Experimental Mechanism of Iridium-Catalyzed C-H Borylation of Arenes and Strategies for Regioselectivity

报告人: 陈军

导　师: 陆平 青年研究员

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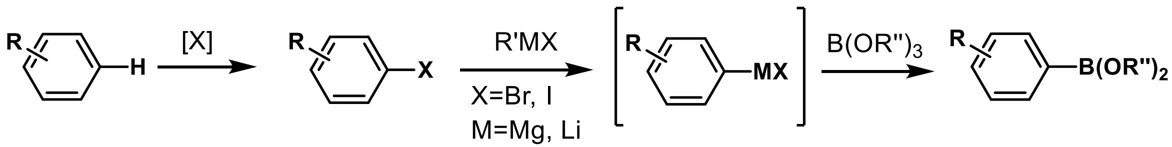
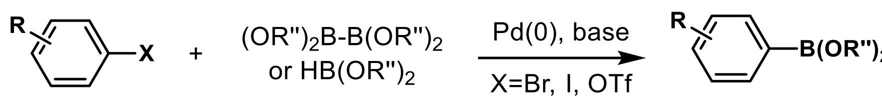
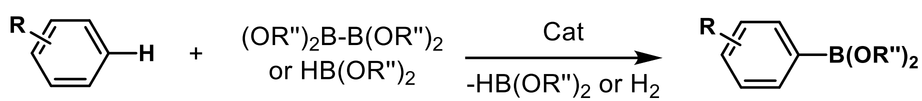
1.1 Syntheses of Arylboronate Esters







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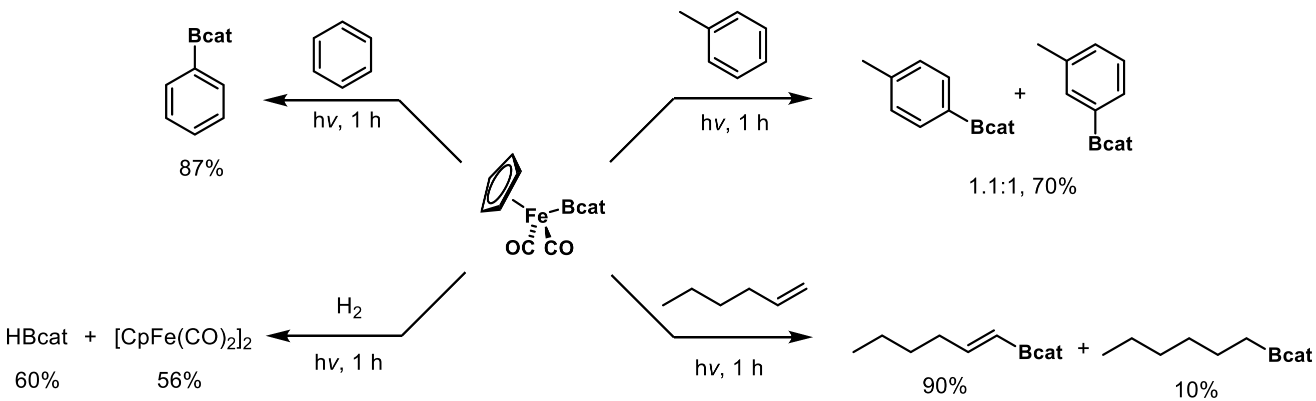
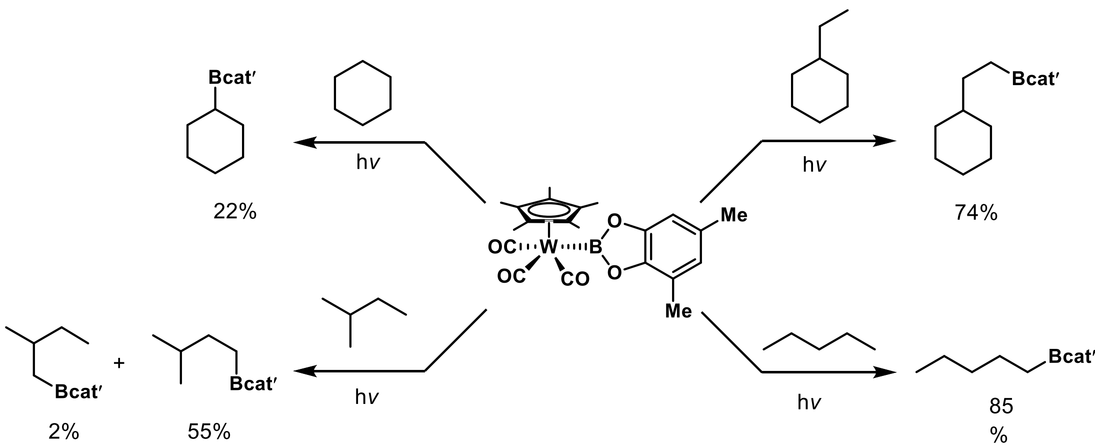
John F. Hartwig. *Chem. Rev.* **2010**, *110*, 890–931

1. Introduction

1.2. Stoichiometric Photochemical Reactions



C-H Borylation with $CpFe(CO)_2(Bcat)$

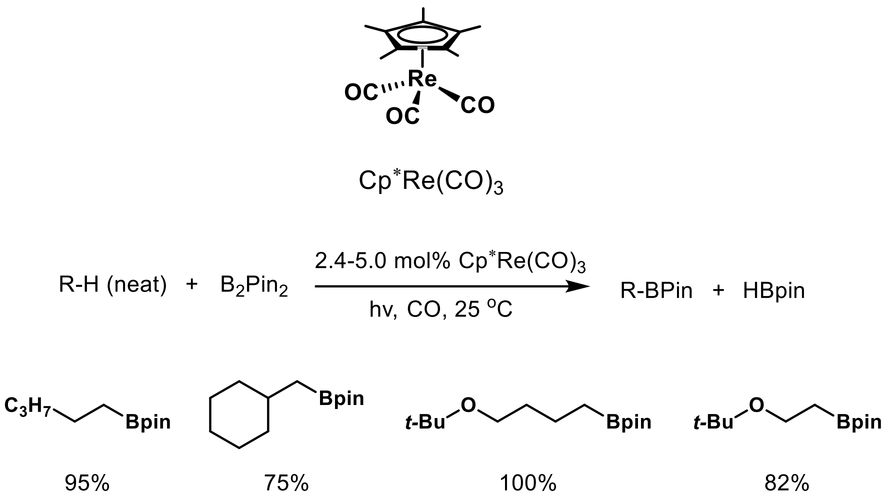


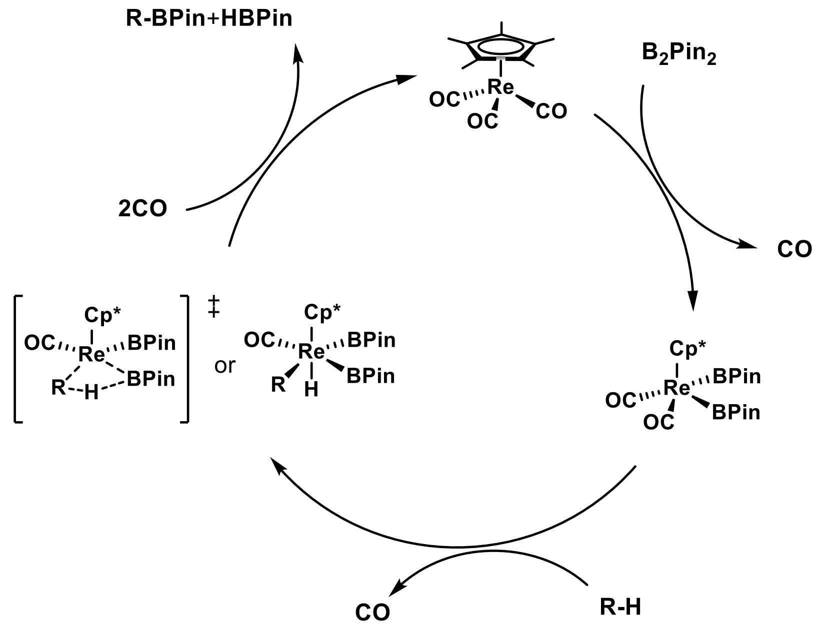
C-H Borylation with $Cp^*W(CO)_3(Bcat')$

John F. Hartwig. *J. Am. Chem. Soc*. **1995**, *117*, 11357-11358
John F. Hartwig. *Science.* **1997**, *277*, 211-213

1. Introduction

1.3. Catalytic Photochemical Reactions



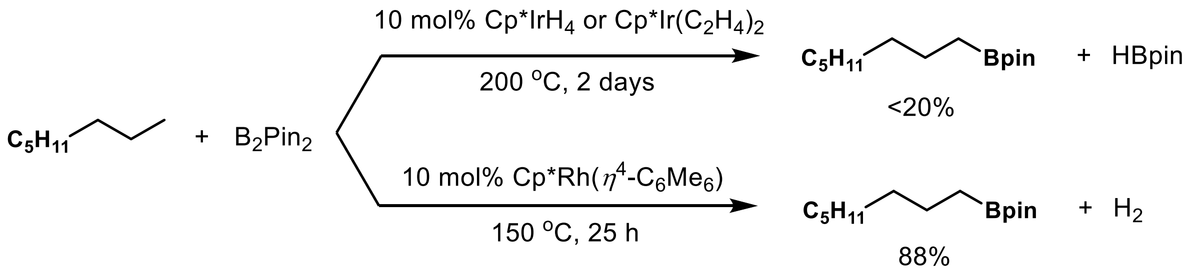


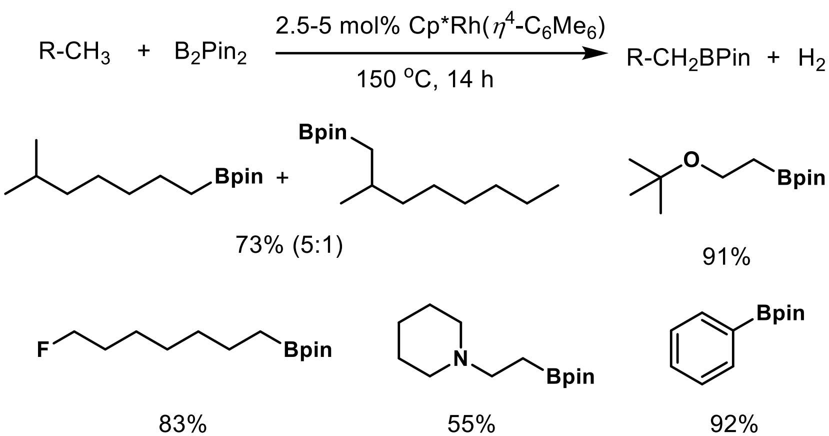
Proposed mechanism

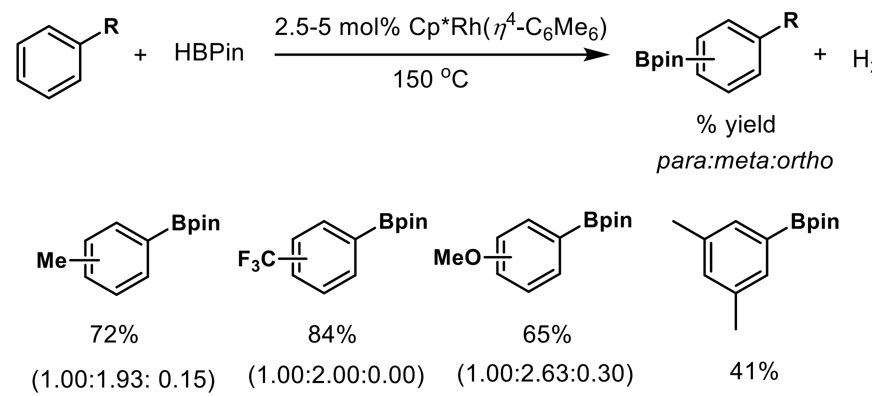
John F. Hartwig. *Angew. Chem. Int. Ed*. **1999**, *38*, 3391-3393

1. Introduction

1.3. Catalytic Thermal Reactions





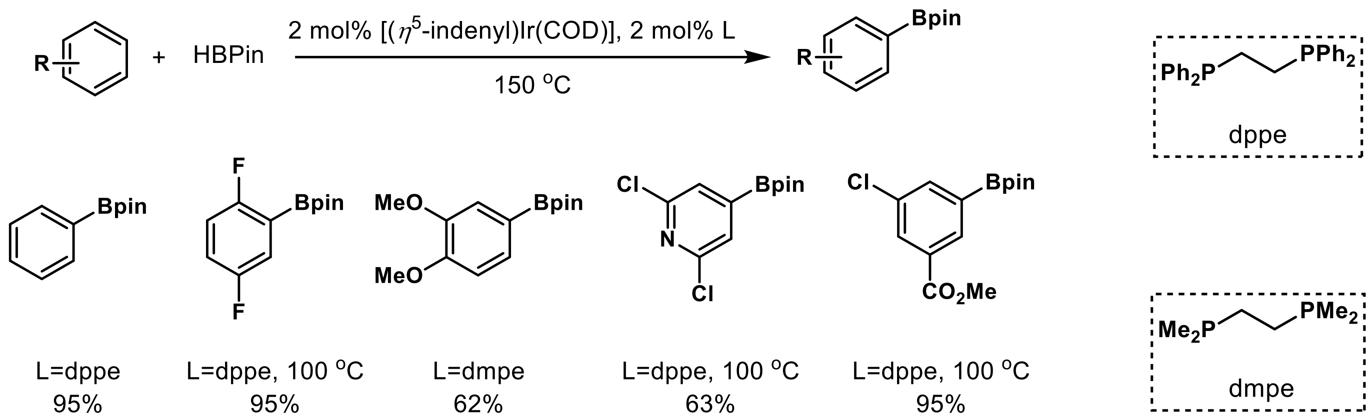


Milton R. Smith, III. *J. Am. Chem. Soc.* **1999**, *121*, 7696-7697
Milton R. Smith, III. *J. Am. Chem. Soc.* **2000**, *122*, 12868-12869
John F. Hartwig. *Science.* **2000**, *287*, 1995-1997

1. Introduction

1.3. Catalytic Thermal Reactions

Arene Borylation with Iridium Catalyst Containing *Phosphine* Ligands



The active catalyst was proposed to contain PMe_3 as a ligand

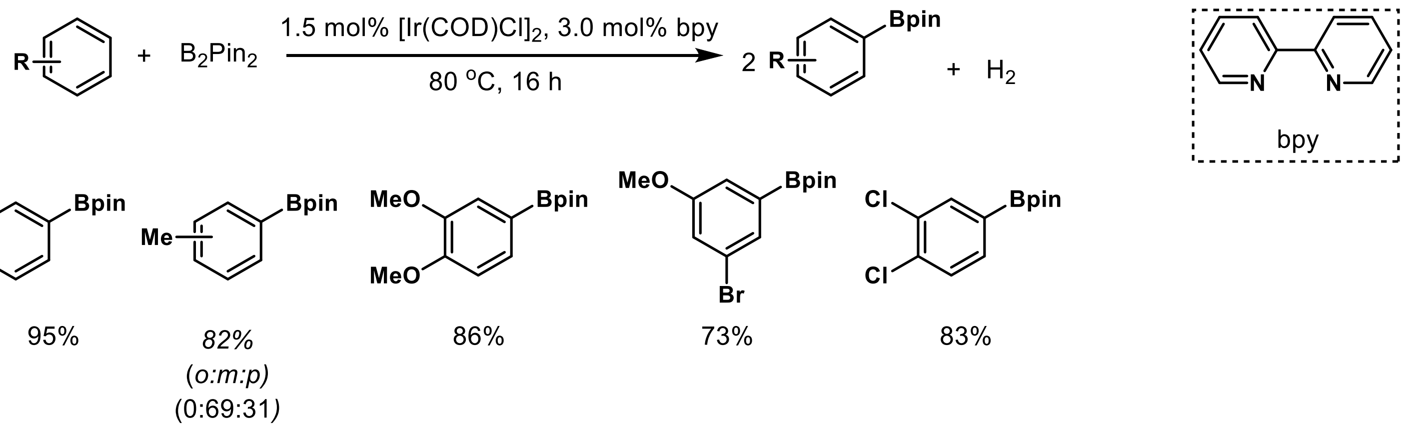
Ir(I) monoboryl or Ir(III) trisboryl complexes?

Milton R. Smith, III. *Science.* **2002**, *295*, 305-308.

1. Introduction

1.3. Catalytic Thermal Reactions

Arene Borylation with Iridium Catalyst Containing *nitrogen* Ligands



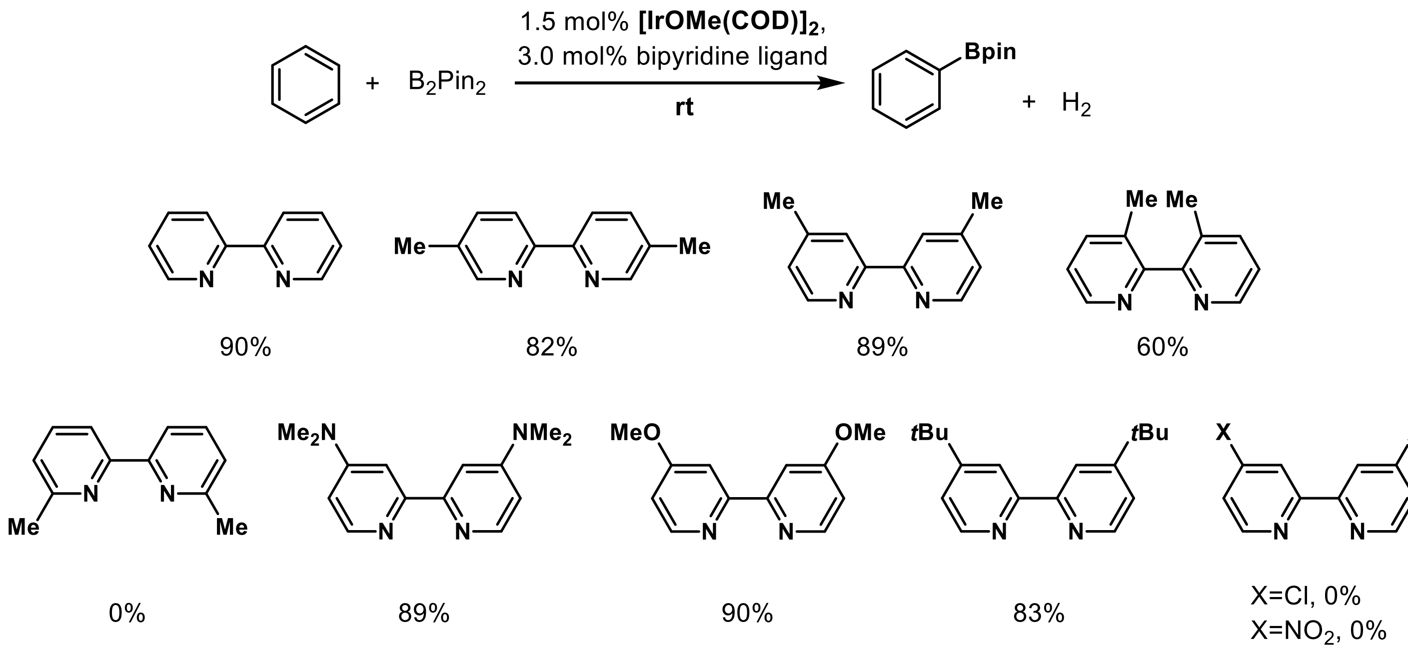
Mild condition!

Tatsuo Ishiyama.; Norio Miyaura.; John F. Hartwig. *J. Am. Chem. Soc.* **2002**, *124*, 390-391

1. Introduction

1.3. Catalytic Thermal Reactions

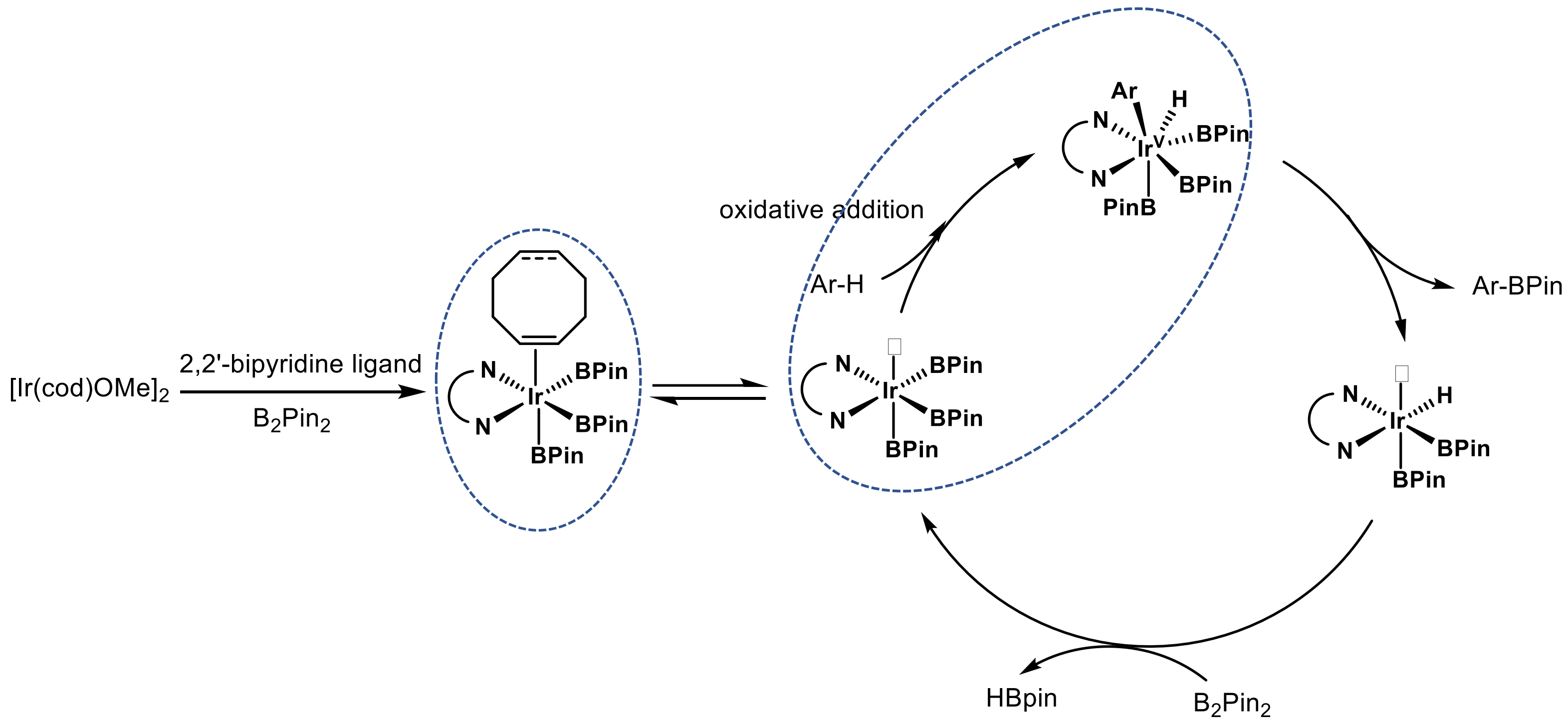
Effect of *nitrogen* ligands on the borylation of benzene



Mild Condition Pay the Way for Studying the Mechanism of C-H Borylation of Arenes

Tatsuo Ishiyama.; Norio Miyaura. *Angew. Chem. Int. Ed*. **2002**, *41*, 3056-3058.

2. Mechanism of the C-H Borylation of Arenes by Bipyridine-Ligated Iridium Complexes

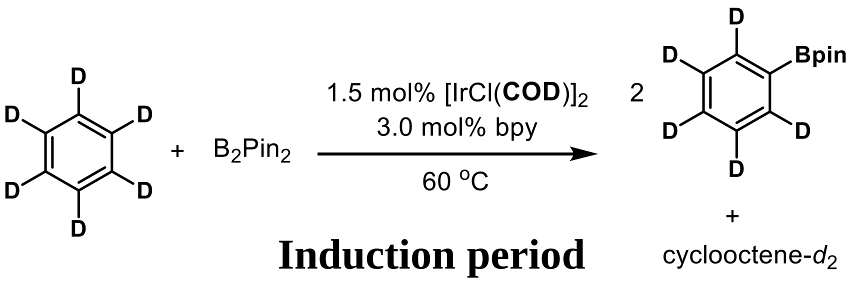


1. **Isolation of active intermediate**
2. **Isotopic labeling experiments**
3. **Kinetic study**

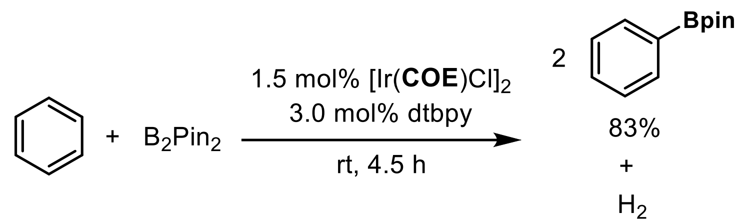
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

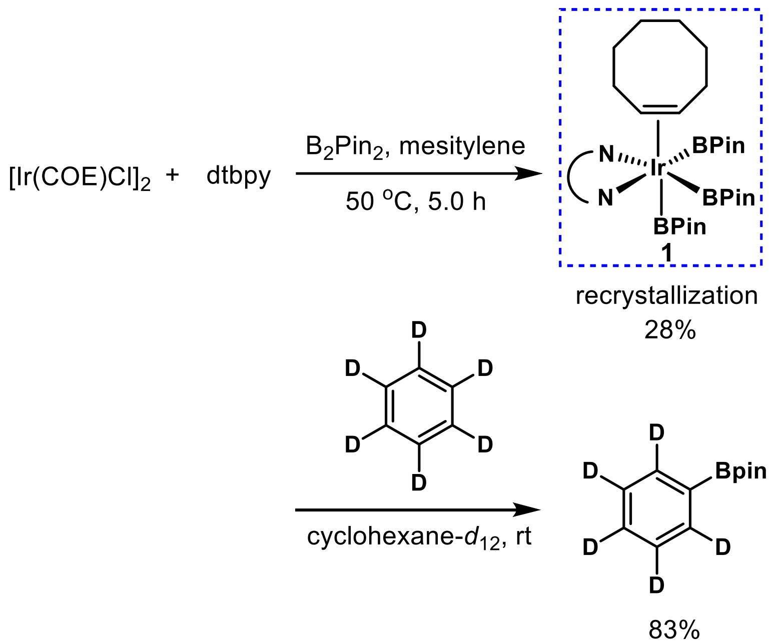
2.1. Isolation of Iridium Trisboryl Complexes 1 and Stoichiometric Reactions

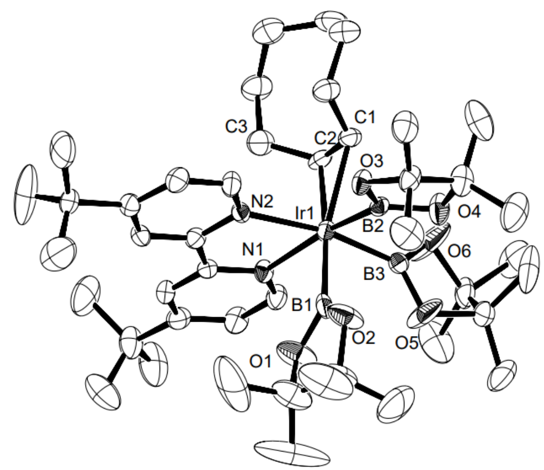


Induction period



No induction period





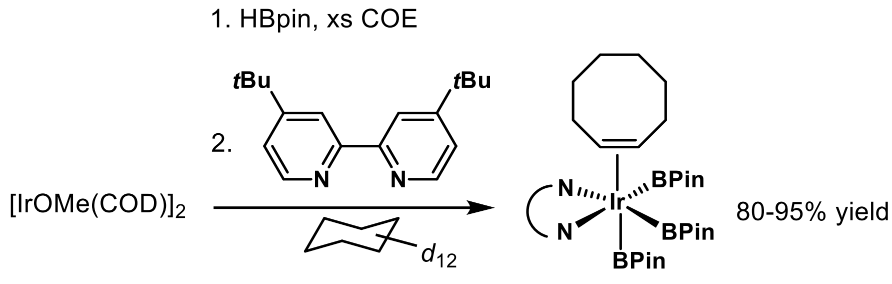
X-Ray structure

[Ir(dtbpy)(η^2-COE)(Bpin)$_3$] is an intermediate or leads directly to an intermediate in this borylation system

Tatsuo Ishiyama.; Norio Miyaura.; John F. Hartwig. *J. Am. Chem. Soc*. **2002**, *124*, 390-391

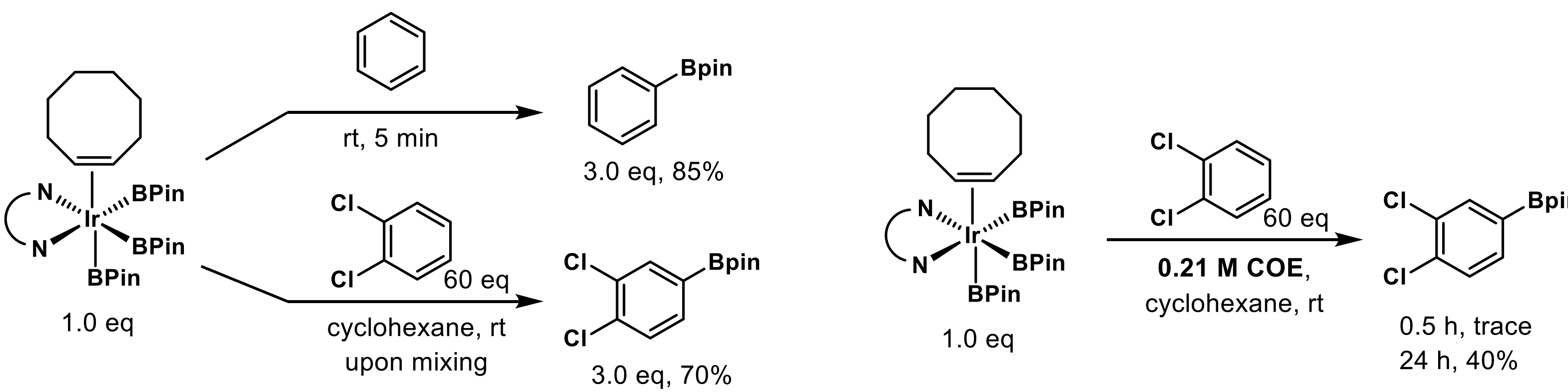
2. Mechanism

2.1. Isolation of Iridium Trisboryl Complexes 1 and Stoichiometric Reactions



1

Efficient synthesis of [Ir(dtbpy)(η^2-COE)(Bpin)$_3$]



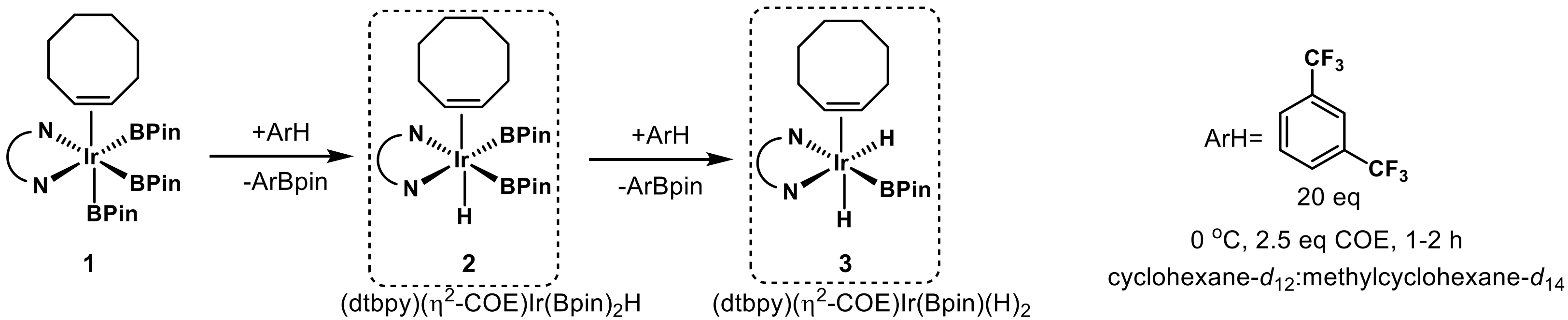
Stoichiometric reactions

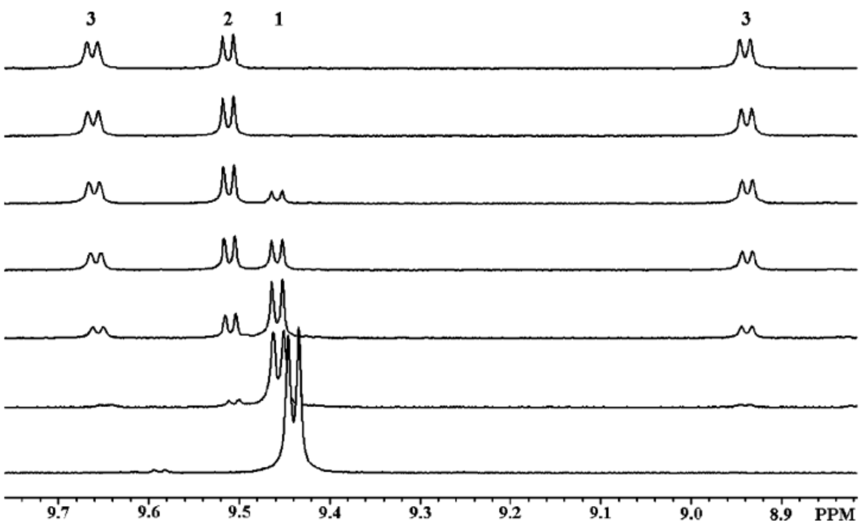
[Ir(COD)(OMe)]$_2$ as the iridium source fits with the general result that the most active catalysts are generated from [Ir(COD)(OMe)]$_2$

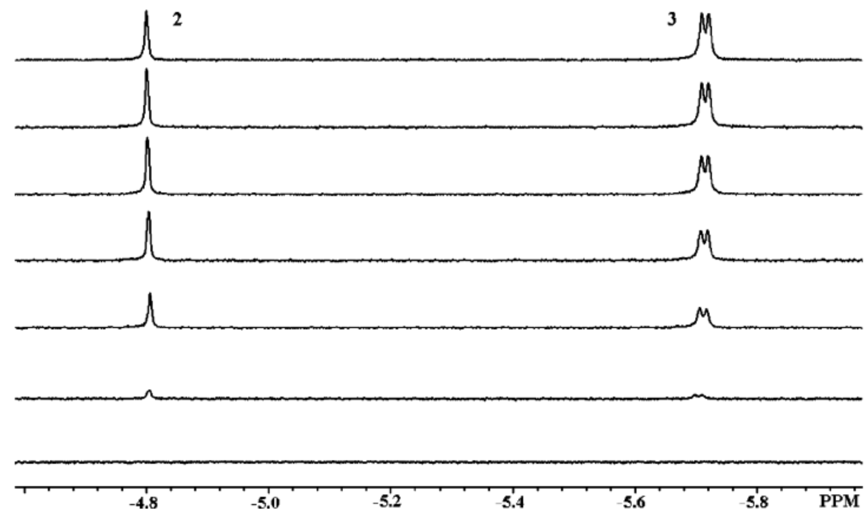
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.1. Isolation of Iridium Trisboryl Complexes 1 and Stoichiometric Reactions







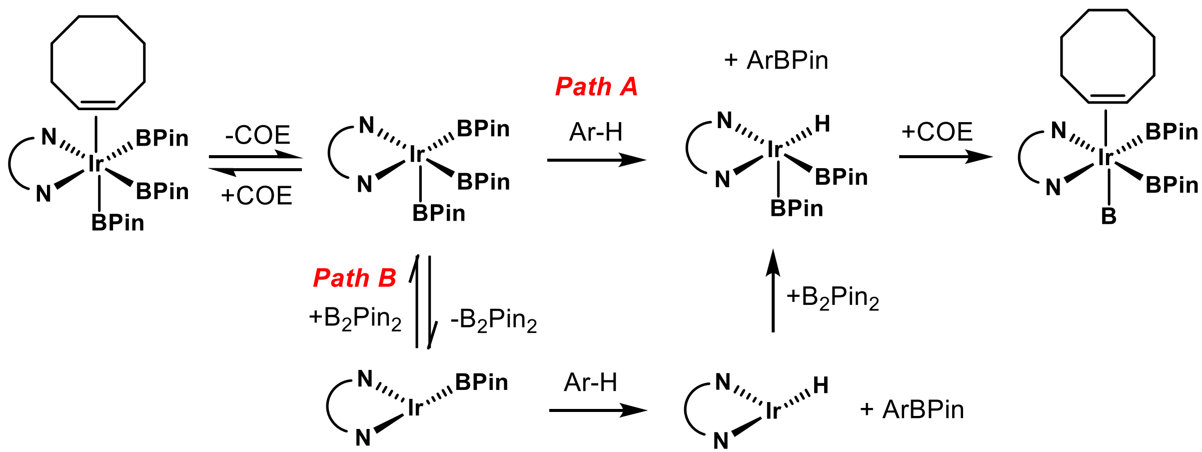
^{1}H NMR spectra of the aromatic region for the **dtbpy** ligand

^{1}H NMR spectra of **hydride** region for the Ir complex

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

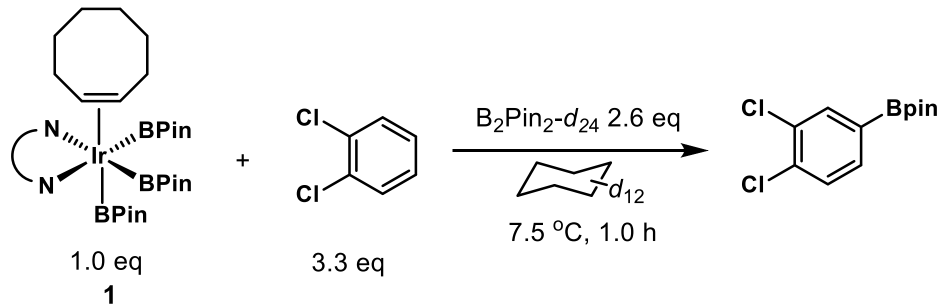
2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species

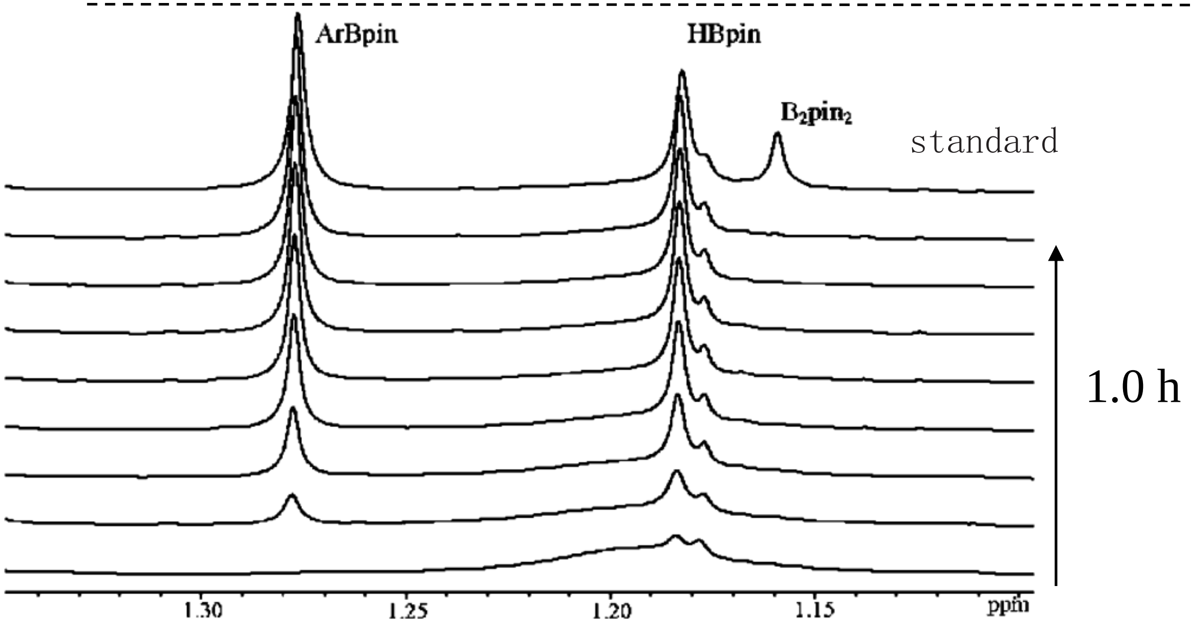


John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species





^{1}H NMR spectra, no formation of B_2Pin_2

Relative Rates for Elimination of B_2pin_2 from 1 and for C-H Activation

$$K_{B\text{-}B\ \mathrm{elimination}} \ll K_{\mathrm{C\text{-}H\ activation}}$$

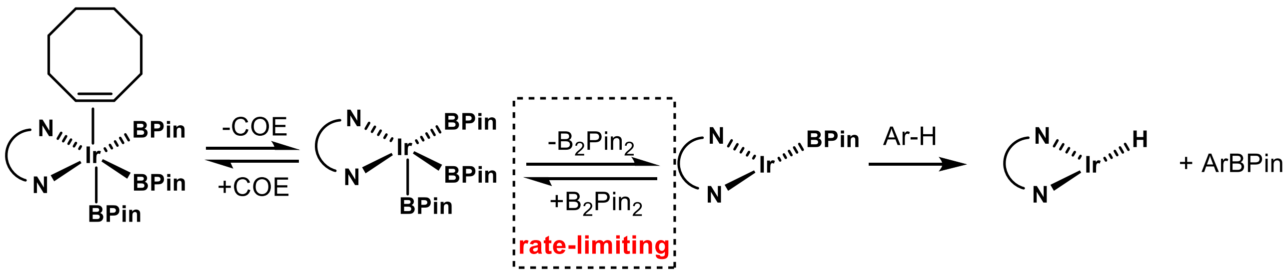
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

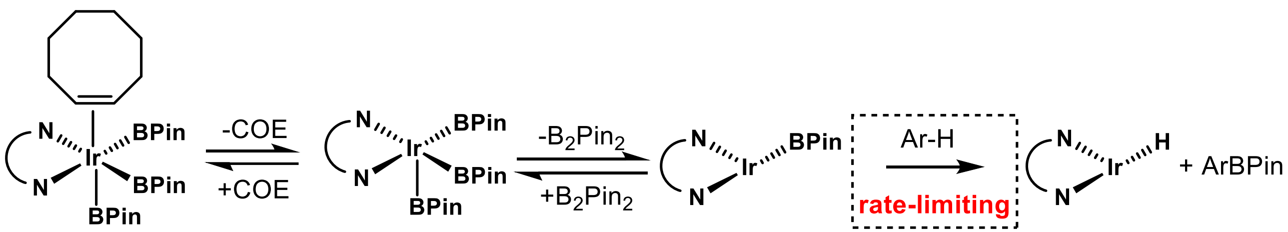
2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species

Kinectic study

first-order in the concentration of arene
zero-order in the concentration of B_2Pin_2



zero-order in arene



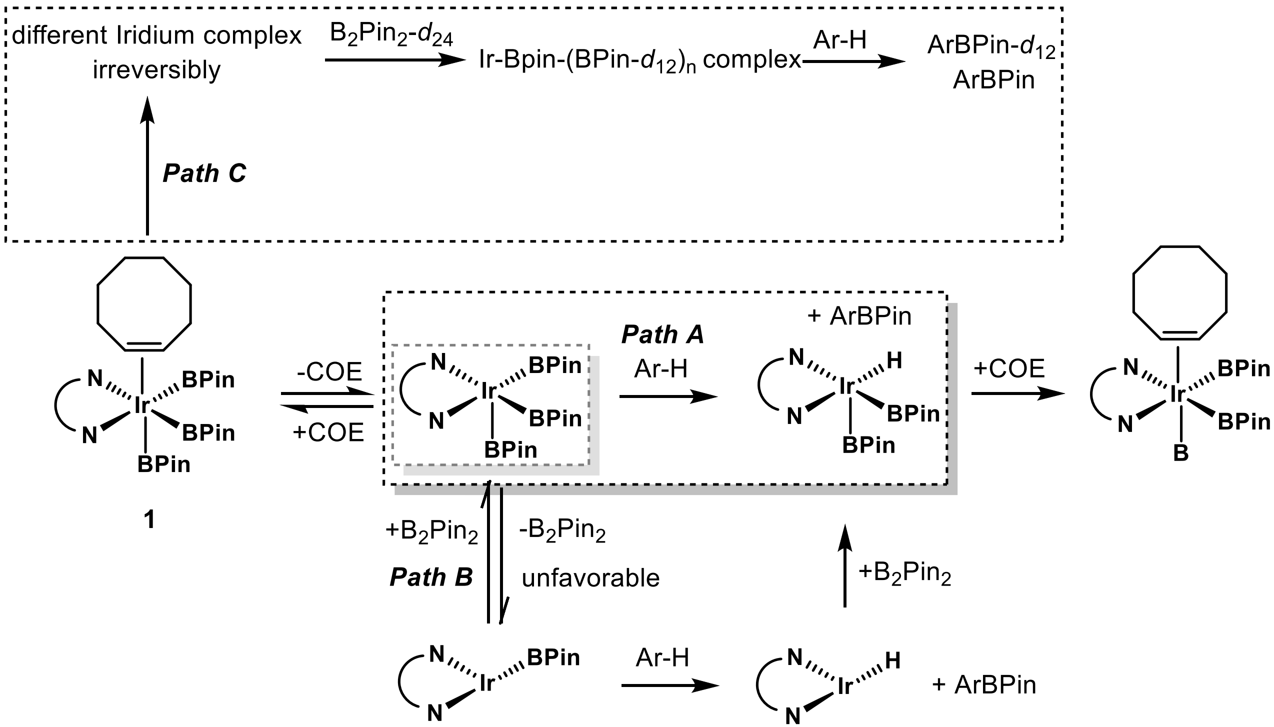
inverse-firse-order in B_2Pin_2

If C-H activation by Ir(I) species!

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species

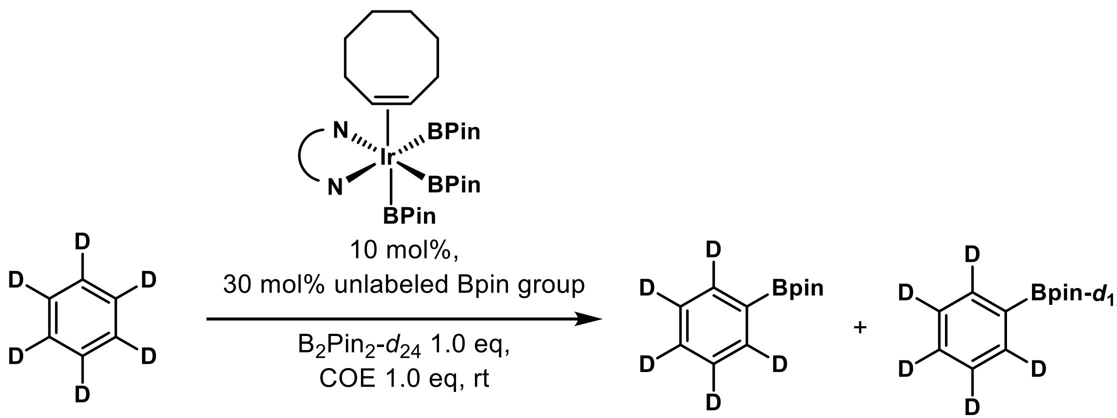


Possible intermediates from 1 to catalyze borylation

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species

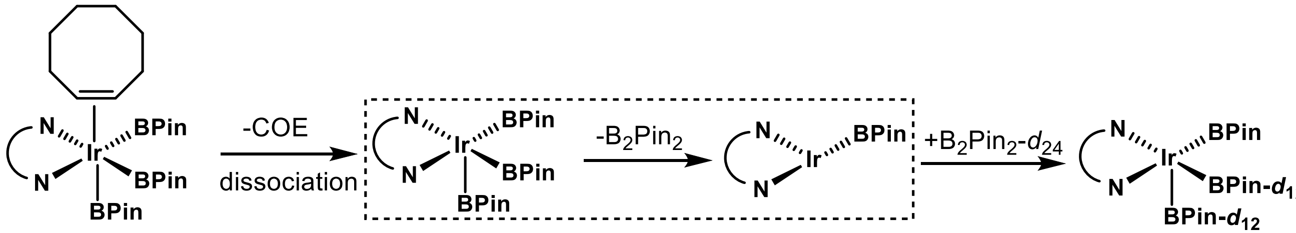


conversion	4 h 10% conversion	17 h 50% conversion	100% conversion
ArBPin / ArBPin-d_{12}	68 / 32	47 / 53	17 / 83

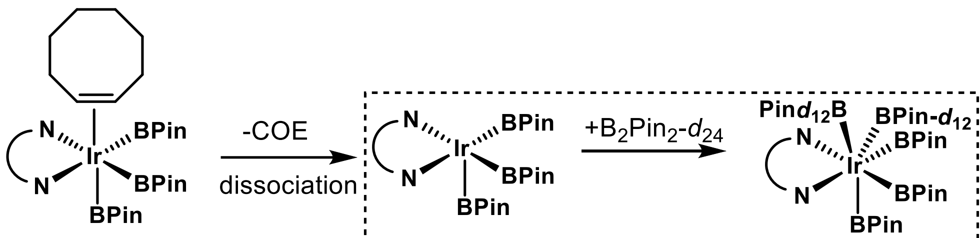
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species

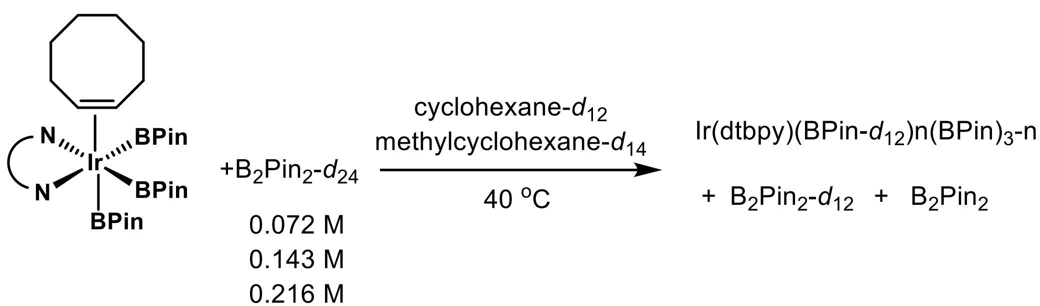


zero-order with the concentration of B_2Pin_2-d_{24}



first-order with the concentration of B_2Pin_2-d_{24}

Exchange of B_2Pin_2-d_{24} with 16 electrons trisboryl complex

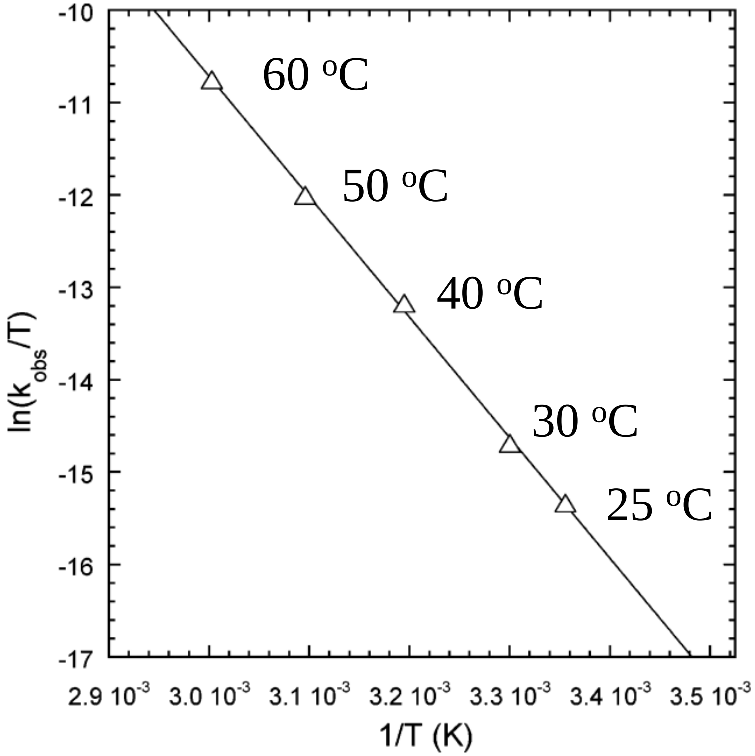


The rate constant for the exchange process depended linearly on the concentration of B_2pin_2-d_{24}

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.2 C-H Activation by Ir(III) Species *vs* Ir(I) Species



Eyring plot for exchange reaction of B_2pin_2/B_2pin_2-d_{24}(2.88*10^{-1} M) with **1** (2.10*10^{-2} M)

$\ln(k/T) = \ln(\sigma \cdot kB/h) + \Delta S^{\neq}/R - \Delta H^{\neq}/R \cdot 1/T$

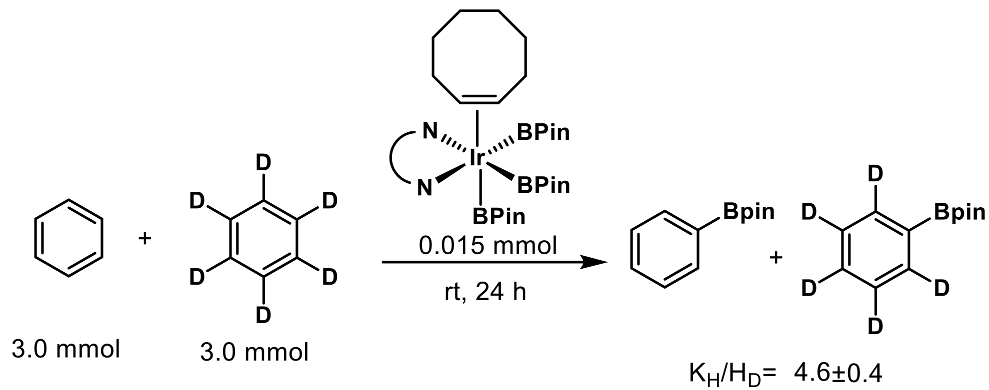
$\Delta H^{\neq}$ = 25.9±1.3 kcal mol^{-1}
$\Delta S^{\neq}$ = 9±1 eu

COE dissociation first
Bimolecular association second

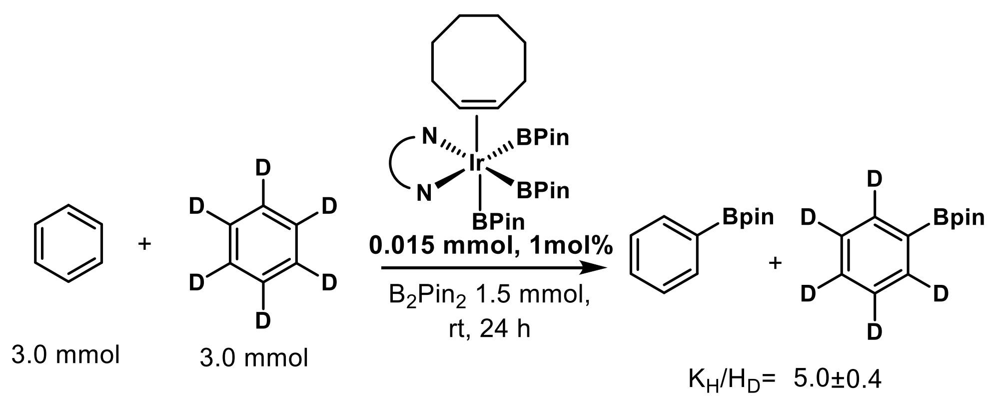
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.3 Isotope Effects



Isotope Effects on the Stoichiometric Reaction Trisboryl with Arene

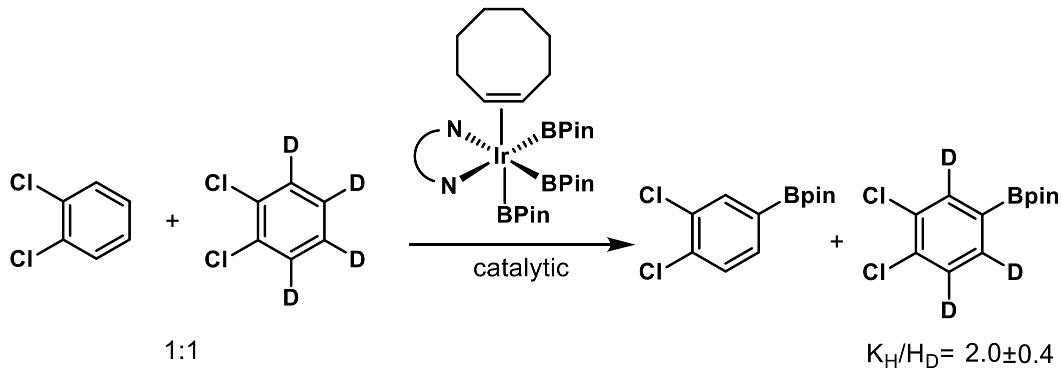


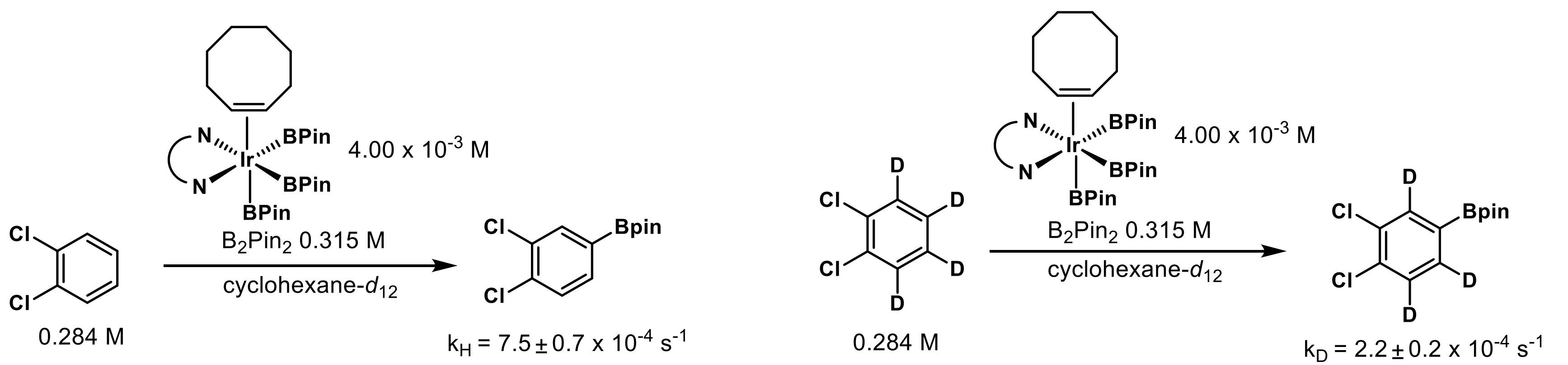
Isotope Effects on the Catalytic Reaction Trisboryl with Arene

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.3 Isotope Effects





$$K_H/K_D=3.3\pm0.6$$

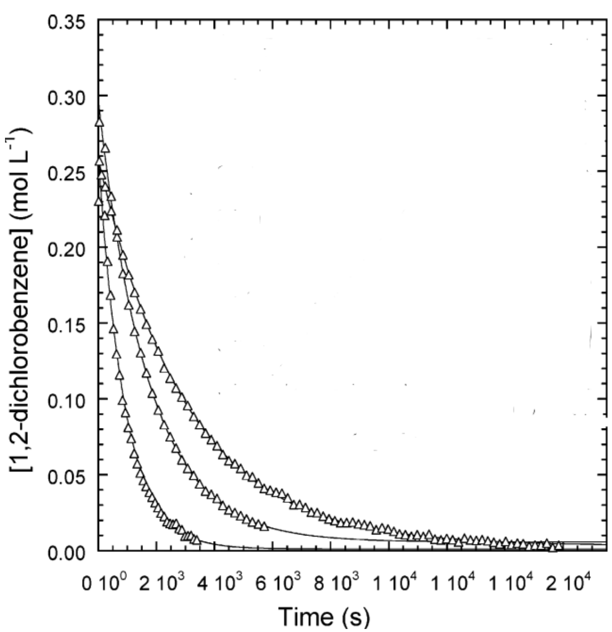
Isotope Effects on the Catalytic Reaction Trisboryl with Arene

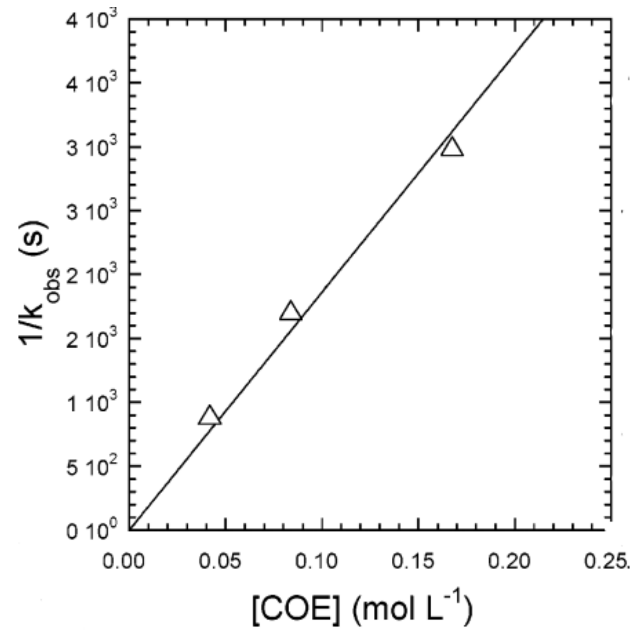
C-H bond cleavage is turnover-limiting !

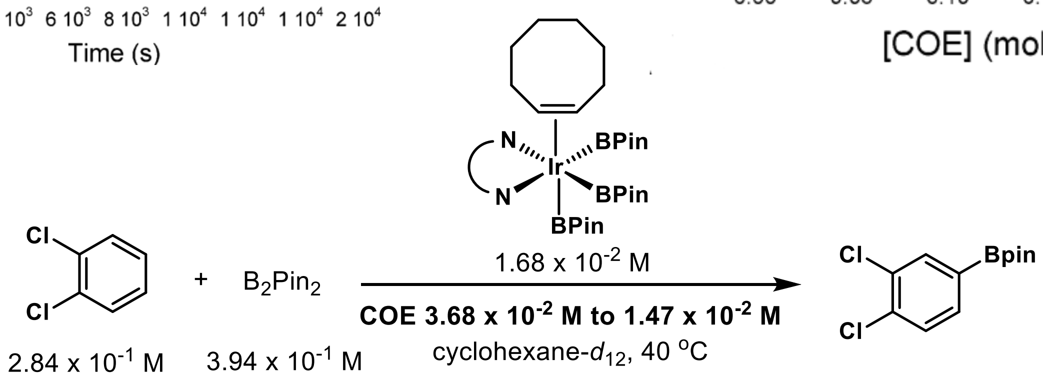
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.4 Kinetic Studies





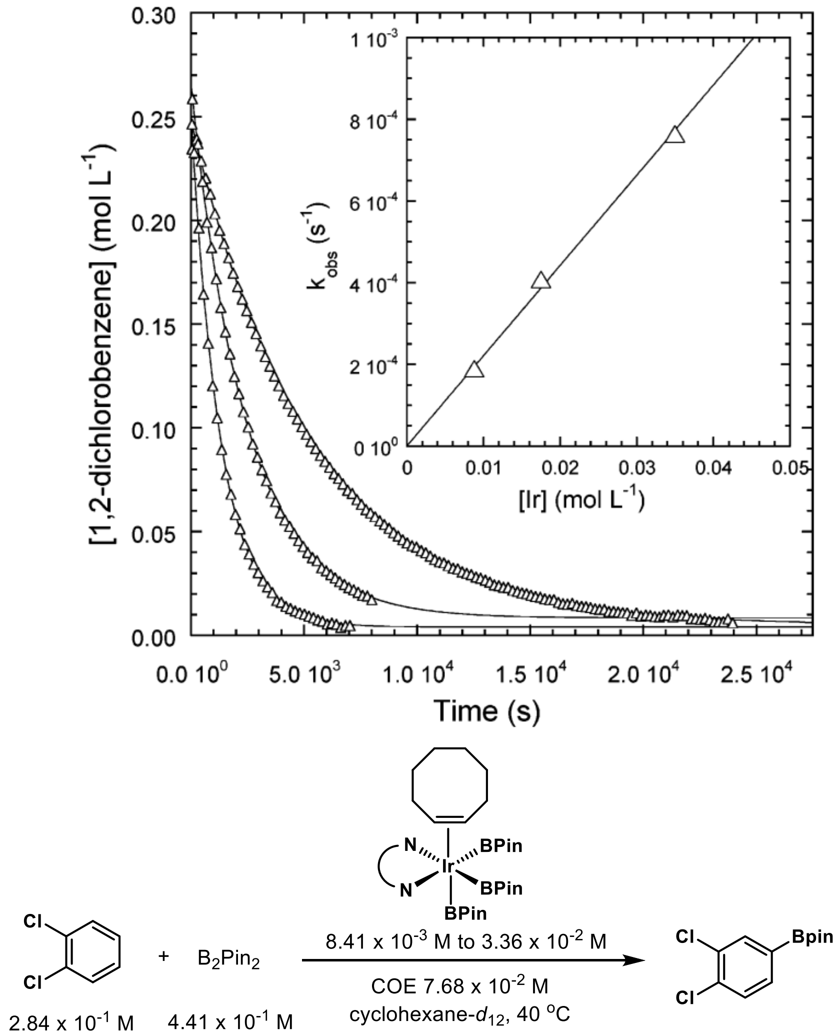


inverse first-order in the concentration of COE

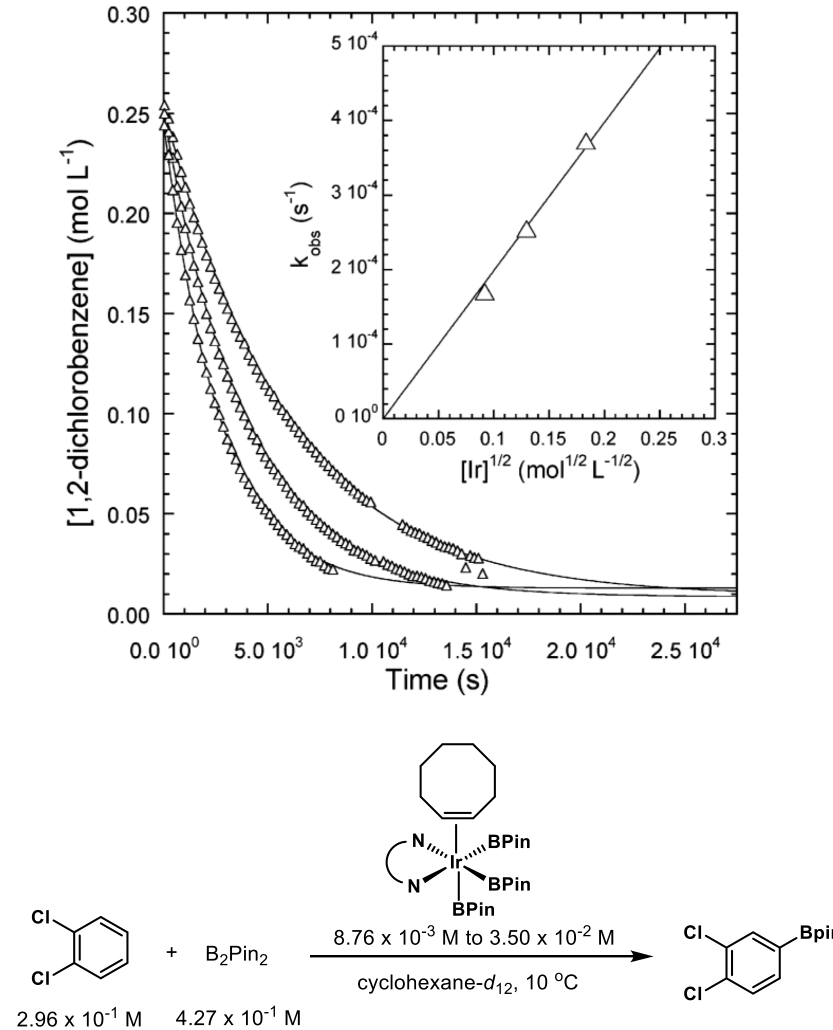
John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

2. Mechanism

2.4 Kinetic Studies



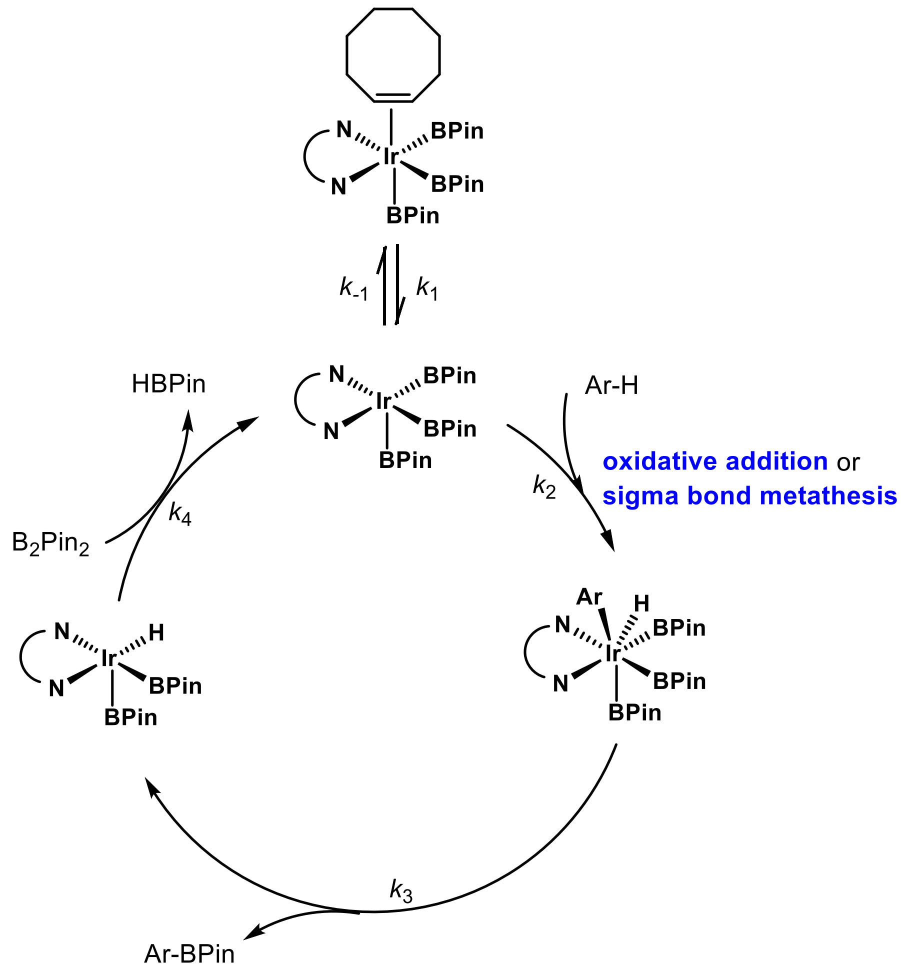
first-order in the concentration of Iridium



half-order in the concentration of Iridium

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

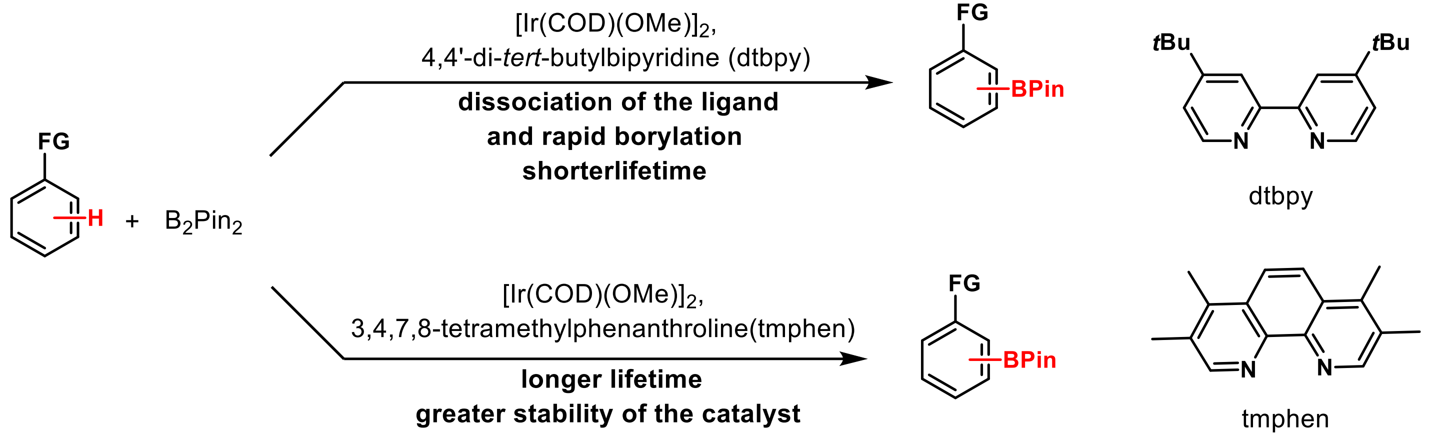
2. Mechanism

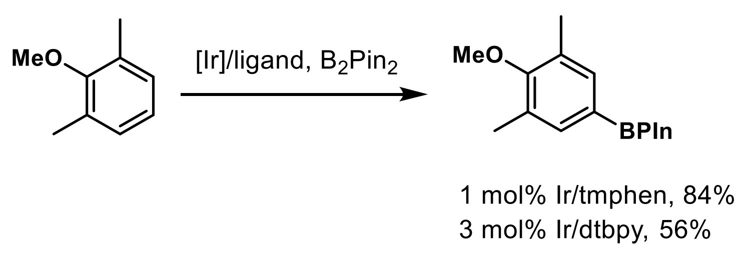


Proposed mechanism

John F. Hartwig. *J. Am. Chem. Soc.* **2005**, *127*, 14263-14278

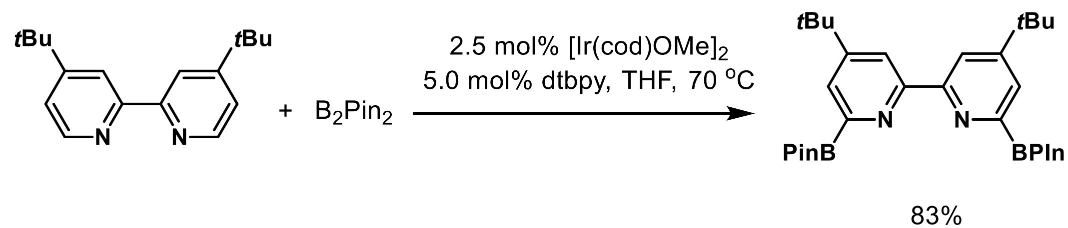
2. Mechanism

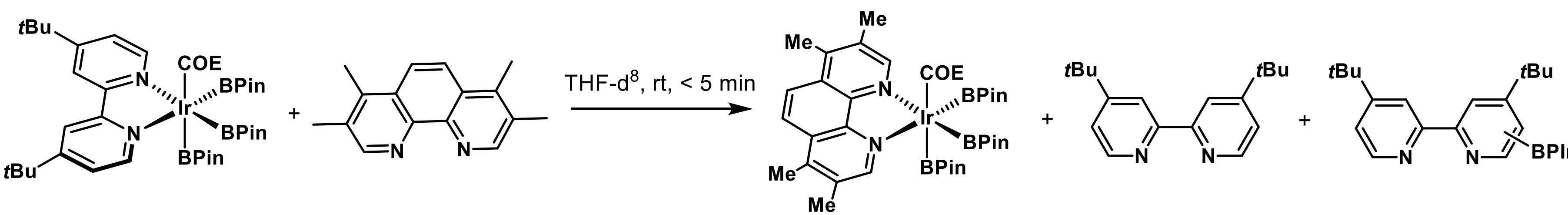




John F. Hartwig. *J. Am. Chem. Soc.* **2019**, *141*, 16479−16485

2. Mechanism

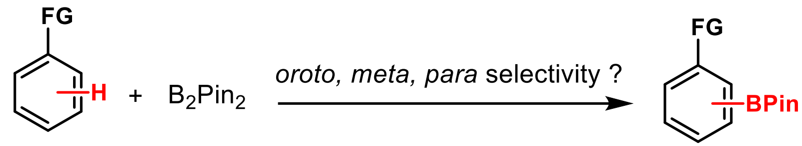




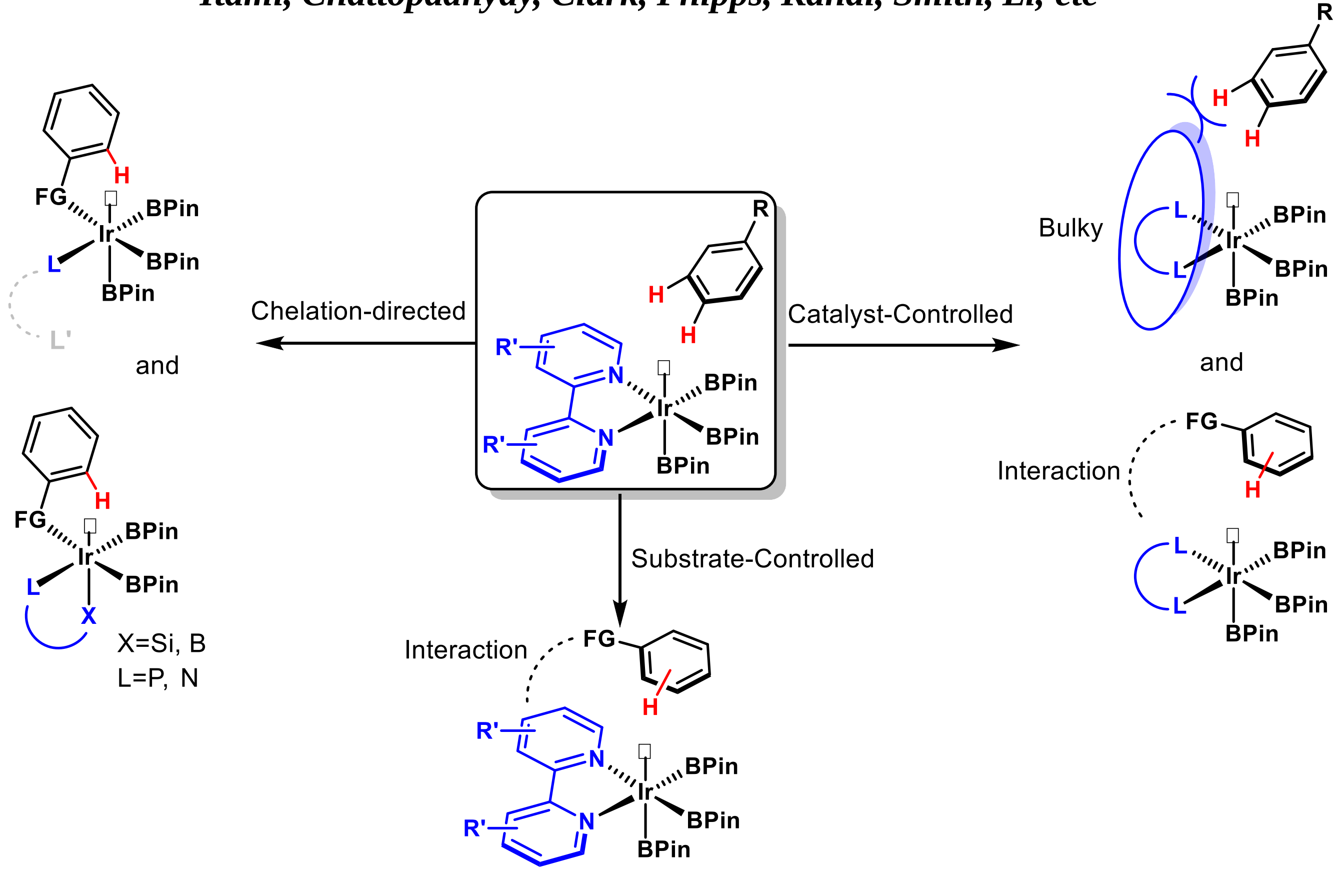
Ligand Exchange and Borylation of dtbpy

John F. Hartwig. *J. Am. Chem. Soc.* **2019**, *141*, 16479−16485

3. Strategies for Regioselective C-H Borylation of Arenes



Major contributions by groups of Sawamura, Ishiyama, Nakao, Itami, Chattopadhyay, Clark, Phipps, Kanai, Smith, Li, etc



Buddhadeb Chattopadhyay. *Tetrahedron Lett*. **2018**, *59* 1269-1277.
Yoshiaki Nakao. *Chem. Lett*. **2019**, *48*, 1092-1100

3. Strategies for Regioselective C-H Borylation of Arenes

3.1 Chelate-directed

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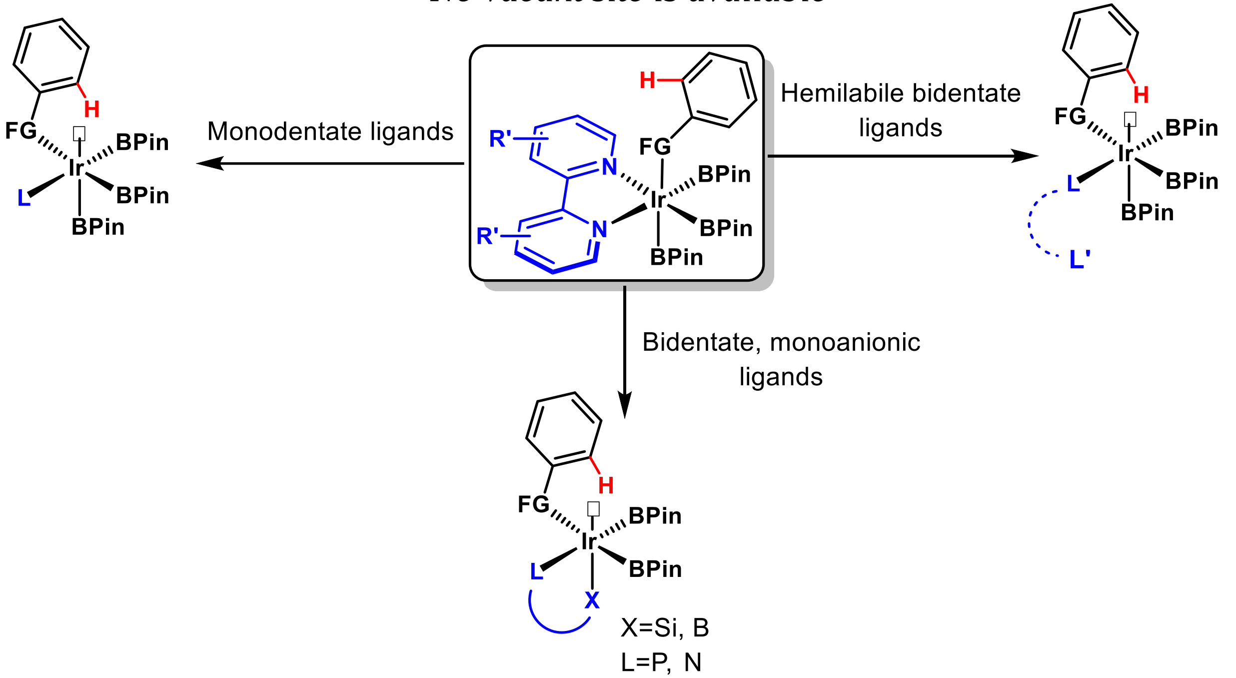
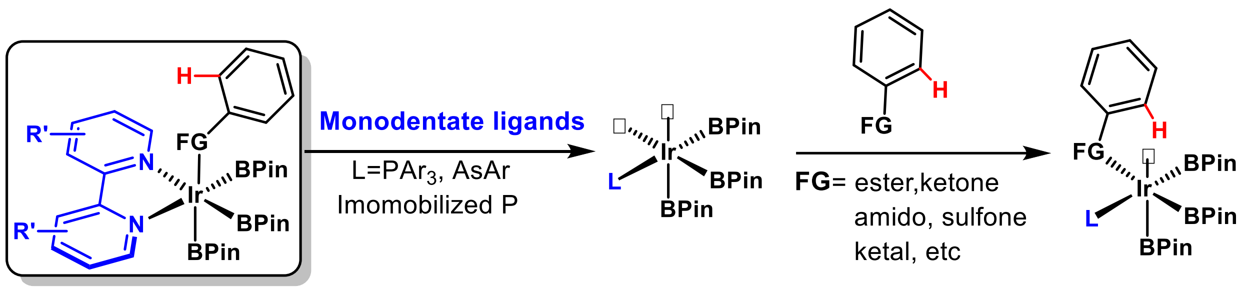
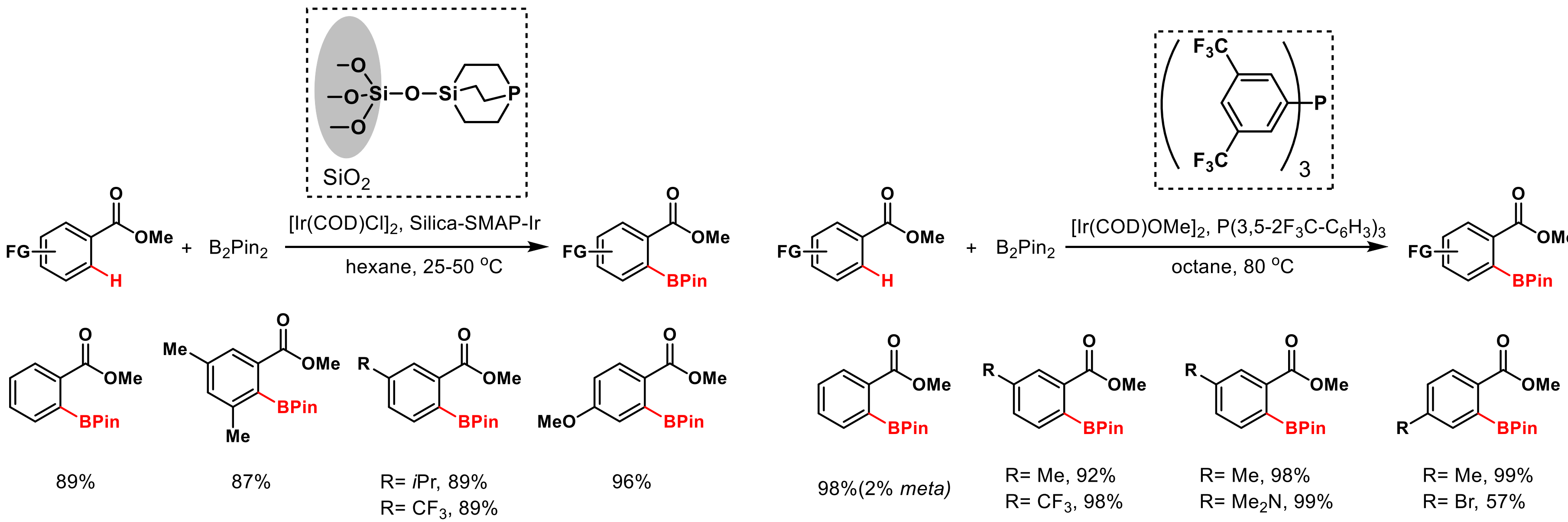


Yoshiaki Nakao. *Chem. Lett*. **2019**, *48*, 1092-1100

3. Strategies for Regioselective C-H Borylation of Arenes

3.1 Chelate-directed

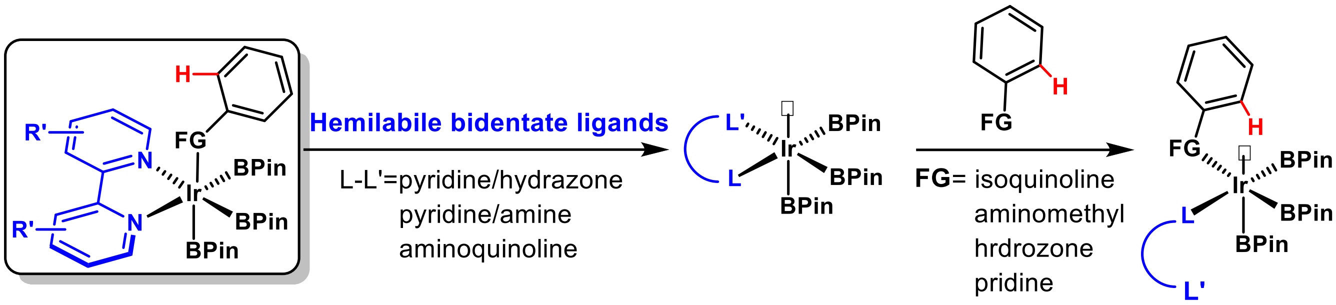


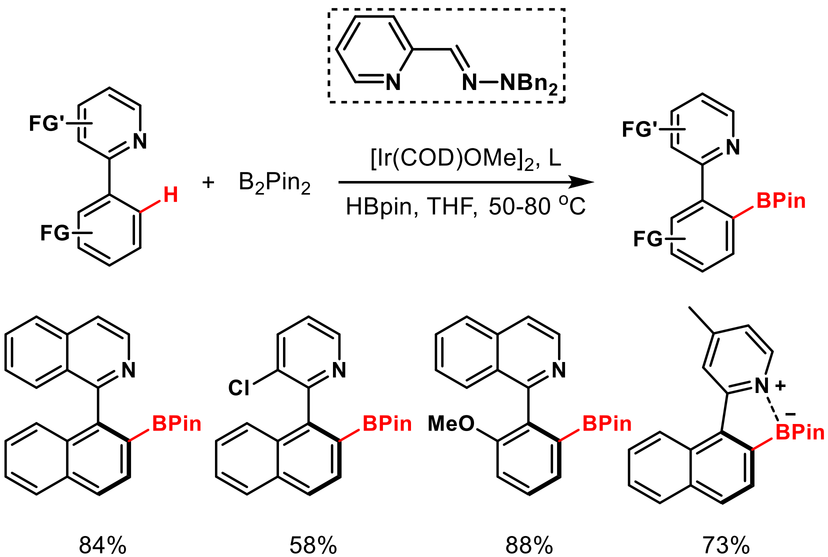


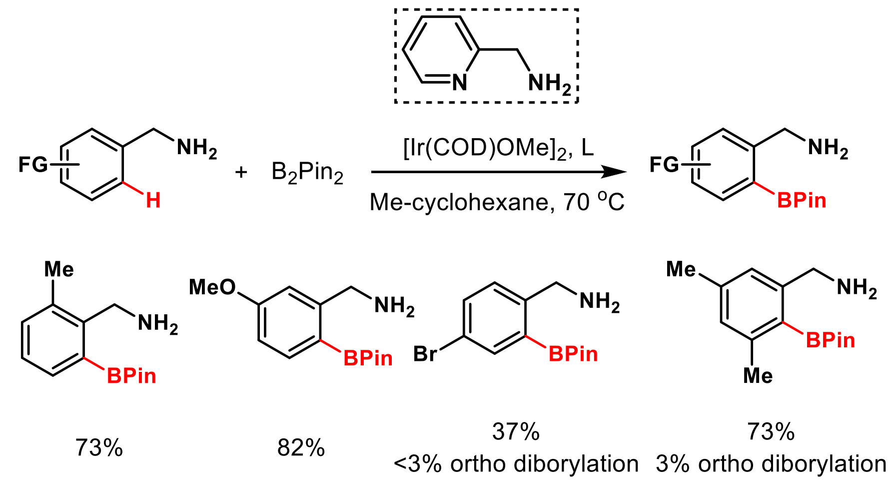
Masaya Sawamura. *J. Am. Chem. Soc.* **2009**, *131*, 5058-5059
Tatsuo Ishiyama.; Norio Miyaura. *Chem. Commun.* **2010**, *46*, 159-161

3. Strategies for Regioselective C-H Borylation of Arenes

3.1 Chelate-directed





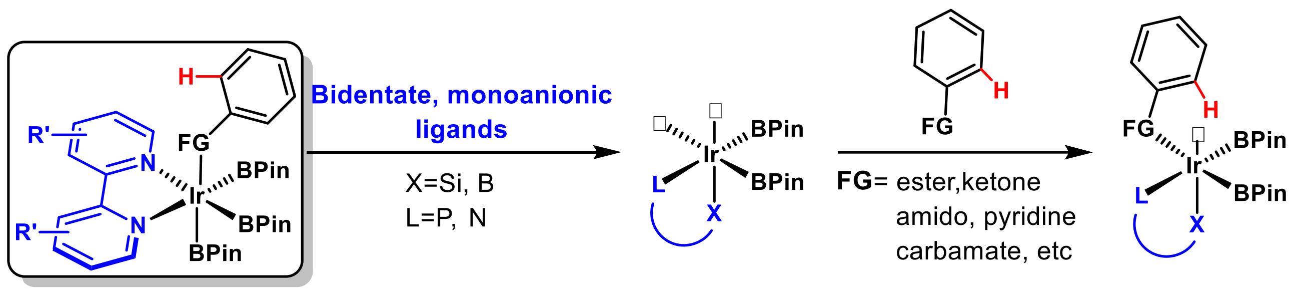


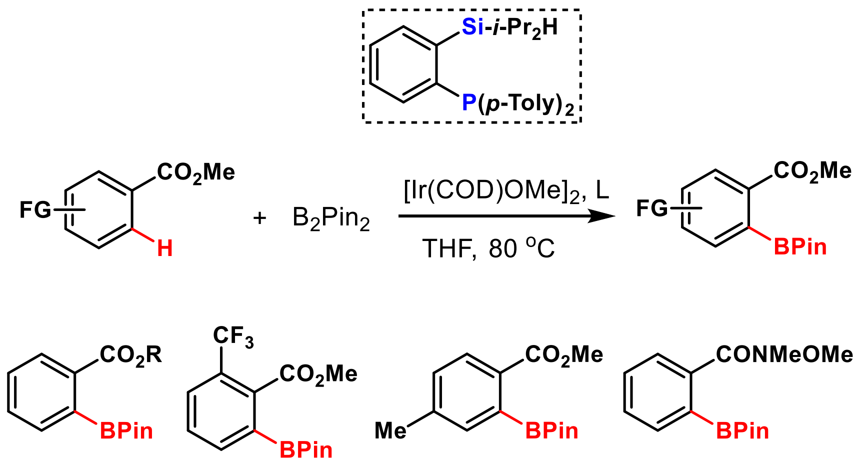
Rosario Ferndez.; JosM. Lassaletta. *Angew. Chem. Int. Ed*. **2011**, *50*, 11724-11728

Timothy B. Clark. *Org. Lett*. **2012**, *14*, 3558-3561

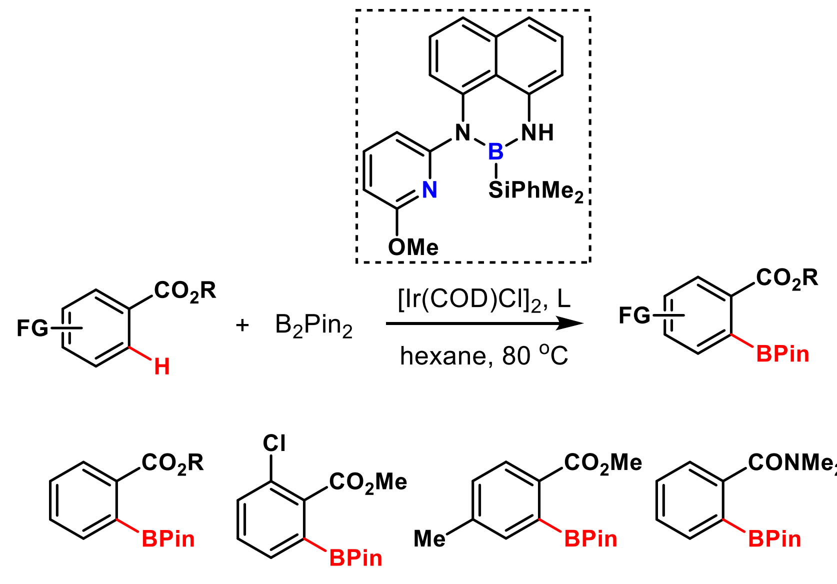
3. Strategies for Regioselective C-H Borylation of Arenes

3.1 Chelate-directed





72% | 82% | 70% 10% ortho diborylation | 84%



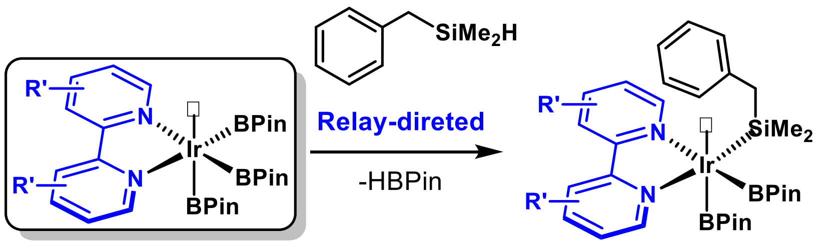
R=Me, 68% 13% ortho diborylation R=tBu, 78% | 98% | 70% | 47%

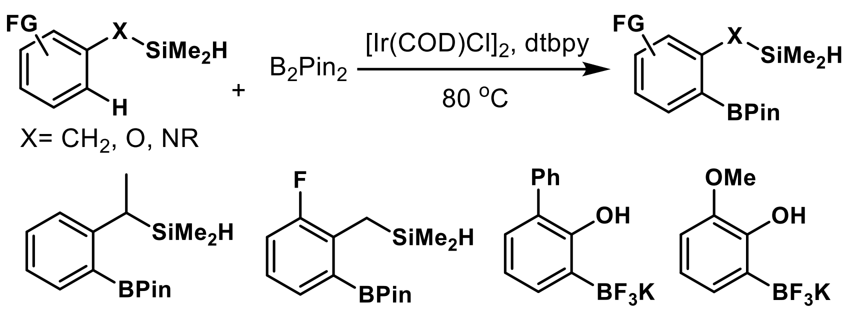
Pengfei Li. *J. Am. Chem. Soc.* **2017**, *139*, 91-94

Shane W. Krska.; Robert E. Maleczka, Jr.; Milton R. Smith, III. *J. Am. Chem. Soc*. **2014**, *136*, 14345-14348

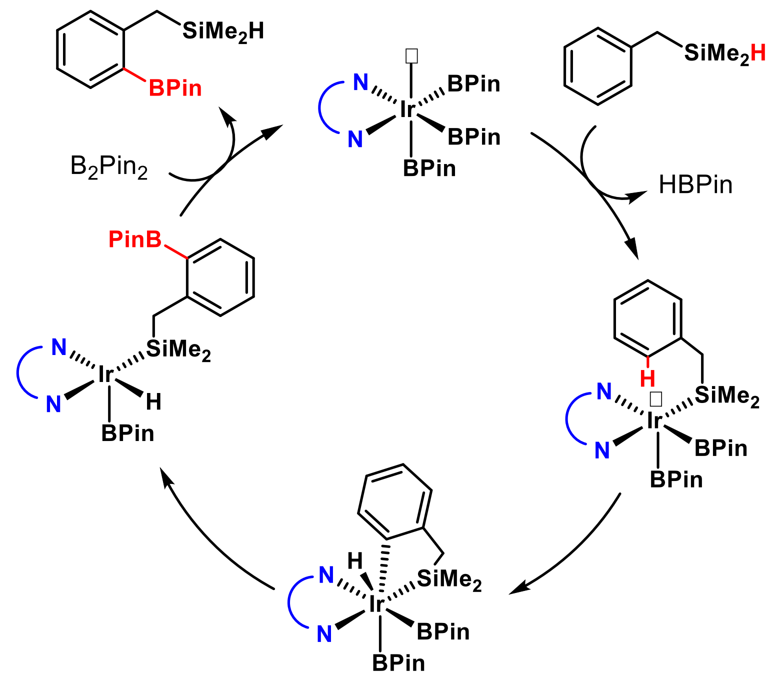
3. Strategies for Regioselective C-H Borylation of Arenes

3.1 Chelate-directed





75% 82% 89% 86%

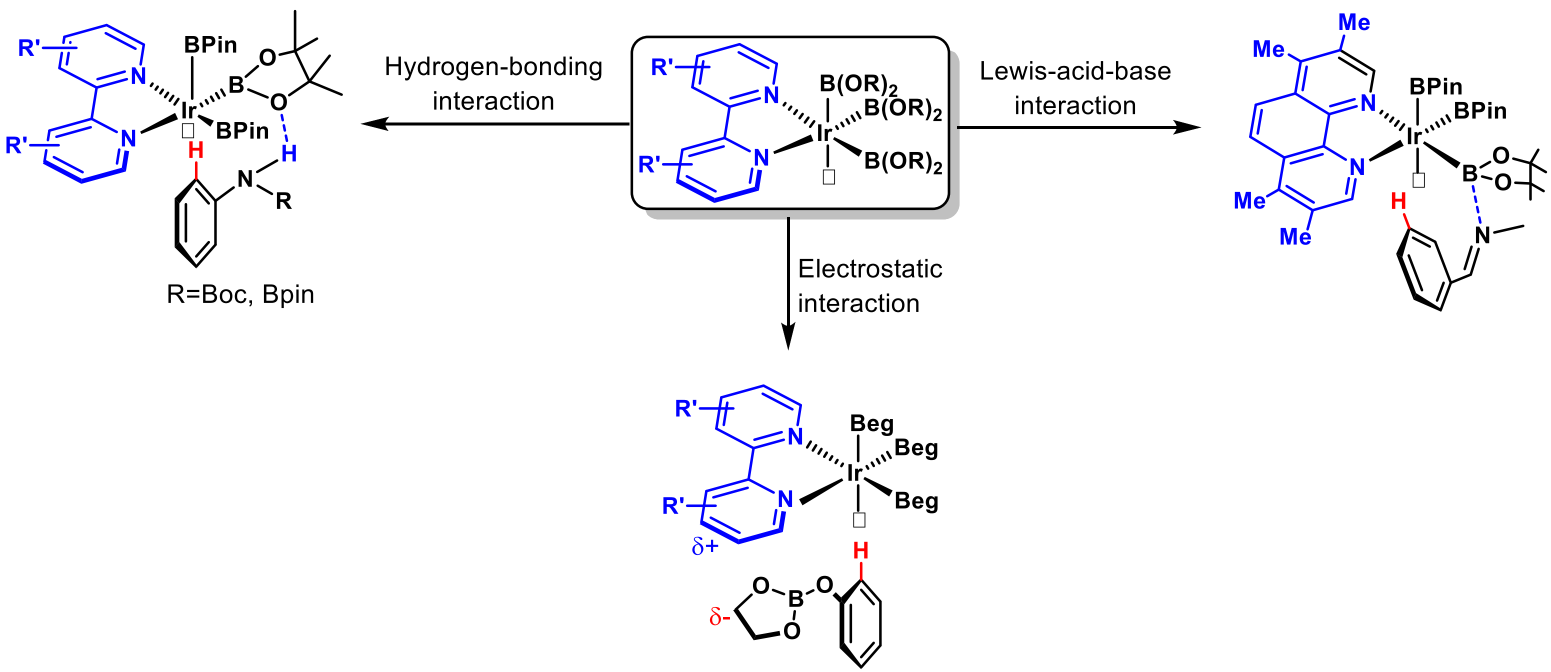


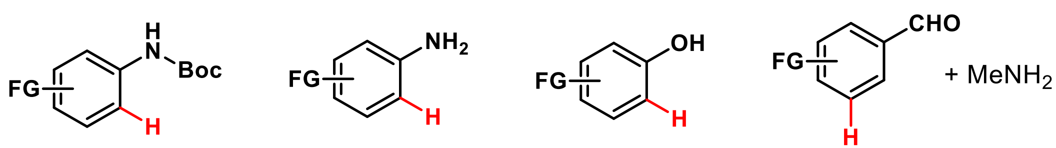
Proposed mechanism

John. F. Hartwig. *J. Am. Chem. Soc.* **2008**, *130*, 7534-7535

3. Strategies for Regioselective C-H Borylation of Arenes

3.2 Substrate-controlled

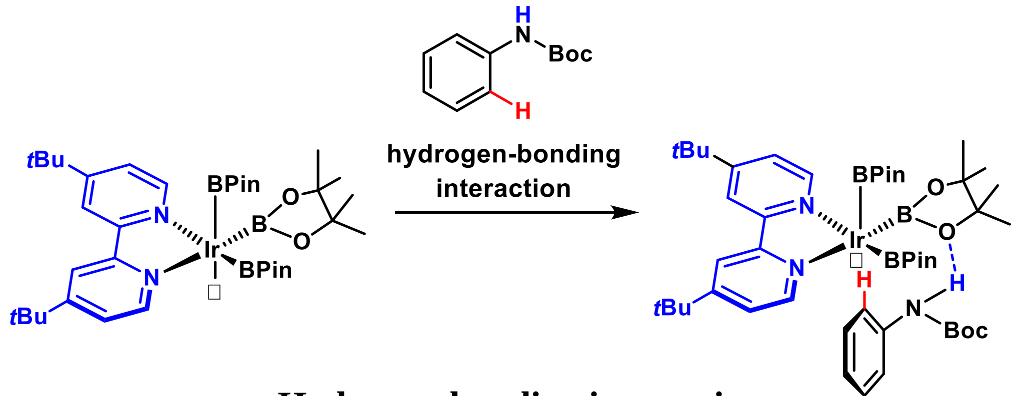




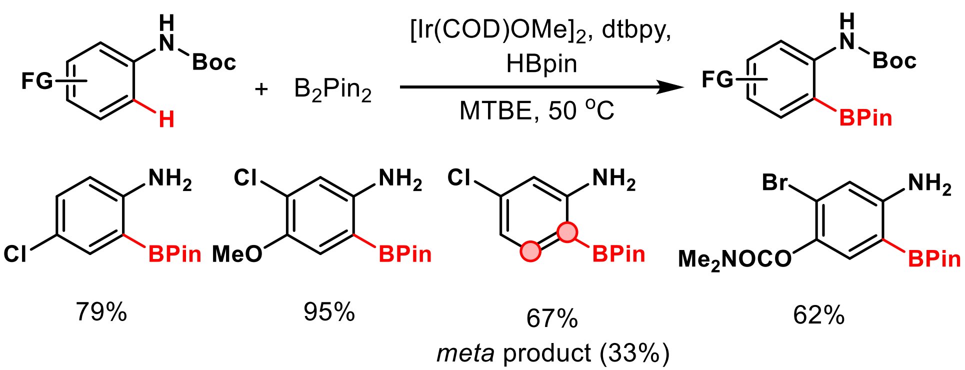
Yoshiaki Nakao. *Chem. Lett*. **2019**, *48*, 1092-1100

3. Strategies for Regioselective C-H Borylation of Arenes

3.2 Substrate-controlled



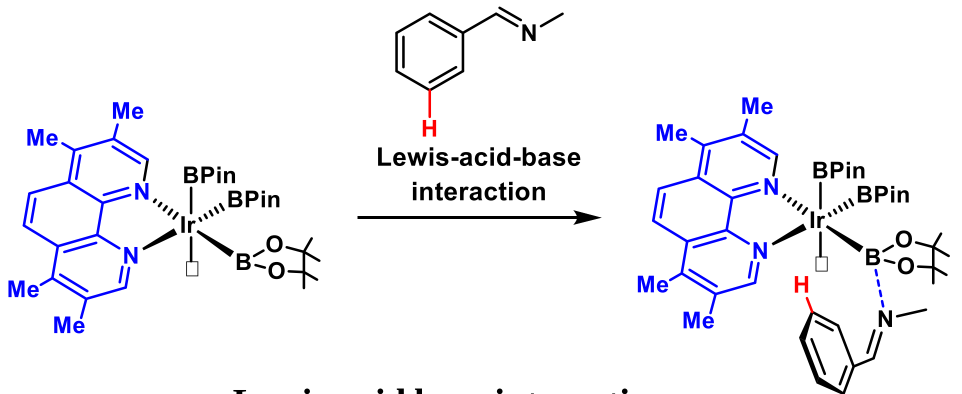
Hydrogen-bonding interaction



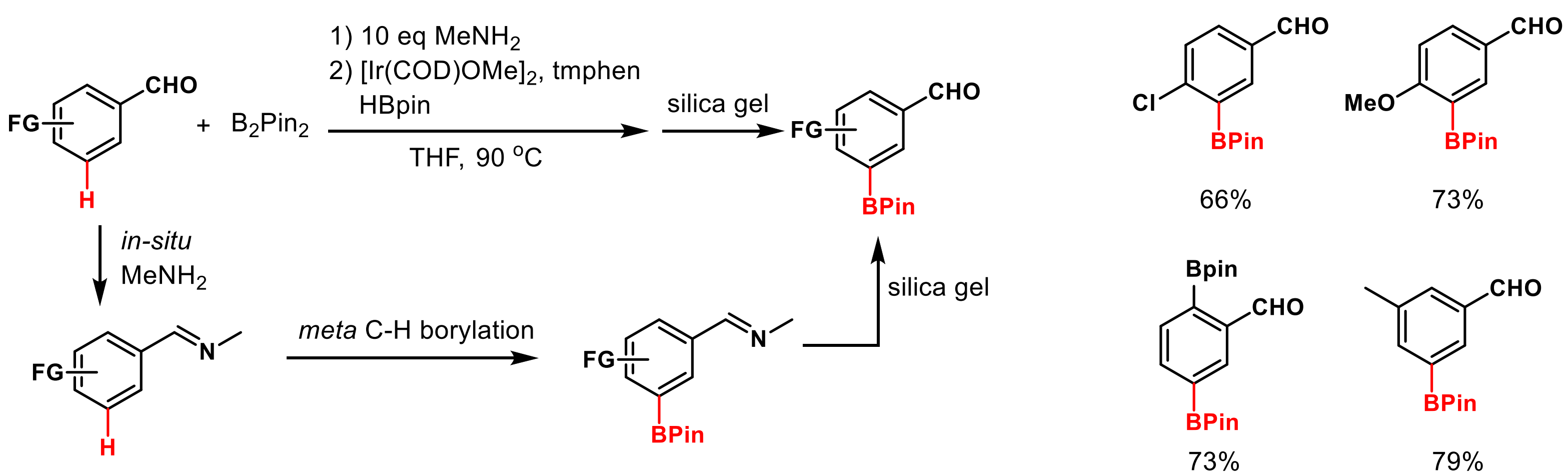
Robert E. Maleczka, Jr.; Milton R. Smith, III. *J. Am. Chem. Soc.* **2012**, 134, 11350-11353

3. Strategies for Regioselective C-H Borylation of Arenes

3.2 Substrate-controlled



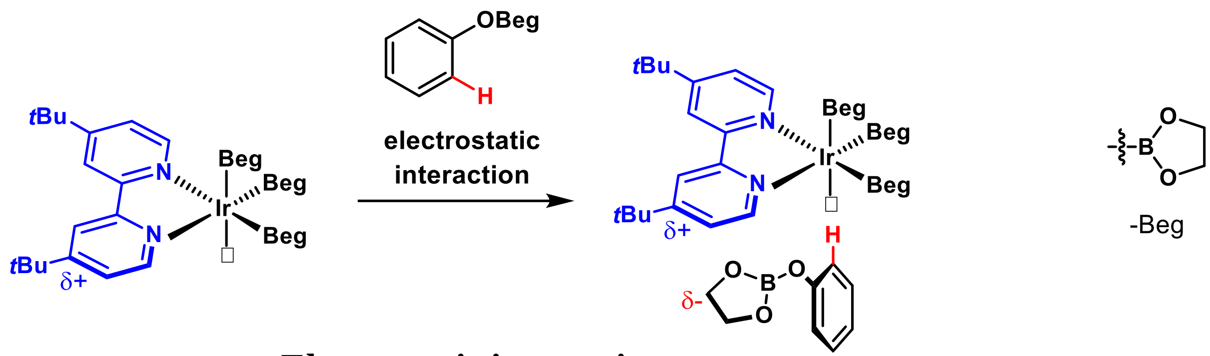
Lewis-acid base interaction



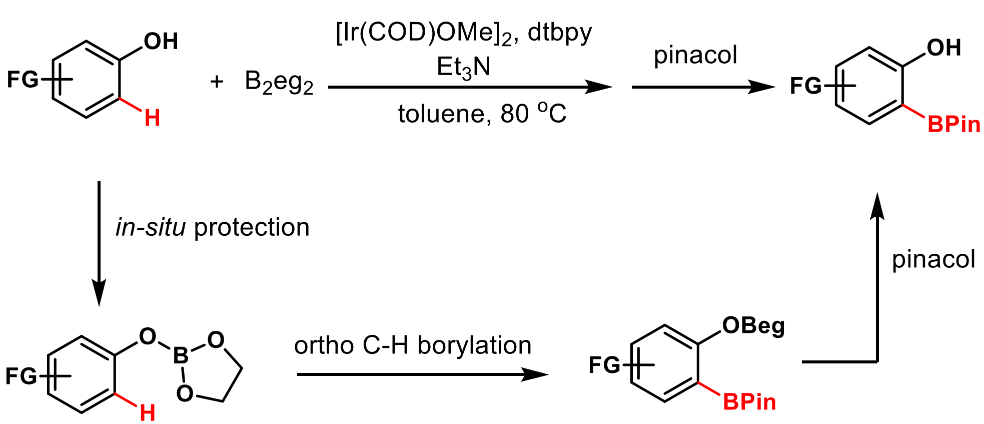
Buddhadeb Chattopadhyay. *J. Am. Chem. Soc*. **2016**, *138*, 84-87

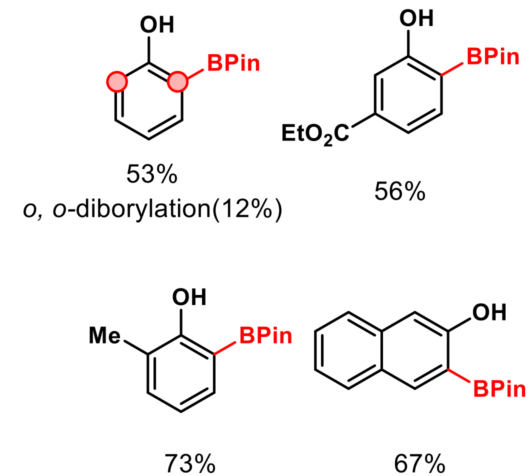
3. Strategies for Regioselective C-H Borylation of Arenes

3.2 Substrate-controlled



Electrostatic interaction

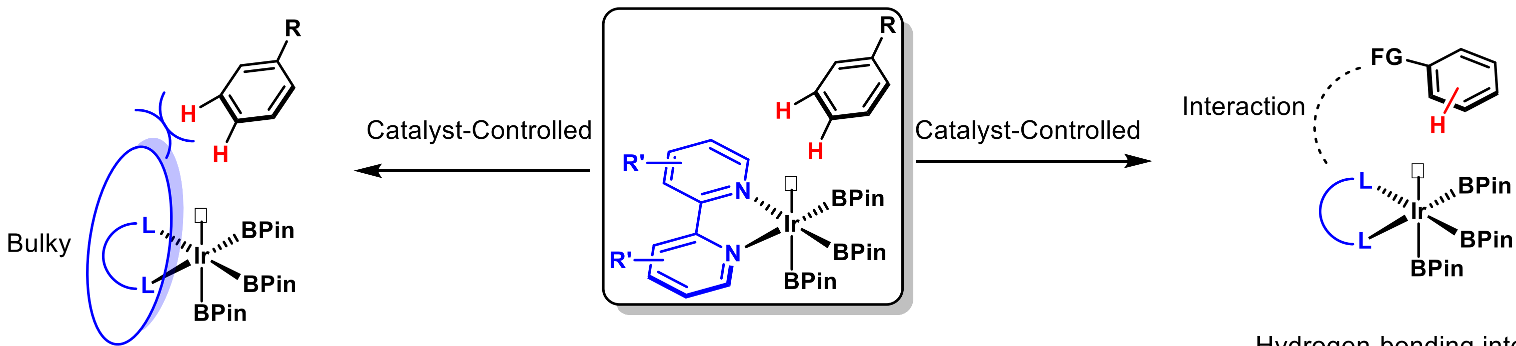




Robert E. Maleczka, Jr.; Milton R. Smith, III. *J. Am. Chem. Soc.* **2017**, *139*, 7864-7871

3. Strategies for Regioselective C-H Borylation of Arenes

3.3 Catalyst-controlled



Repulsive steric interactions

Hydrogen-bonding interaction

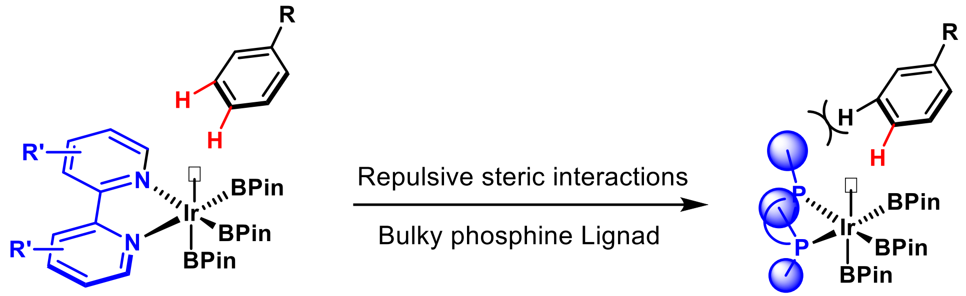
Lewis-acid -base interaction

Ion-pairing interaction

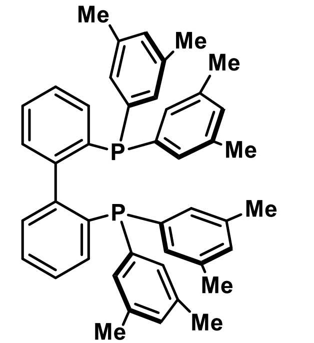
Interactions mediated by an alkali metal (M)

3. Strategies for Regioselective C-H Borylation of Arenes

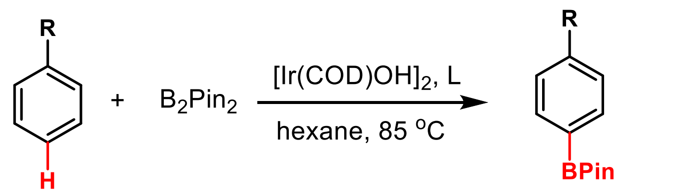
3.3 Catalyst-controlled



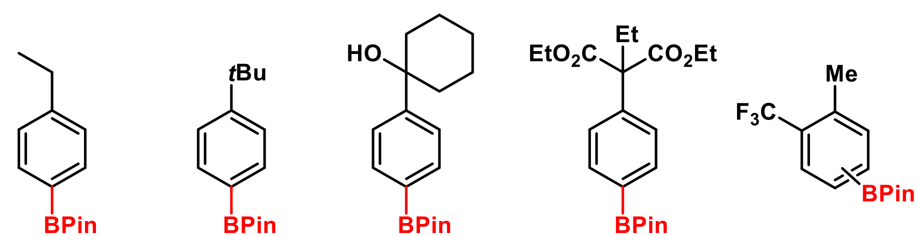
Repulsive steric interactions



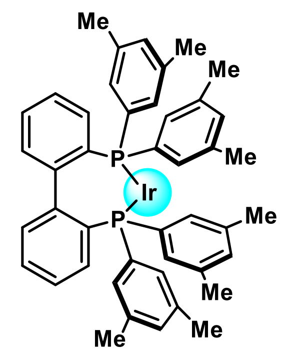
Bulky phosphine Lignad



yield, *para/meta*



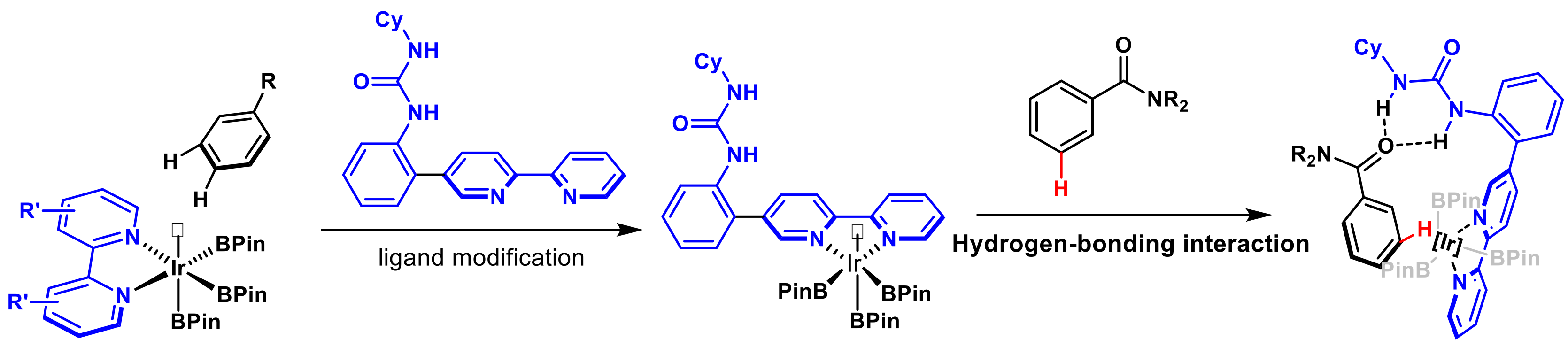
80%(31/68) 84%(90/10) 58%(71/29) 64%(87/13) 68%*(50/50)*



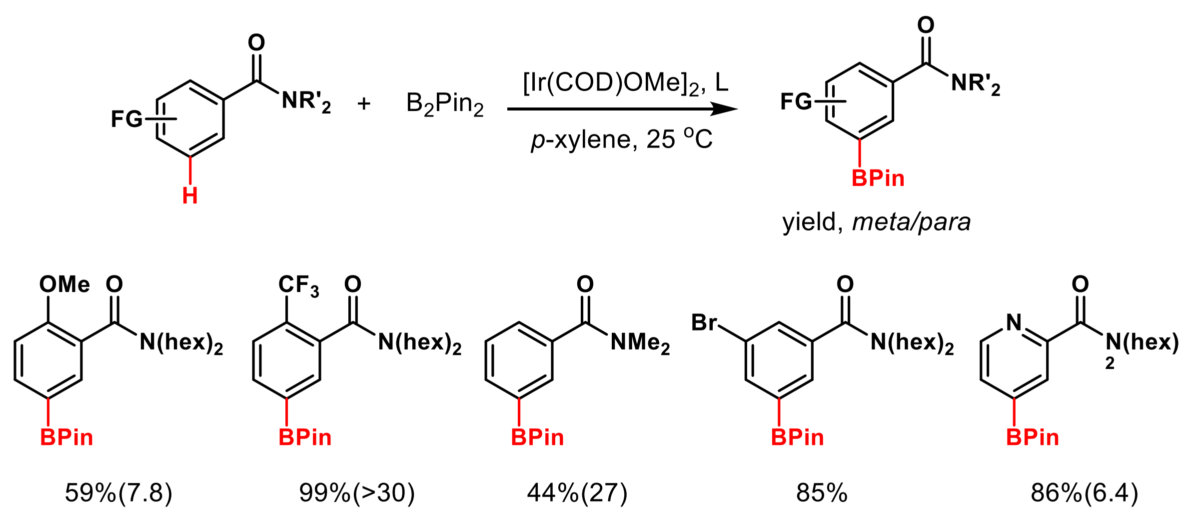
Kenichiro Itami. *J. Am. Chem. Soc*. **2015**, *137*, 5193-5198

3. Strategies for Regioselective C-H Borylation of Arenes

3.3 Catalyst-controlled



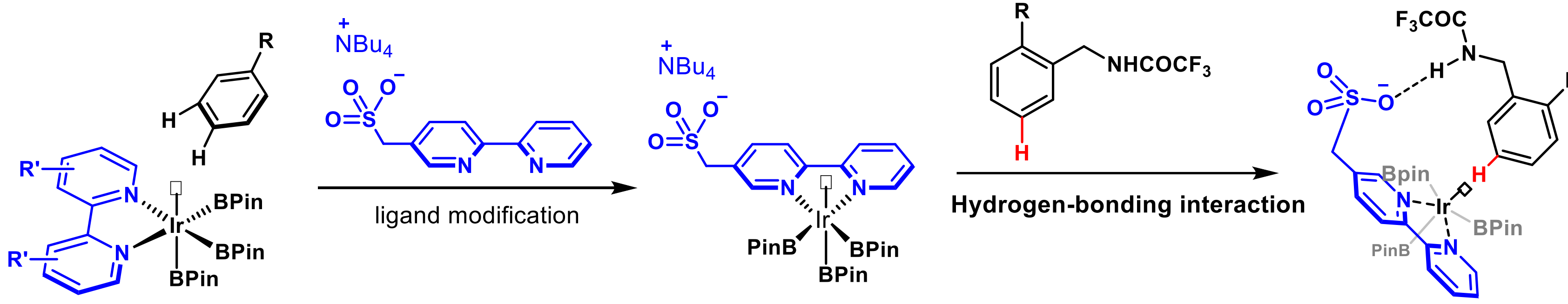
Hydrogen-bonding interaction



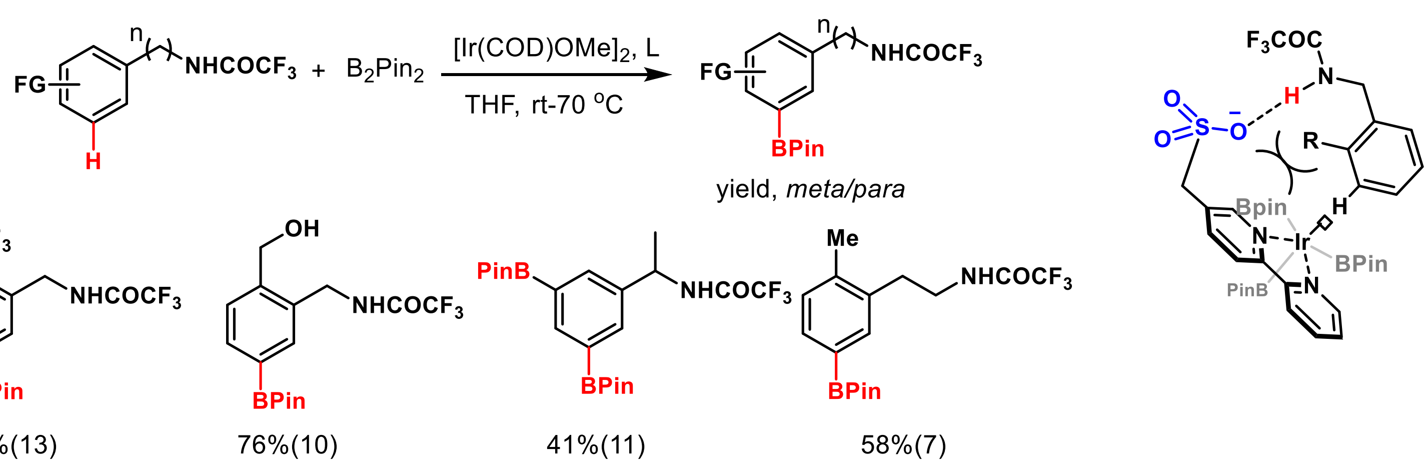
Motomu Kanai. *Nature Chem*. **2015**, *7*, 712-717

3. Strategies for Regioselective C-H Borylation of Arenes

3.3 Catalyst-controlled



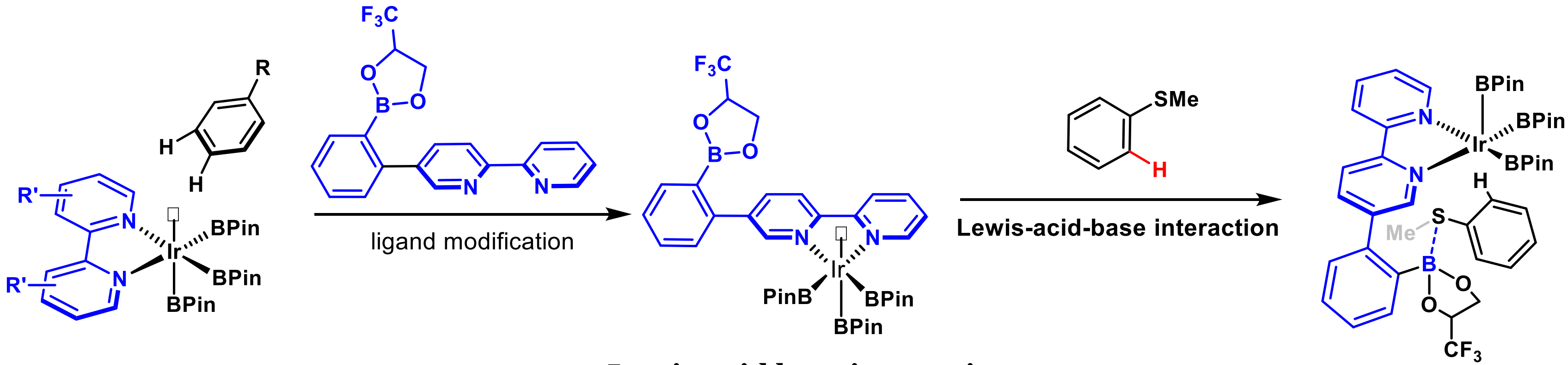
Hydrogen-bonding interaction



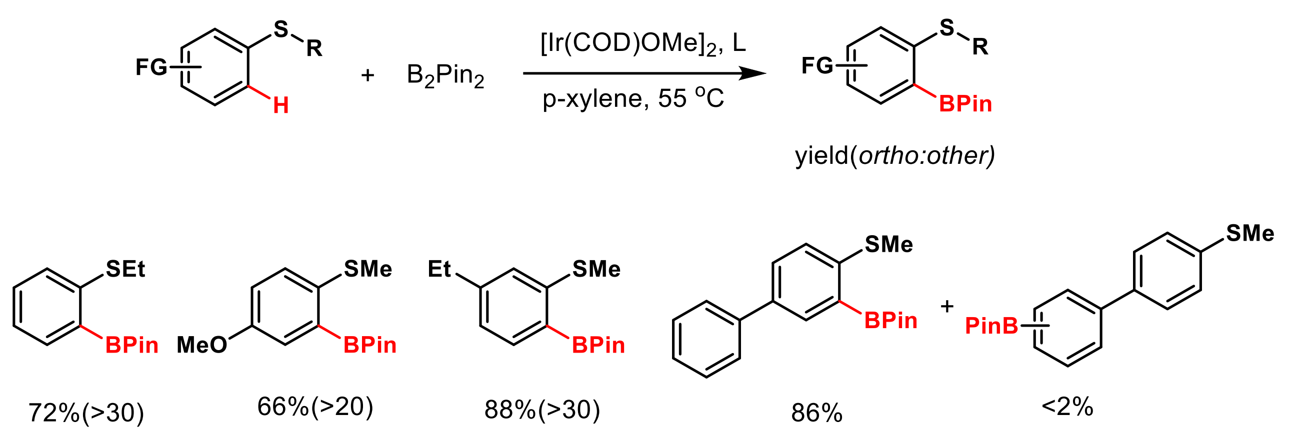
Robert J. Phipps. *Angew. Chem. Int. Ed*. **2017**, *56*, 13351-13355

3. Strategies for Regioselective C-H Borylation of Arenes

3.3 Catalyst-controlled



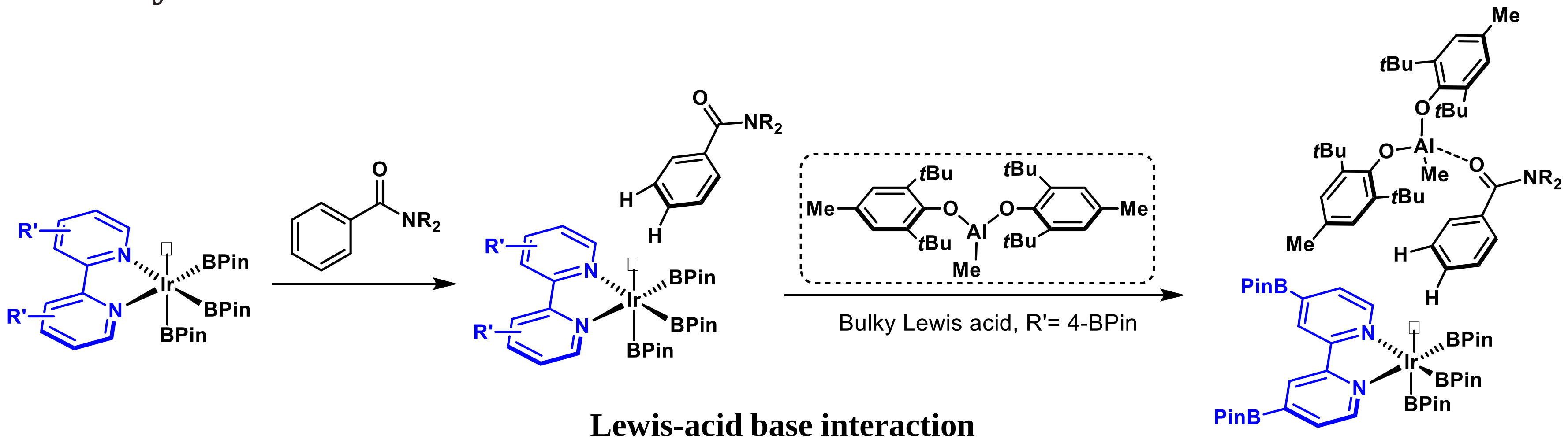
Lewis-acid base interaction



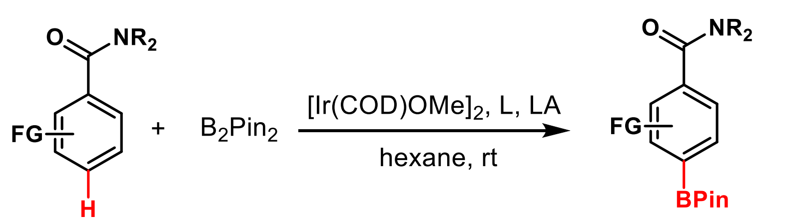
Motomu Kanai. *Angew. Chem. Int. Ed*. **2017**, *56*, 1495-1499

3. Strategies for Regioselective C-H Borylation of Arenes

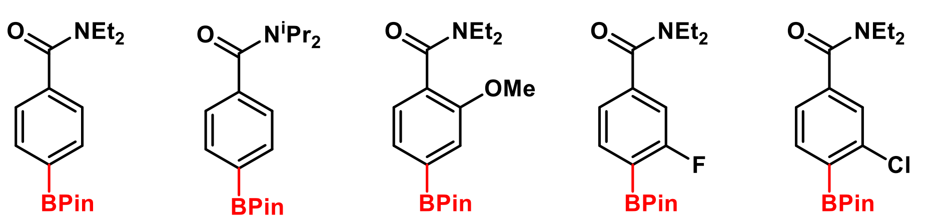
3.3 Catalyst-controlled



Lewis-acid base interaction



yield, *para/meta*

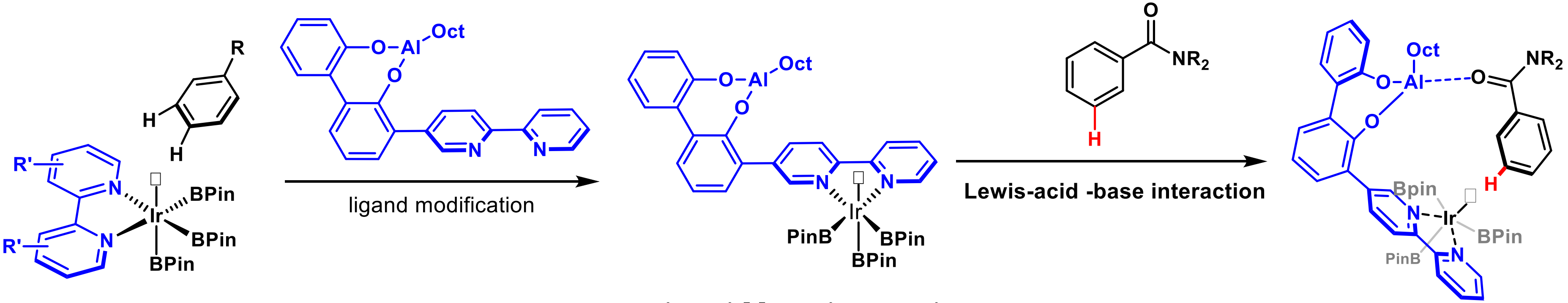


92%(6.9) 95%(>20) 90%(>20) 93%(13) 96%(0.21/1.0)

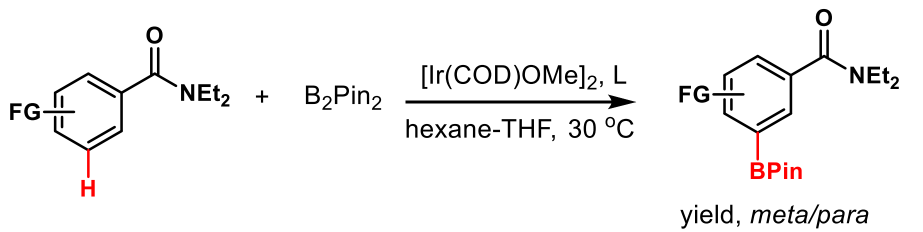
Yoshiaki Nakao. *Angew. Chem. Int. Ed*. **2017**, *56*, 4853-4857

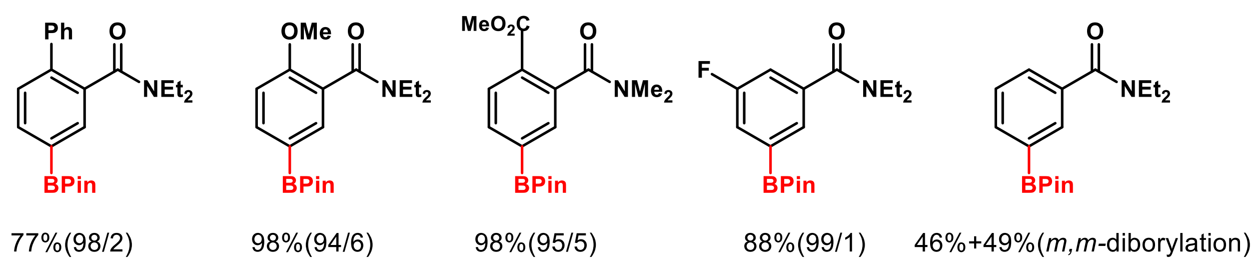
3. Strategies for Regioselective C-H Borylation of Arenes

3.3 Catalyst-controlled



Lewis-acid base interaction

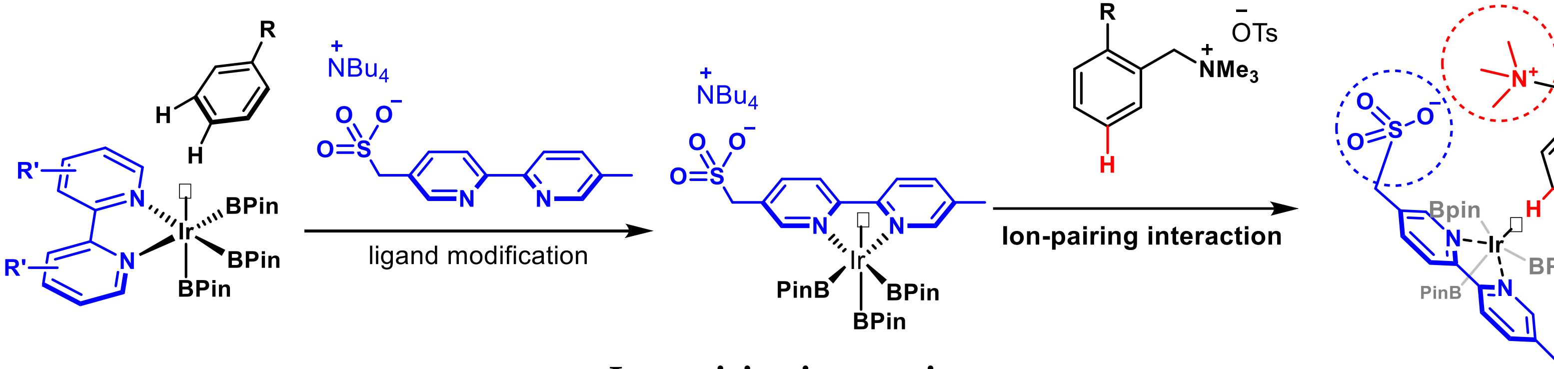




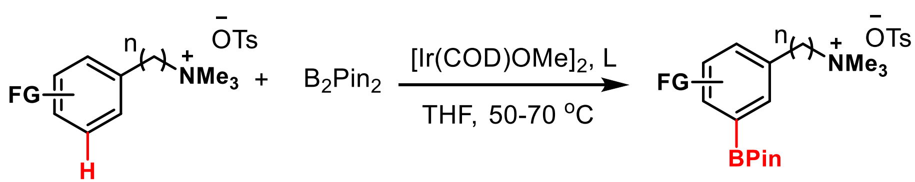
Yoshiaki Nakao. *J. Am. Chem. Soc*. **2019**, *141*, 7972-7979

3. Strategies for Regioselective C-H Borylation of Arenes

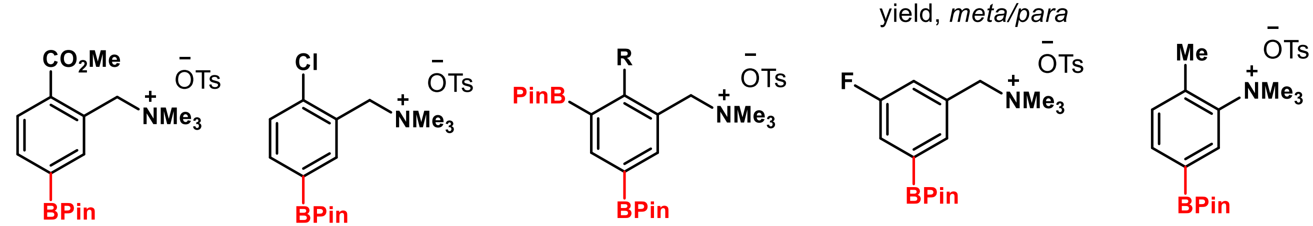
3.3 Catalyst-controlled



Ion-pairing interaction



yield, *meta/para*

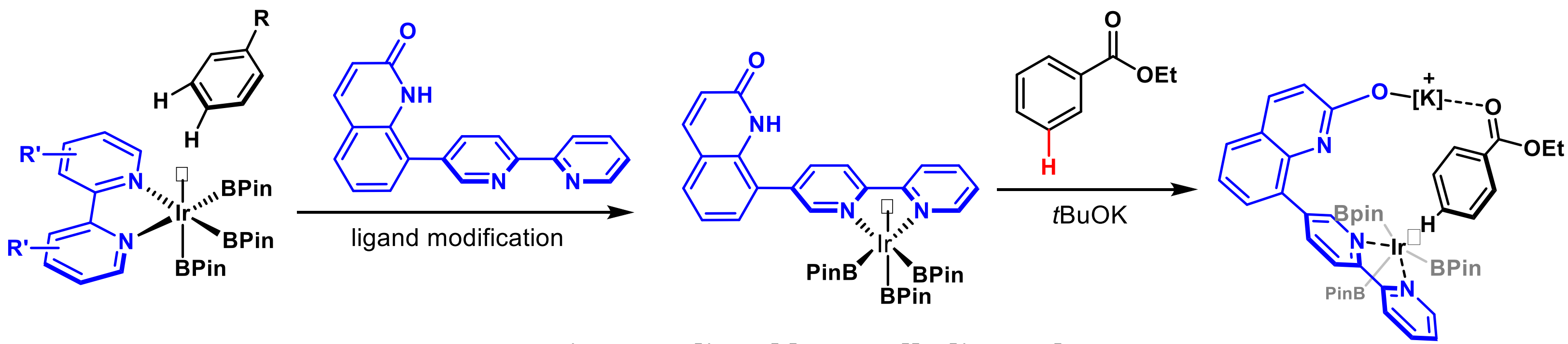


71%(13) | 77%(11) | R=F, 61%(12)
R=H, 92%(>20) | 76%(20) | 85%(8)

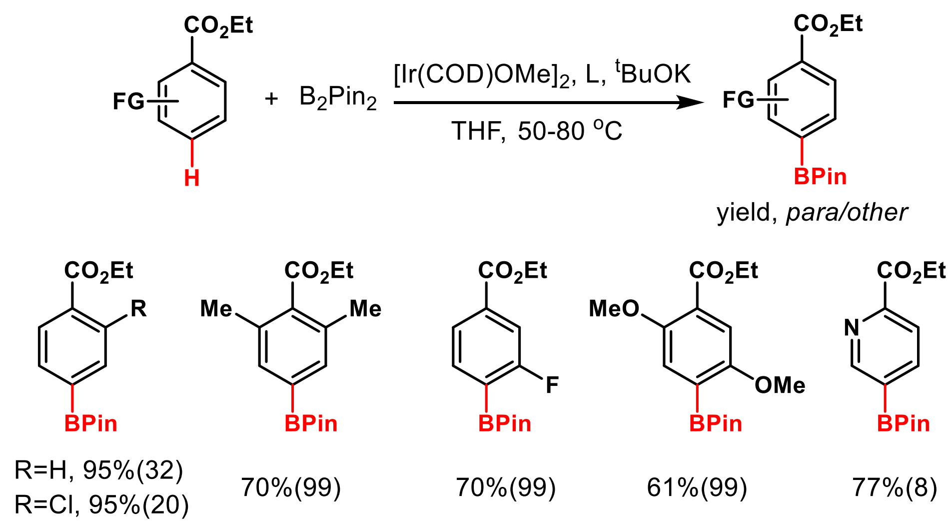
Robert J. Phipps. *J. Am. Chem. Soc.* **2016**, *138*, 12759-12762

3. Strategies for Regioselective C-H Borylation of Arenes

3.3 Catalyst-controlled



Interactions mediated by an alkali metal

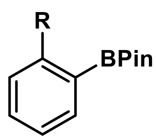


Buddhadeb Chattopadhyay. *J. Am. Chem. Soc*. **2017**, *139*, 7745-7748

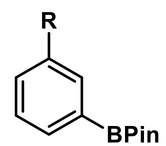
4. Summary

1. The mechanism have been studied by experiments and accepted by others.

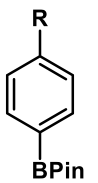
2.



Chelate directed
Relay directed
Hydrogen-bonding interaction
Electrostatic interaction
Lewis-acid base interaction



Hydrogen-bonding interaction
Ion-pairing interaction



Interactions mediated by an K^+
Repulsive Steric Interactions
Lewis-acid base interaction

3. **Challenges**

Simple arene such as toluene, ethylbenzene are still the challenges to control the regioselectivity.

Thanks for your attention!