

Phosphine-directed C-H Functionalization

汇报人：齐树陶

导师：张俊良 教授

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Content

- **Background**

- 1.1 Brief introduction of phosphine-directed C–H functionalization

- 1.2 Previous works (P-accelerated direct C–H functionalization)

- **Recent achievement in phosphine-directed C–H functionalization**

- **Summary**

Content

- **Background**

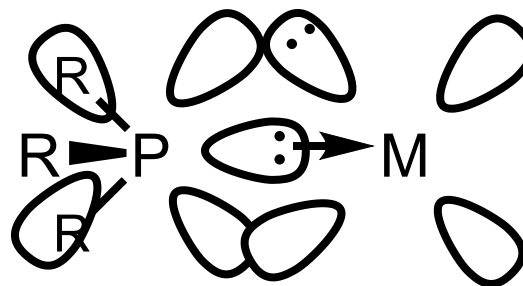
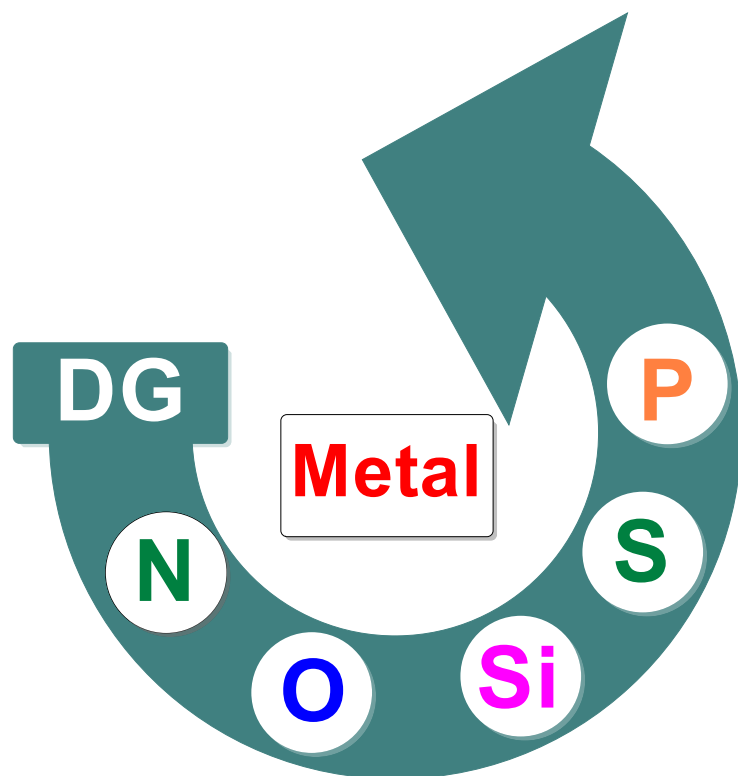
- 1.1 Brief introduction of phosphine-directed C–H functionalization

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- Summary

1.1 Brief Introduction of Phosphine-directed C-H Functionalization

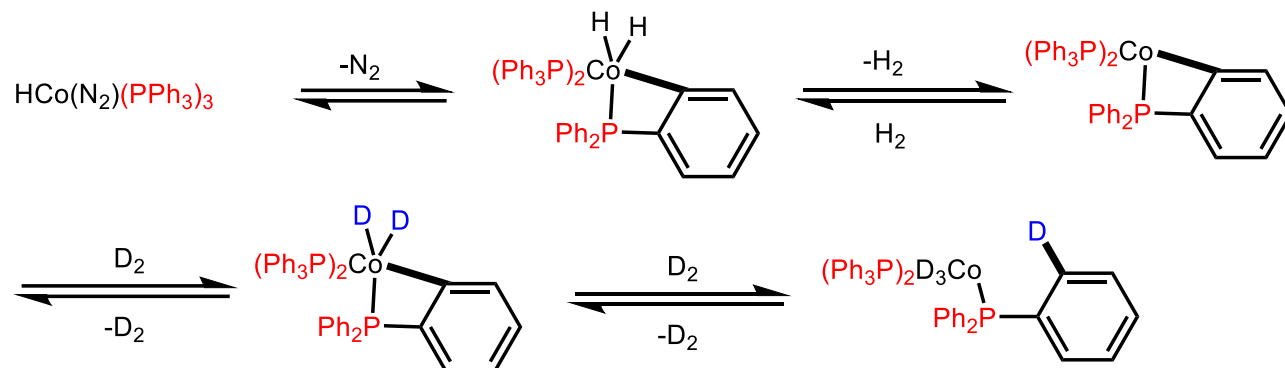


Challenges

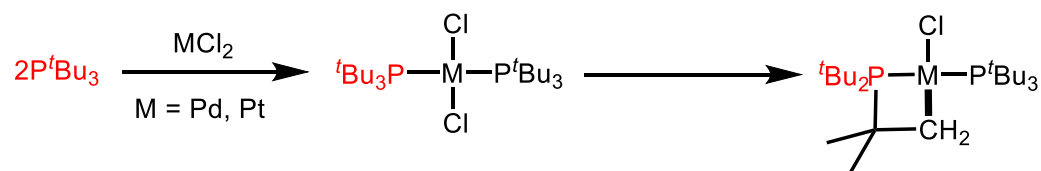
- 1. Strong coordination with metals**
- 2. Easy to be oxidized**

1.1 Brief Introduction of Phosphine-directed C-H Functionalization

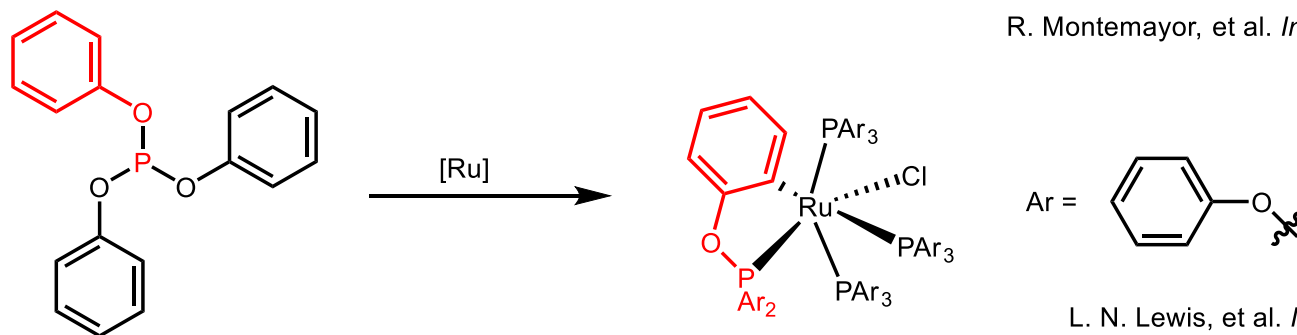
Early Examples in Stoichiometric Reactions



G. W. Parshall, et al. *J. Am. Chem. Soc.* **1968**, *90*, 1669



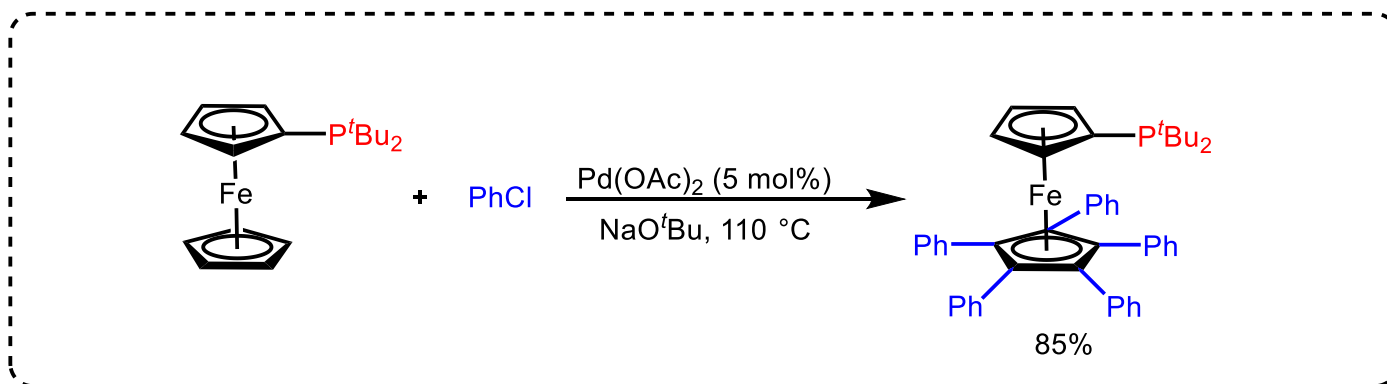
R. Montemayor, et al. *Inorg. Chem.* **1977**, *16*, 2183



L. N. Lewis, et al. *Inorg. Chem.* **1985**, *24*, 44335

1.1 Brief Introduction of Phosphine-directed C-H Functionalization

First Catalytic Example

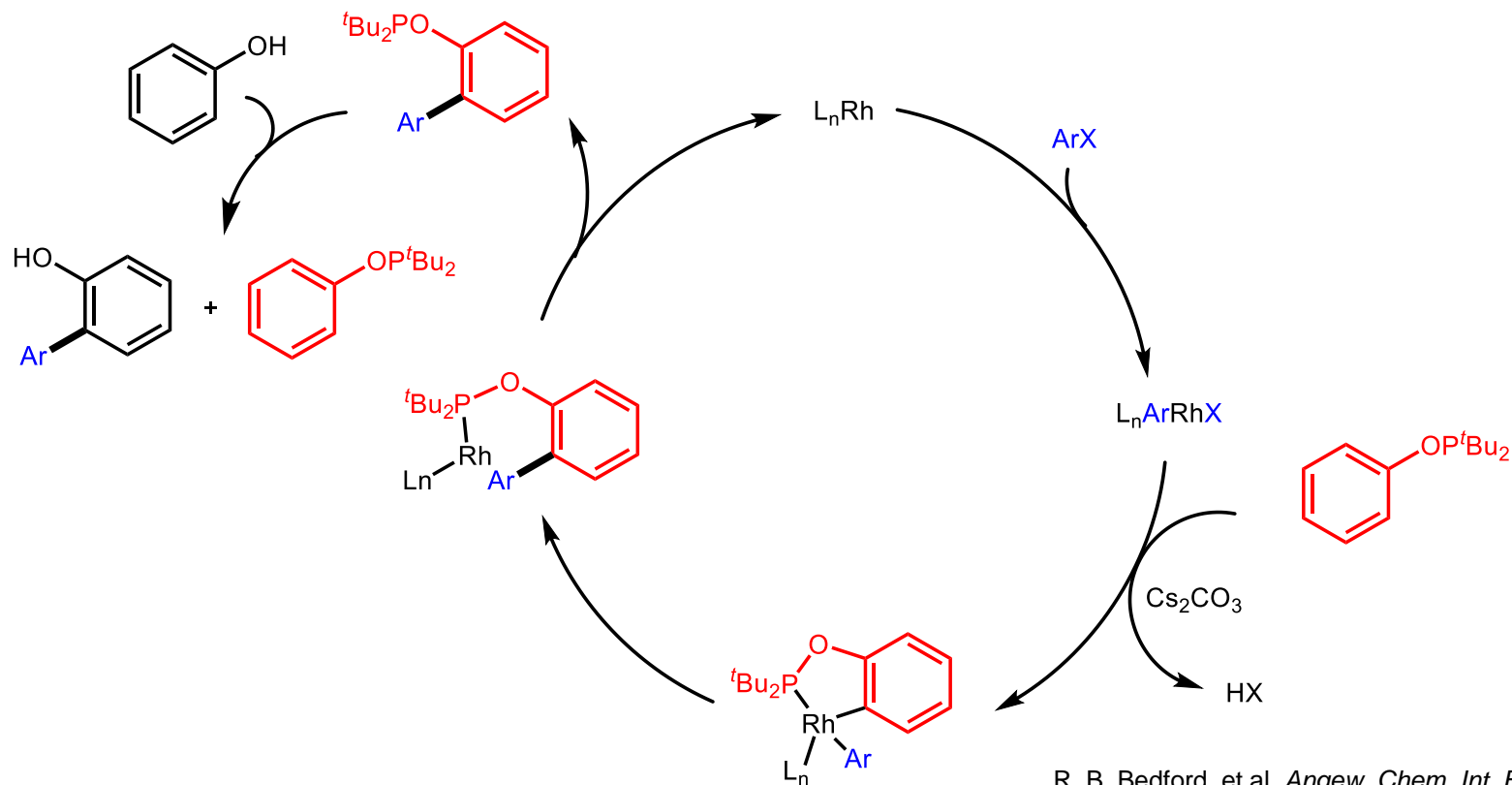
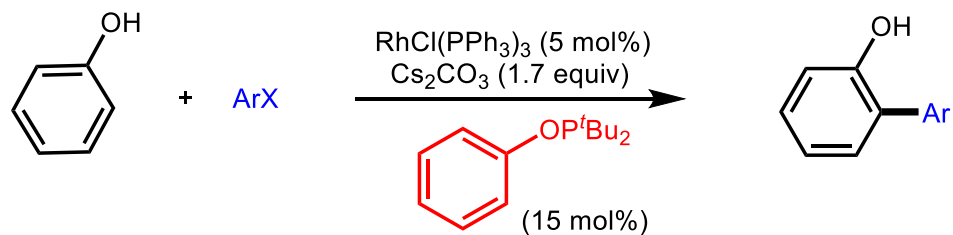


J. Hartwig

Only One Example!

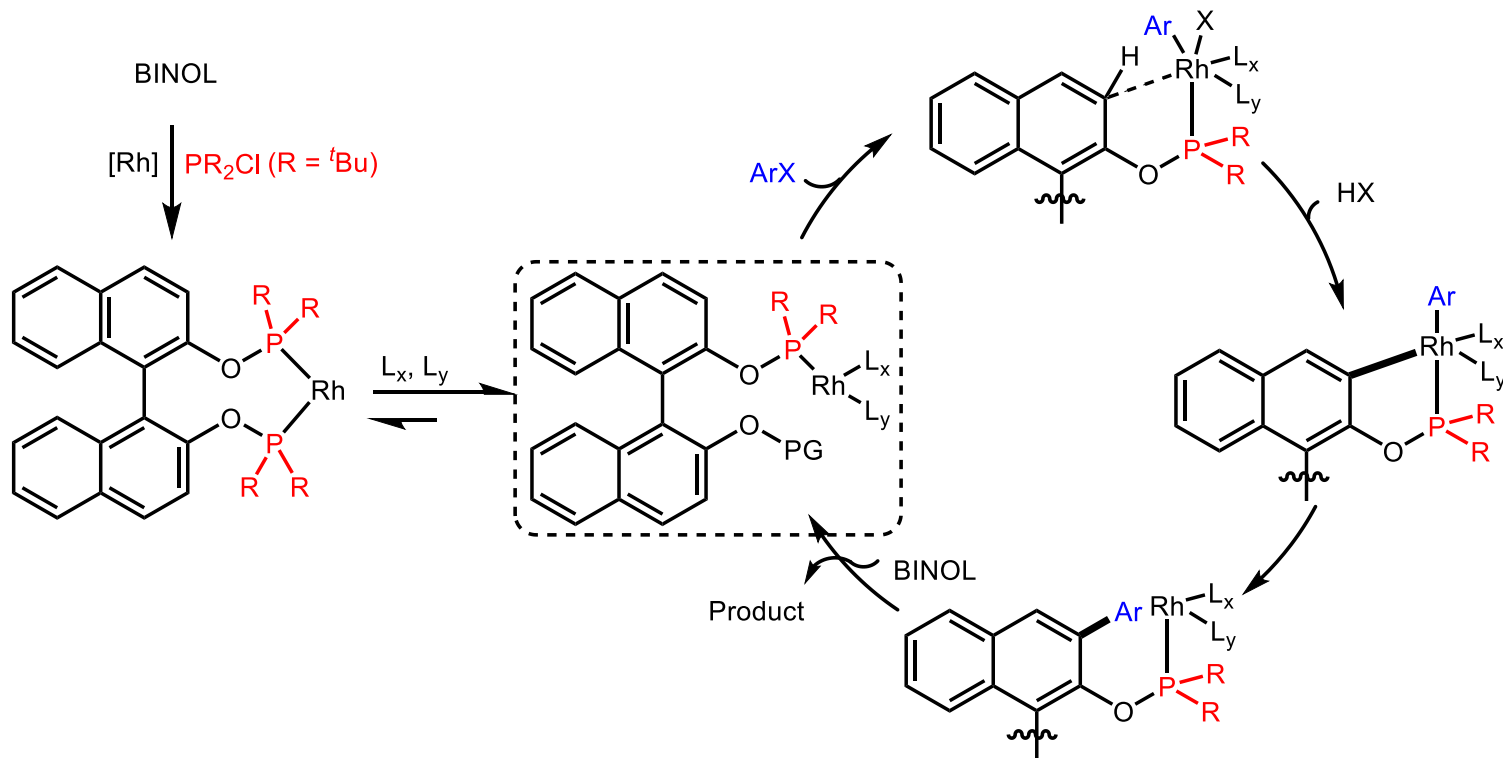
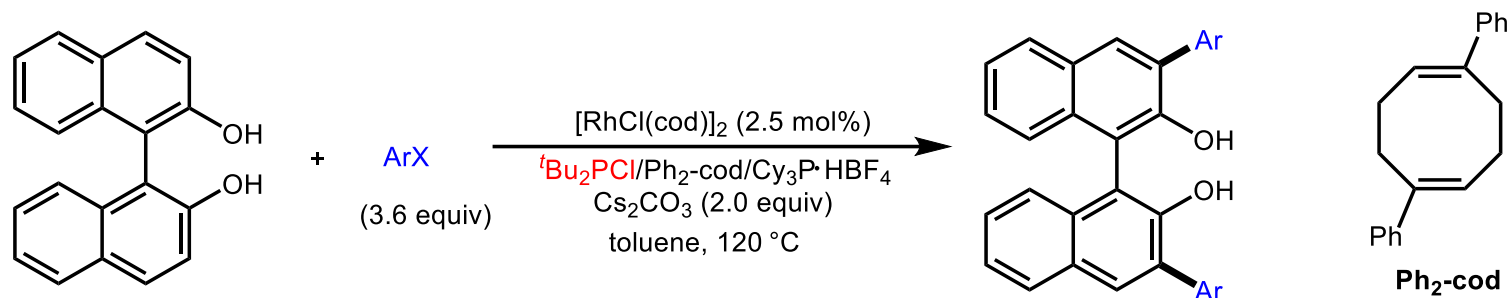
1.2 P-accelerated Direct C-H Functionalization

Early Examples



1.2 P-accelerated Direct C-H Functionalization

Recent Examples



Content

- Background

 - 1.1 Brief introduction of phosphine-directed C–H functionalization

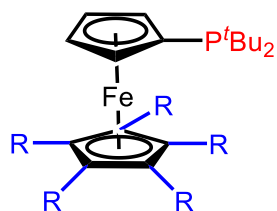
 - 1.2 Previous works (P-accelerated direct C–H functionalization)

- **Recent achievement in phosphine-directed C–H functionalization**

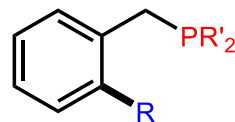
- Summary

2. Phosphine-directed C-H Functionalization

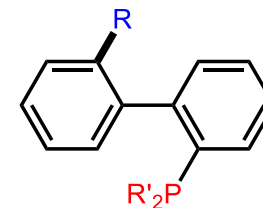
The Main Skeletons of Recent Research



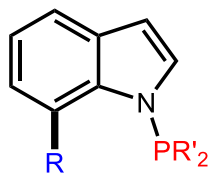
R = Ph Hartwig *JACS* 2000



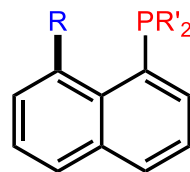
R = B Clark *ACIE* 2014



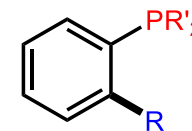
R = Ar Shi *ACIE* 2017
Zeng *OL* 2019
R = Si Shi *ACIE* 2018
R = Alkyl Shi *Nat. Commun.* 2018
Soule *ACIE* 2018



R = Alkyl Shi *JACS* 2017
R = Ar Shi *Sci. Adv.* 2017



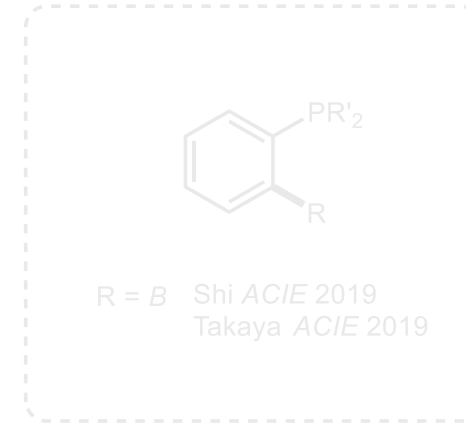
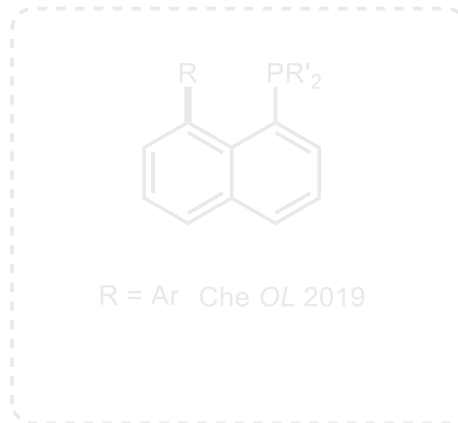
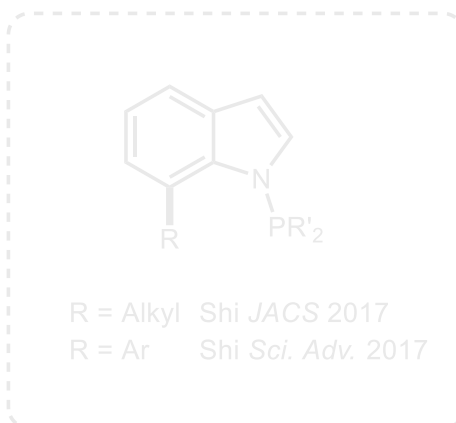
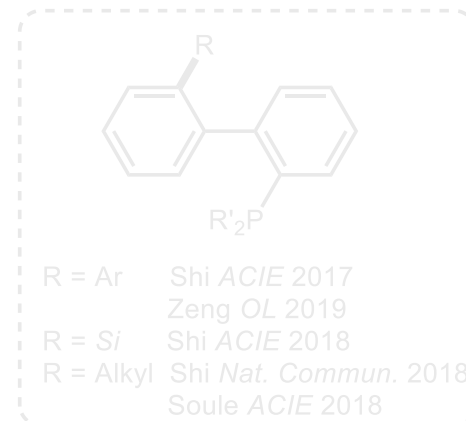
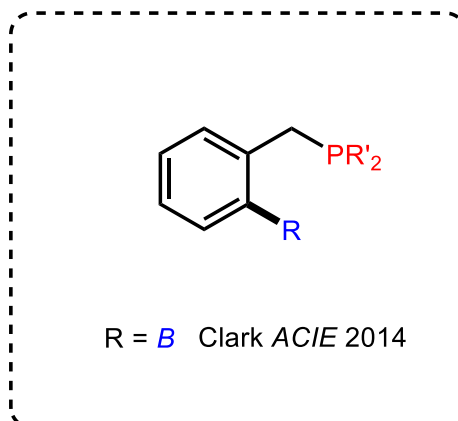
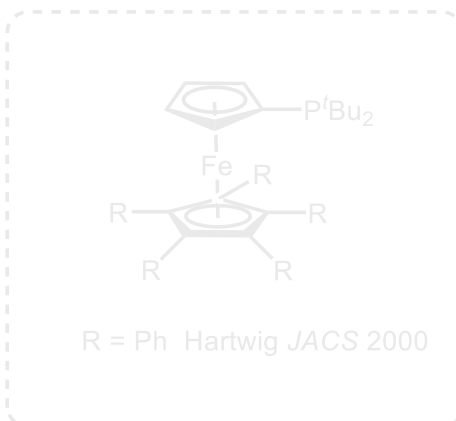
R = Ar Che *OL* 2019



R = B Shi *ACIE* 2019
Takaya *ACIE* 2019

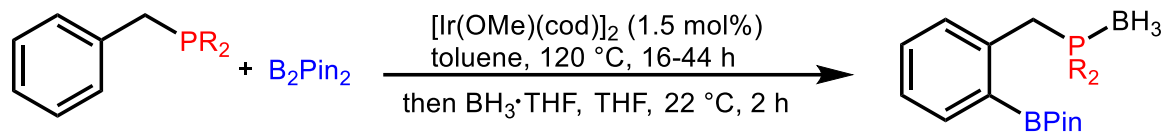
2. Phosphine-directed C-H Functionalization

The Main Skeletons of Recent Research



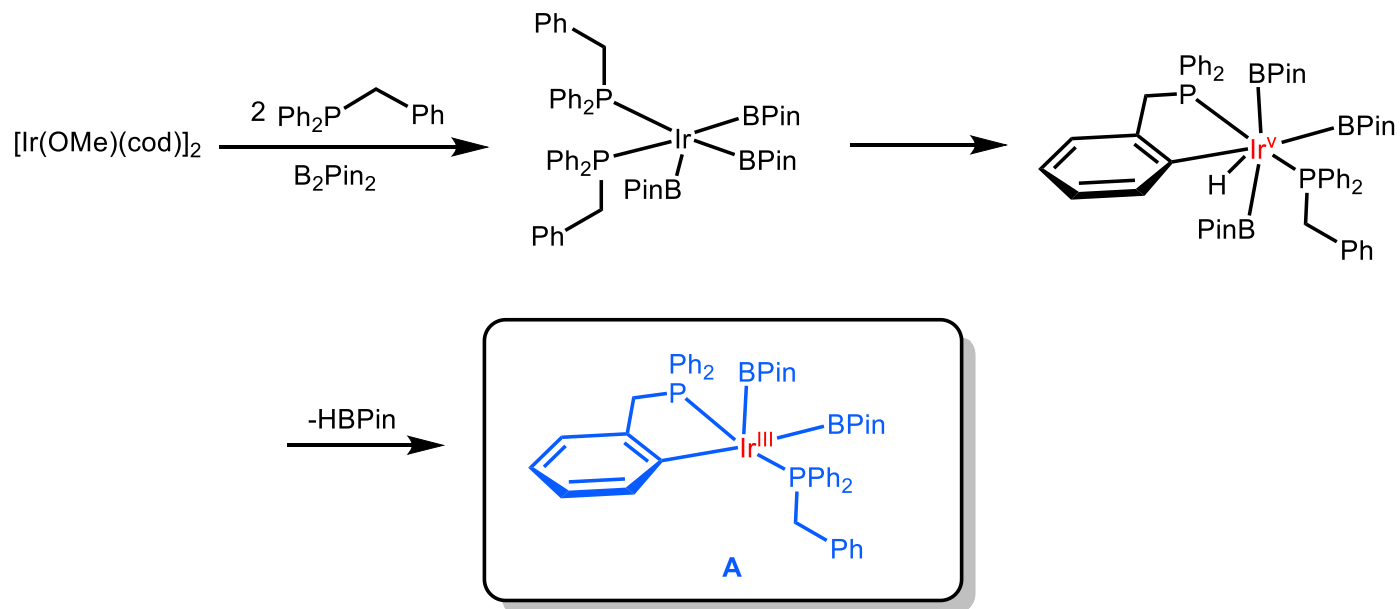
2. Phosphine-directed C-H Functionalization

First Example of Phosphine-directed C-H Borylation



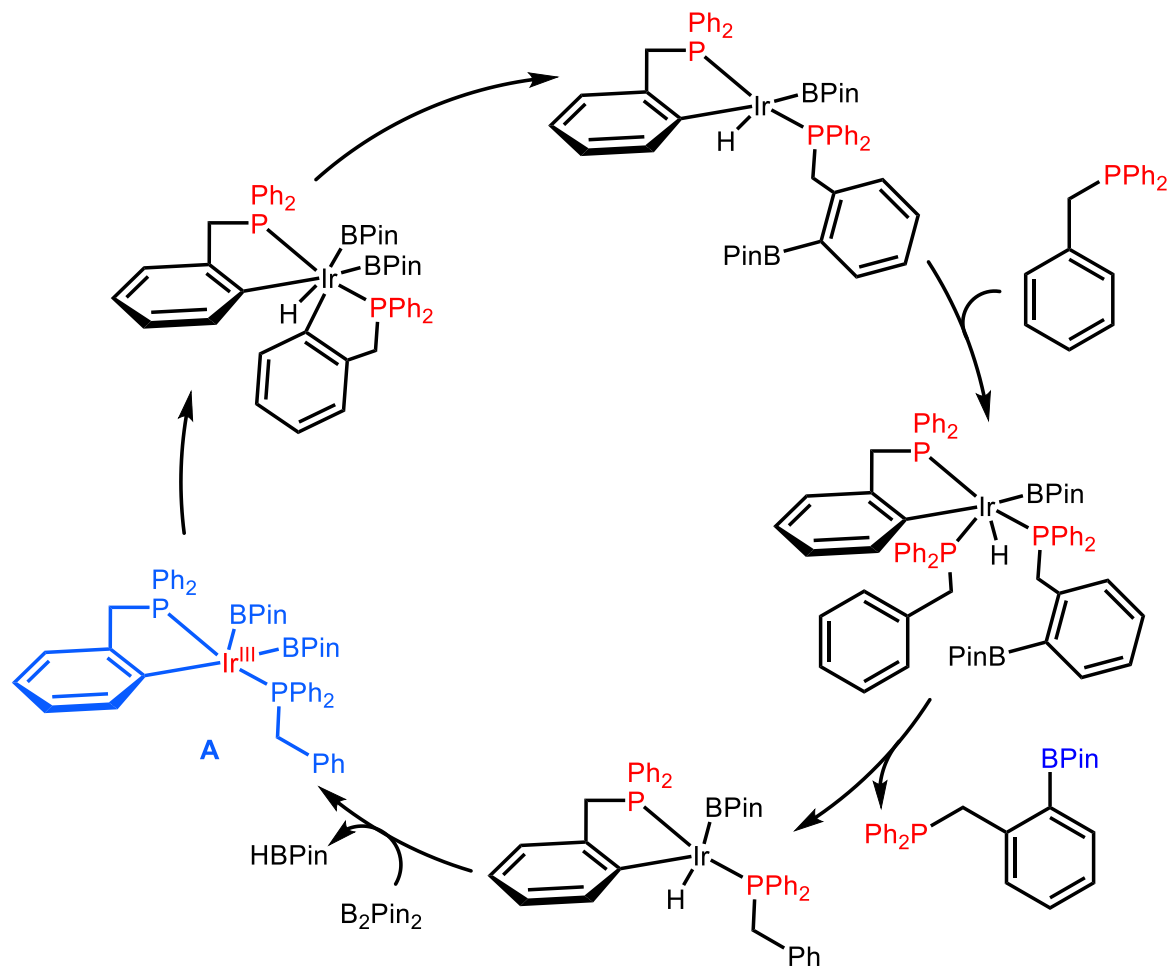
R = Ph
R = Cy
R = Ad

R = Ph, 75%
R = Cy, 51%
R = Ad, 66%



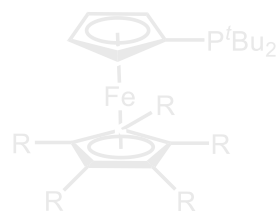
2. Phosphine-directed C-H Functionalization

Proposed Mechanism

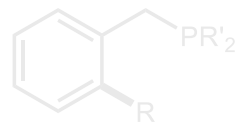


2. Phosphine-directed C-H Functionalization

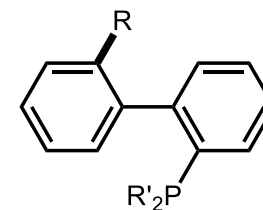
The Main Skeletons of Recent Research



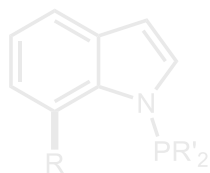
R = Ph Hartwig *JACS* 2000



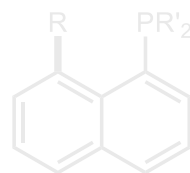
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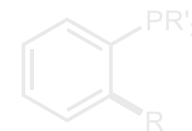
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R = Ar Shi *Sci. Adv.* 2017



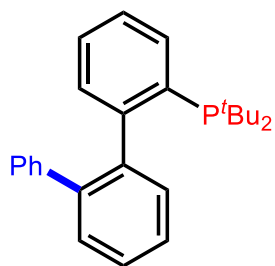
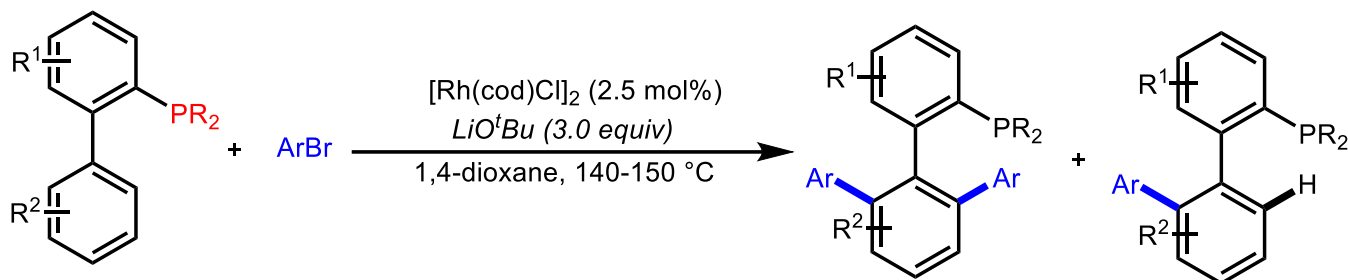
R = Ar Che *OL* 2019



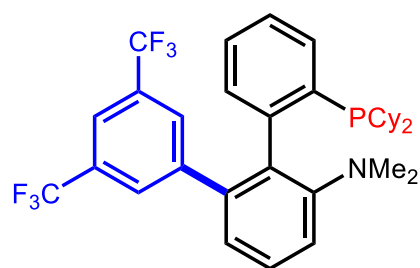
R = B Shi *ACIE* 2019
Takaya *ACIE* 2019

2. Phosphine-directed C-H Functionalization

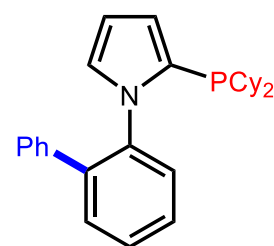
Phosphine-directed C-H Arylation



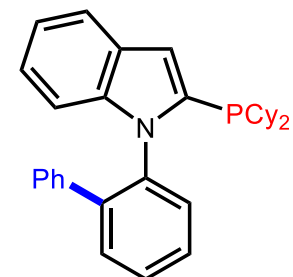
71%



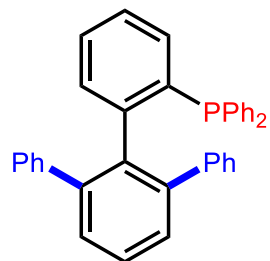
83%



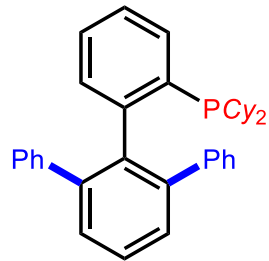
86%



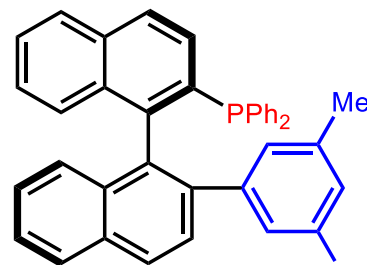
80%



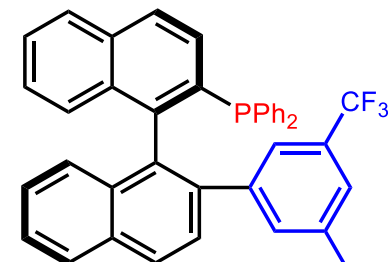
86%



94%



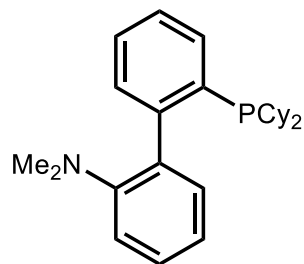
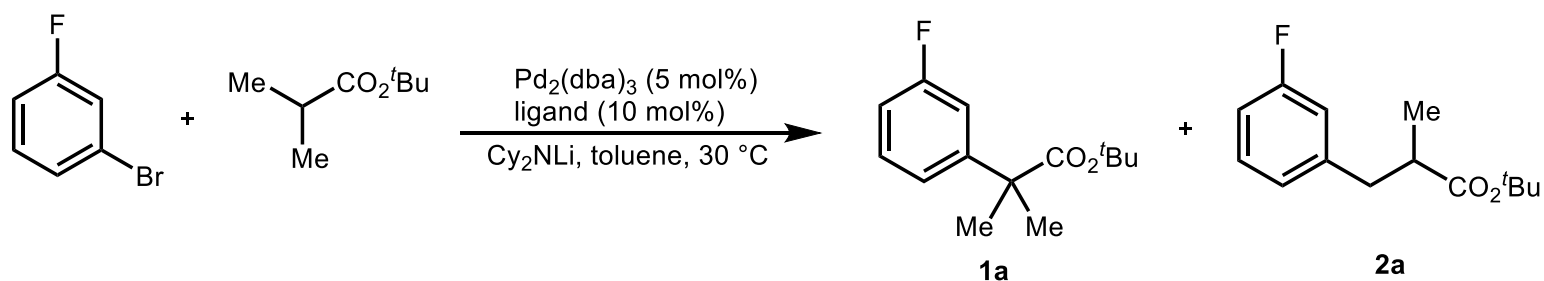
47%



58%

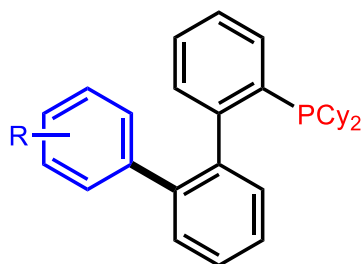
2. Phosphine-directed C-H Functionalization

Application of New Type of Ligands



Davephos

1a/2a = 47:53 (95%)



Better Regioselectivity

R = H, **1a/2a** = 42:58 (88%)

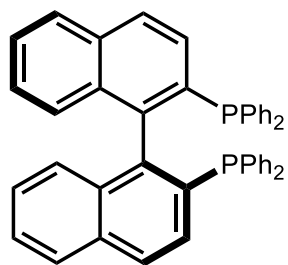
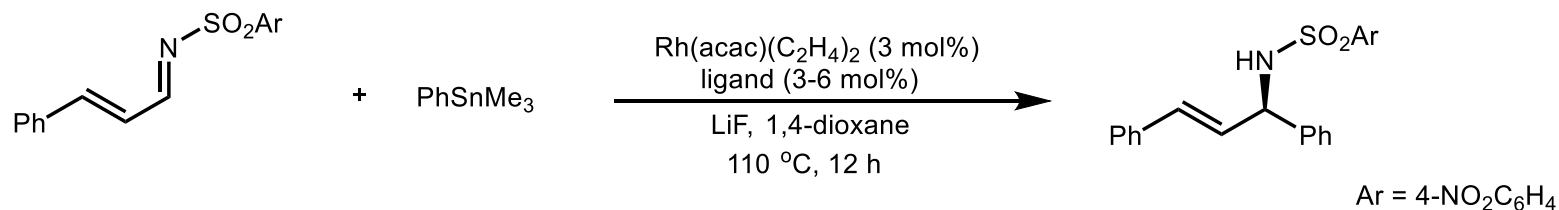
R = 4-OMe, **1a/2a** = 39:61 (83%)

R = 4-NMe₂, **1a/2a** = 37:63 (86%)

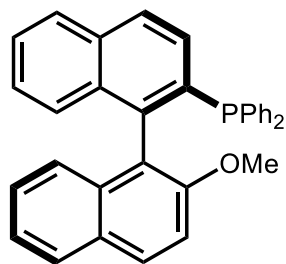
R = 3,5-(OMe)₂, **1a/2a** = 29:71 (76%)

2. Phosphine-directed C-H Functionalization

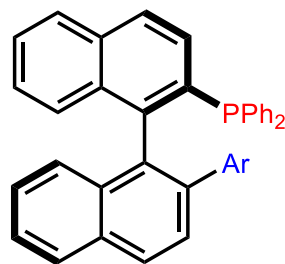
Application of New Type of Ligands



(S)-BINAP
trace



(R)-MeO-MOP
75%, 88% ee



(R)-Ar'-MOP

Ar = Ph, 74%, 92% ee

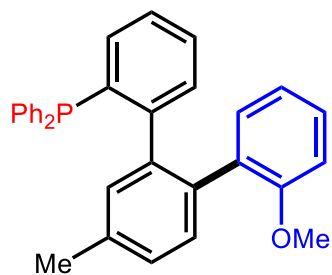
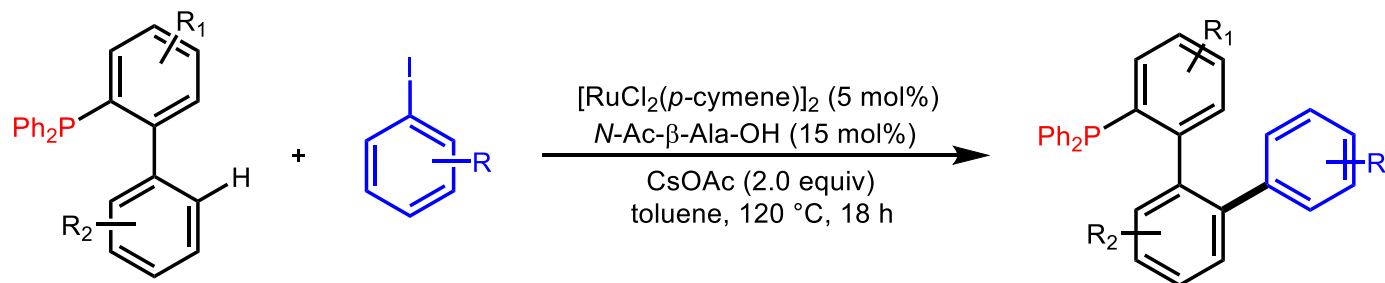
Ar = 4-OMeC₆H₄, 78%, 95% ee

Ar = 3,5-(OMe)₂C₆H₃, 76%, 98% ee

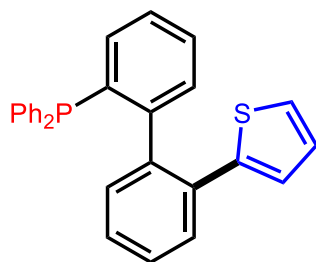
Better Stereoselectivity

2. Phosphine-directed C-H Functionalization

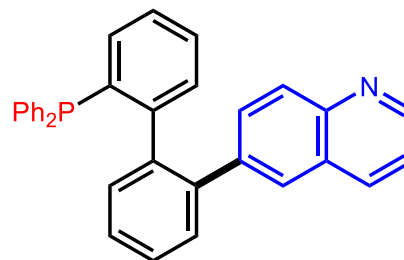
Phosphine-directed C-H Arylation



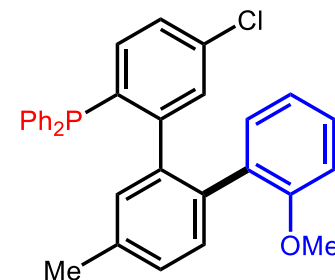
64%



50%



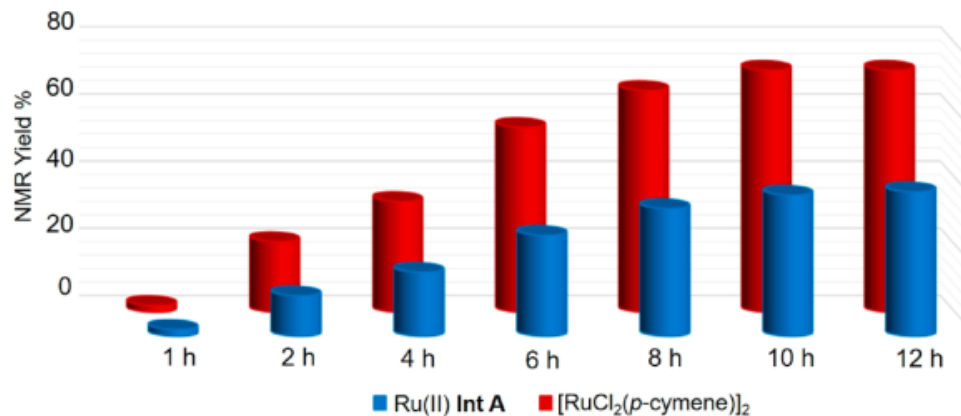
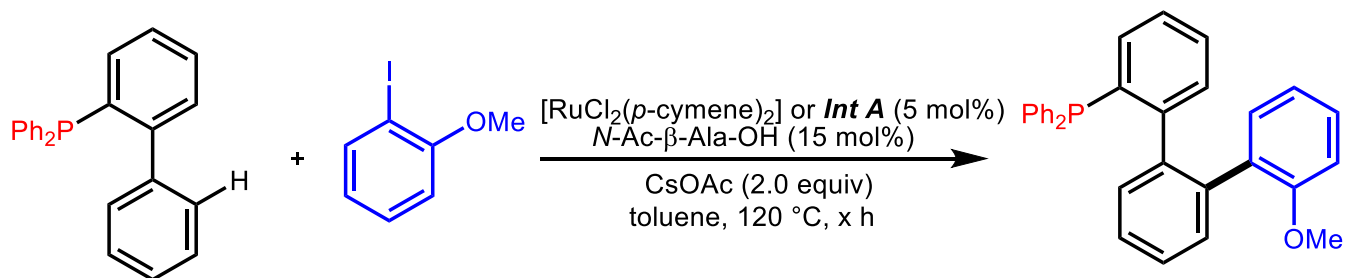
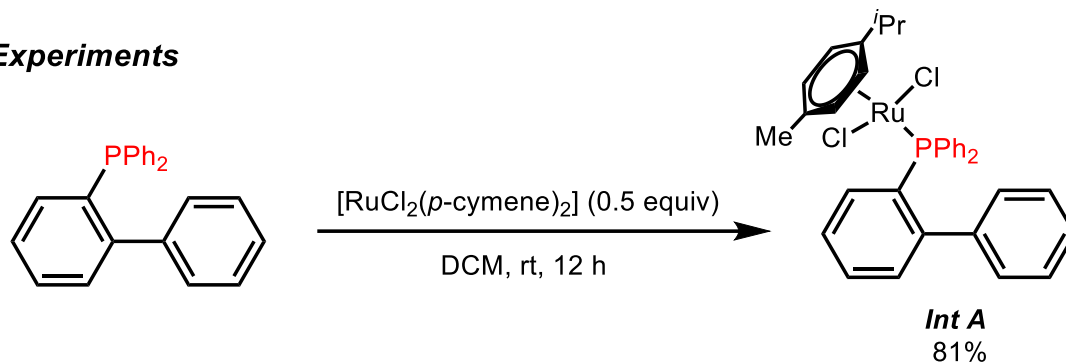
54%



88%

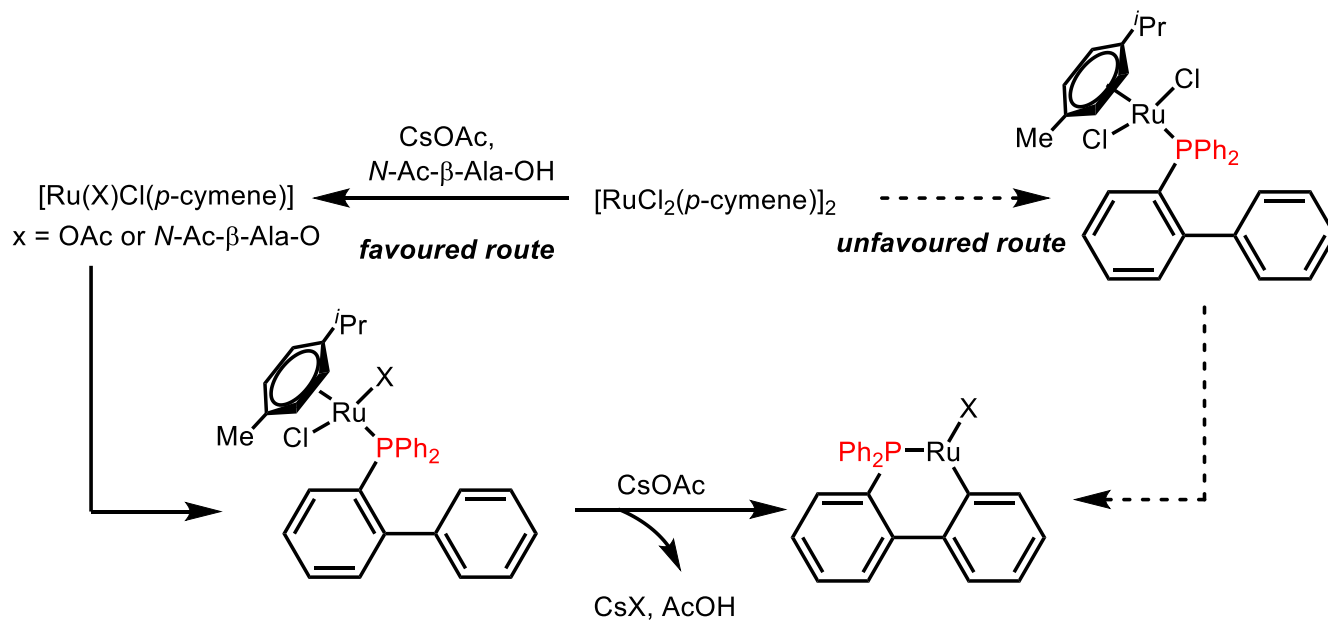
2. Phosphine-directed C-H Functionalization

Mechanistic Experiments



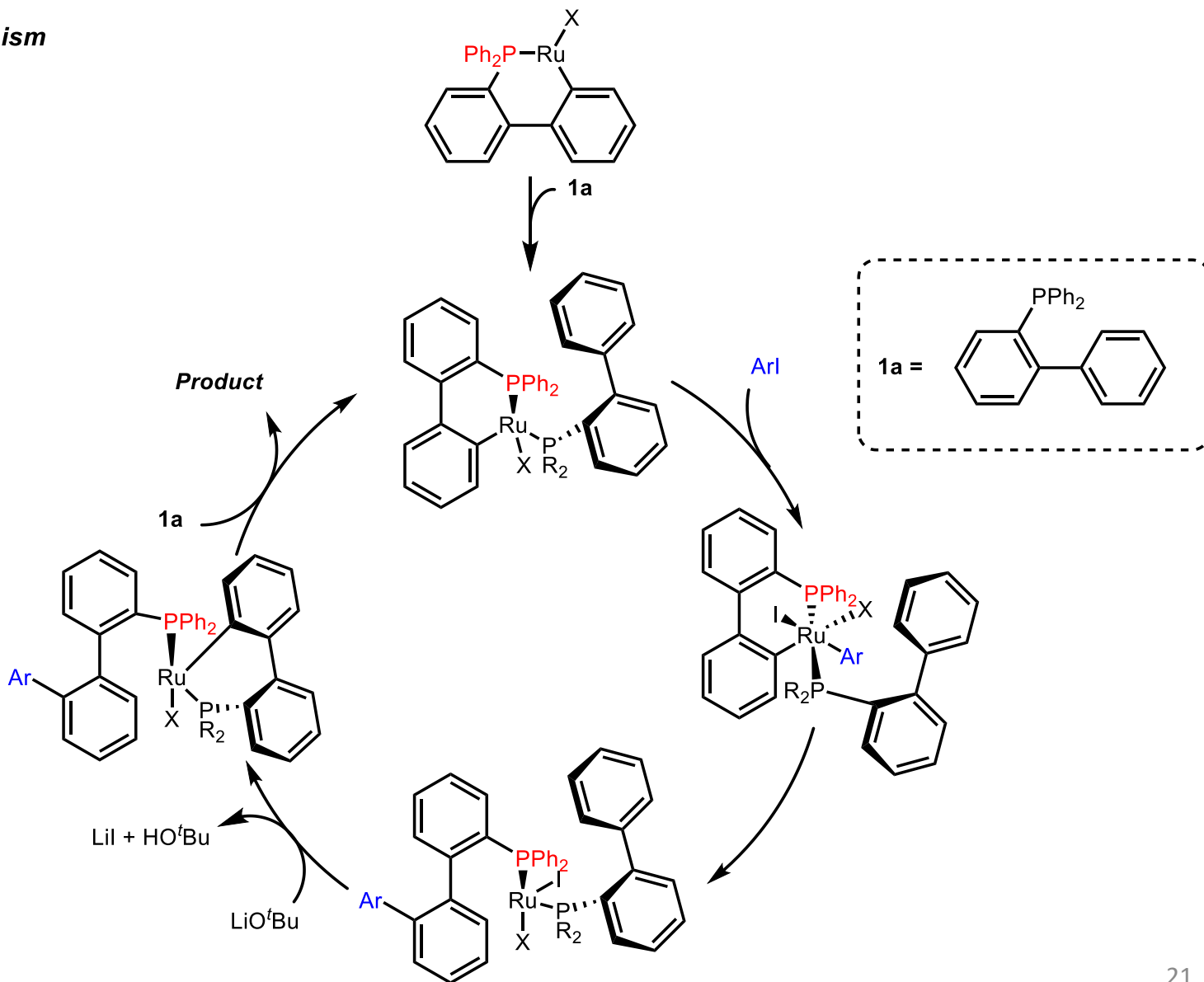
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Mechanistic Experiments



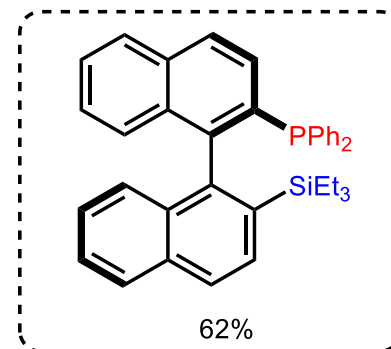
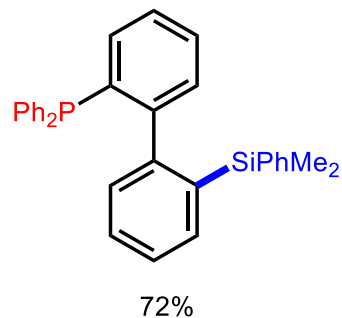
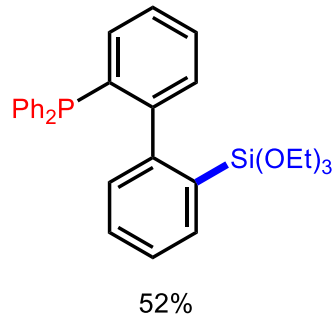
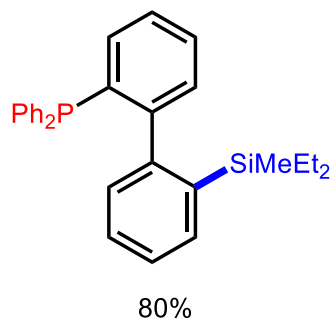
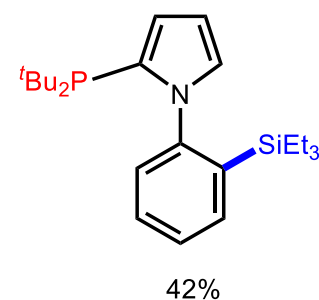
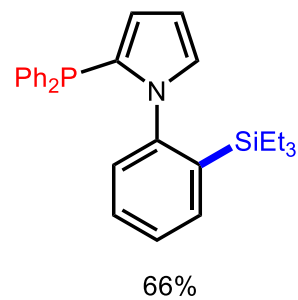
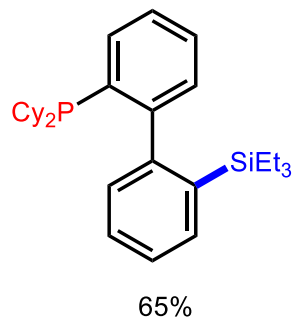
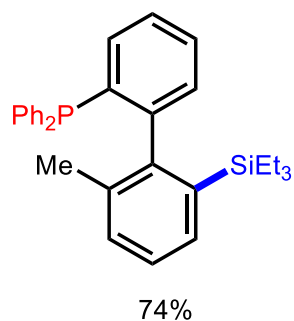
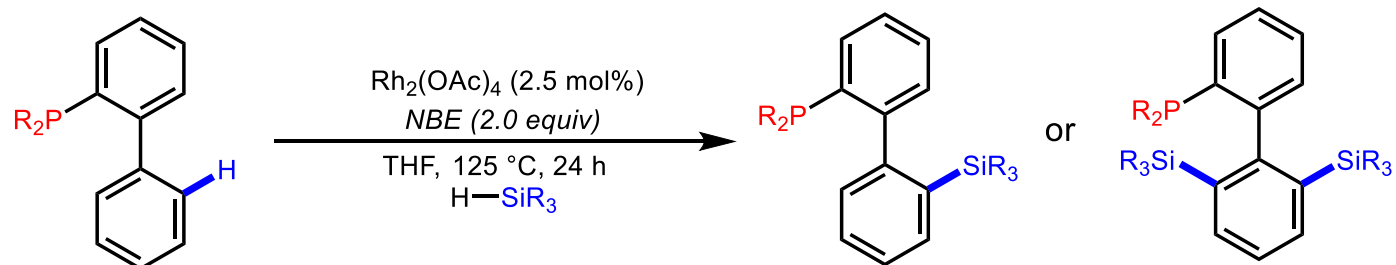
2. Phosphine-directed C-H Functionalization

Proposed Mechanism



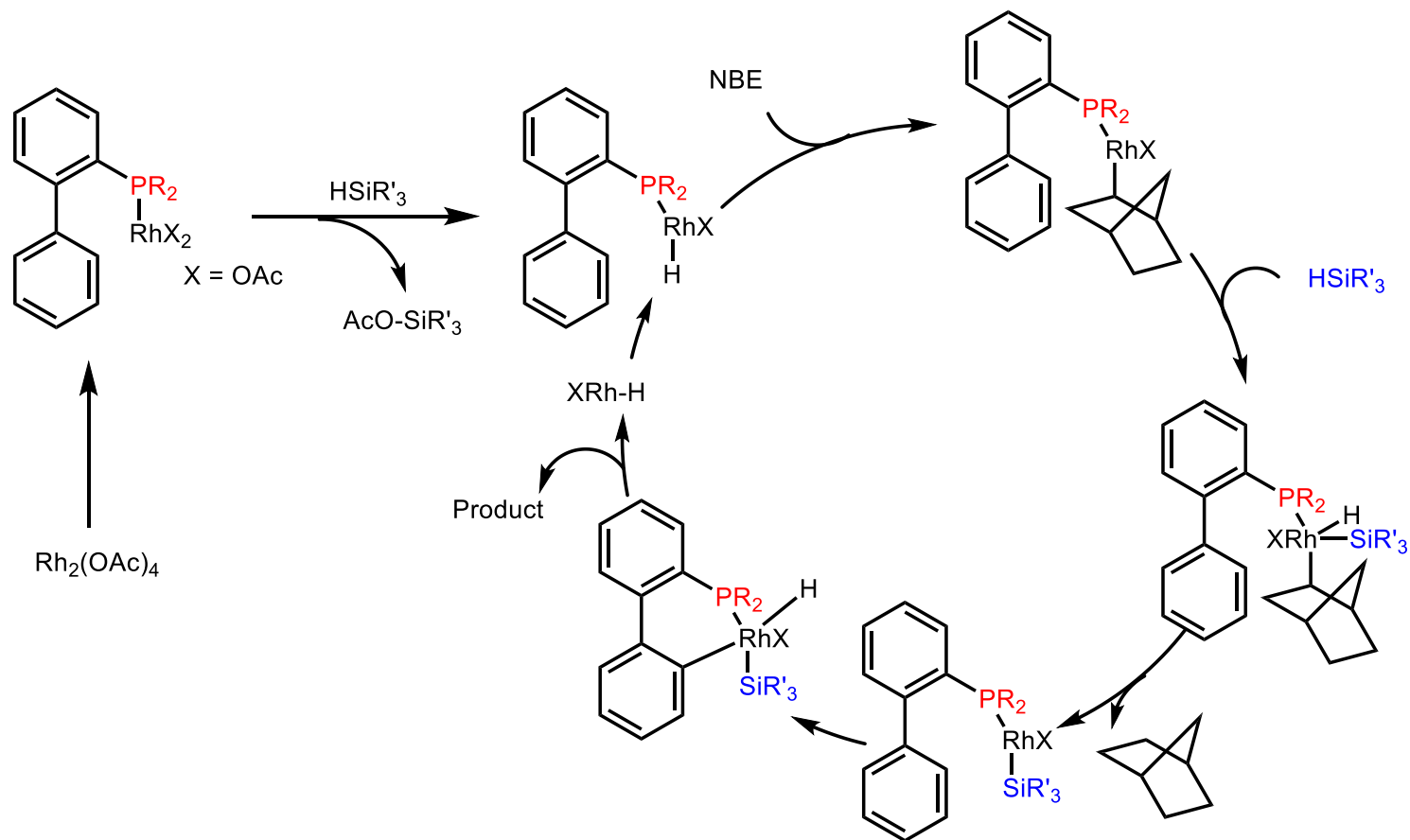
2. Phosphine-directed C-H Functionalization

Phosphine-directed C-H Silylation



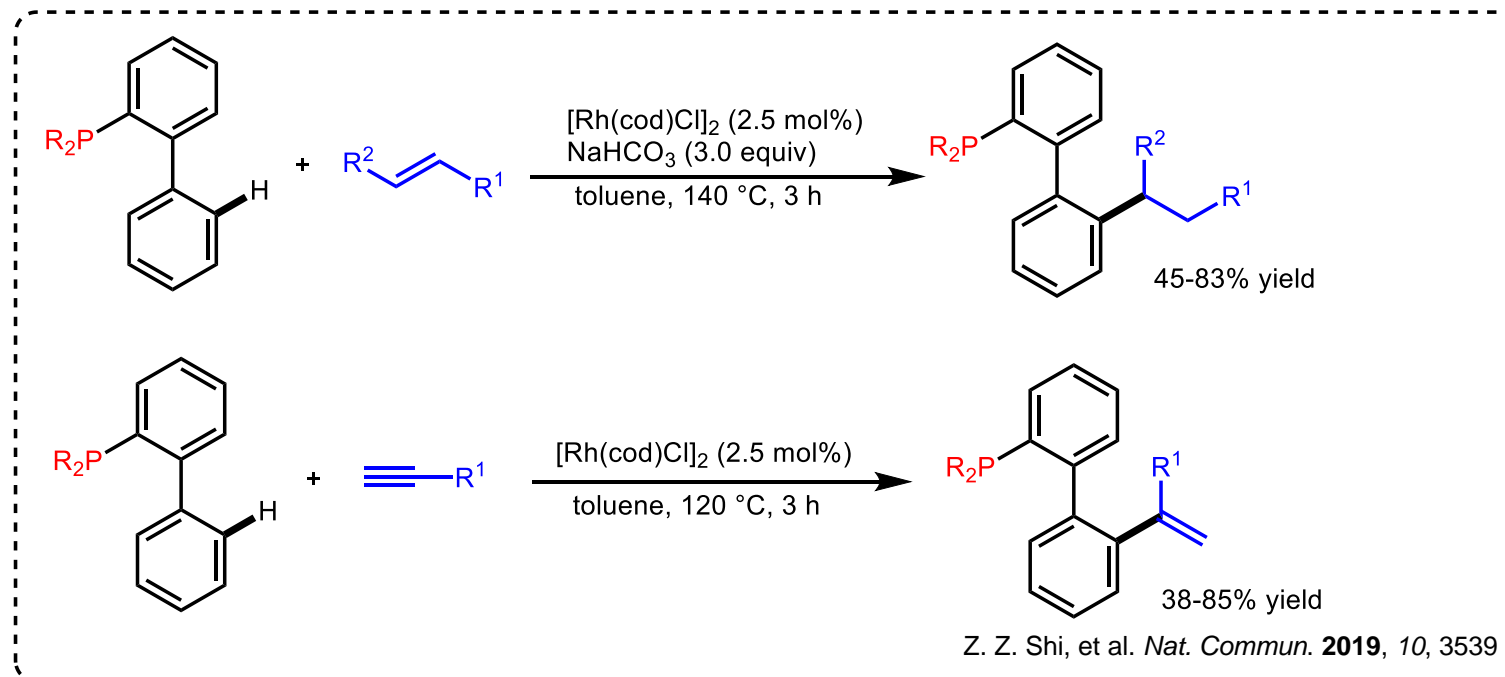
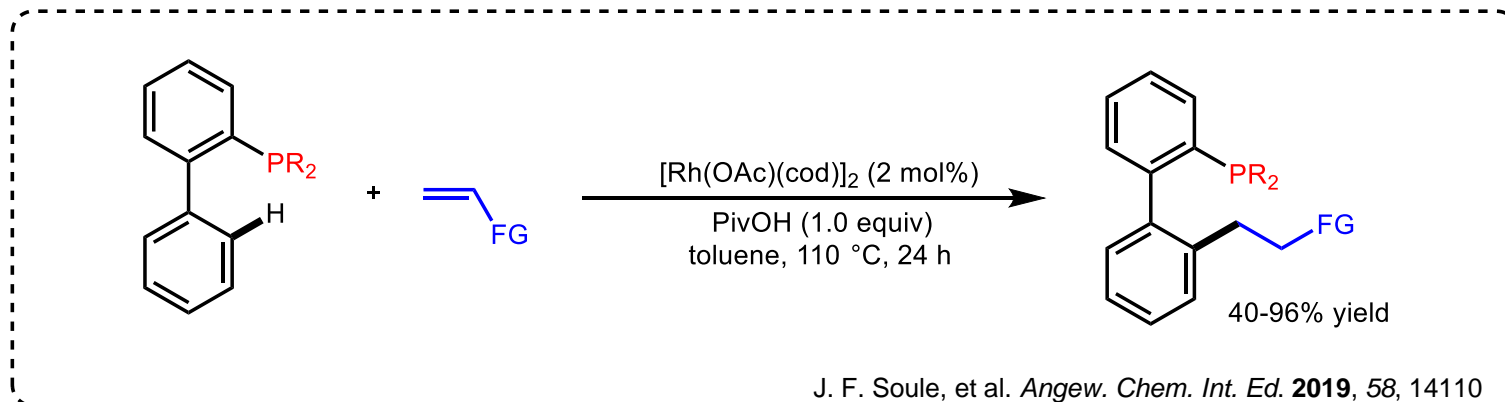
2. Phosphine-directed C-H Functionalization

Proposed Mechanism



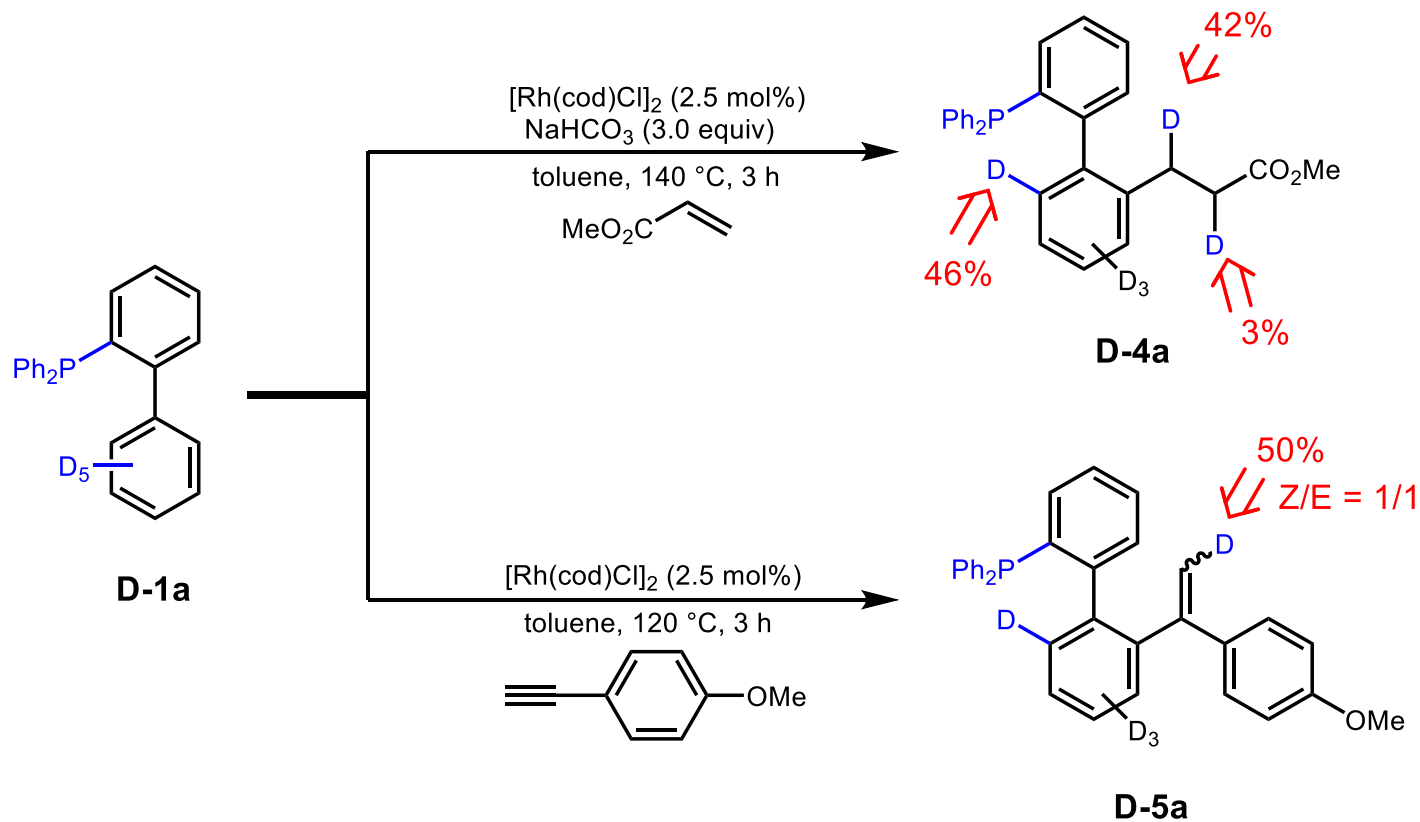
2. Phosphine-directed C-H Functionalization

Phosphine-directed C-H Alkylation



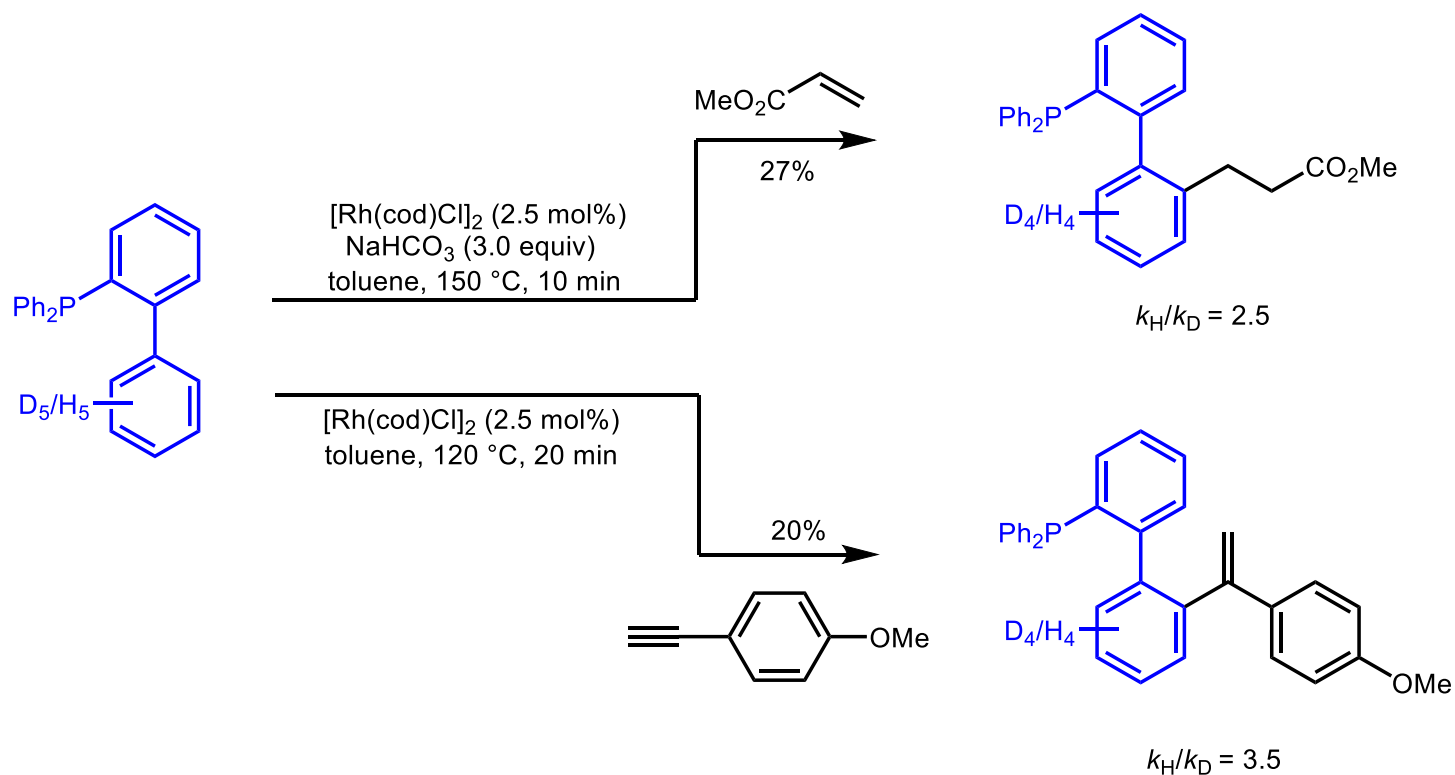
2. Phosphine-directed C-H Functionalization

Mechanistic Experiments



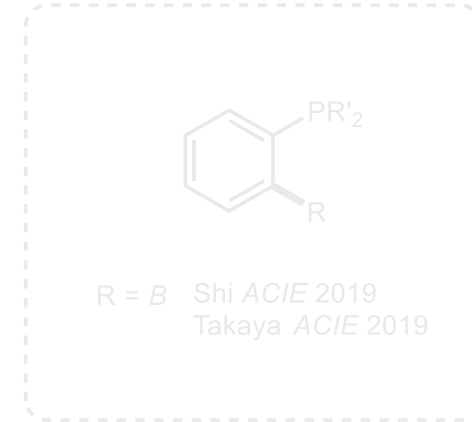
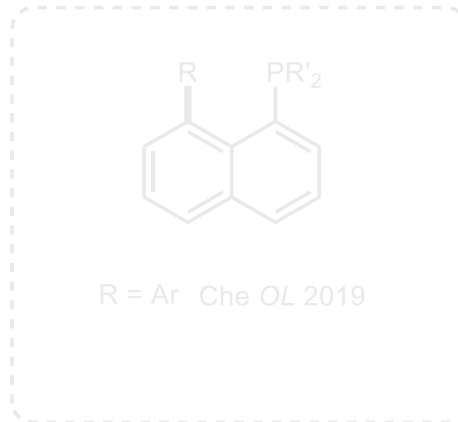
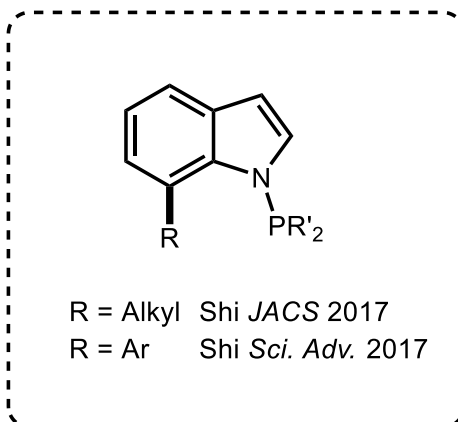
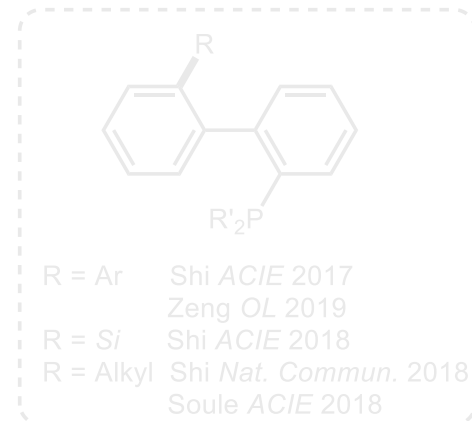
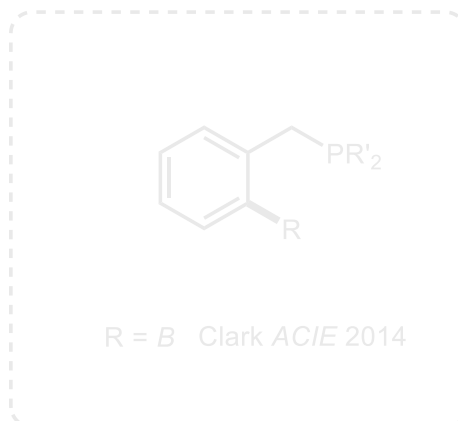
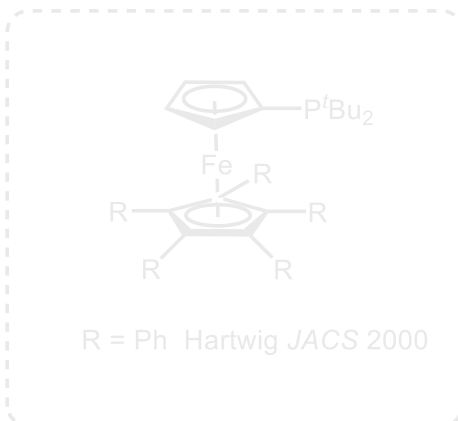
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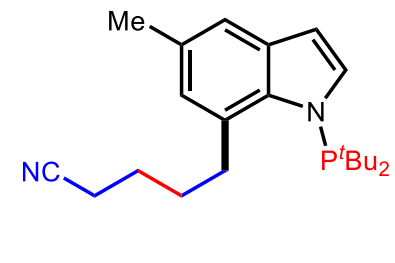
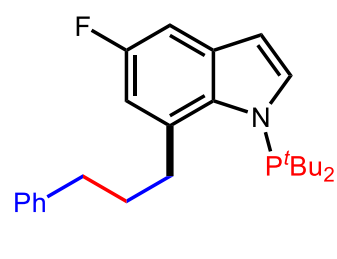
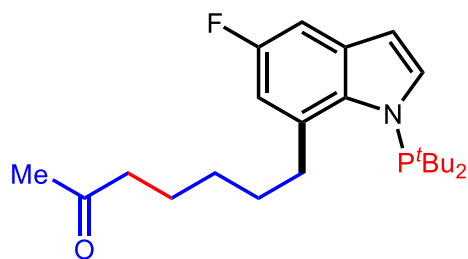
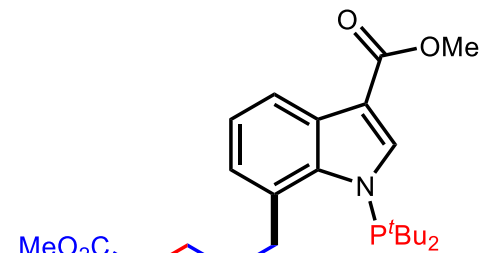
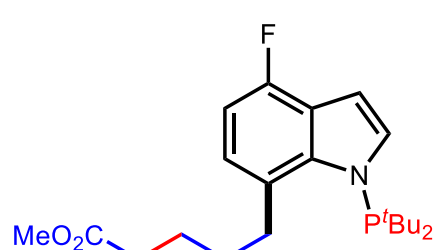
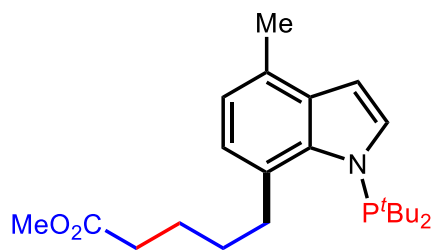
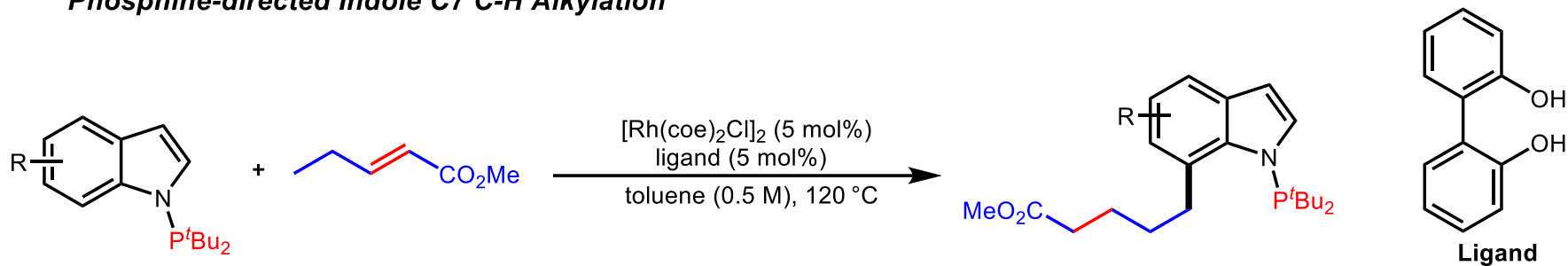
2. Phosphine-directed C-H Functionalization

The Main Skeletons of Recent Research



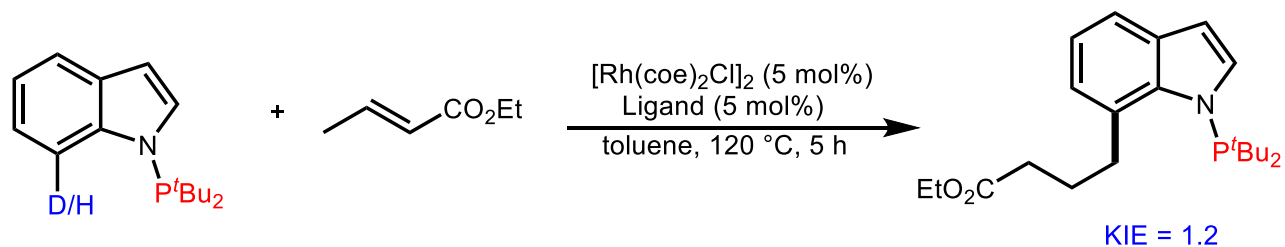
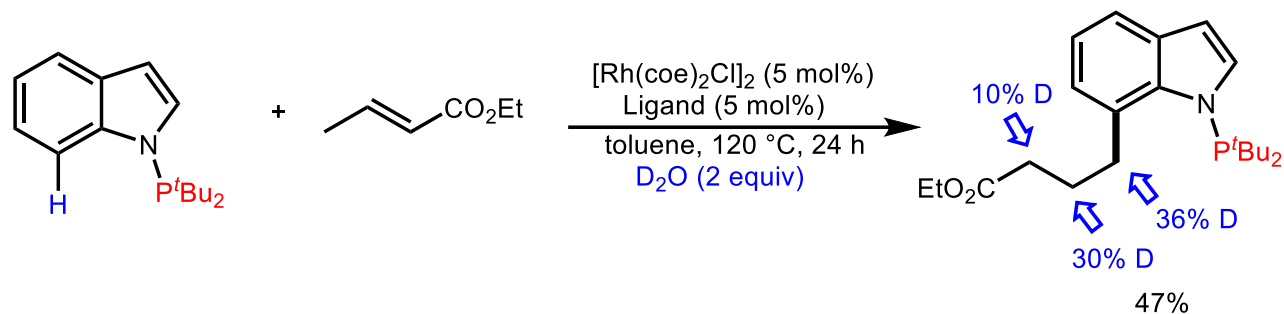
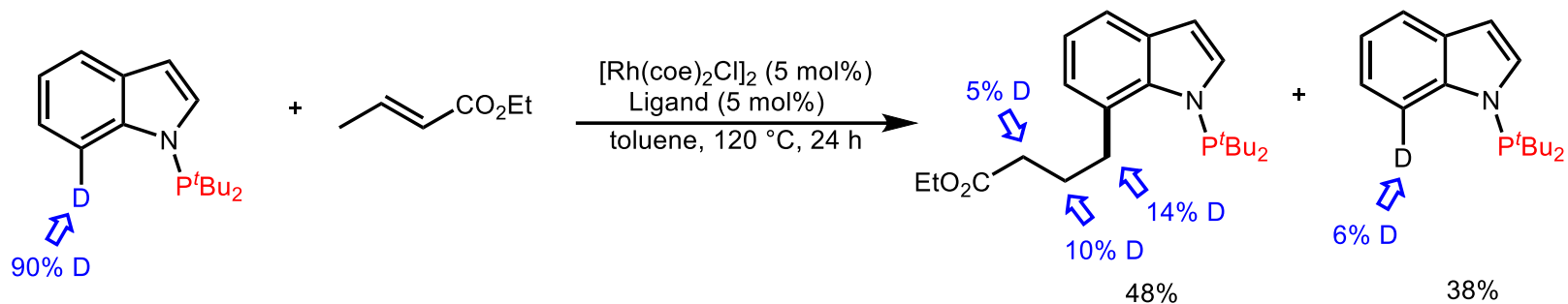
2. Phosphine-directed C-H Functionalization

Phosphine-directed Indole C7 C-H Alkylation



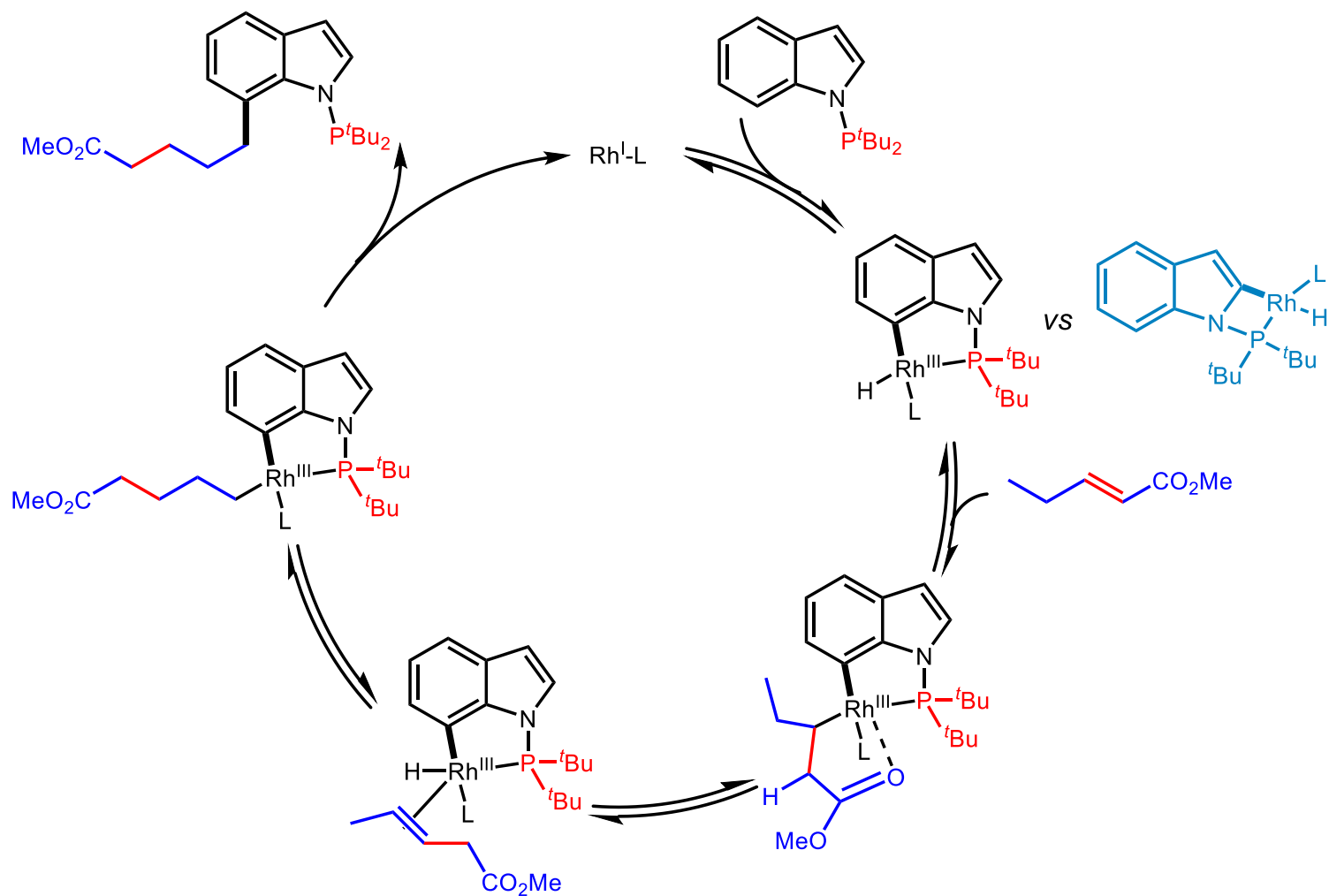
2. Phosphine-directed C-H Functionalization

Mechanistic Experiments



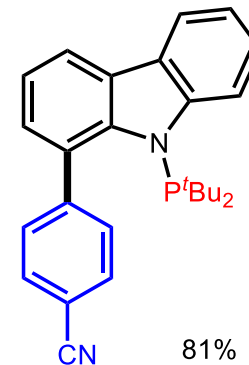
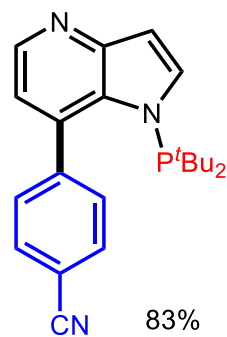
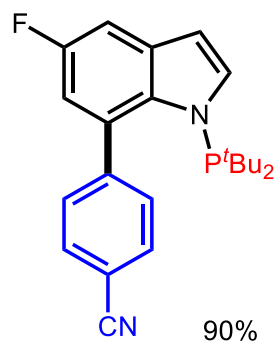
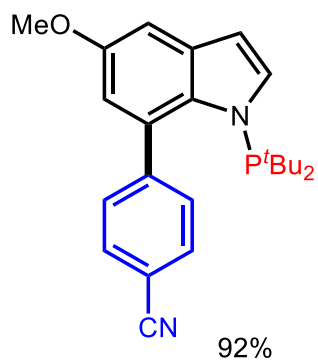
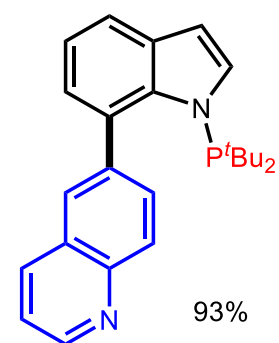
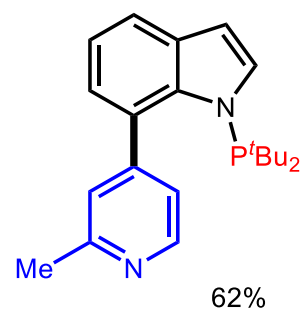
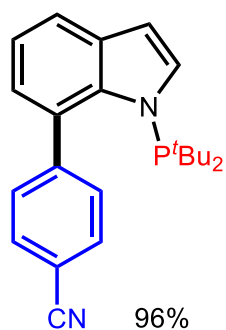
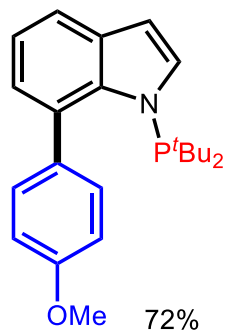
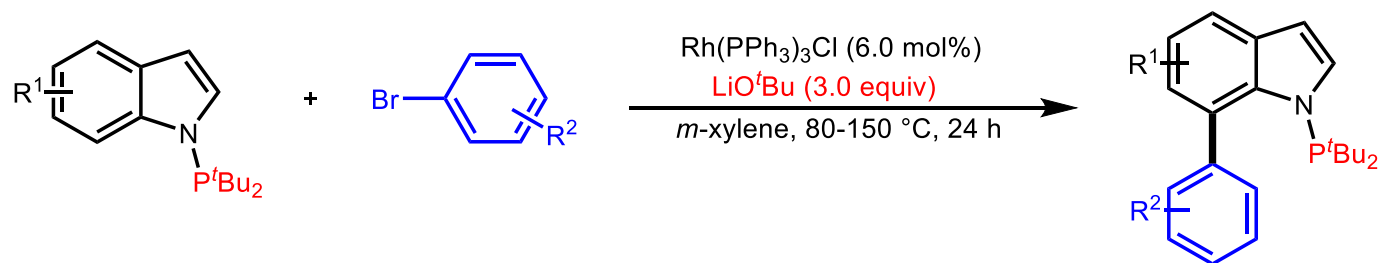
2. Phosphine-directed C-H Functionalization

Proposed Catalytic Cycle



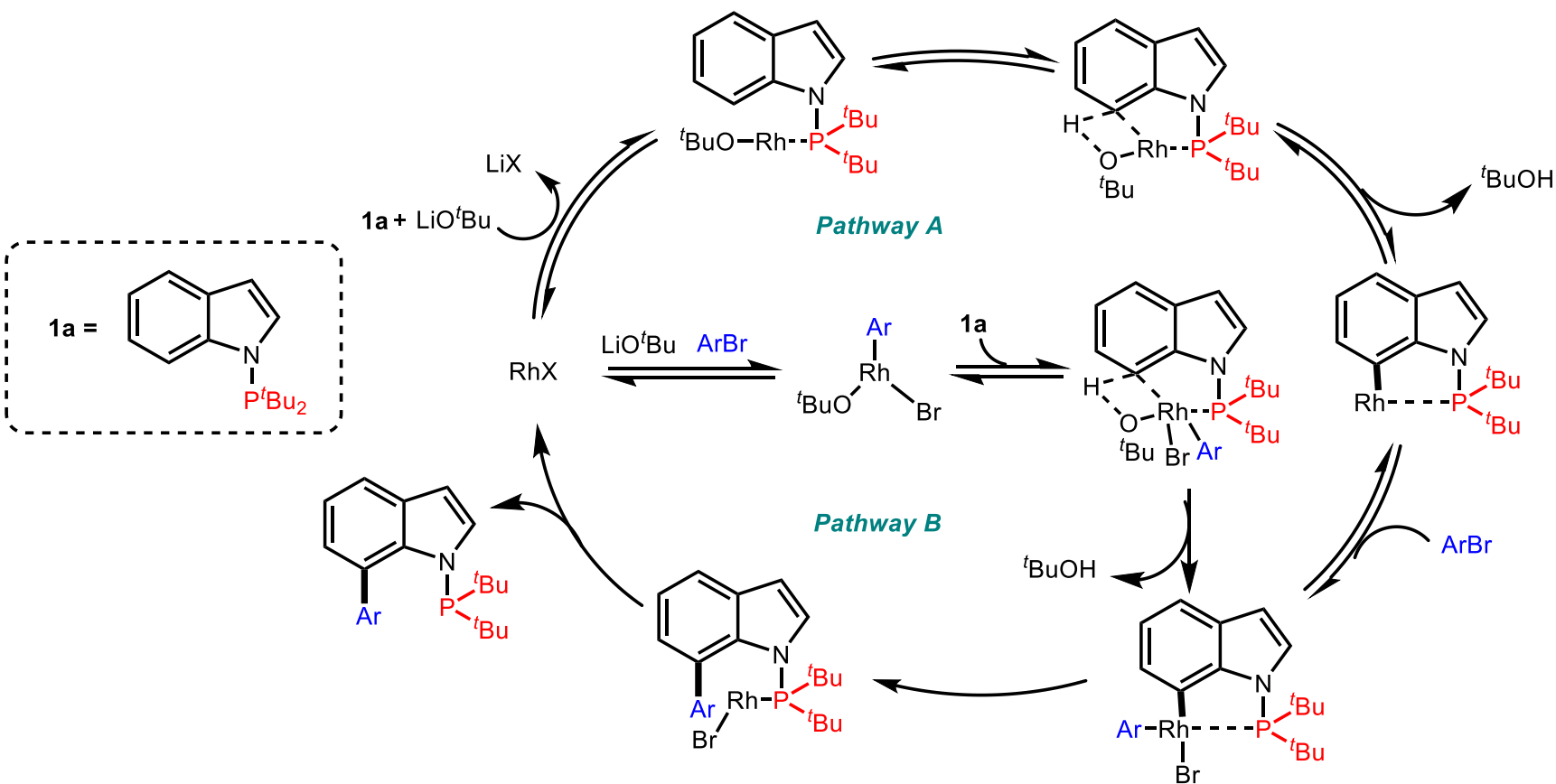
2. Phosphine-directed C-H Functionalization

Phosphine-directed Indole C7 Arylation



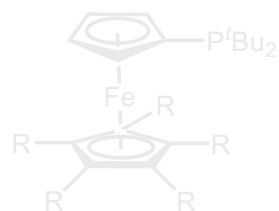
2. Phosphine-directed C-H Functionalization

Proposed Catalytic Cycle

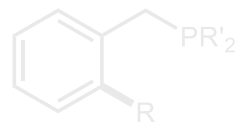


2. Phosphine-directed C-H Functionalization

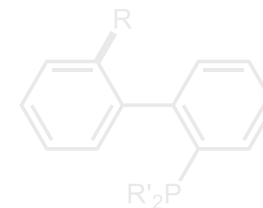
The Main Skeletons of Recent Research



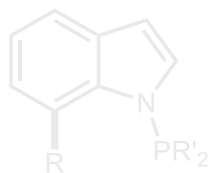
$R = Ph$ Hartwig *JACS* 2000



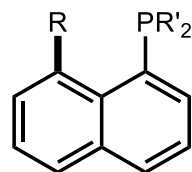
$R = B$ Clark *ACIE* 2014



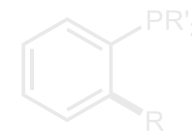
$R = Ar$ Shi *ACIE* 2017
Zeng *OL* 2019
 $R = Si$ Shi *ACIE* 2018
 $R = Alkyl$ Shi *Nat. Commun.* 2018
Soule *ACIE* 2018



$R = Alkyl$ Shi *JACS* 2017
 $R = Ar$ Shi *Sci. Adv.* 2017



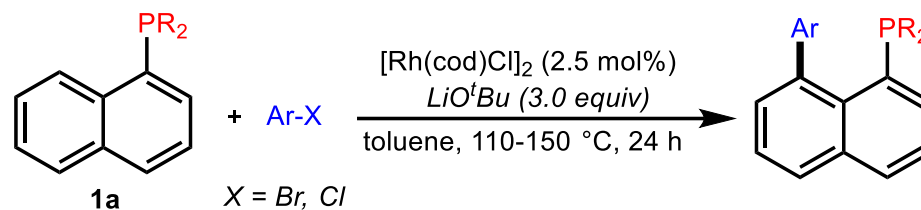
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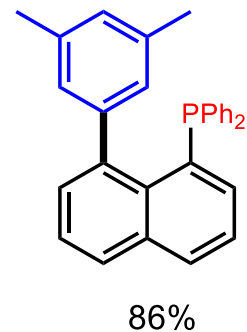
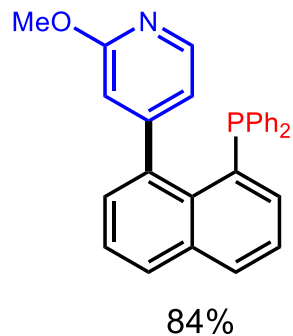
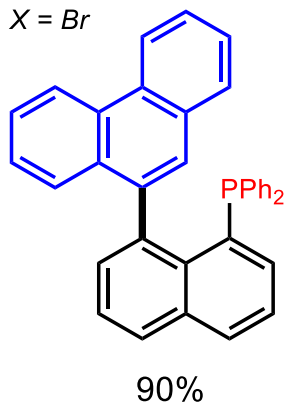
$R = B$ Shi *ACIE* 2019
Takaya *ACIE* 2019

2. Phosphine-directed C-H Functionalization

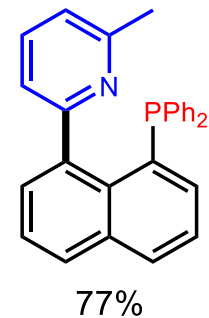
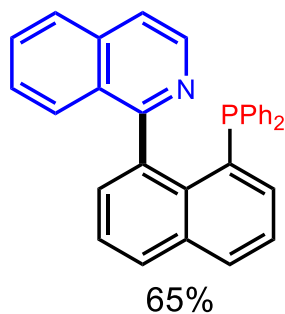
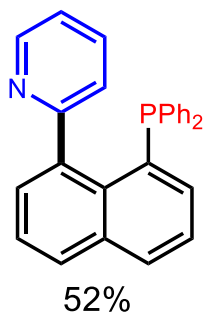
Phosphine-directed C-H Arylation



$X = \text{Br}$

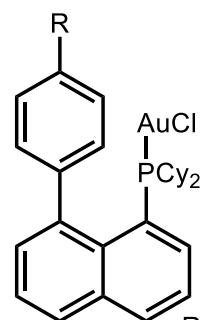
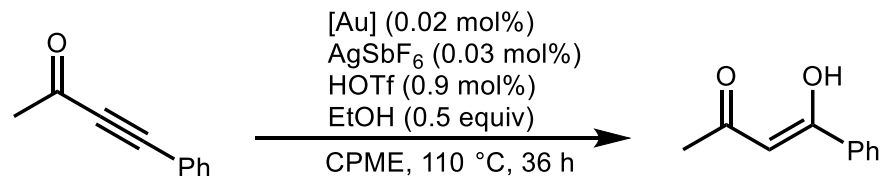


$X = \text{Cl}$

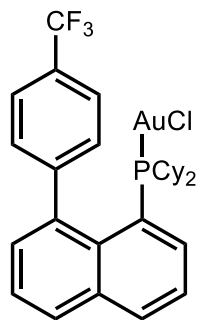


2. Phosphine-directed C-H Functionalization

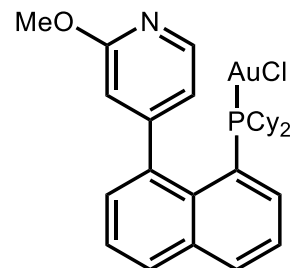
Application of New Type Ligands



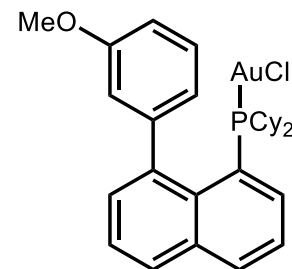
R = carbazole
conv. = 41%
ton = 2050



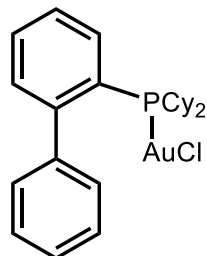
conv. = 54%
ton = 2700



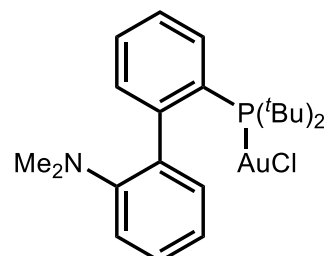
conv. = 56%
ton = 2800



conv. = 65%
ton = 3250



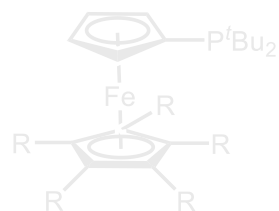
conv. = 34%
ton = 1700



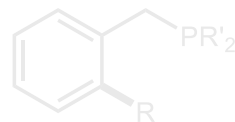
conv. = 44%
ton = 2200

2. Phosphine-directed C-H Functionalization

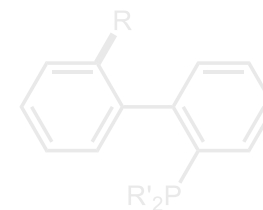
The Main Skeletons of Recent Research



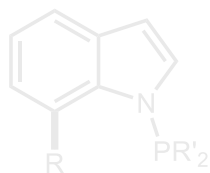
R = Ph Hartwig *JACS* 2000



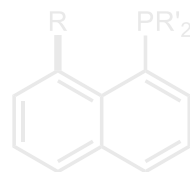
R = B Clark *ACIE* 2014



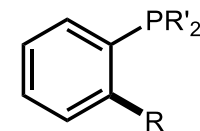
R = Ar Shi *ACIE* 2017
Zeng *OL* 2019
R = Si Shi *ACIE* 2018
R = Alkyl Shi *Nat. Commun.* 2018
Soule *ACIE* 2018



R = Alkyl Shi *JACS* 2017
R = Ar Shi *Sci. Adv.* 2017



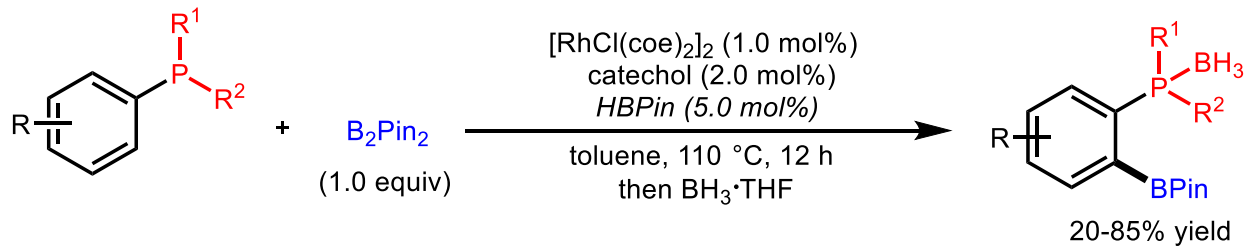
R = Ar Che *OL* 2019



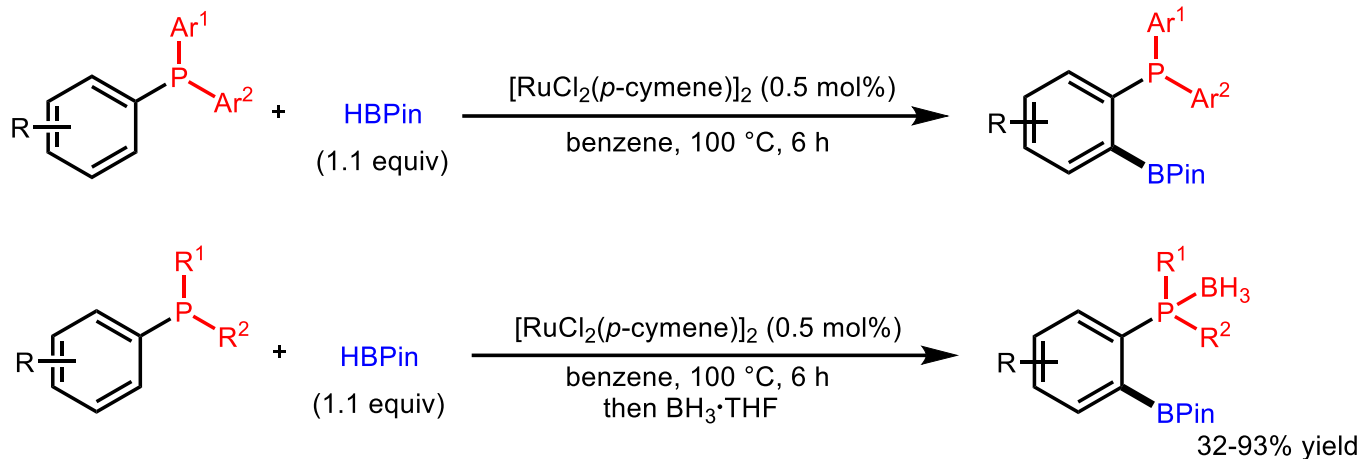
R = B Shi *ACIE* 2019
Takaya *ACIE* 2019

2. Phosphine-directed C-H Functionalization

Phosphine-directed C-H Borylation



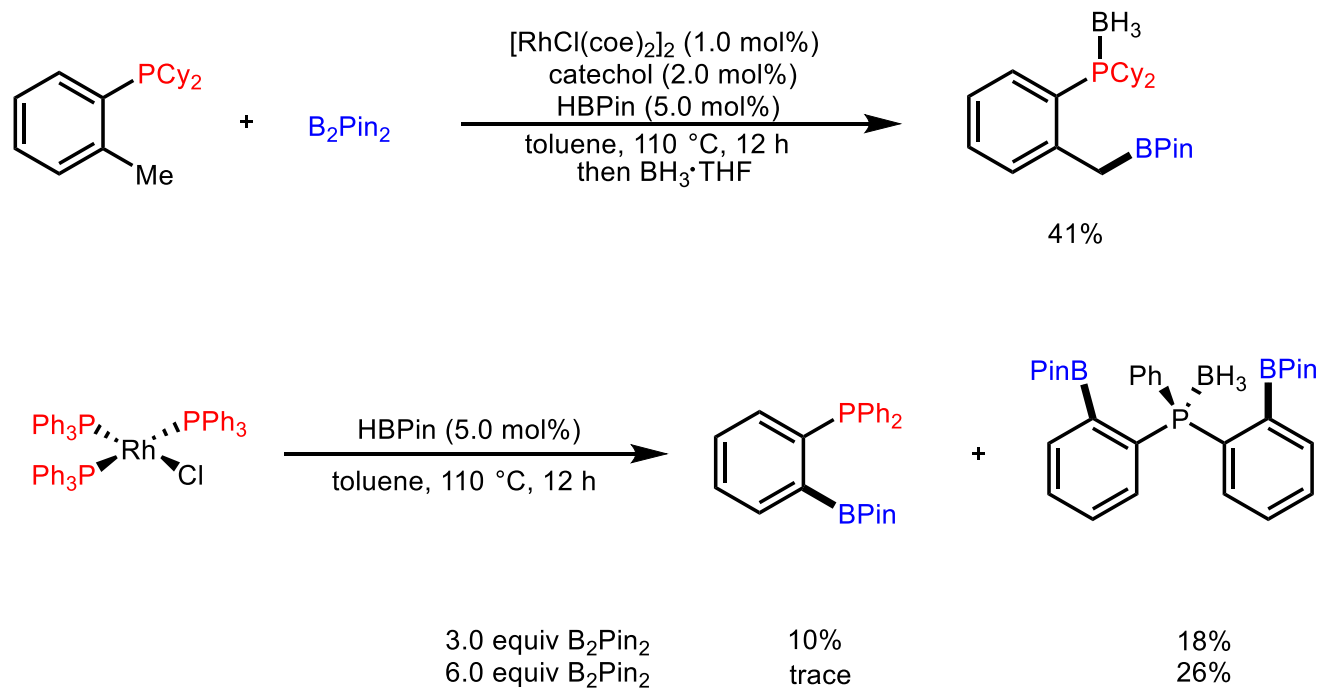
Z. Z. Shi, et al. *Angew. Chem. Int. Ed.* **2019**, 58, 2078



J. Takaya, et al. *Angew. Chem. Int. Ed.* **2019**, 58, 2850

2. Phosphine-directed C-H Functionalization

Phosphine-directed C-H Borylation



Content

- Background

 - 1.1 Brief introduction of phosphine-directed C–H functionalization

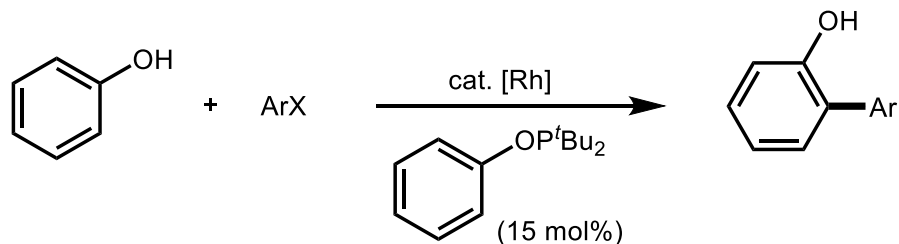
 - 1.2 Previous works (P-accelerated direct C–H functionalization)

- Recent achievement in phosphine-directed C–H functionalization

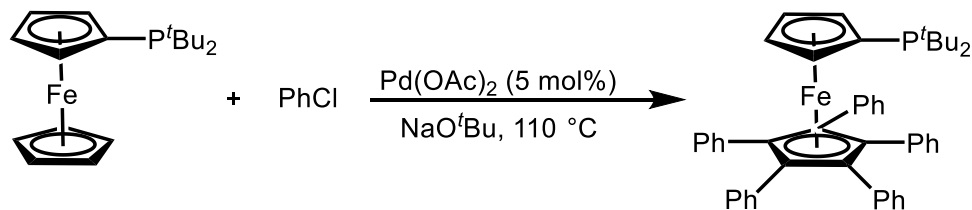
- Summary

3. Summary

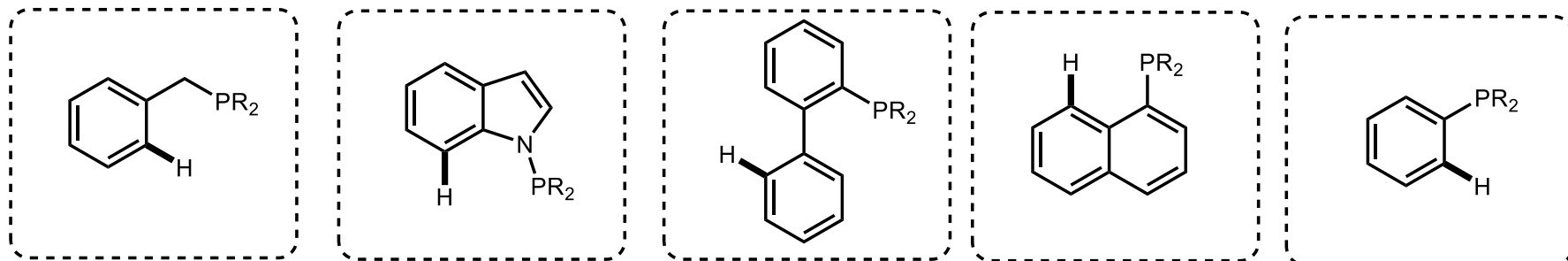
P-accelerated direct C-H functionalization



First Example of phosphine-directed C-H functionalization



Recent achievements in phosphine-directed C-H functionalization



Thanks For Your Attention