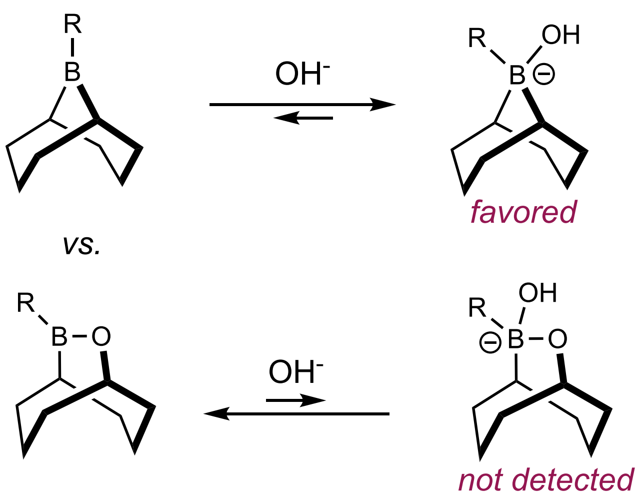
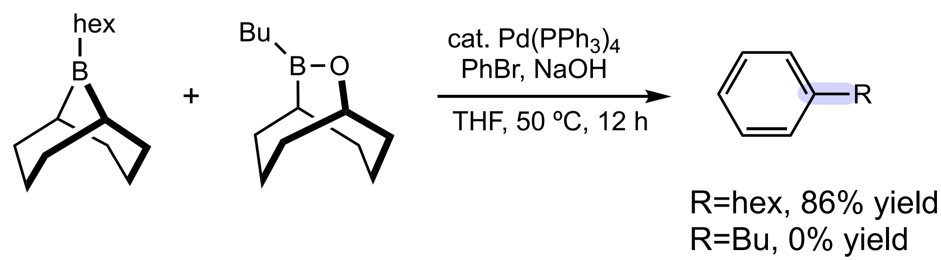


- Borane is more Lewis-acidic (less Lewis-acidic borinic ester)

competition experiment:



- Cross-coupling product originate solely from borane
- Fast TM of borane through the boronate pathway
  Slow TM of borinic ester through oxo-palladium path

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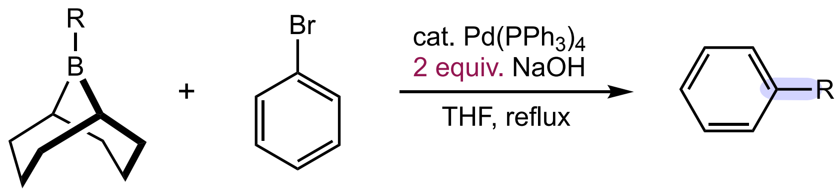
Early experimental evidence

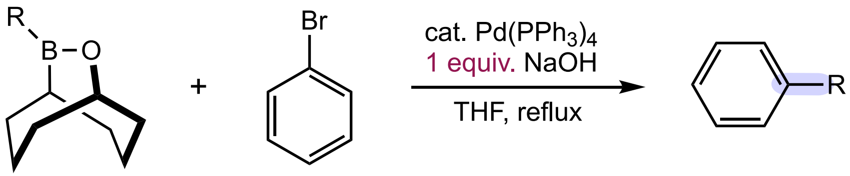


fast

rate = k $[PhBr]^1[borane]^0[NaOH]^0$

TOL step: oxidative addition of PhBr

boronate pathway



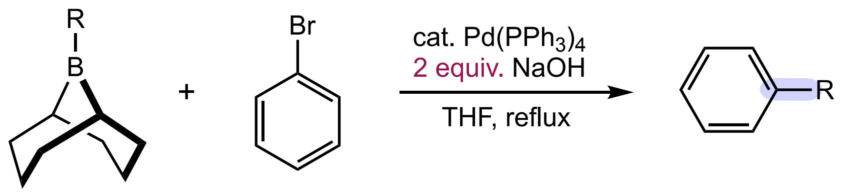
slow

rate = k $[PhBr]^0[borinate]^0[NaOH]^1$

TOL step: hydrolysis of $(PPh_3)_2Pd(Br)(Ph)$

oxo-palladium pathway

Early experimental evidence



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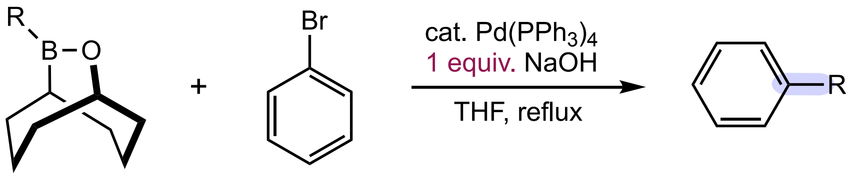

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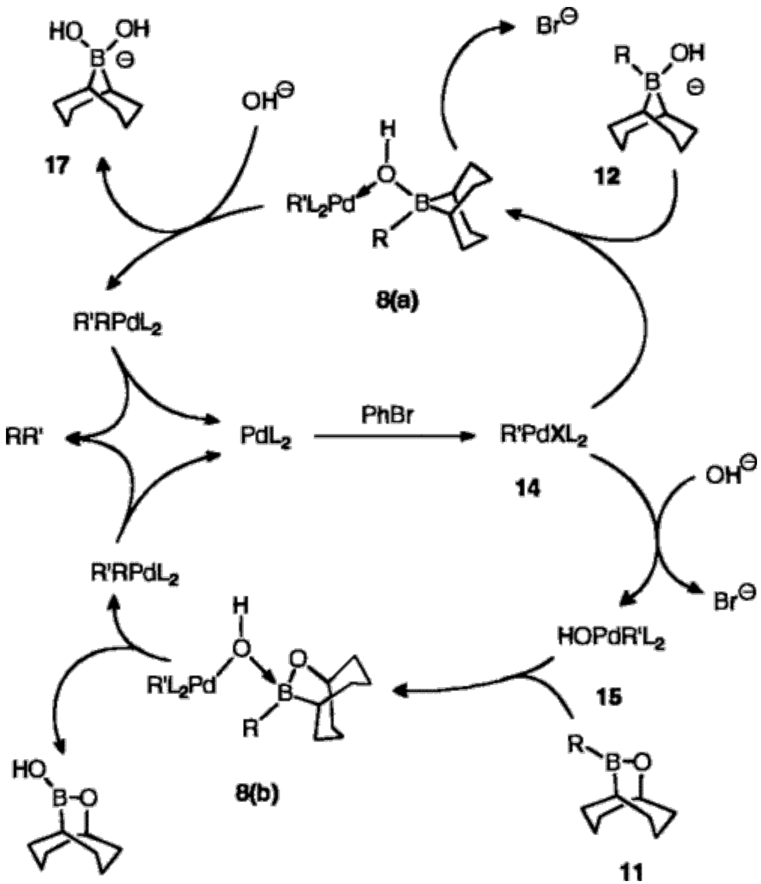
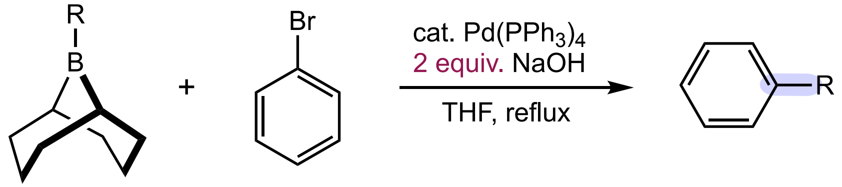


Early experimental evidence



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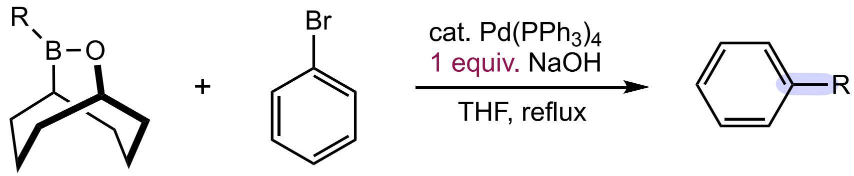

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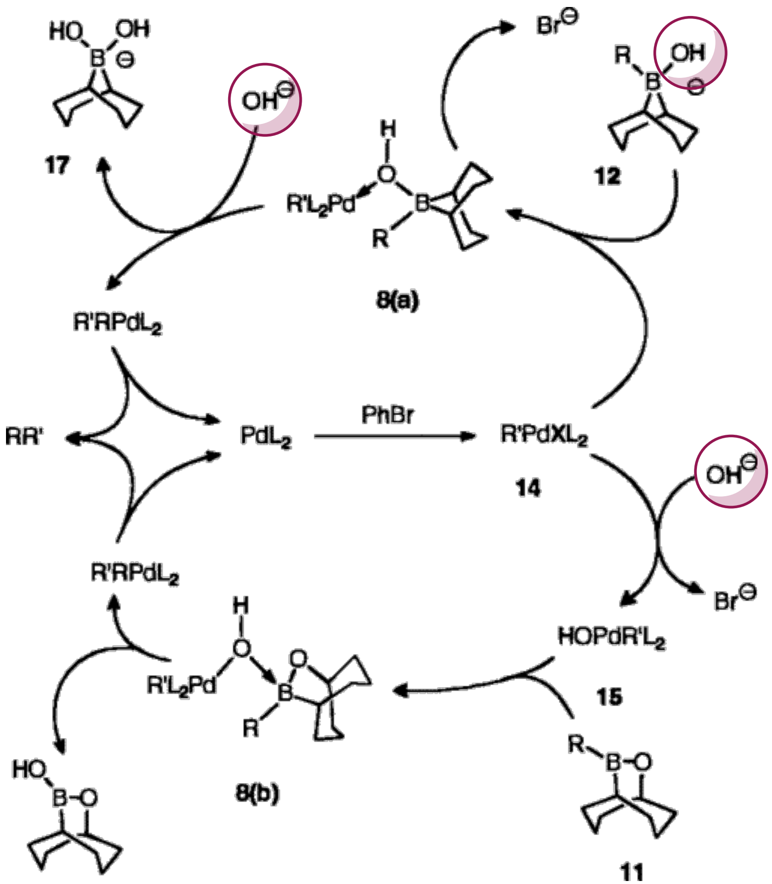
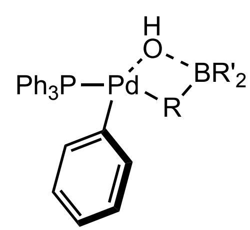
oxo-palladium pathway



Possible role of bases:

- Formation of **12** (more nucleophilic)
- Complexation of $R_2B(OH)$ byproducts
- Hydrolysis of $(Ph)Pd(Br)(PPh_3)_2$
- Accelerated coupling rates for 11
- Catalyst regeneration

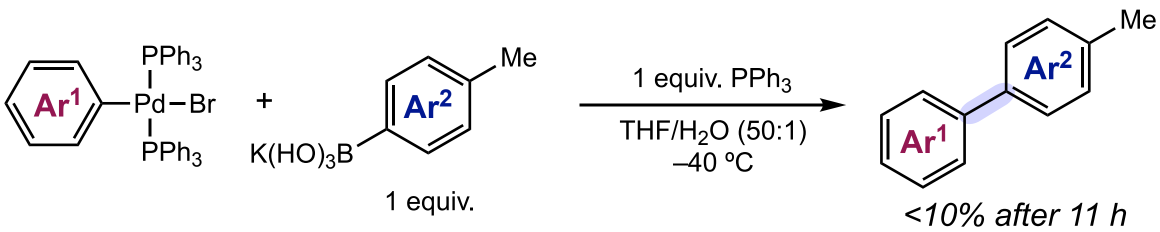


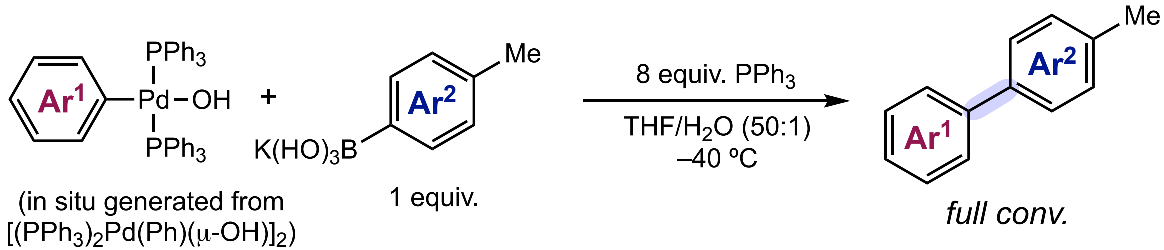
R delivered through
a 4-membered TS
(retention of configuration)

Kinetic studies

Stoichiometric reactions

Hartwig (2011)





Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116.

Kinetic studies

■ ***Stoichiometric reactions***

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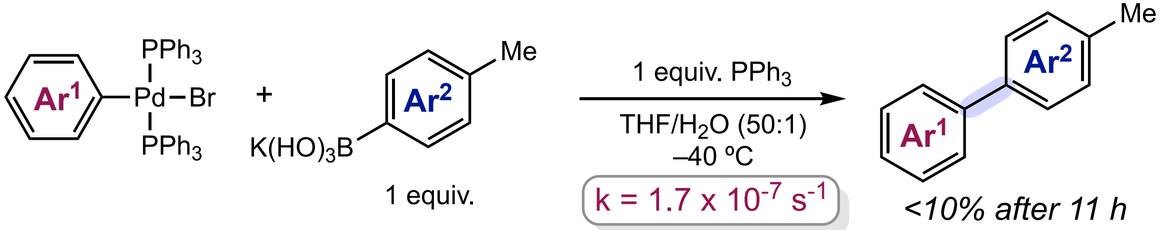

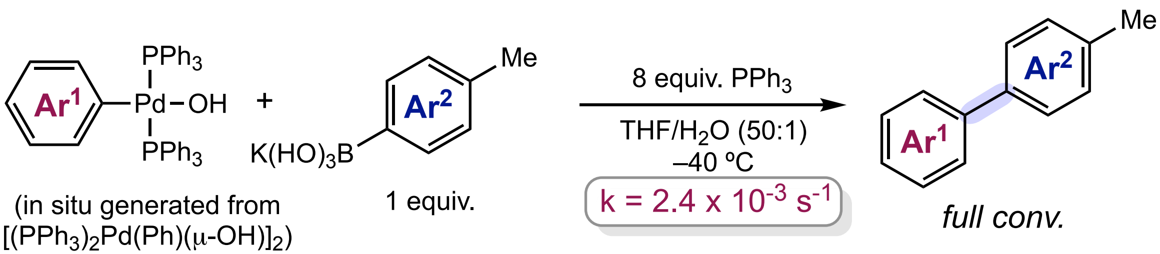

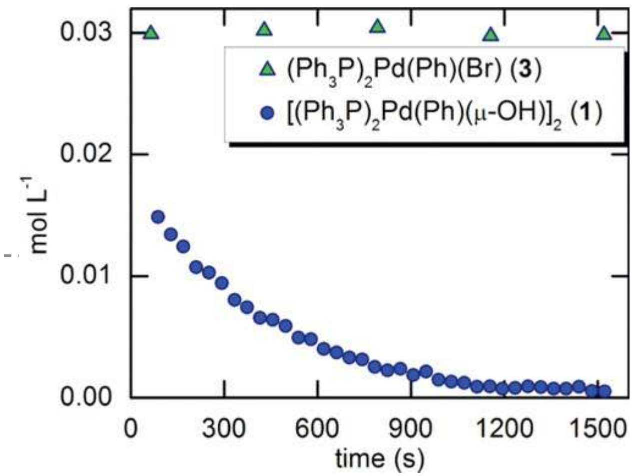

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Kinetic studies

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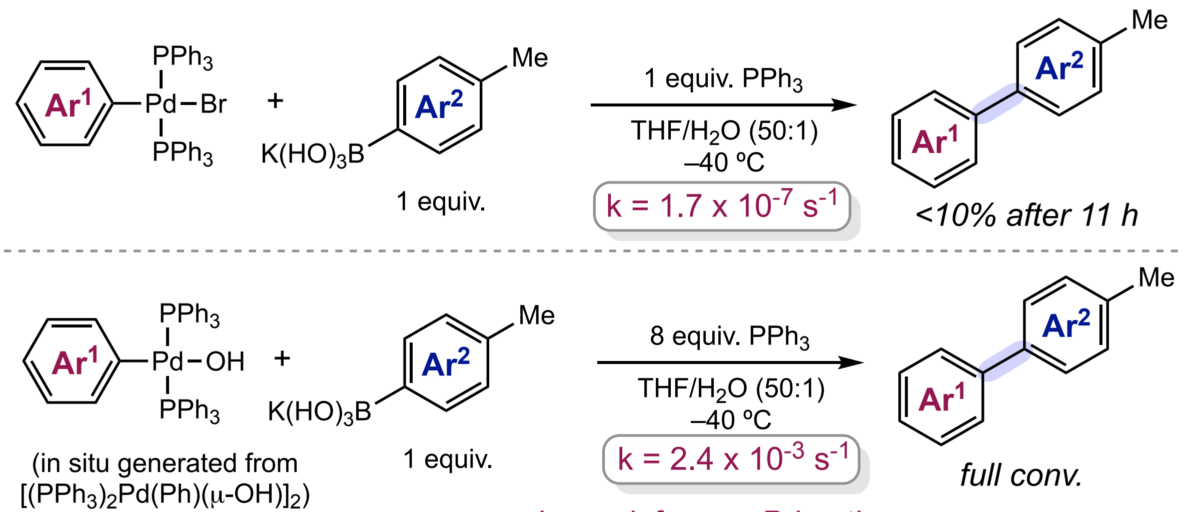
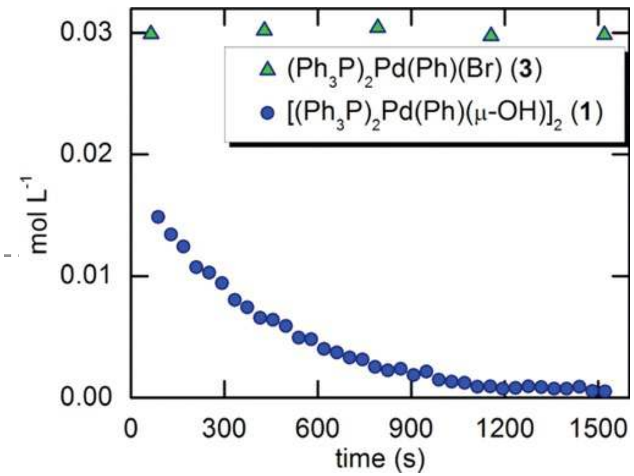
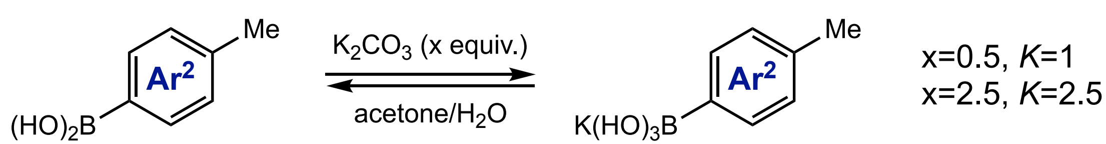
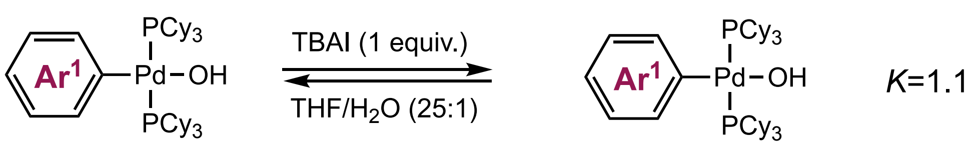




larger k for oxo-Pd pathway by a factor of 10^4

Equillibrium constant





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Kinetic studies

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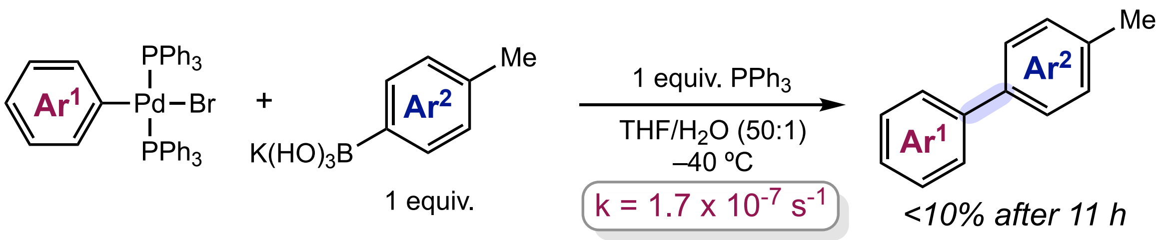

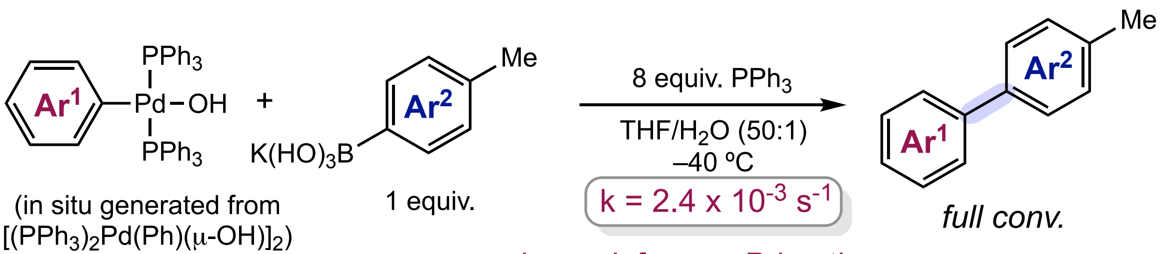

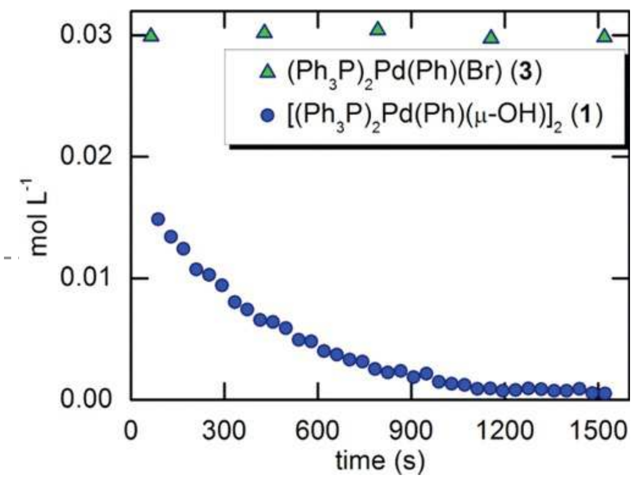

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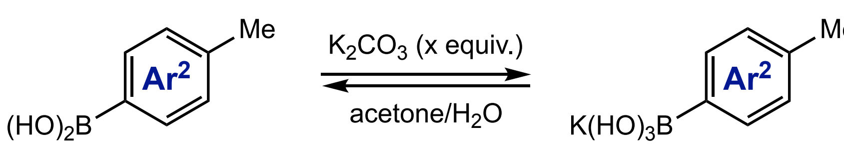
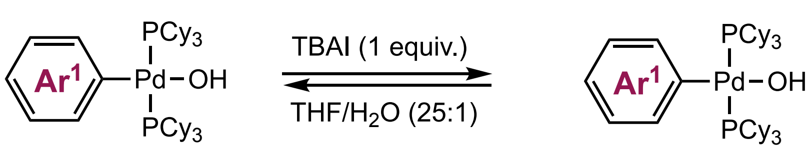
Equillibrium constant



x=0.5, K=1
x=2.5, K=2.5



K=1.1

- Similar populations of
  (1) boronic acid and borate ion
  (2) [Pd]X and [Pd]OH
  in the presence of water & K_2CO_3
- oxo-palladium pathway is ~4 orders of magnitude faster
- SMC under these conditions proceeds through oxo-Pd pathway.

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Kinetic studies

Stoichiometric reactions

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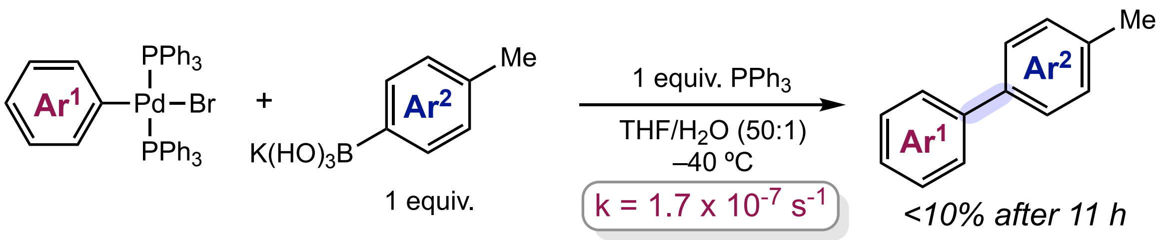
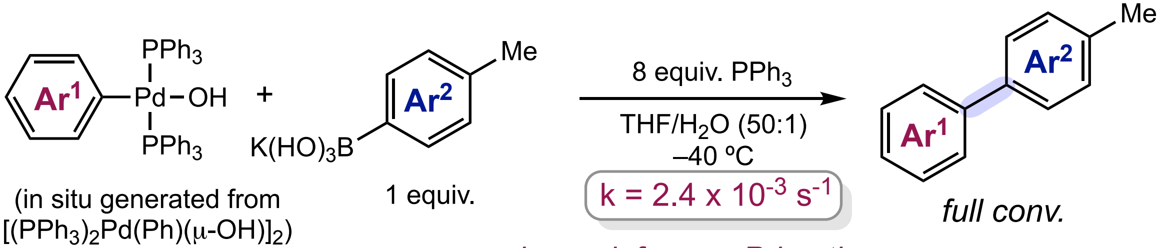
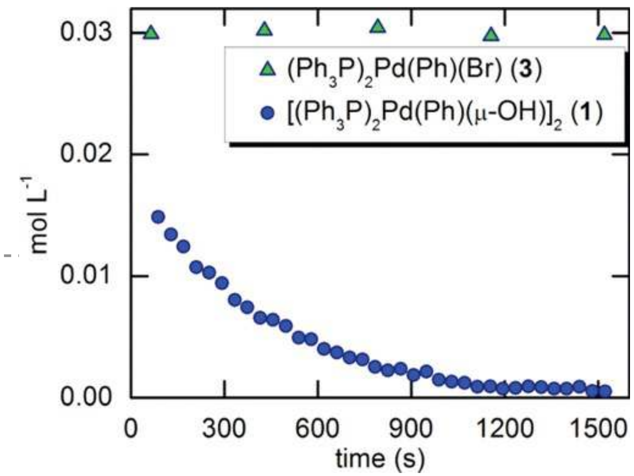
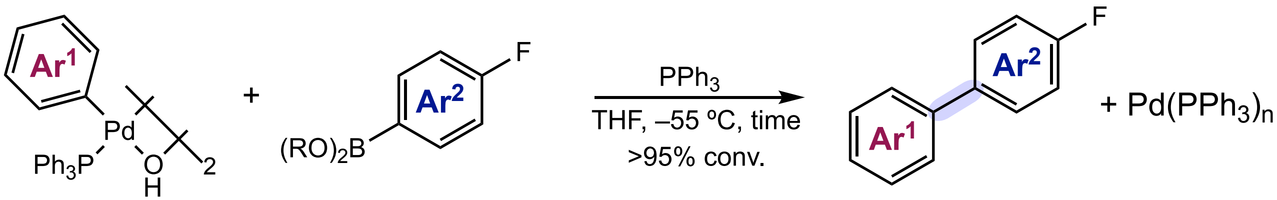


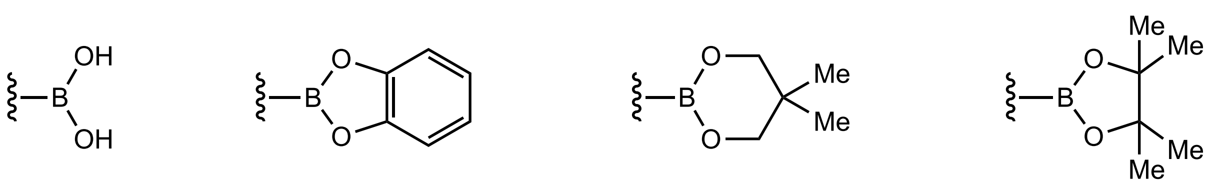




larger k for oxo-Pd pathway by a factor of 10^4

Boronic esters





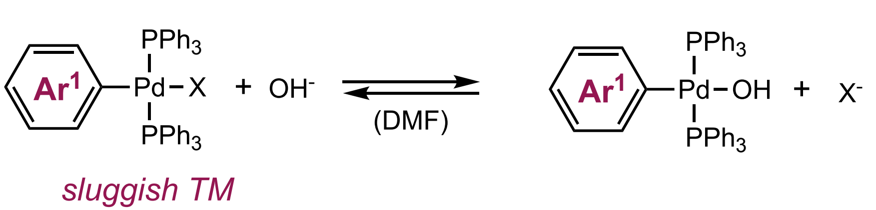
<2 min | *<2 min* | *<2 min* | *1.5 h*

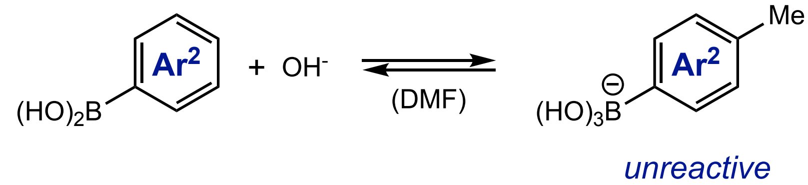
but, still much faster than boronate pathway

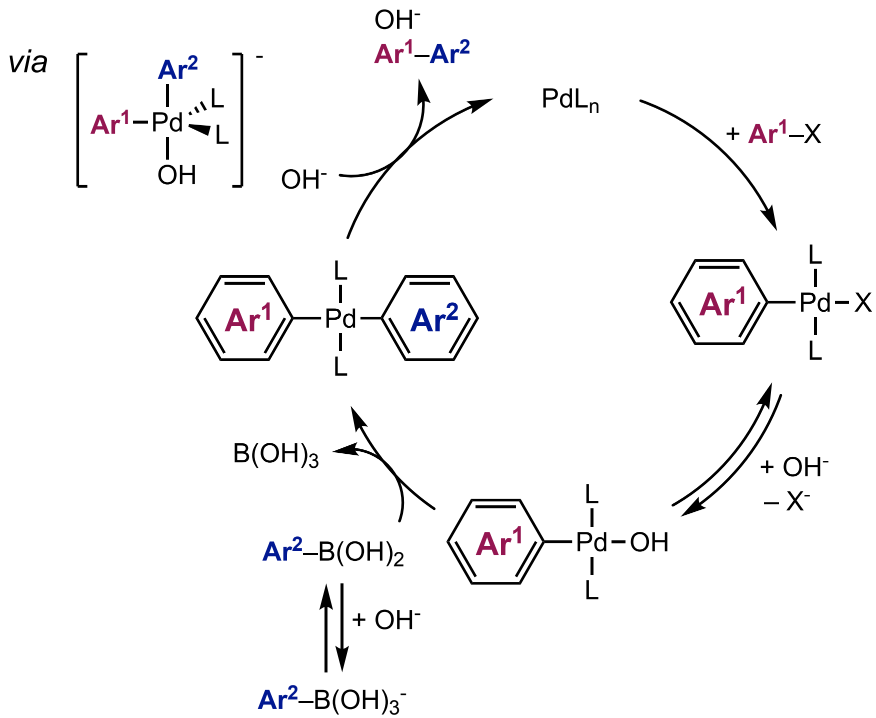
Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 2116.

Kinetic studies

Amatore and Jutand (2011)







Triple role of OH^-

- Formation of *trans*-$[ArPd(OH)(PPh_3)_2]$
- Unexpected promotion of RE
- Formation of the unreactive anionic $ArB(OH)_3^-$

Amatore, C.; Jutand, A.; Le Duc, G. *Chem. - Eur. J.* **2011**, *17*, 2492.
Amatore, C.; Jutand, A.; Le Duc, G. *Angew. Chem. Int. Ed.* **2012**, *51*, 1379.

Kinetic studies

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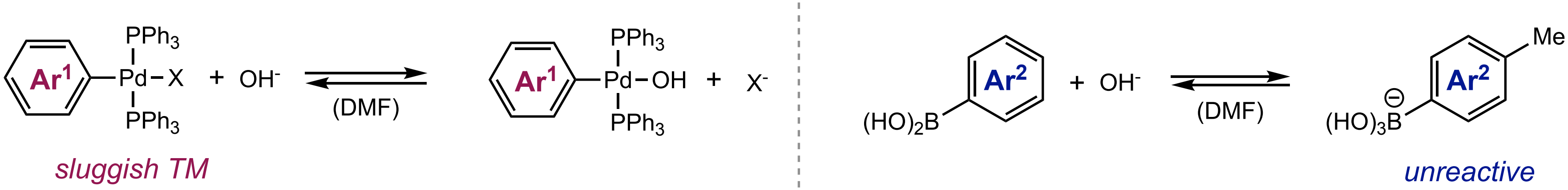
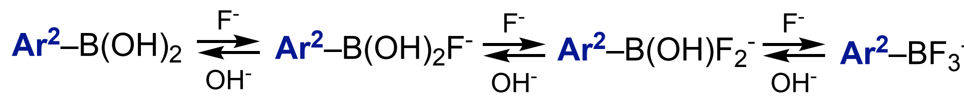
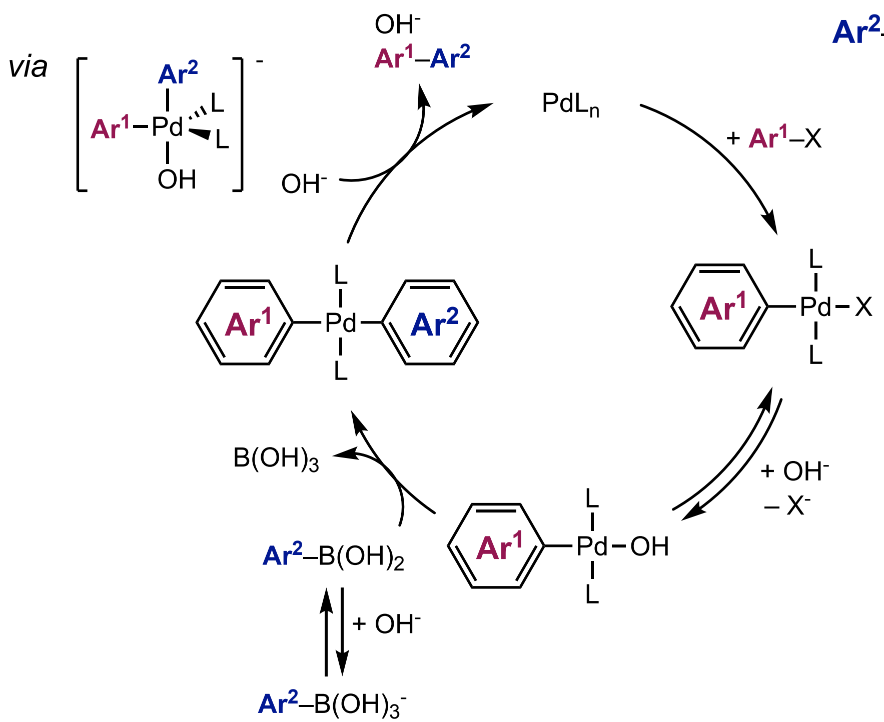


Similar observation for F-

in DMF





Triple role of OH- / F-

- Formation of *trans*-[ArPd(OH/F)$(PPh_3)_2$]
- Unexpected promotion of RE
- Formation of the unreactive borate anions

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Kinetic studies

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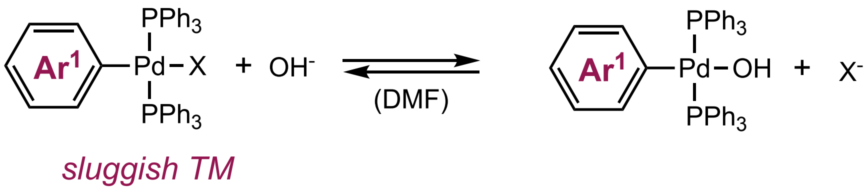

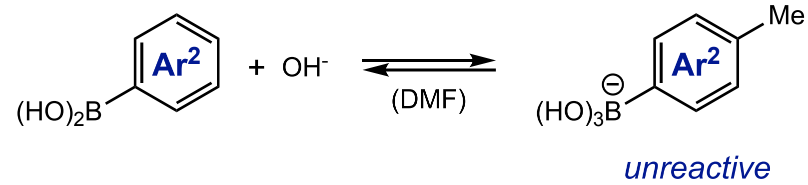

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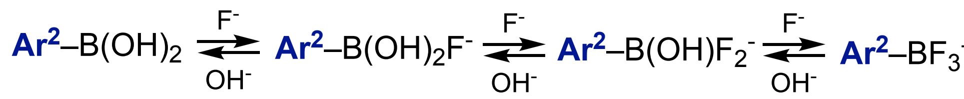

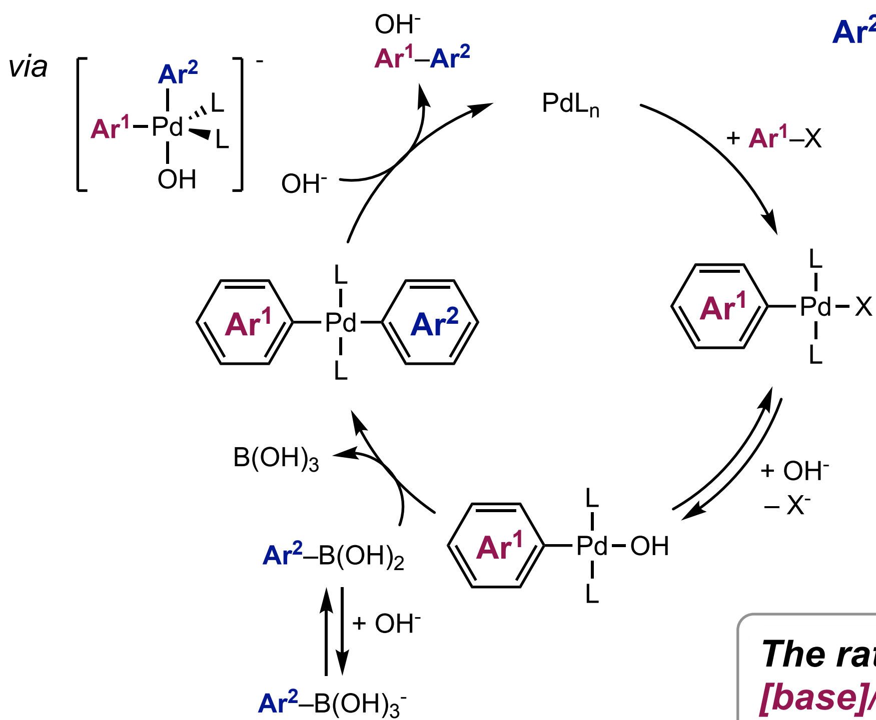

Triple role of OH- / F-

- Formation of *trans*-[ArPd(OH/F)(PPh_3)$_2$]
- Unexpected promotion of RE
- Formation of the unreactive borate anions

> ***The rate of the overall reaction is controlled by the ratio [base]/[Ar'B(OH)2] when the base is either F- or OH-.***

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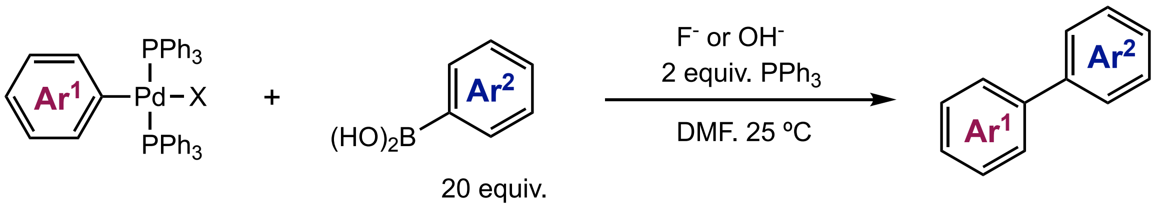

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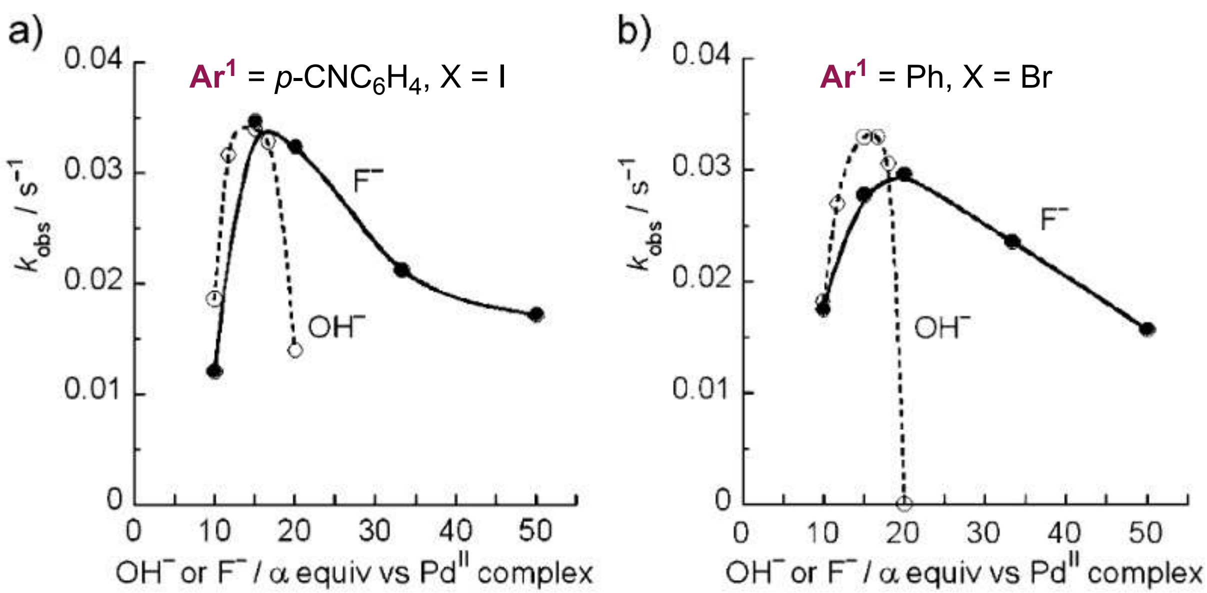
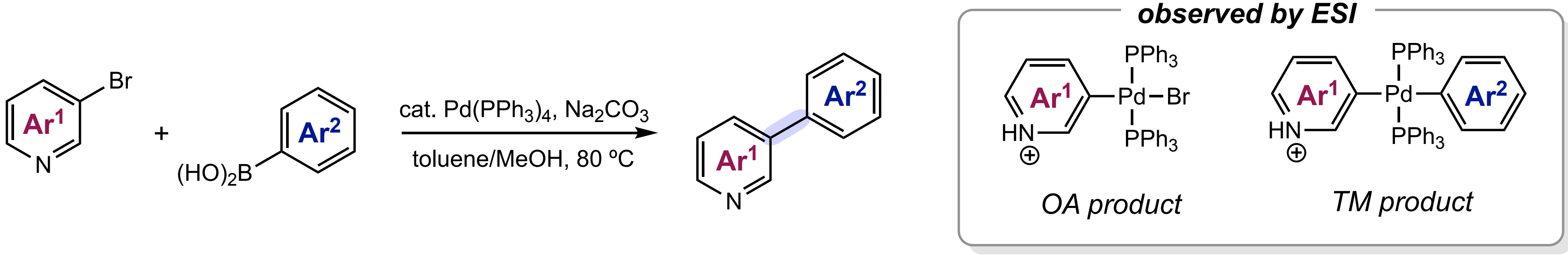


Oxo-palladium pathway is favored over boronate pathway.

Amatore, C.; Jutand, A.; Le Duc, G. *Chem. - Eur. J.* **2011**, *17*, 2492.
Amatore, C.; Jutand, A.; Le Duc, G. *Angew. Chem. Int. Ed.* **2012**, *51*, 1379.

Observation of elusive reaction intermediate

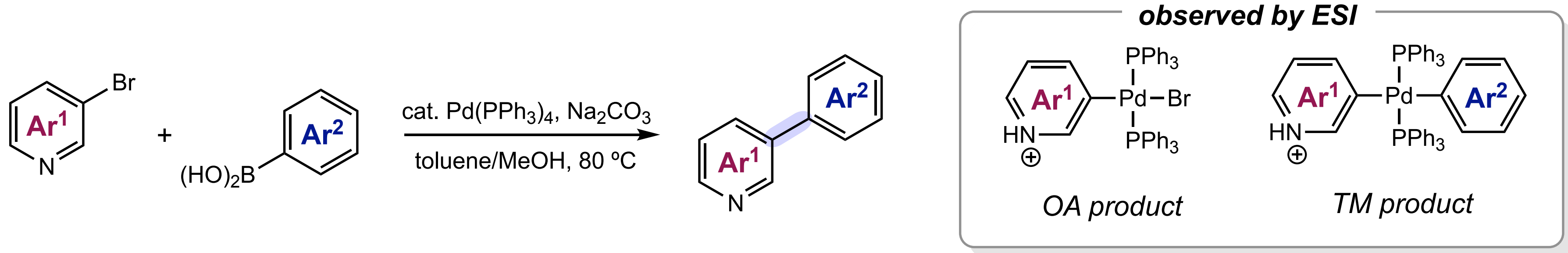
By ESI-Ms



Aliprantis, A. O.; Canary, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 6985.

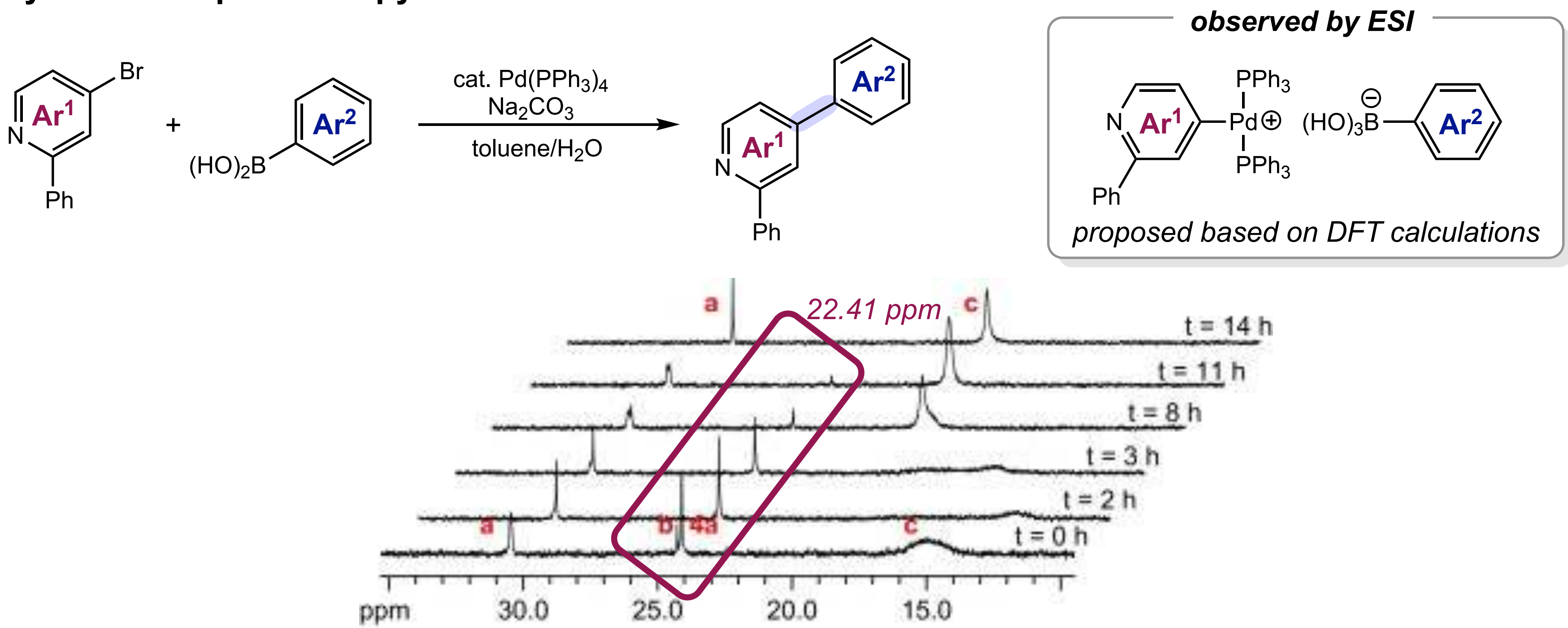
Observation of elusive reaction intermediate

By ESI-Ms



Aliprantis, A. O.; Canary, J. W. *J. Am. Chem. Soc.* **1994**, *116*, 6985.

By ^{31}P NMR spectroscopy

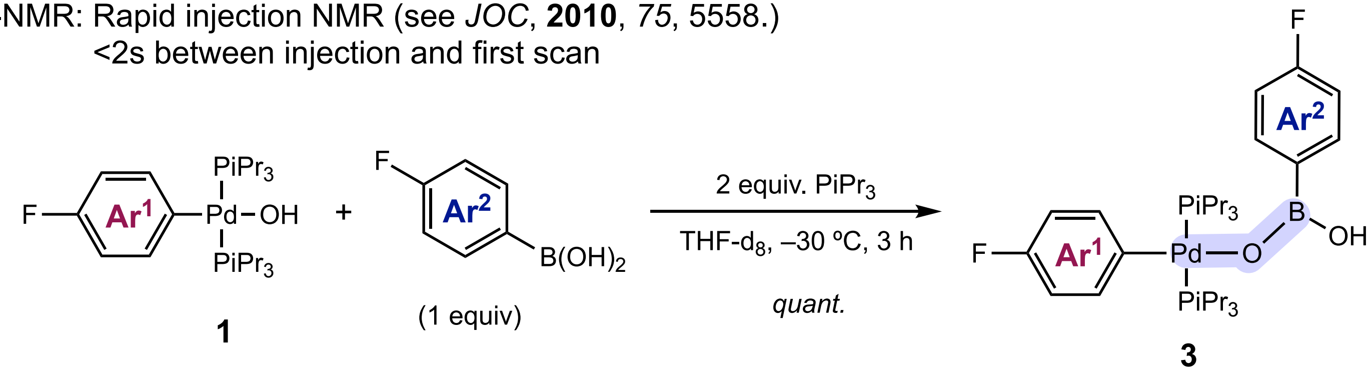


Sicre, C.; Braga, A. A. C.; Maseras, F.; Cid, M. M. *Tetrahedron* **2008**, *64*, 7437.

Direct observation of TM product using RI-NMR technique

Denmark (2016)

RI-NMR: Rapid injection NMR (see *JOC*, **2010**, *75*, 5558.)
<2s between injection and first scan

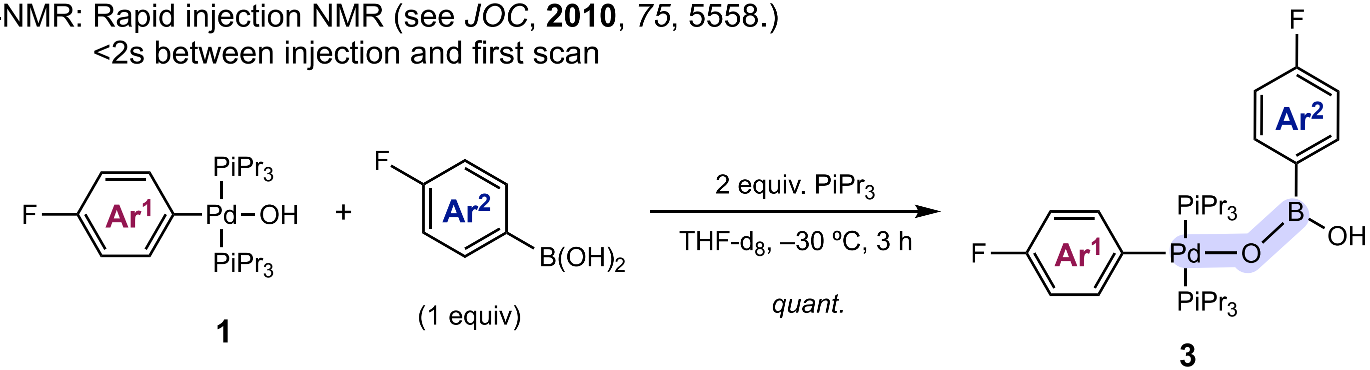


Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Denmark (2016)

RI-NMR: Rapid injection NMR (see *JOC*, **2010**, *75*, 5558.)
<2s between injection and first scan



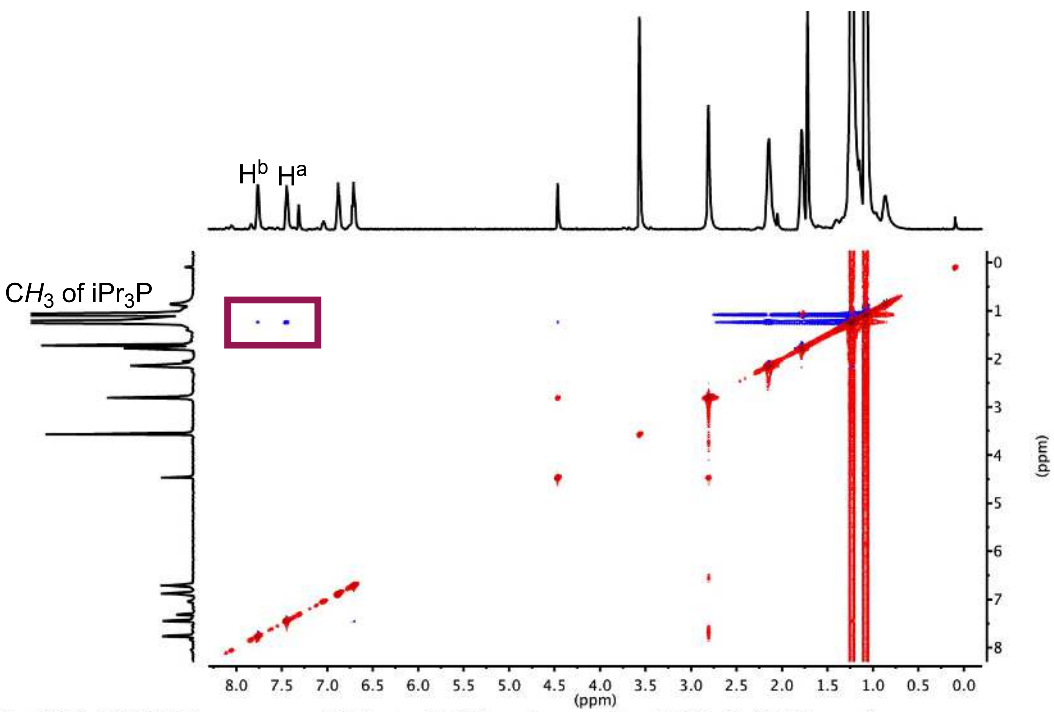
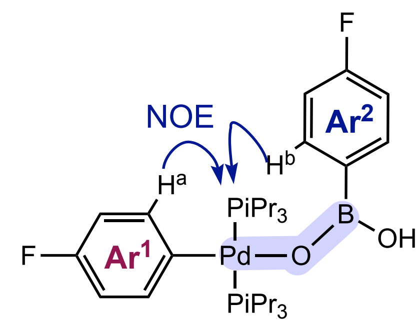


Fig S 10. NOESY spectrum of **11** at −30 °C, referenced to THF-d_8 (1.72 ppm).



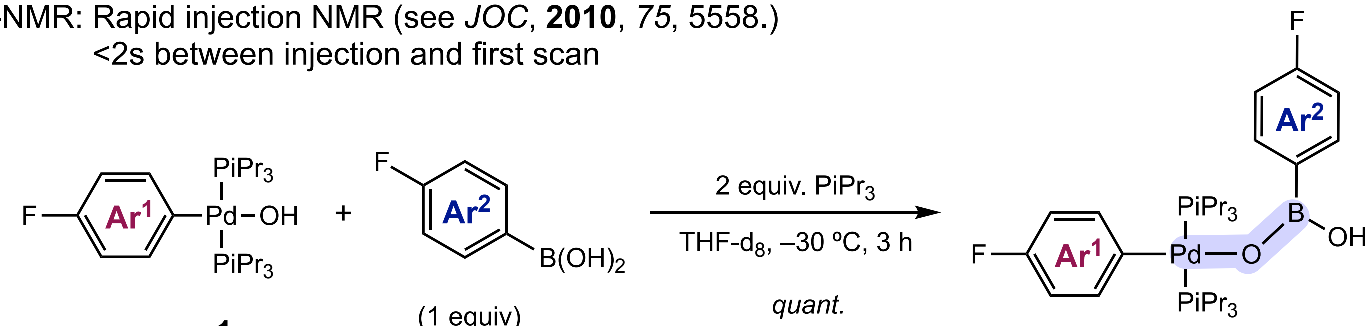
from NOSEY:
trans-bisphosphino sq. pl. Pd complex

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Denmark (2016)

RI-NMR: Rapid injection NMR (see *JOC*, **2010**, *75*, 5558.)
<2s between injection and first scan



1 **3**

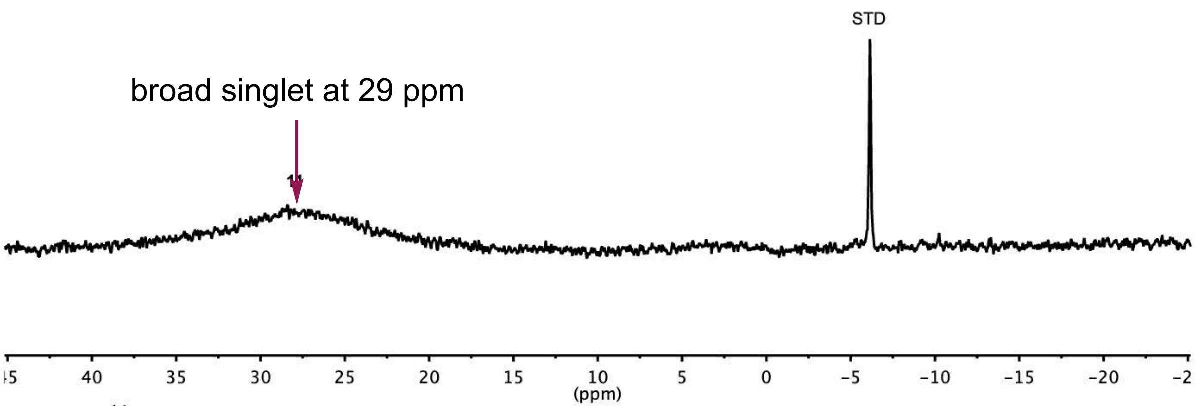
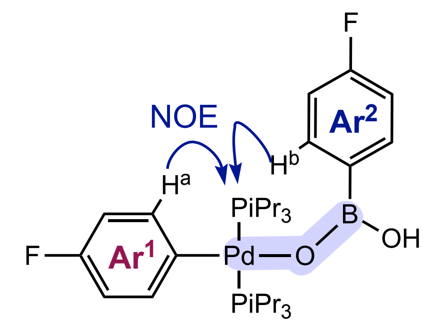


Fig S 5. ^{11}B NMR spectrum of **11** at −30 °C, referenced to Ph_4BNa (−6.14 ppm).



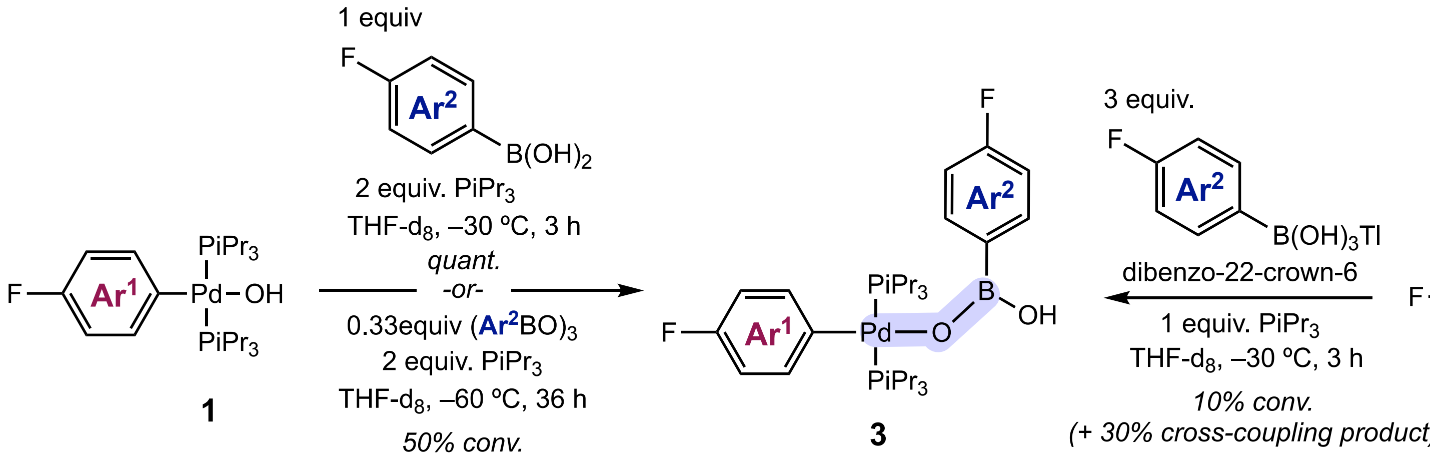
from NOSEY:
trans-bisphosphino sq. pl. Pd complex

from ^{11}B NMR:
tri-coordinate boron compound

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Independent synthesis of 3

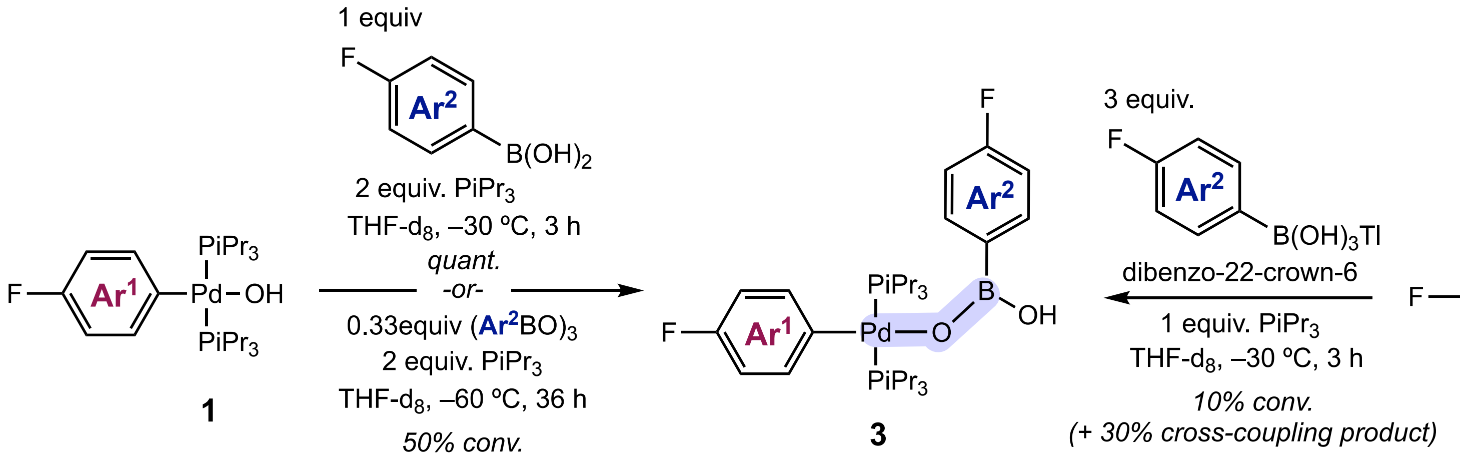


3 can be formed w/o the intermediacy of Ar[Pd](OH) complex

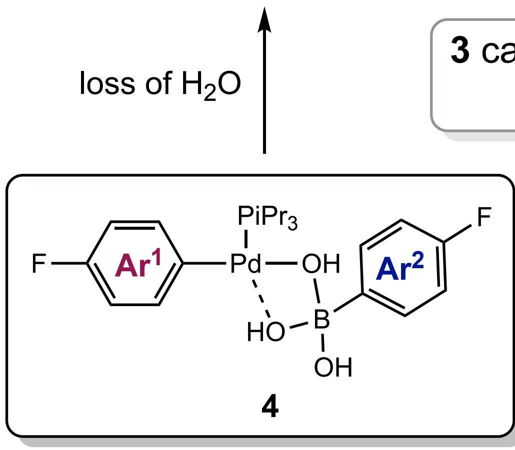
Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Independent synthesis of 3



3 can be formed w/o the intermediacy of Ar[Pd](OH) complex



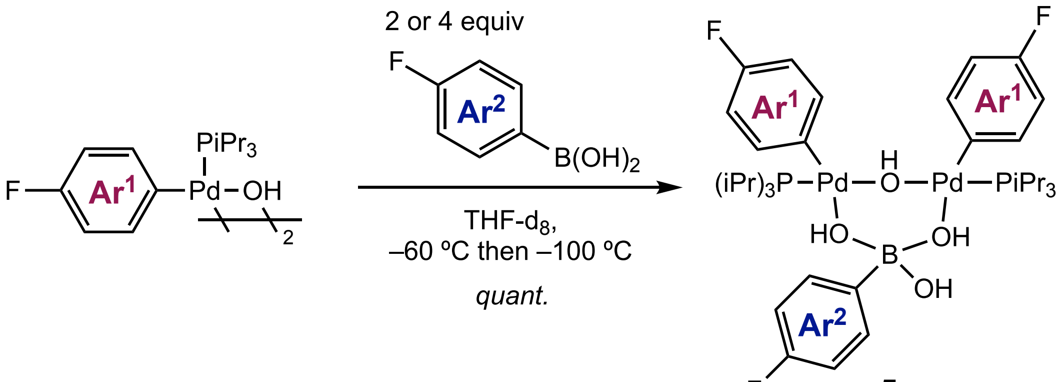
- Formed initially, then rapid loss of H_2O
- addition of H_2O to **3** —> No change
- addition of OH^- ($CsOH$-H_2O) —> No change

*Reaction not observed due to steric hindrance resulting from two iPr_3P ligands on **3**?*

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Preparation of tetracoordinate boron reaction intermediate:



5
2:1 adduct

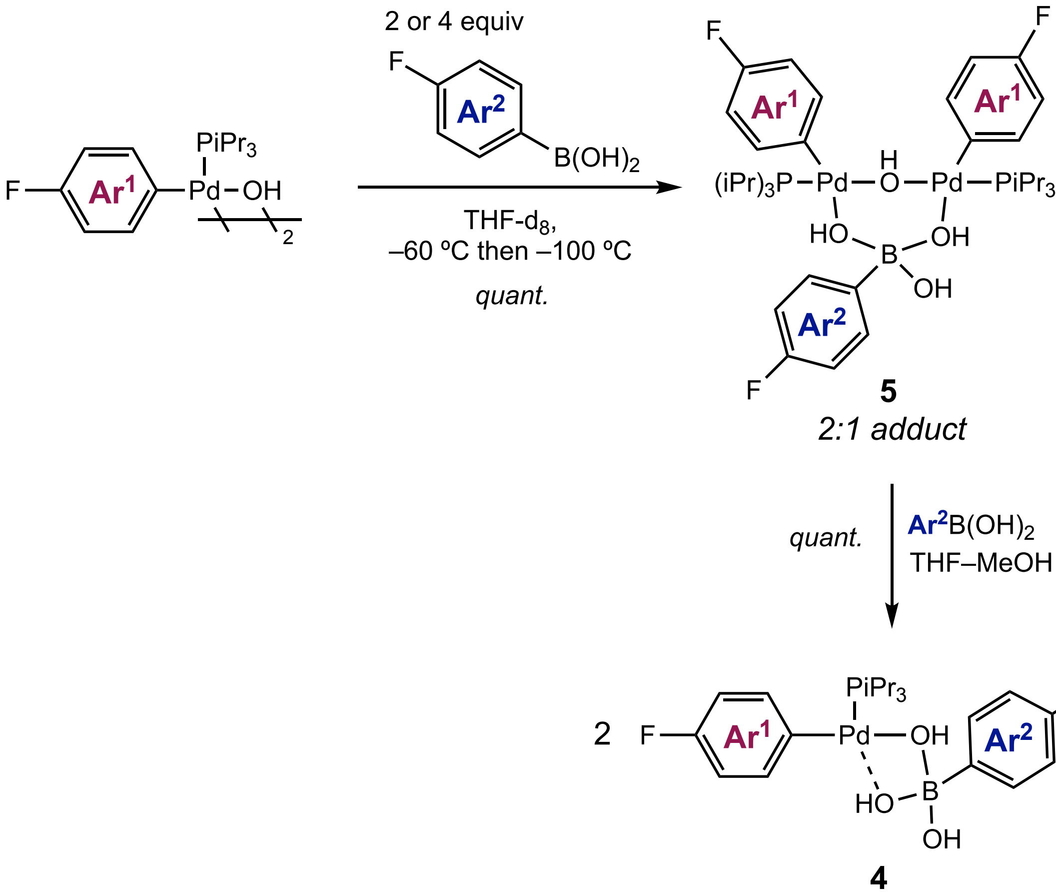
No change with an excess of **Ar^2**B(OH)$_2$

Cross peak between **5** and **Ar^2**B(OH)$_2$ in EXSY even at 100 ºC

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Preparation of tetracoordinate boron reaction intermediate:



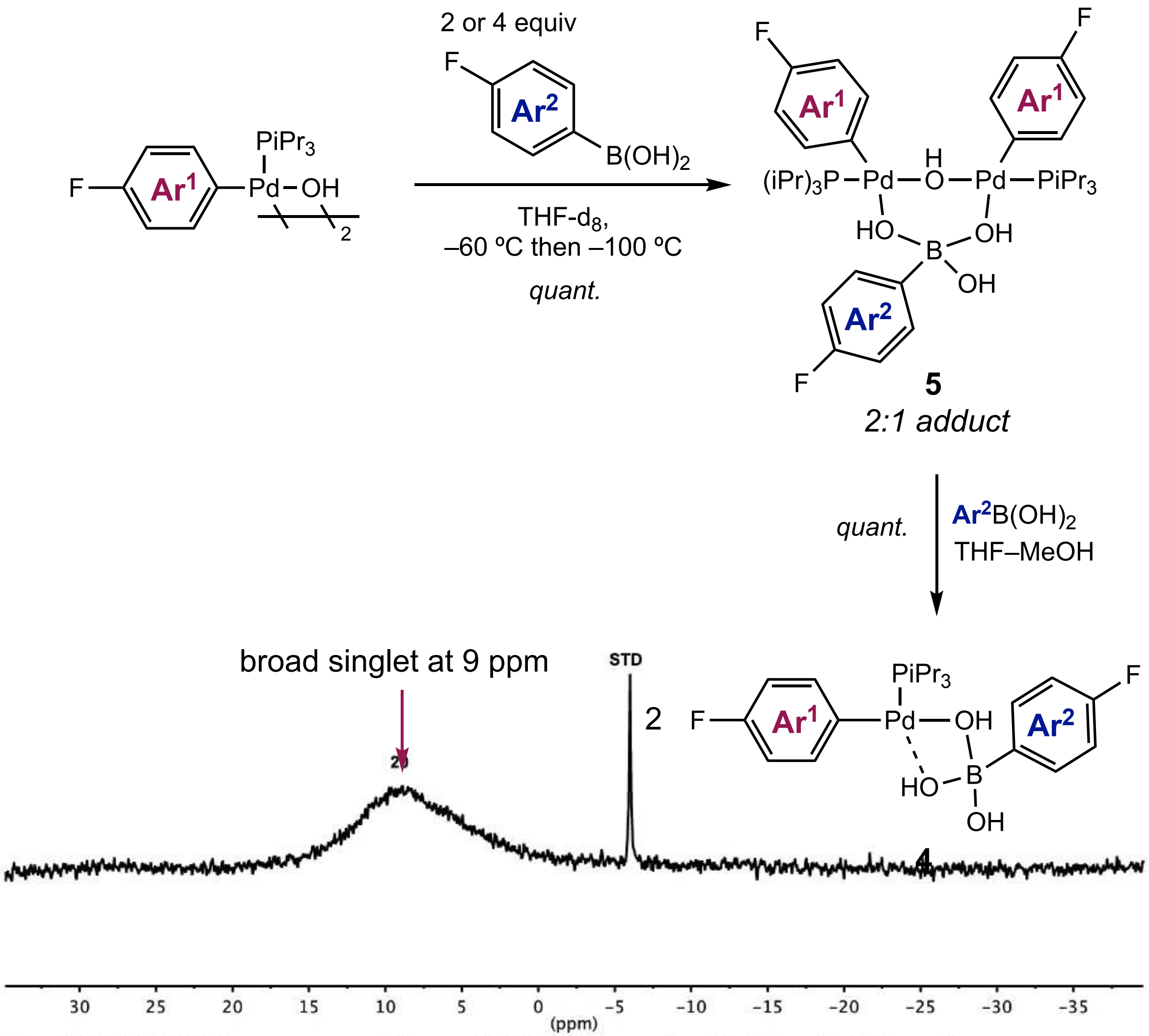
No change with an excess of **Ar**[2]B$(OH)_2$

Cross peak between **5** and **Ar**[2]B$(OH)_2$ in EXSY even at 100 ºC

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Direct observation of TM product using RI-NMR technique

Preparation of tetracoordinate boron reaction intermediate:



No change with an excess of **Ar**^{2}B(OH)$_2$

Cross peak between **5** and **Ar**^{2}B(OH)$_2$ in EXSY even at 100 ºC

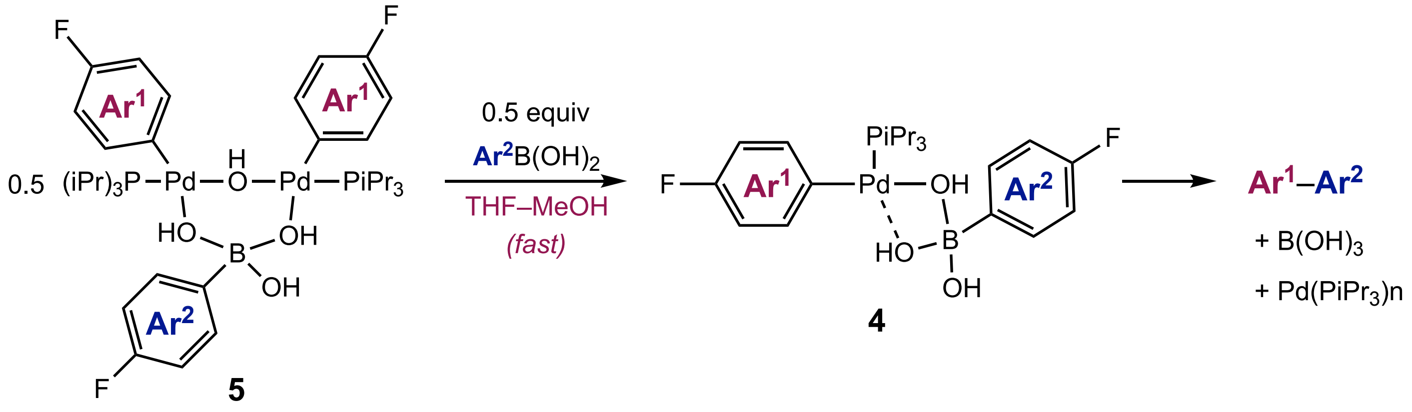
4-coordinate boronate complex!

Fig S 57. ^{11}B NMR spectrum of **20** at −60 °C, referenced to Ph$_4$BNa (−6.14 ppm).

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Kinetic analysis of TM

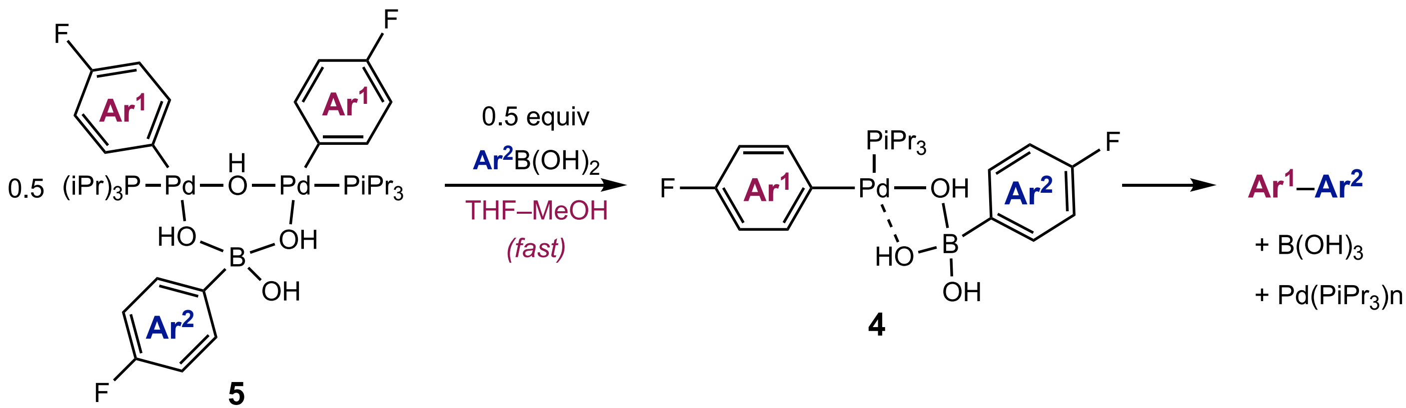
Transfer of Ar from 4-coordinate B to P

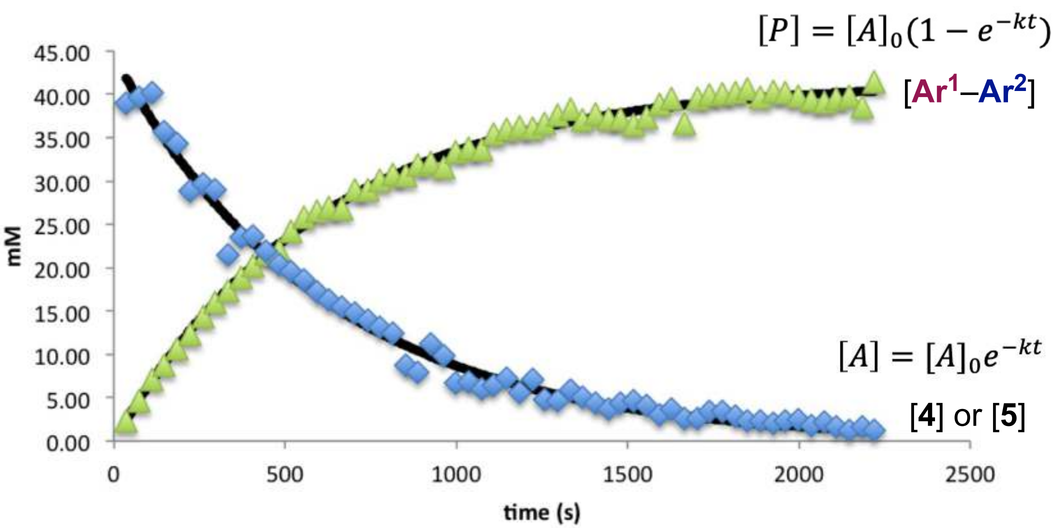


Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Kinetic analysis of TM

Transfer of Ar from 4-coordinate B to P





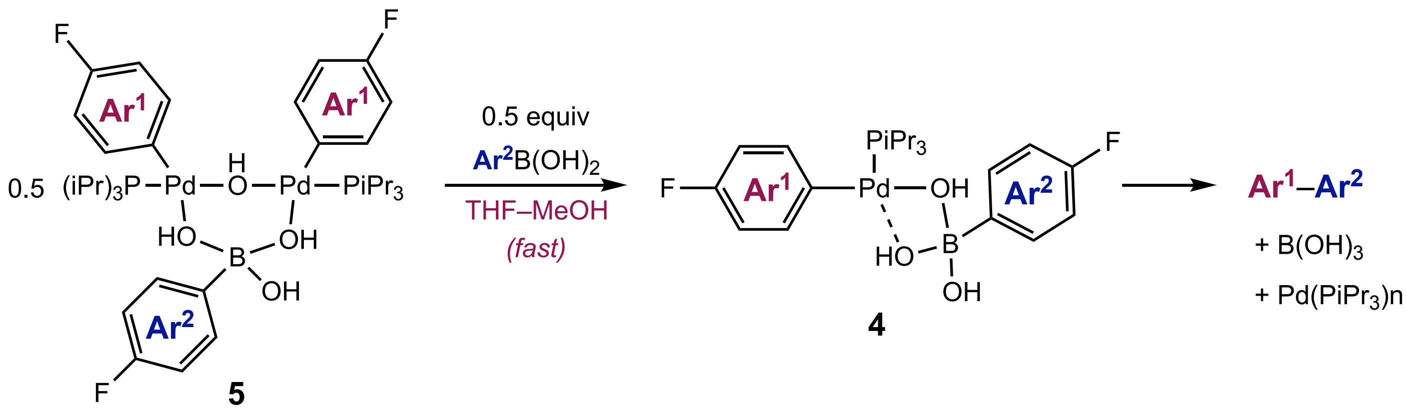
in THF-MeOH (from **4** to prdt)
k_{obs}(-**4**) = 1.41(1) x 10^{-3} s^{-1}
k_{obs}(+prdt) = 1.55(3) x 10^{-3} s^{-1}

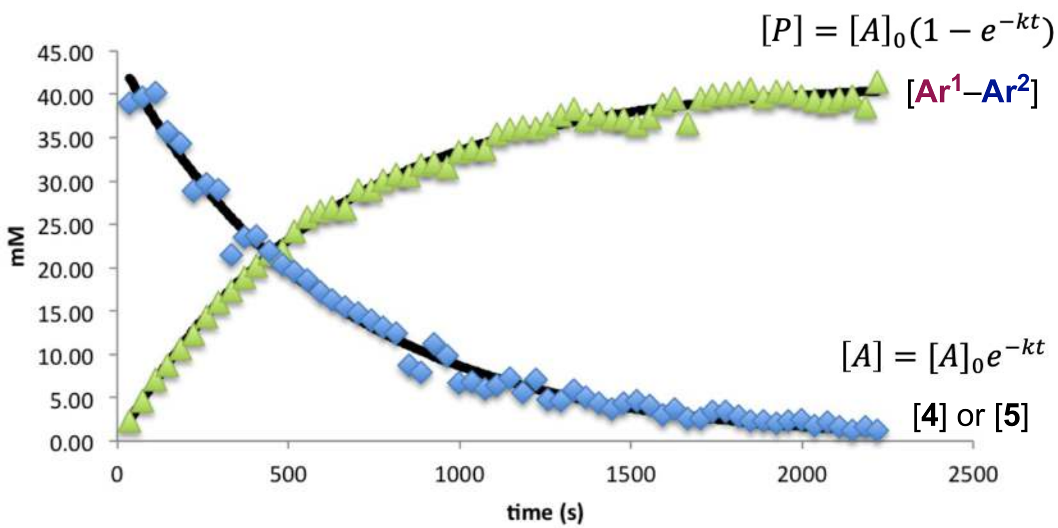
in THF (from **5** to prdt)
k_{obs}(-**5**) = 7.6(2) x 10^{-4} s^{-1}
k_{obs}(+prdt) = 5.78(4) x 10^{-4} s^{-1}

Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Kinetic analysis of TM

Transfer of Ar from 4-coordinate B to P





in THF-MeOH (from **4** to prdt)
k_{obs}(-**4**) = 1.41(1) x 10^{-3} s^{-1}
k_{obs}(+prdt) = 1.55(3) x 10^{-3} s^{-1}

in THF (from **5** to prdt)
k_{obs}(-**5**) = 7.6(2) x 10^{-4} s^{-1}
k_{obs}(+prdt) = 5.78(4) x 10^{-4} s^{-1}

Decay of **5** and formation of product coincide!

Similarity of rate constants observed in THF and THF-MeOH mixture supports that **5** is converted to **4** before transmetalation.

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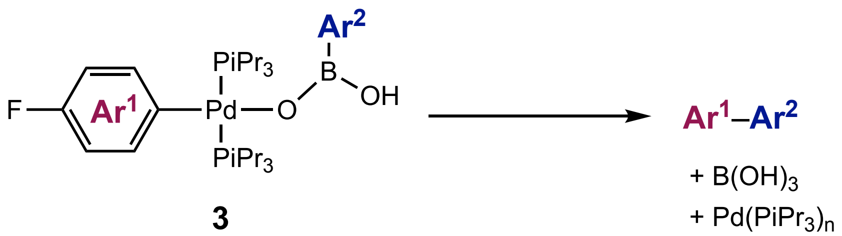
Kinetic analysis of TM

Transfer of Ar from 3-coordinate B to P

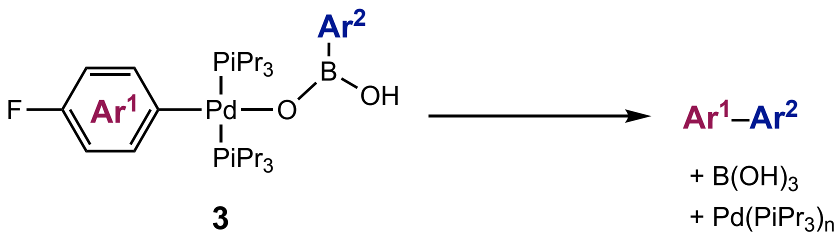


Thermally stable at –30 ºC
in the presence of excess $PiPr_3$.

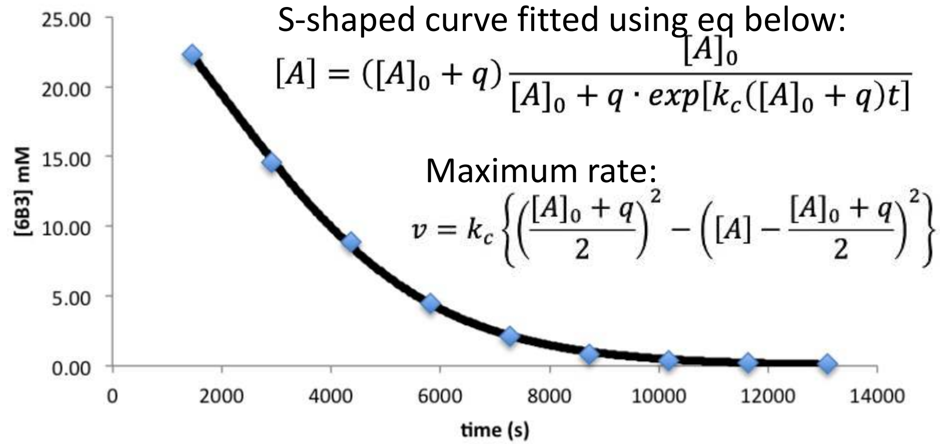
Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Kinetic analysis of TM

Transfer of Ar from 3-coordinate B to P



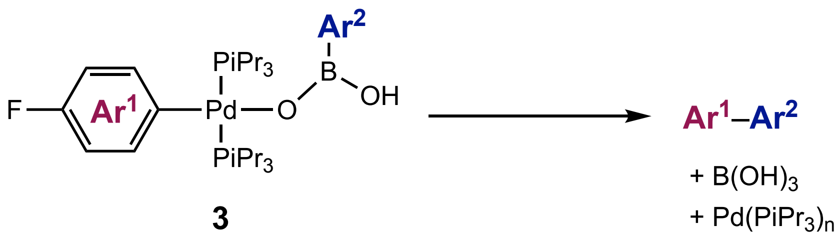
Thermally stable at –30 ºC
in the presence of excess $PiPr_3$.



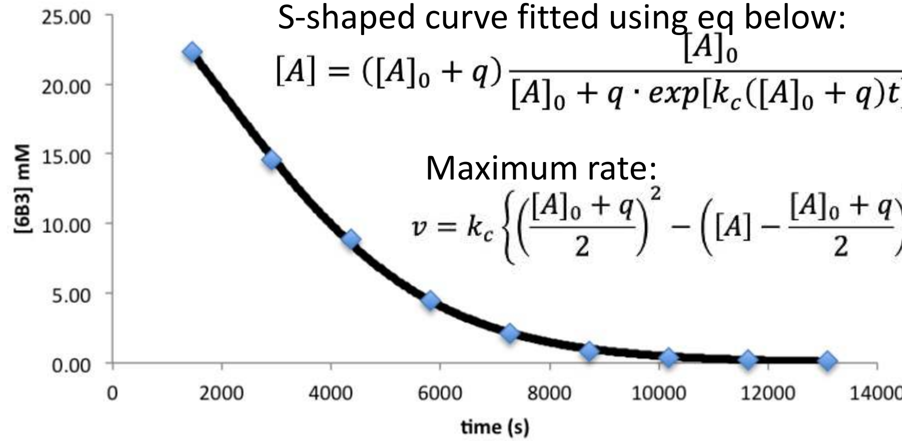
Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Kinetic analysis of TM

Transfer of Ar from 3-coordinate B to P



Thermally stable at –30 ºC
in the presence of excess $PiPr_3$.



S-shaped curve fitted using eq below:

$$[A] = ([A]_0 + q)\frac{[A]_0}{[A]_0 + q \cdot exp[k_c([A]_0 + q)t]}$$

Maximum rate:

$$v = k_c\left\{\left(\frac{[A]_0 + q}{2}\right)^2 - \left([A] - \frac{[A]_0 + q}{2}\right)^2\right\}$$

Plot of $\log[v_{max}]$ vs. $\log[P^iPr_3]$

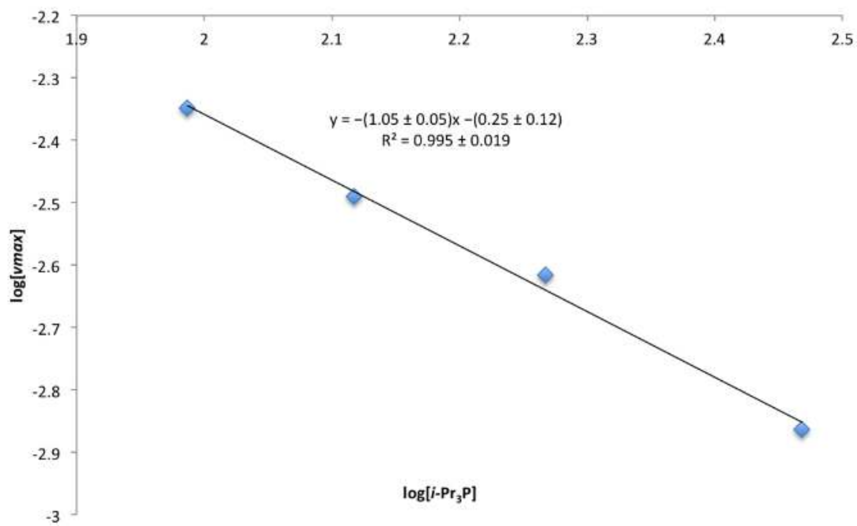
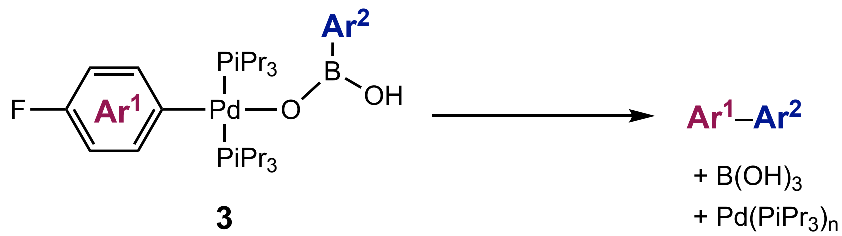


Fig S 92. Order Determination of *i*-Pr_3P.

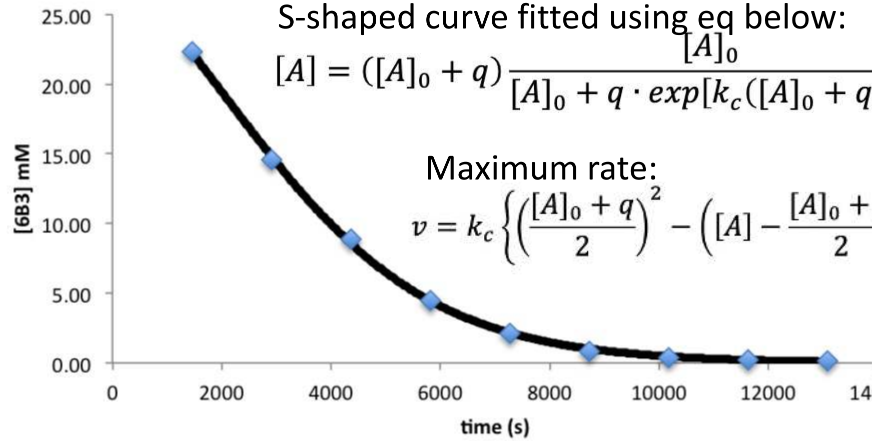
Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

Kinetic analysis of TM

Transfer of Ar from 3-coordinate B to P



Thermally stable at –30 ºC
in the presence of excess $PiPr_3$.



S-shaped curve fitted using eq below:

$$[A] = ([A]_0 + q)\frac{[A]_0}{[A]_0 + q\cdot exp[k_c([A]_0 + q)t]}$$

Maximum rate:

$$v = k_c\left\{\left(\frac{[A]_0 + q}{2}\right)^2 - \left([A] - \frac{[A]_0 + q}{2}\right)^2\right\}$$

Plot of $\log[v_{max}]$ vs. $\log[P^iPr_3]$

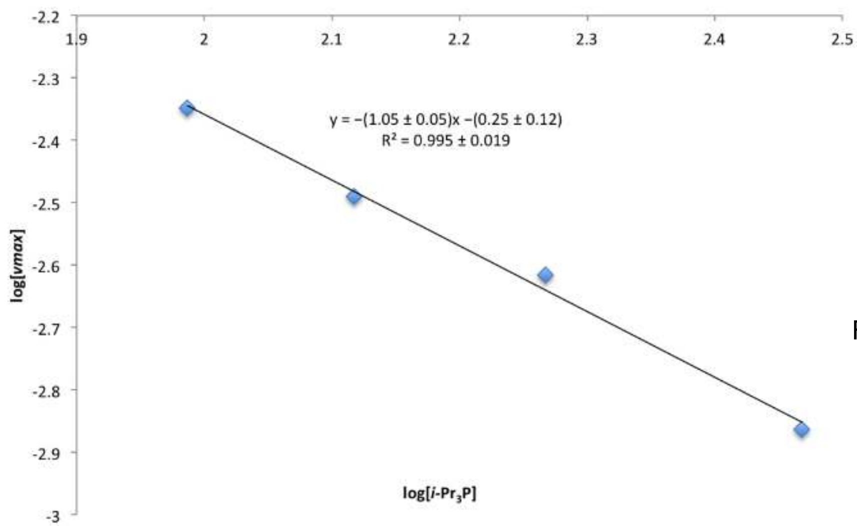
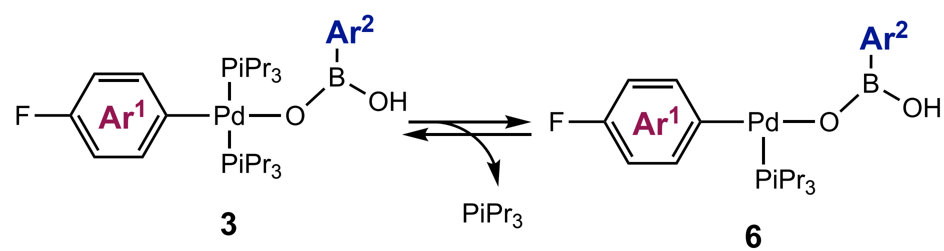


Fig S 92. Order Determination of i-Pr_3P.

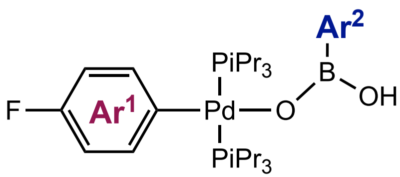
- *Inverse* dependence on phosphine
- *Dissociation of phosphine is a pre-equilibrium process*



Thomas, A. A.; Denmark, S. E. *Science*, **2016**, *352*, 329.

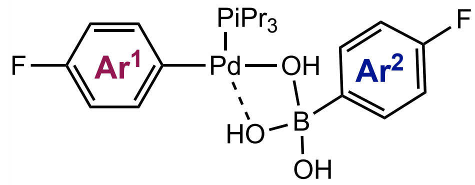
Pre-transmetalation complexes observed so far

3-coord. B complexes

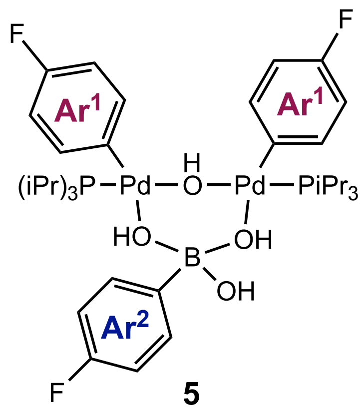


3

4-coord. B complexes



4



5

- contain a Pd–O–B linkage & are able to transfer Ar groups from B to Pd.
- Empty coordination site on Pd is needed for the TM to take place. (phosphine dissociation)

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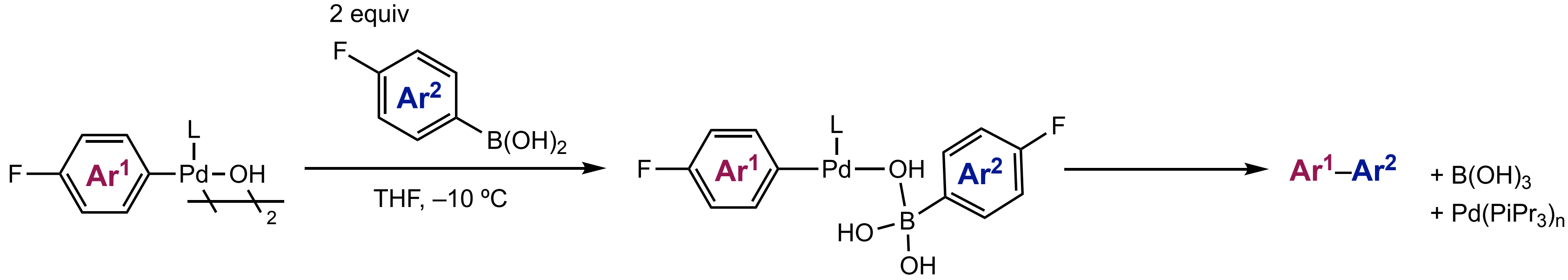
Pre-transmetalation complexes

Phosphine ligands:

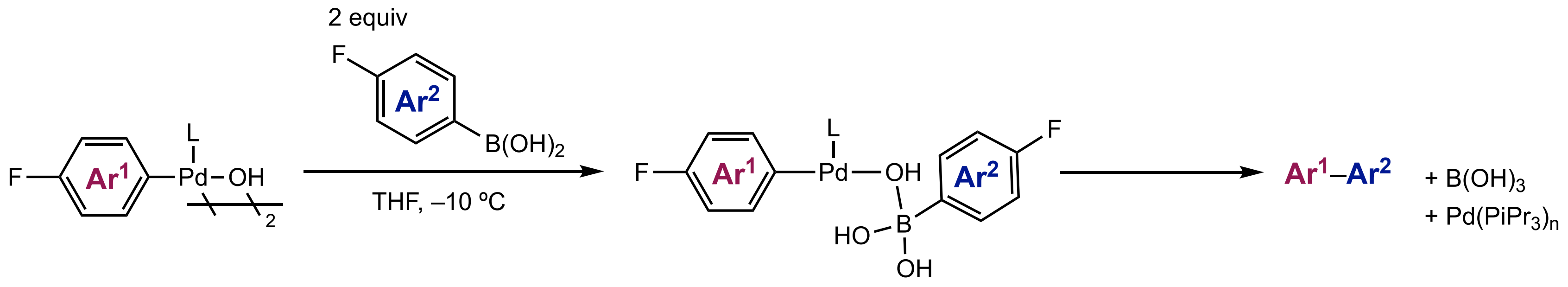


L =	dppf	$PiPr_3$	PPh_3
k_{obs} =	$2.75(2) \times 10^{-3}\ s^{-1}$	$8.09(3) \times 10^{-3}\ s^{-1}$	$9.95(2) \times 10^{-3}\ s^{-1}$
k_{rel} =	1	2.9	3.6

Thomas, A. A.; Wang, H.; Zahrt, A. F.; Denmark, S. E. *J. Am. Chem. Soc.* **2017**, *139*, 3805

Pre-transmetalation complexes

Phosphine ligands:



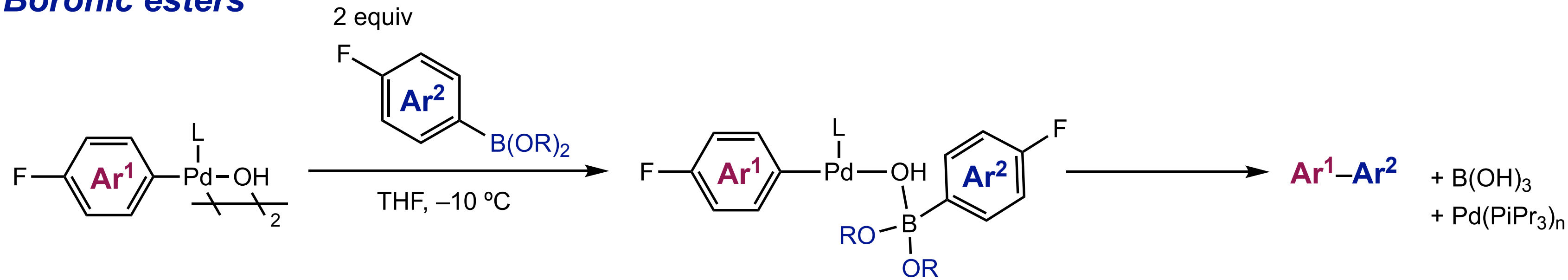
L =	dppf	$PiPr_3$	PPh_3
k_{obs} =	2.75(2) x 10^{-3} s^{-1}	8.09(3) x 10^{-3} s^{-1}	9.95(2) x 10^{-3} s^{-1}
k_{rel} =	1	2.9	3.6

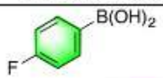
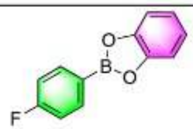
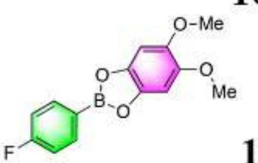
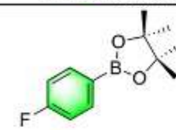
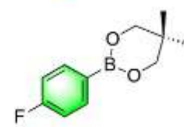
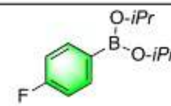
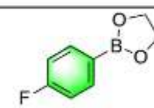
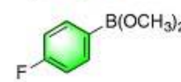
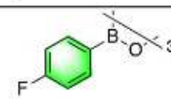
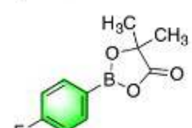
- Smallest k with dppf: Ligand dissociation prior to TM (coordinatively unsaturated Pd center)
- Faster rate with PPh_3: More electrophilic Pd center —> faster TM

Thomas, A. A.; Wang, H.; Zahrt, A. F.; Denmark, S. E. *J. Am. Chem. Soc.* **2017**, *139*, 3805

Pre-transmetalation complexes

Boronic esters



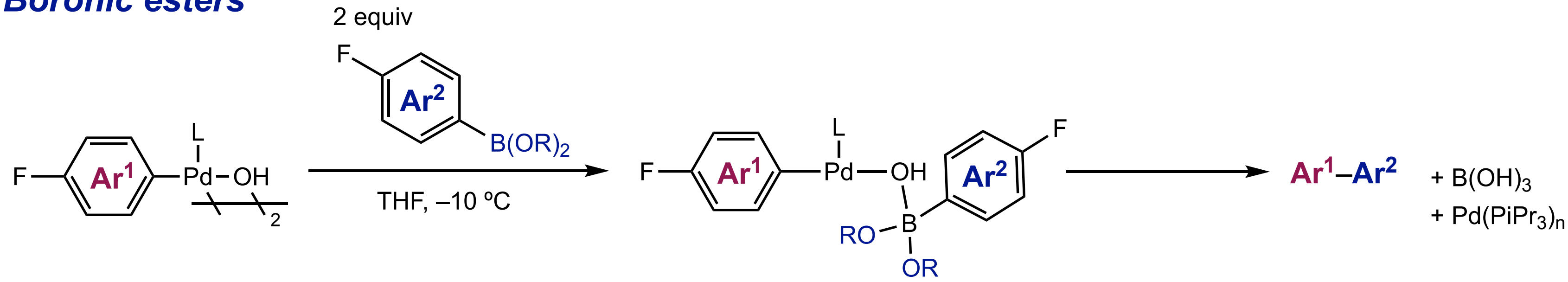
substrate	complex	[a]form k, 10^{-3} s^{-1}	k_{rel}
 **2**	**4**	0.578 ± 0.013	1.00
 **8**	**9**	2.46 ± 0.39	4.27
 **10**	**11**	0.0013 ± 0.0004	0.0022
 **12**	**14**	2.73 ± 0.54	4.20
 **13**	**15**	3.34 ± 0.21	5.78
 **16**	**18**	– (prdt formation: 5.5 h)	–
 **22**	**23**	(prdt formation: 0.3 h)	
 **20**	**21**	0.824 ± 0.016	1.42
 **17**	**19**	13.3 ± 0.7	23.01
 **7**	**6**	12.4 ± 0.2	21.45
 **28**	**30**	5.39 ± 0.07	9.33
 **29**	**31**	0.226 ± 0.031	0.39

- Faster rate with PPh_3: More electrophilic Pd cen

Thomas, A. A.; Zahrt, A. F.; Delaney, C. P.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 4401

Pre-transmetalation complexes

Boronic esters

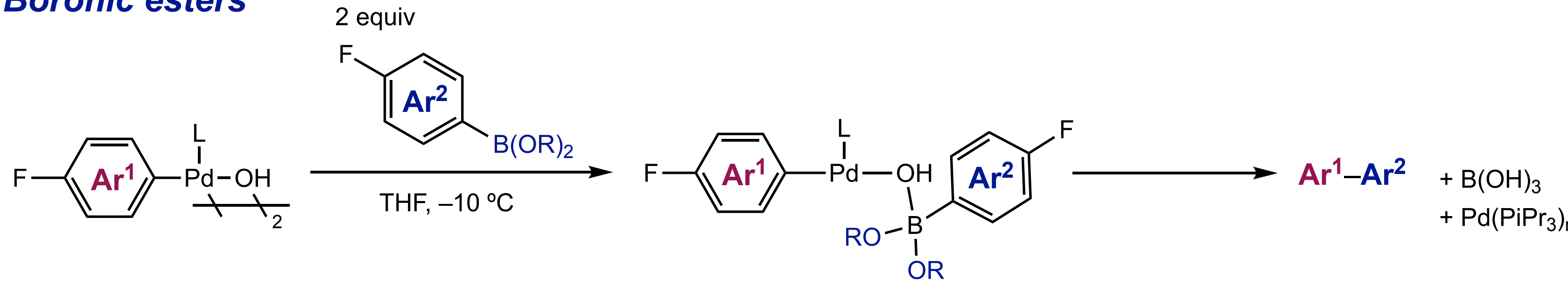


- Ease of **rehybridization of B**:
  steric accessibility, electrophilicity, angular distortion
- Ease of formation of a **coordinatively unsaturated Pd** complex:
  Lewis basicity and steric demand of the oxygen atoms
- **Migratory aptitude of the Ar** group:
  Lewis basicity of O (inverse dependence compared to the factor above)

Thomas, A. A.; Zahrt, A. F.; Delaney, C. P.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 4401

Pre-transmetalation complexes

Boronic esters



- Ease of **rehybridization of B**:
  steric accessibility, electrophilicity, angular distortion

- Ease of formation of a **coordinatively unsaturated Pd** complex:
  Lewis basicity and steric demand of the oxygen atoms

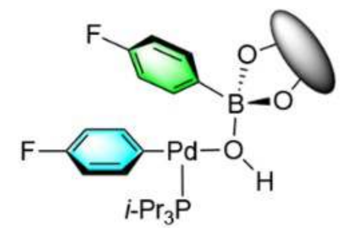
- **Migratory aptitude of the Ar** group:
  Lewis basicity of O (inverse dependence compared to the factor above)

1. Lewis basic oxygen atoms:
   favorable Pd–O interaction —> higher barrier for dissociation and less stable pre-TM intermediate

   Catechol > glycol > boronic acid : (easily dissociated)
2. Lewis basic oxygen atoms:
   hyperconjugative activation of migrating Ar group —> lowering barrier to TM

3. boronic acid (free to rotate) > glycol, catechol (geometric constraint)

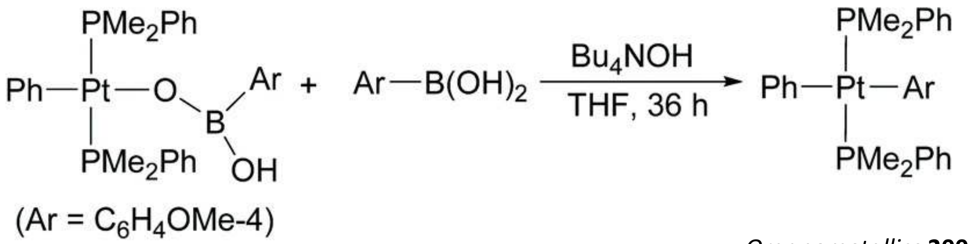
$B(eg) >> BCat > B(OH)_2$



Thomas, A. A.; Zahrt, A. F.; Delaney, C. P.; Denmark, S. E. *J. Am. Chem. Soc.* **2018**, *140*, 4401

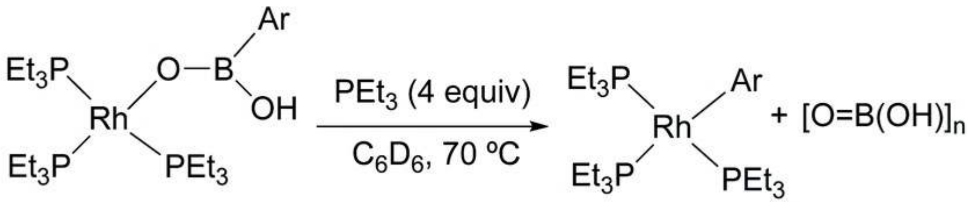
Other metal complexes containing M–O–B bonds

- *Pt: Osakada (2005)*



Organometallics **2005**, *24*, 3815

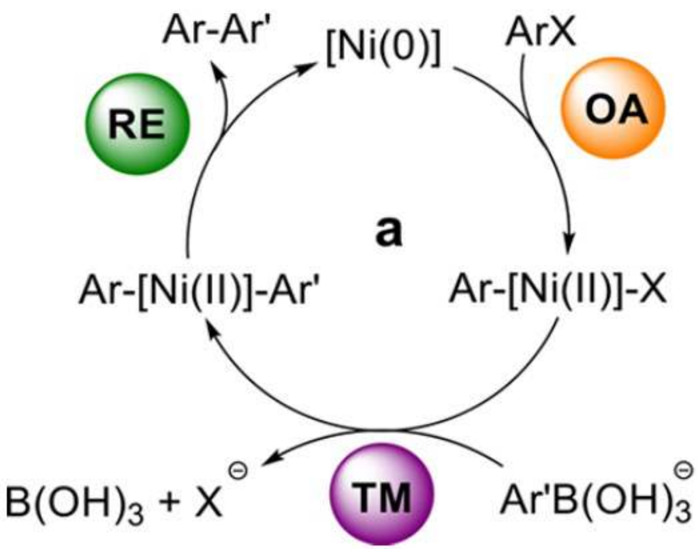
- *Rh: Hartwig (2007)*



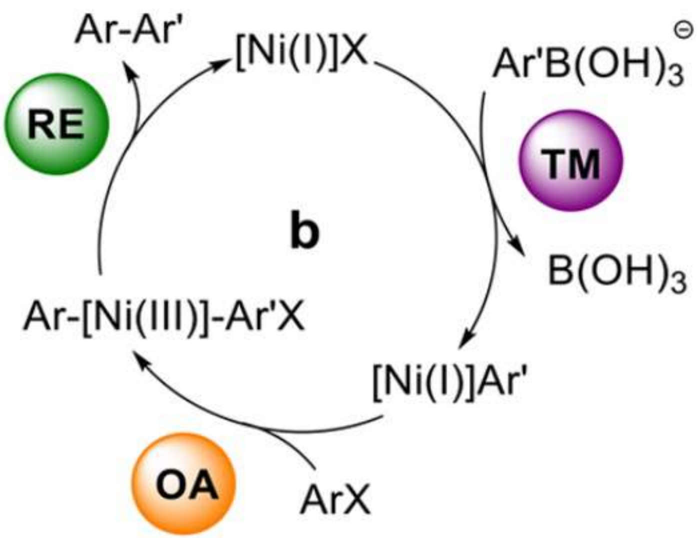
J. Am. Chem. Soc. **2007**, *129*, 1876.

Proposed mechanism for Ni-catalyzed SMC

Ni(0)-Ni(II) cycle

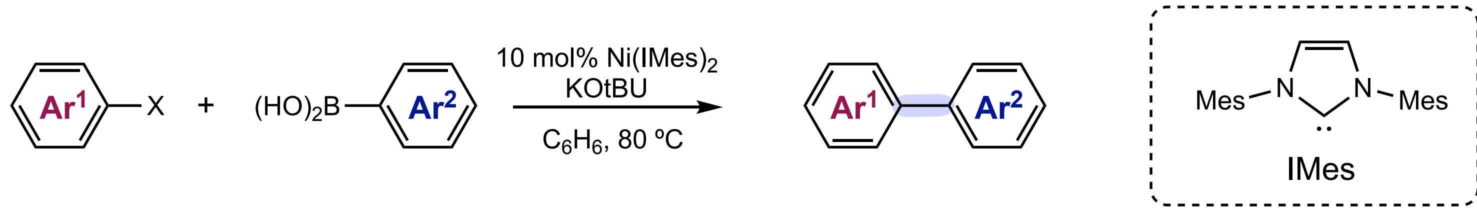


Ni(I)-Ni(III) cycle



- **OA**: either in a concerted fashion or by a single-electron transfer pathway via free radicals
- **RE**: less information is available due to the difficulty of isolating TM product.
- **TOL**: either OA (poorly reactive substrates such as ArCl) or TM (for other electrophiles)

Ni-catalyzed SMC: Ni(I/III) cycle



Reaction of Ni(0) cat and electrophile

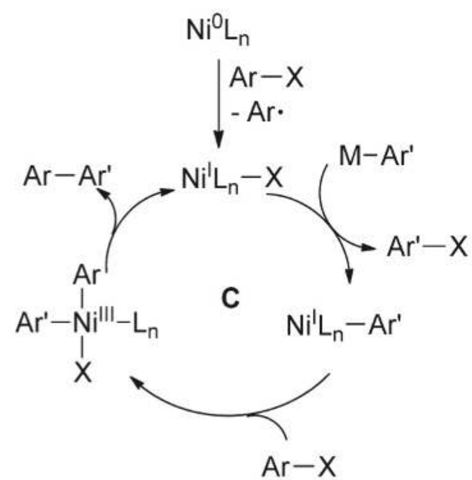
$$Ni(IMes)_2 \xrightarrow{PhX} Ni(IMes)_2X + Ph\bullet$$

X = I, Br, Cl

Never detected OA product
—> general mechanism may not be applicable to Ni-based cross-coupling

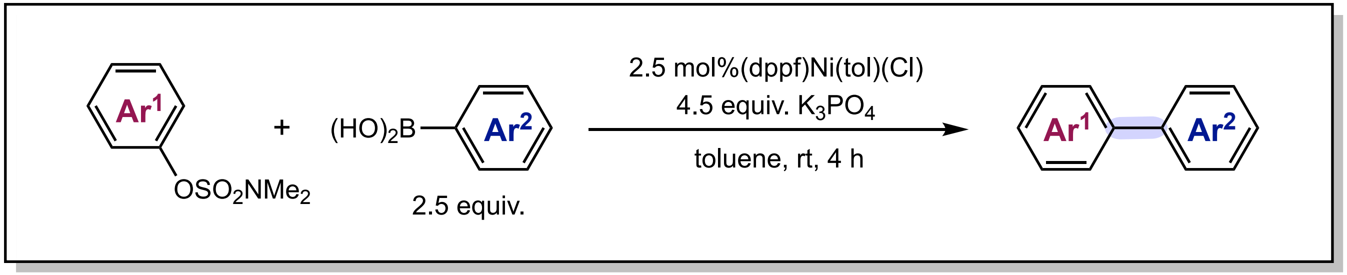
Alternative mechanism was proposed

Transmetalation,
followed by OA and RE

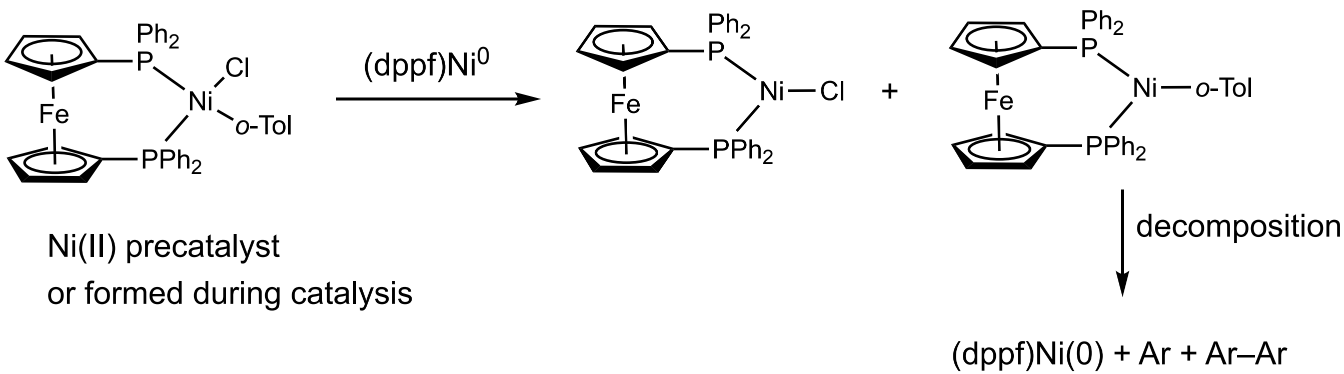


Zhang, K.; Conda-Sheridan, M.; Cooke, S. R.; Louie, J. *Organometallics* **2011**, *30*, 2546.

Ni-catalyzed SMC: Ni(0/II) cycle



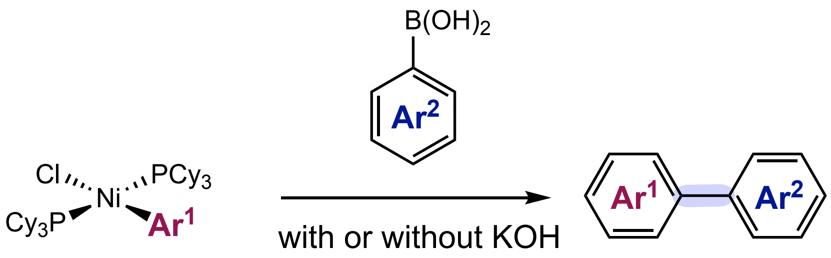
■ **Formation of Ni(I) is deterimental to catalysis**



■ **Ni(0/II) cycle was proposed.**

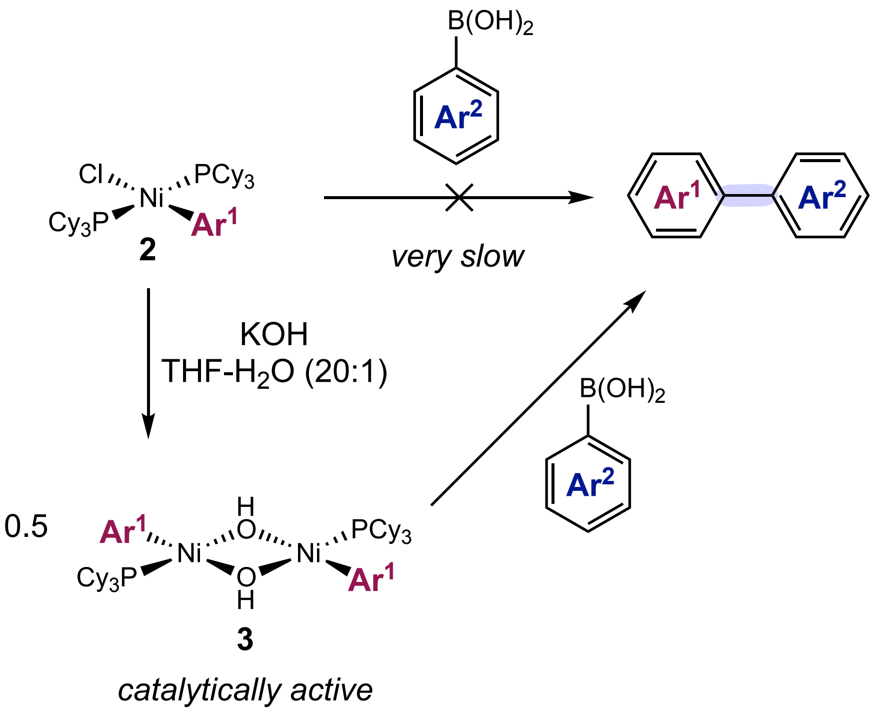
Beromi, M. M.; Nova, A.; Balcells, D.; Brasacchio, A. M.; Brudvig, G. W.; Guard, L. M.; Hazari, N.; Vinyard, D. J. *J. Am. Chem. Soc.* **2017**, *139*, 922

Mechanistic study on B-to-Ni transmetalation



Christian, A. H.; Müller, P.; Monfette, S. *Organometallics* **2014**, *33*, 2134

Mechanistic study on B-to-Ni transmetalation



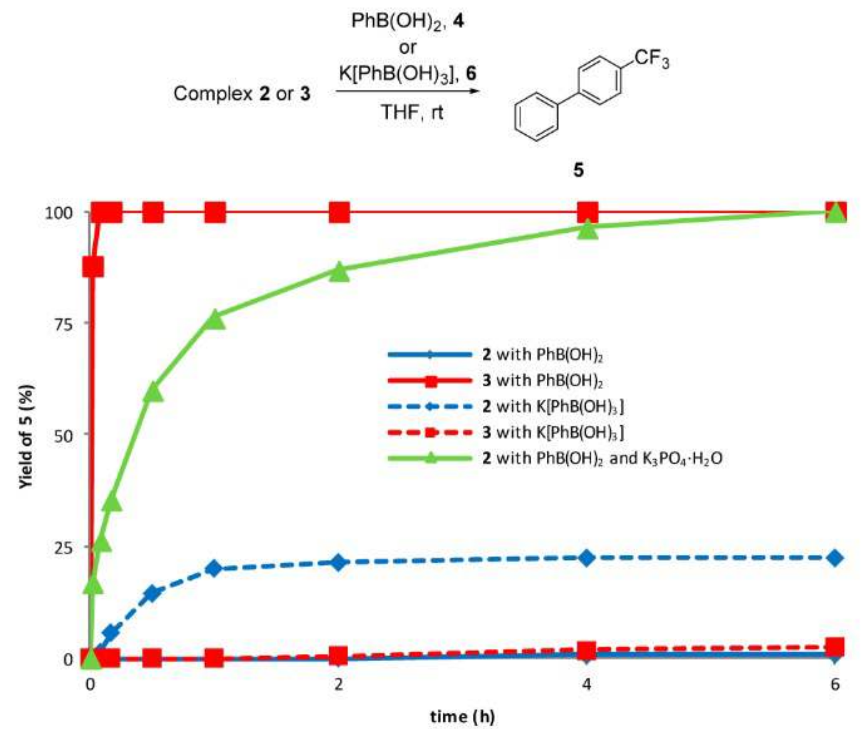


Figure 3. Yield of **5** over time. Conditions: 17 mM [Ni], 1.5 equiv of **4** (solid line) or **6** and 18-crown-6 (dashed line), THF, 22 °C, N_2 atmosphere. Values are ±3% in replicate runs.

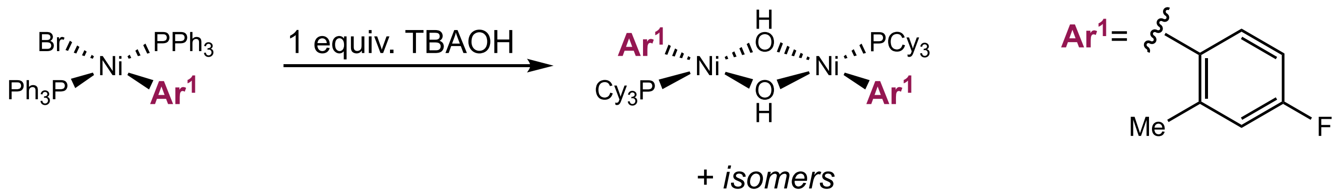
- bridged hydroxo dinickel complex:
  reacts with $PhB(OH)_2$ faster than NiCl complex with $PhB(OH)_2$

- TM does not proceed in the absence of hydroxide

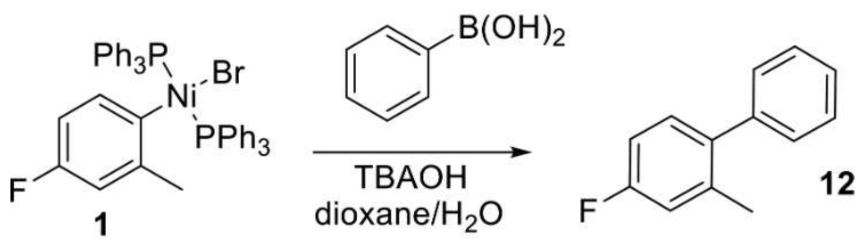
Christian, A. H.; Müller, P.; Monfette, S. *Organometallics* **2014**, *33*, 2134

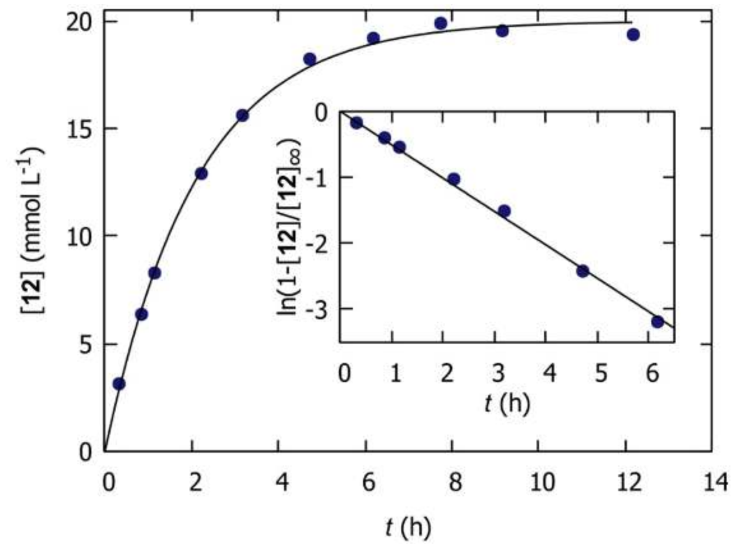
Mechanistic study on B-to-Ni transmetalation

Hydrolysis of NiBr compound:



Scheme 5. Reaction of Complex 1 with PhB(OH)$_2$ in the Presence of TBAOH to form the Biphenyl Product 12





Payard, P.-A.; Perego, L. A.; Ciofini, I.; Grimaud, L. *ACS Catal.* **2018**, *8*, 4812

Mechanistic study on B-to-Ni transmetalation

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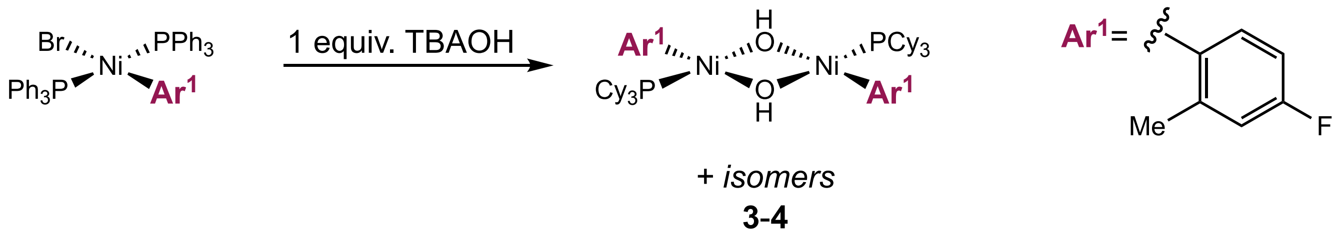
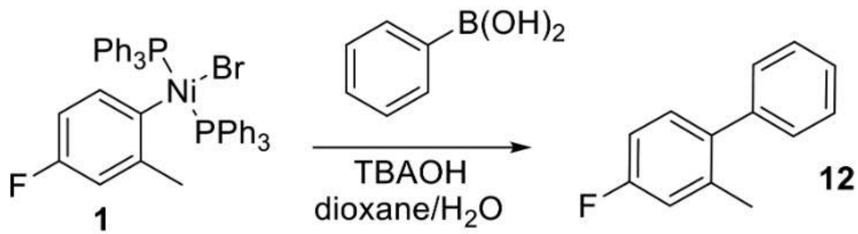
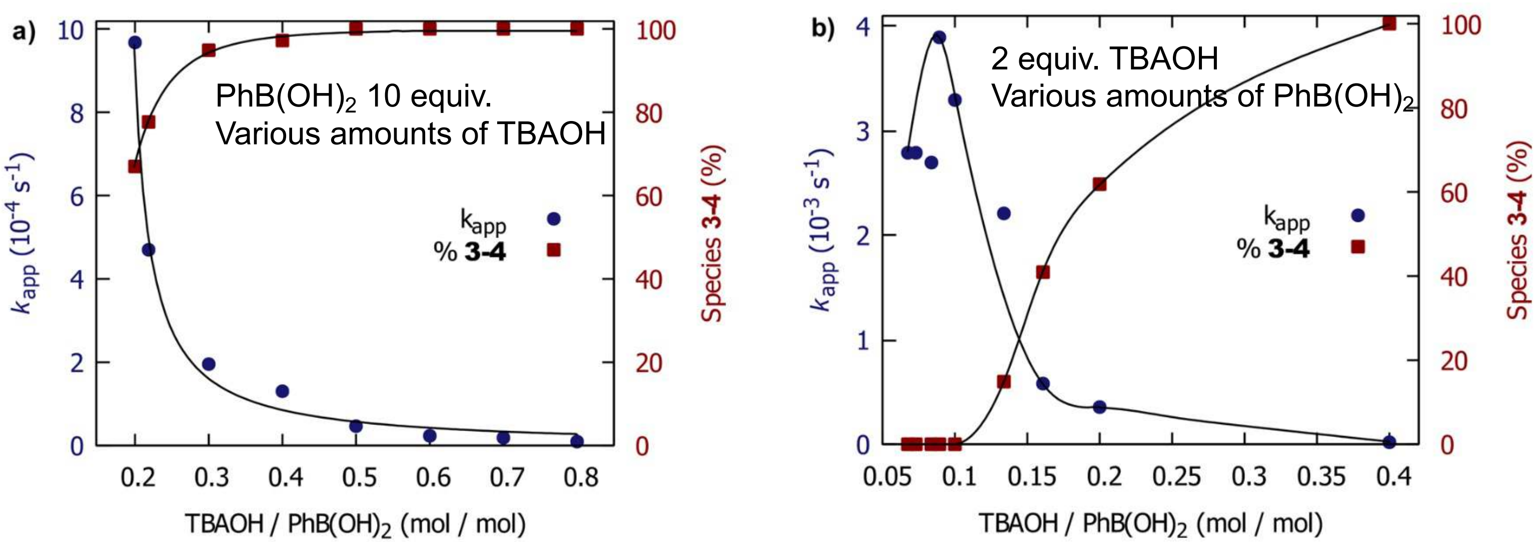


Scheme 5. Reaction of Complex 1 with $PhB(OH)_2$ in the Presence of TBAOH to form the Biphenyl Product 12





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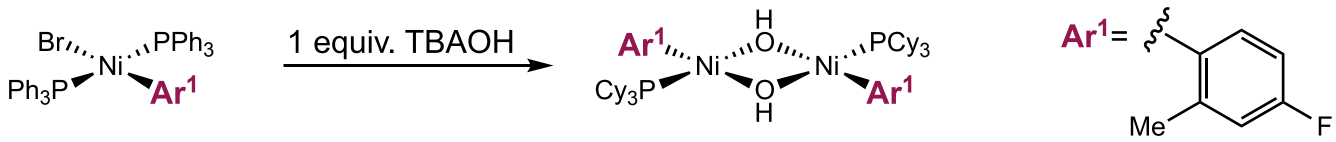
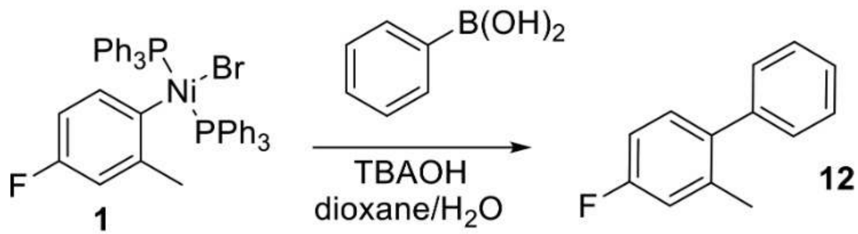
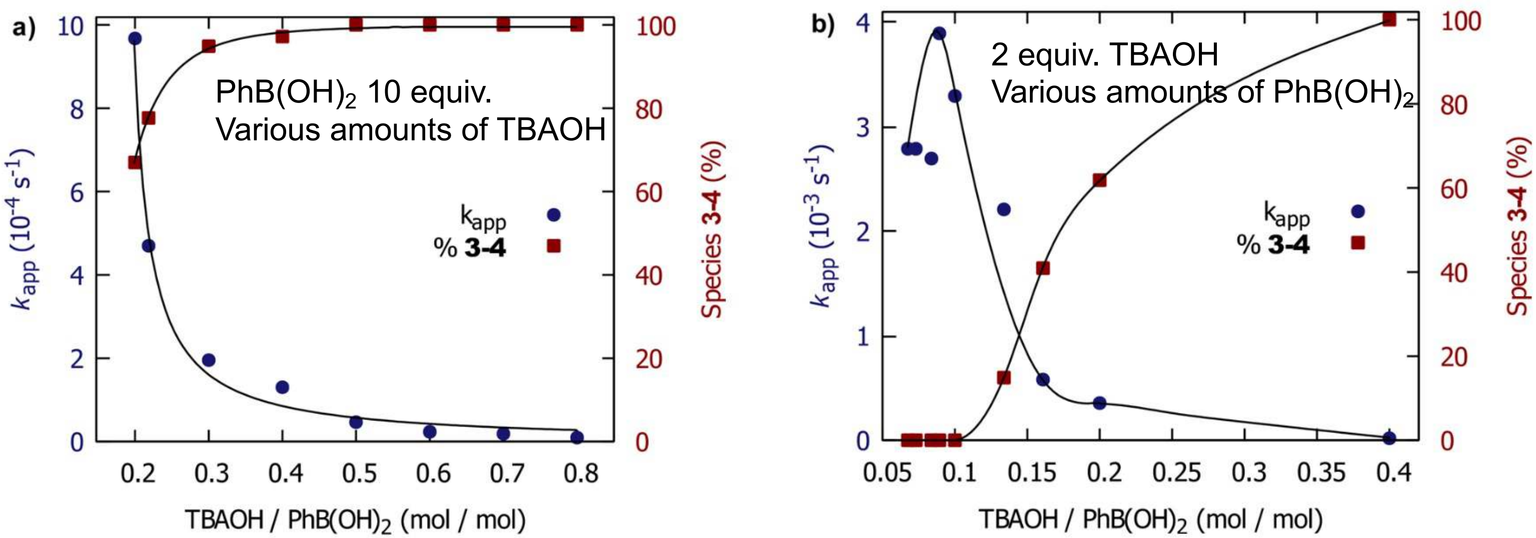


+ *isomers*
3-4

Scheme 5. Reaction of Complex 1 with $PhB(OH)_2$ in the Presence of TBAOH to form the Biphenyl Product 12



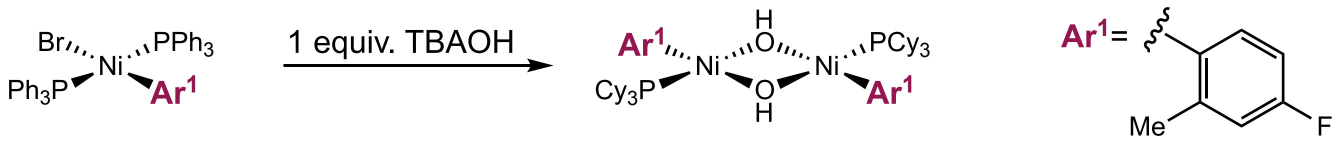
- at low $[TBAOH]/[PhB(OH)_2]$, fast reaction
- [**3-4**] should kept low.
  Plot indicates dimeric **3** and **4** are not directly involved in TM.



Payard, P.-A.; Perego, L. A.; Ciofini, I.; Grimaud, L. *ACS Catal.* **2018**, *8*, 4812

Mechanistic study on B-to-Ni transmetalation

Hydrolysis of NiBr compound:



\+ *isomers*
3-4

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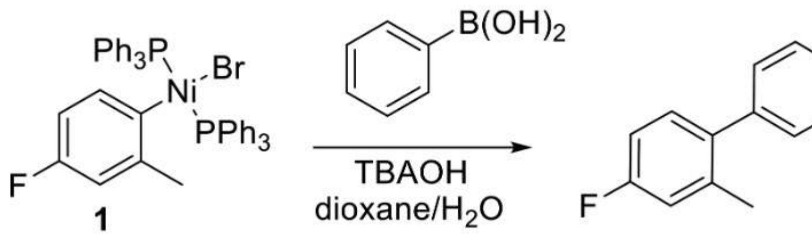


1 **12**

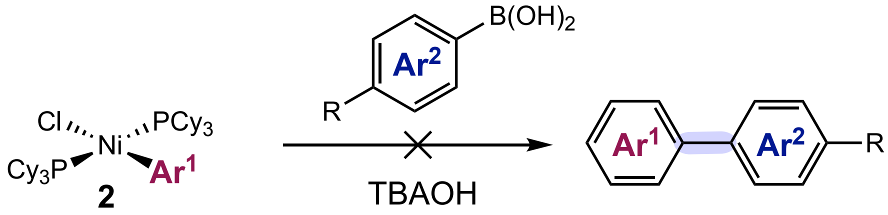
- at low $[TBAOH]/[PhB(OH)_2]$, fast reaction
- [**3-4**] should kept low.
  Plot indicates dimeric **3** and **4** are not directly involved in TM.

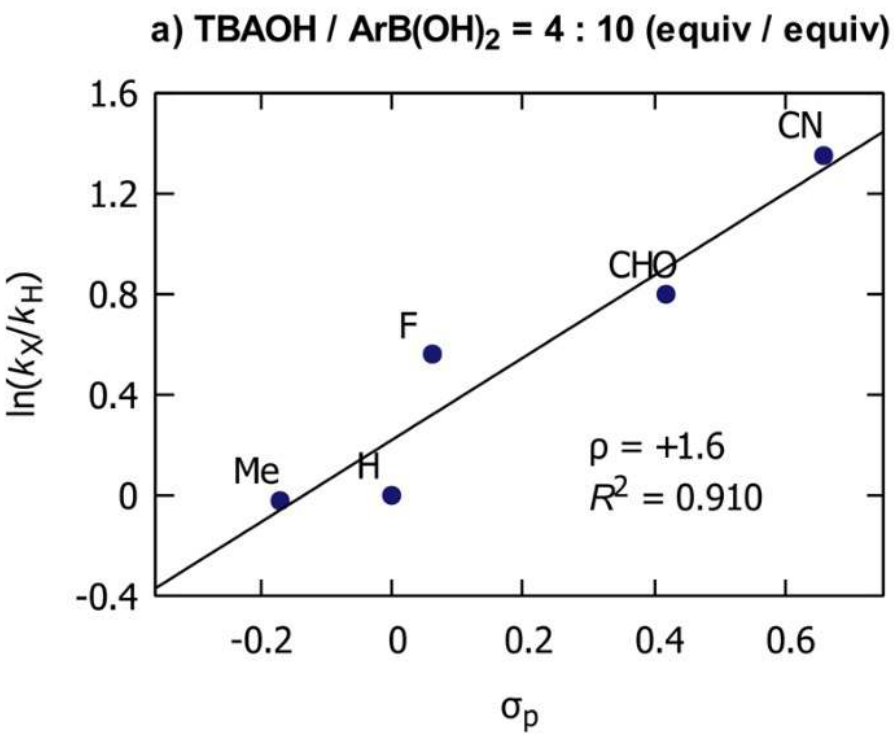
Control of $[OH^-]$ is very important!!

- poorly soluble inorganic bases (carbonate, phosphate) in low-polarity solvent
- amount of water added
- portionwise addition of bases in case reaction is slow.

Payard, P.-A.; Perego, L. A.; Ciofini, I.; Grimaud, L. *ACS Catal.* **2018**, *8*, 4812

Hammett plot at high and low [OH⁻]





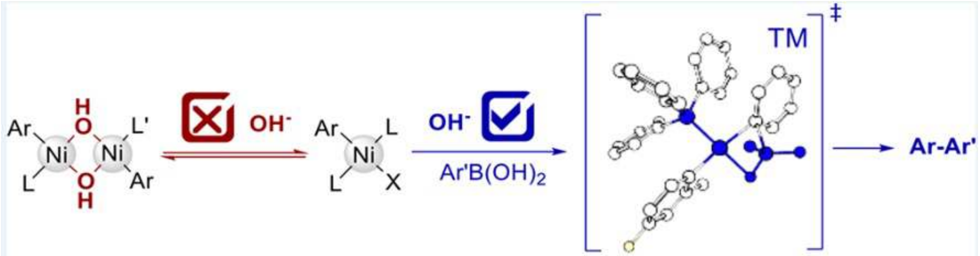
■ at high [OH⁻]

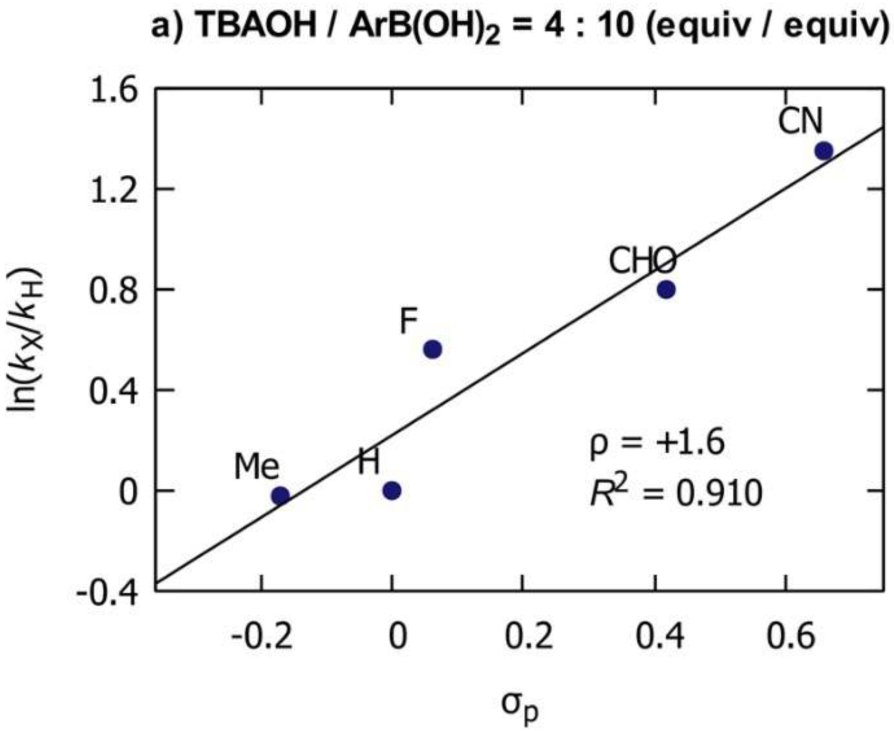
pre-equilibria to Ni(OH) dimer

electron-poor —> more Lewis-acidic
—> reacts with hydroxo-bridged dimer
—> fast reaction

Christian, A. H.; Müller, P.; Monfette, S. *Organometallics* **2014**, *33*, 2134

Hammett plot at high and low [OH$^-$]





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Christian, A. H.; Müller, P.; Monfette, S. *Organometallics* **2014**, *33*, 2134

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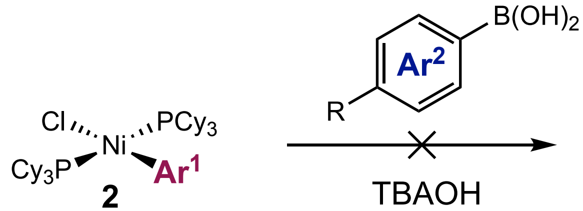
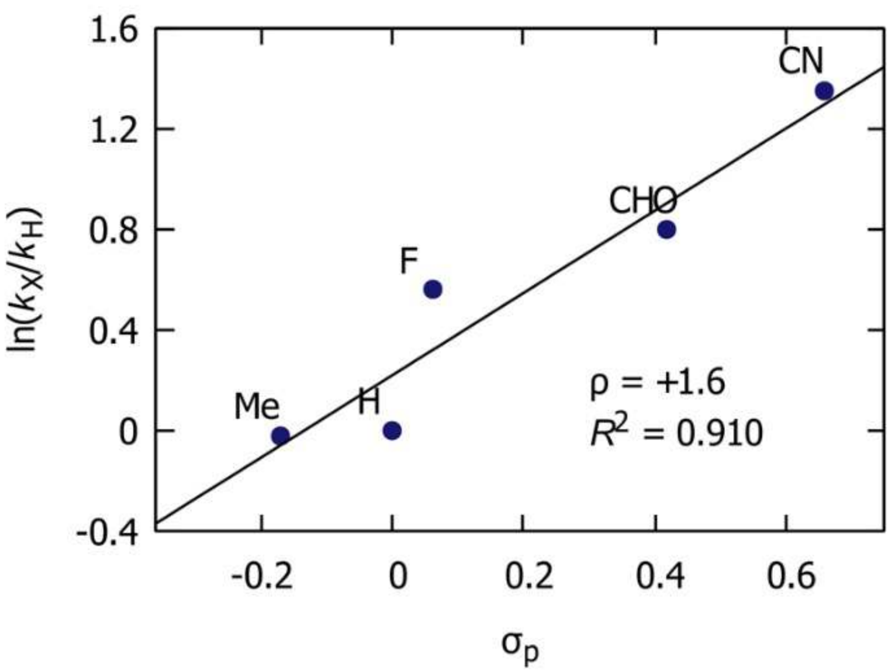
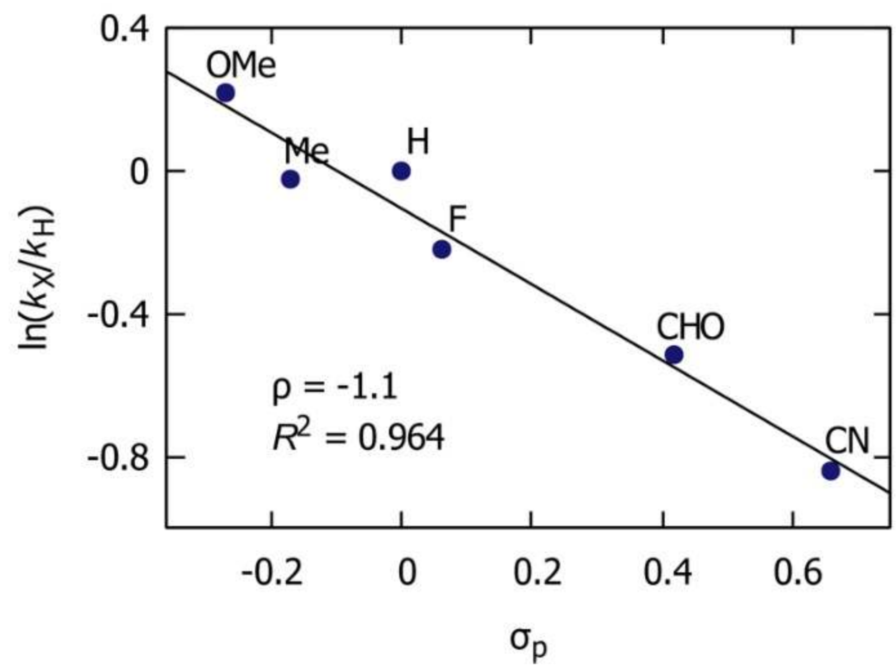


a) TBAOH / ArB(OH)$_2$ = 4 : 10 (equiv / equiv)



b) TBAOH / ArB(OH)$_2$ = 2 : 20 (equiv / equiv)



■ at high [OH$^-$]

pre-equilibria to Ni(OH) dimer

electron-poor —> more Lewis-acidic
—> reacts with hydroxo-bridged dimer
—> fast reaction

■ at low [OH$^-$]

e-rich boronic acid reacts faster

(Ni: electrophile, B: nucleophile)

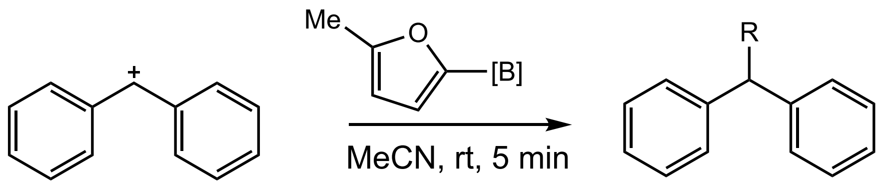
Christian, A. H.; Müller, P.; Monfette, S. *Organometallics* **2014**, *33*, 2134

Boron reagents

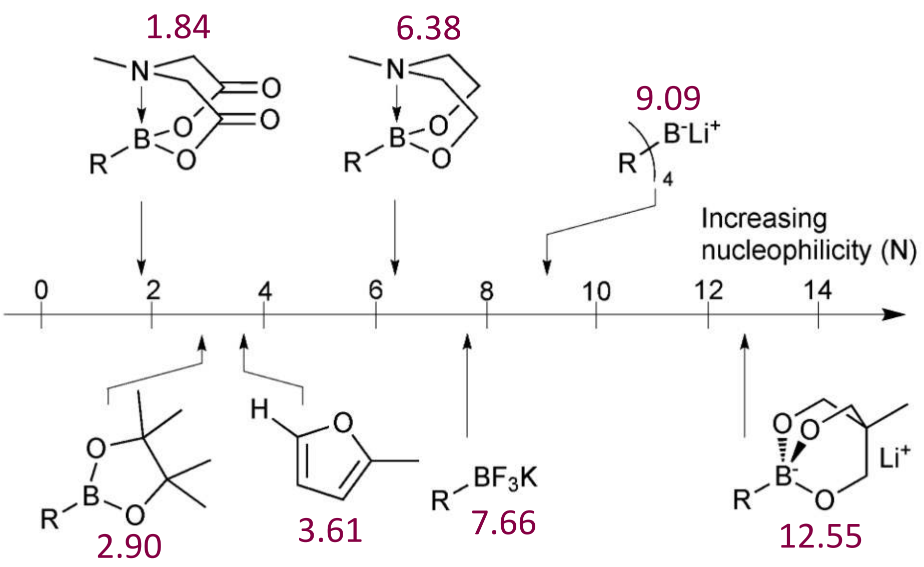
■ *Nucleophilicity*

In SMC, boron reagent tends to
be nucleophilic component.

Mayr's nucleophilicity scale:



benzhydrylium ion



G. Berionni , B. Maji , P. Knochel and H. Mayr,
Chem. Sci., **2012**, *3* , 878

Boron reagents

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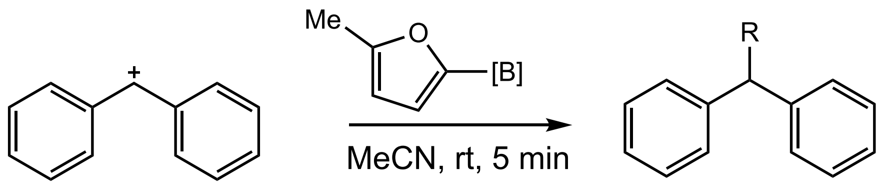
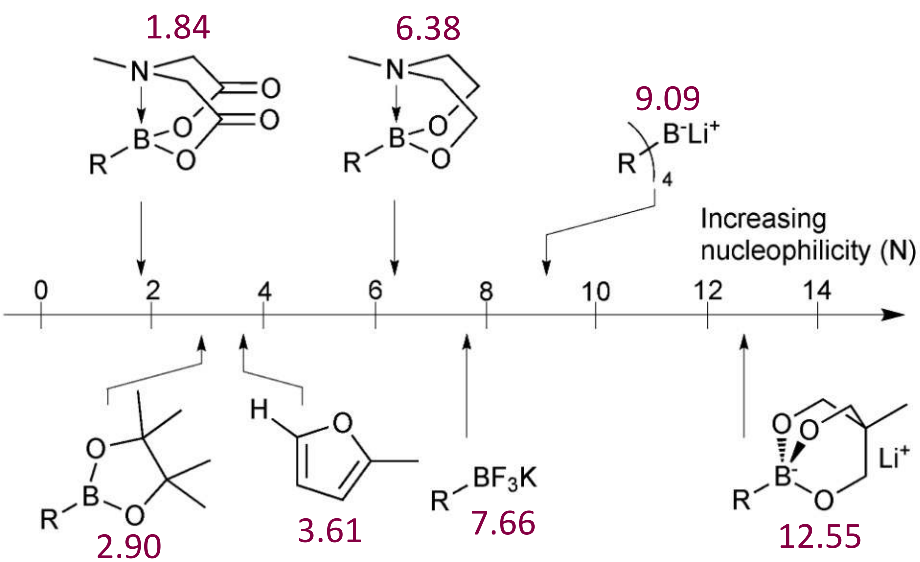


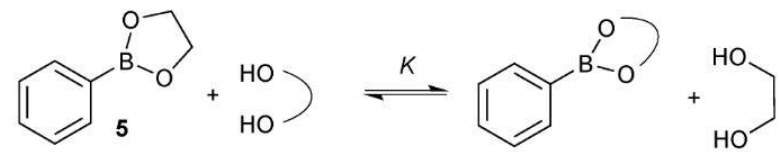
benzhydrylium ion



G. Berionni , B. Maji , P. Knochel and H. Mayr, *Chem. Sci.*, **2012**, *3* , 878

■ *Stability*

The extent of transesterification is used to assess the stability of boronic esters of interest.



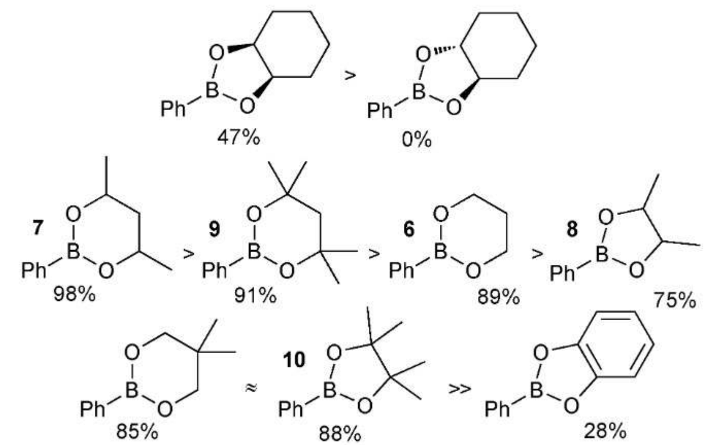


Fig. 4 Stability sequences for a range of boronic esters, with percent transesterification from the glycol boronic ester indicated.

- trans diols: completely unreactive
- 6-membered esters: more thermodynamically stable (favorable orbital overlap btw B and O)
- Methyl group substitution: further stabilization
- Catechol: the decreased pi-donating ability of O to B

Lennox, A. J. J.; Lloyd-Jones, G. C. *Chem. Soc. Rev.*, **2014**, *43*, 412.

Use of boronic esters in transmetalation

■ ***Direct transmetalation***

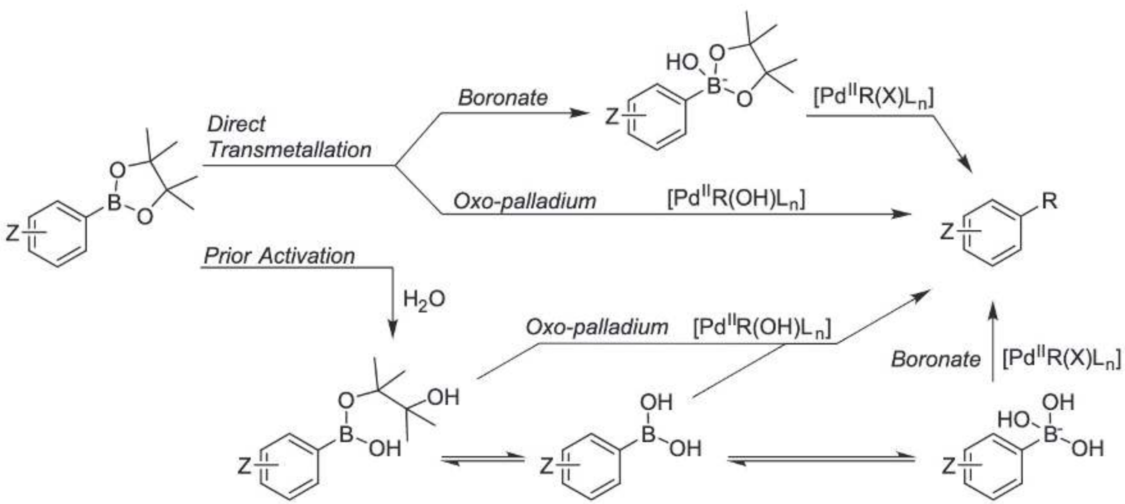
Boranes, Boronic acids

■ ***Pre-activatiopn necessary***

Organotrifluoroborate salt, MIDA boronate, BDan

■ ***Still ambiguous***

Boronic esters; BPin, BNeo, BCat, …
Trihydroxyborate ion



Scheme 8.24 Possible transmetallation mechanisms for the coupling of an arylpinacolboronic ester.

Lennox, A. J. J.; Lloyd-Jones, G. C. Boron Reagent Activation in Suzuki-Miyaura Coupling, Chapter 8 in "Modern Cross Coupling: Evolution and Application" Edited by Thomas Colacot, RSC, 2014