

# **Iridium-Catalyzed Hydrogenation with Chiral P,N Ligands**

贾佳

# Outline

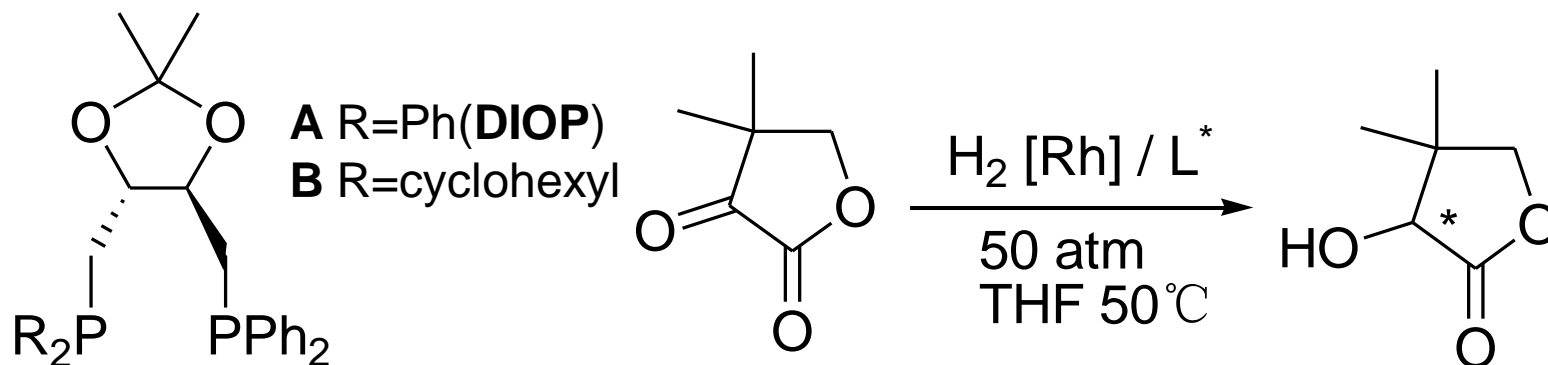
- Brief Introduction
- Hydrogenation of C=C Bonds
- Hydrogenation of C=N Bonds
- Hydrogenation of C=O Bonds
- Conclusion

# Brief Introduction

First example of Iridium catalyst :

$[\text{Ir}(\text{cod})\text{L}_2]\text{PF}_6$  or  $[\text{Ir}(\text{cod})(\text{py})\text{L}]\text{PF}_6$  L=tertiary phosphine

Crabtree *J. Organomet. Chem.* **1977** 205.



Achiwa *Synlett* **1992** 169

Ligand **A**: 45% yield 37% ee  
Ligand **B**: 100% yield 72% ee

# Why P,N Ligands

$P^{\text{trans}}$  mainly exerts an electronic effect

$P^{\text{cis}}$  mainly exerts a steric effect



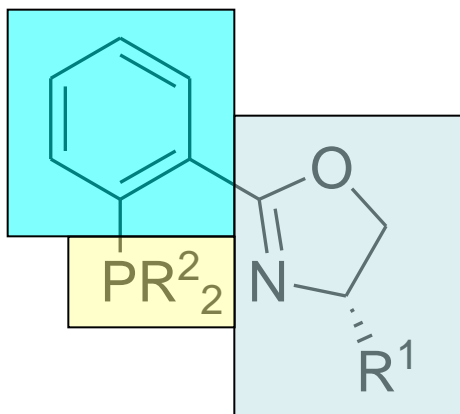
does not necessarily guarantee the performance

## A Mixed Donor P,N Ligands

a "soft" P-Ligand with  $\pi$ -acceptor properties

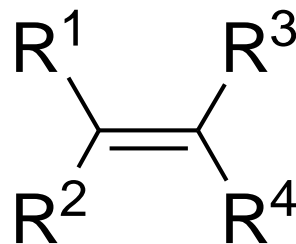
a "hard" N-Ligand acting primarily as an  $\sigma$ -donor

# Hydrogenation of C=C Bonds

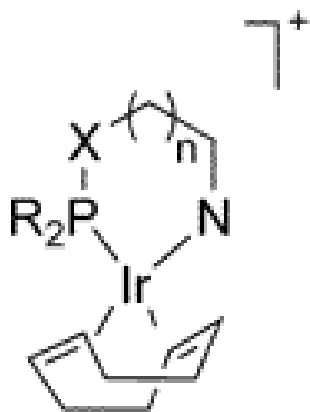


PHOX Pfaltz *ACIE* **1998** 2897

does not need a polar group adjacent to C=C bond



unfunctional olefins



BARF<sup>-</sup>

generalized catalyst

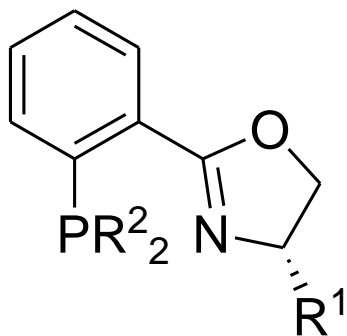
# Hydrogenation of Trisubstituted Olefins

A modular process of Iridium-P,N Ligands catalytic system *limited substrate scope*

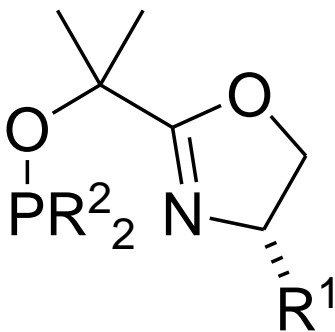


## Represented Ligands *based on P atoms*

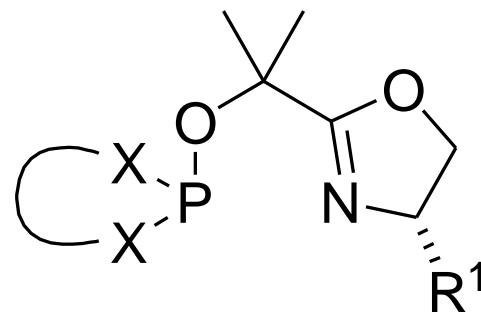
Phosphine



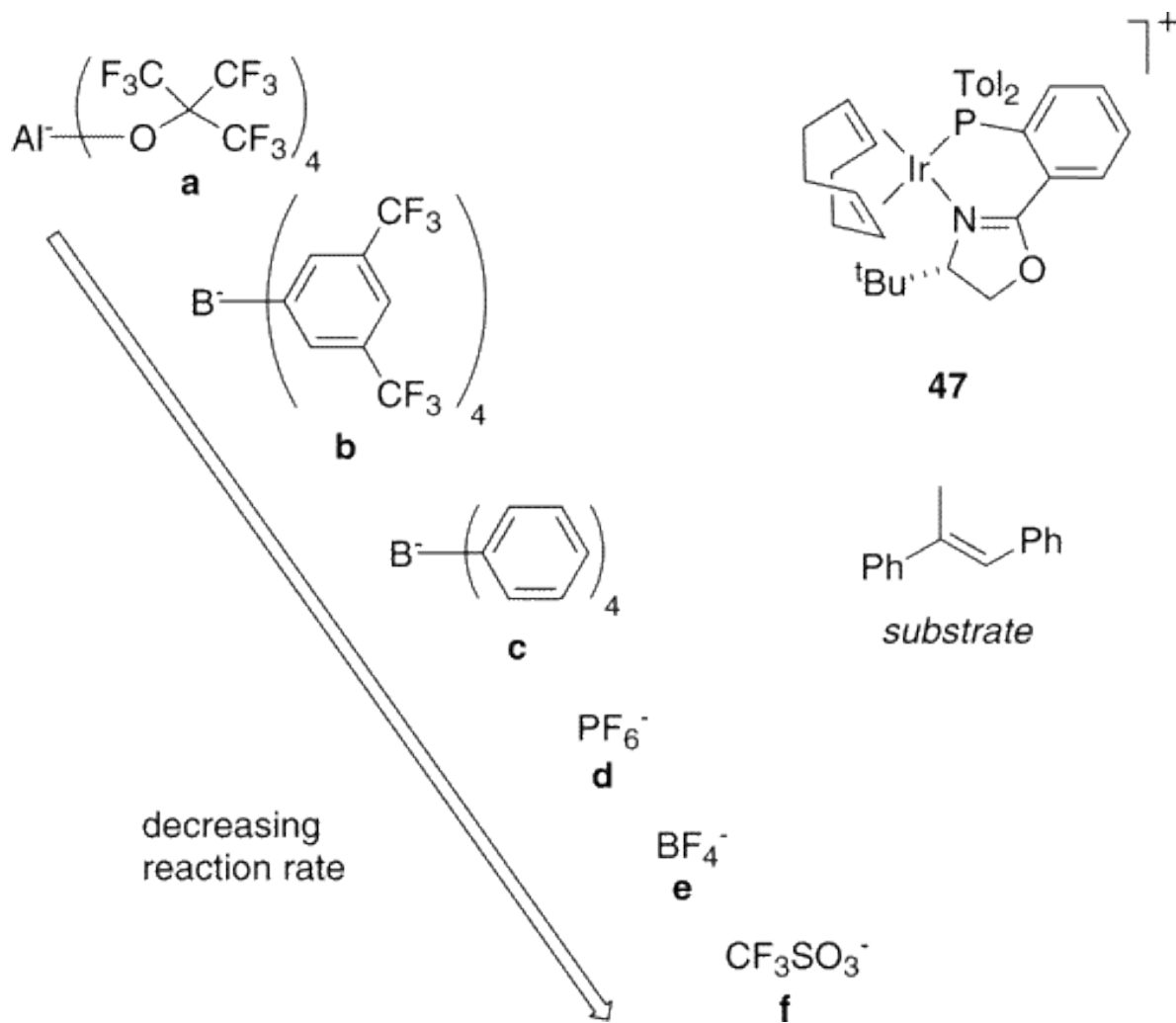
Phosphinite



Phosphite



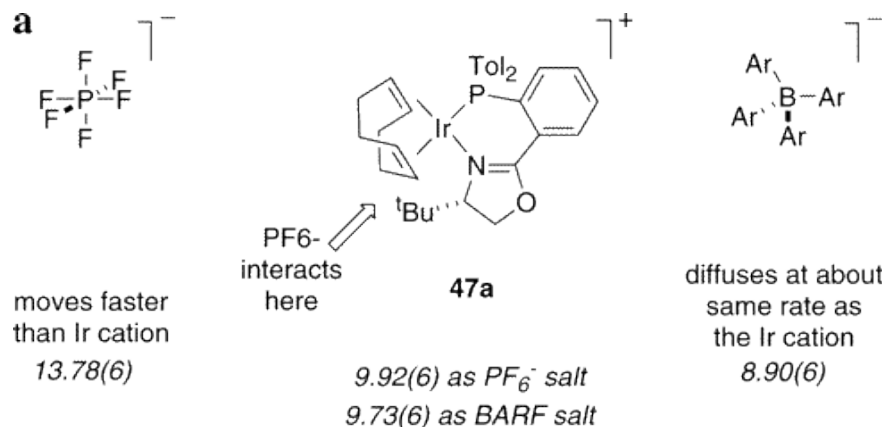
# Unexpected Anion Effect



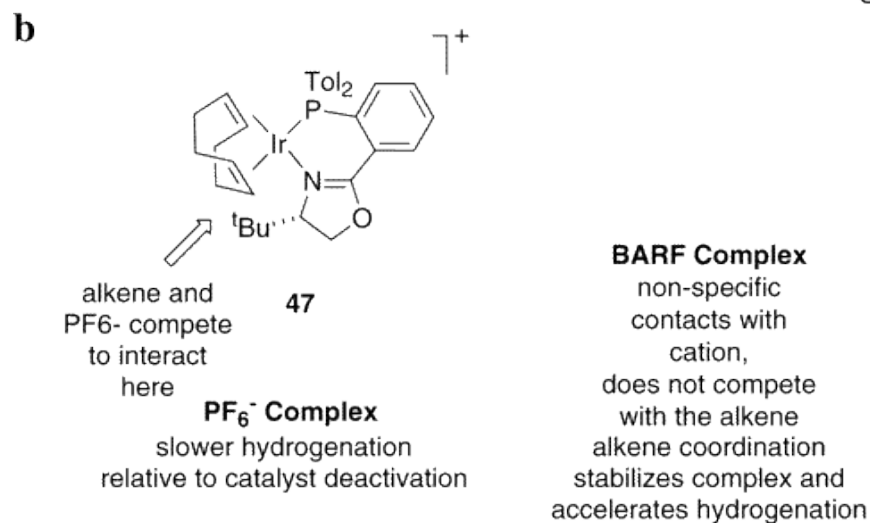
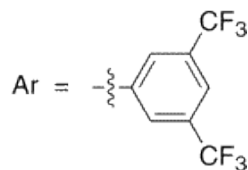
a & b TOF<sub>max</sub> > 5000

b is less sensitive to water and to adventitious oxygen.

# Unexpected Anion Effect



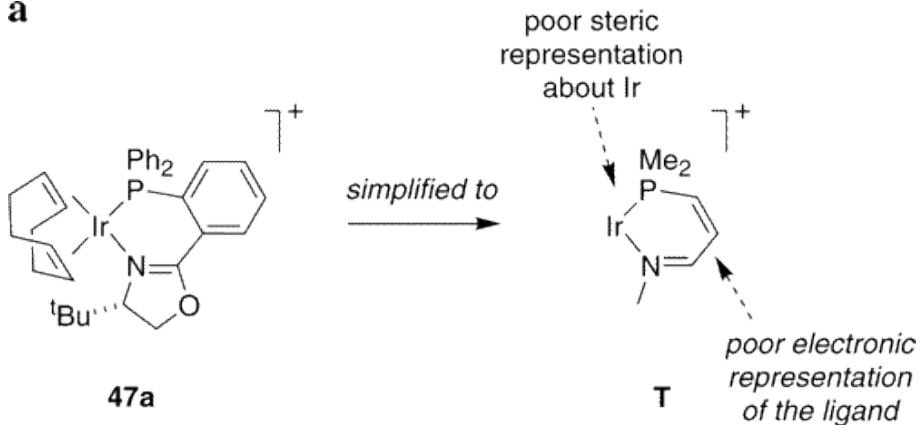
$\text{PF}_6^-$  anion is less strongly associated with the metal than the  $\text{BARF}^-$  but the interactions it does have are more specific.



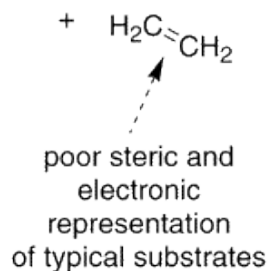
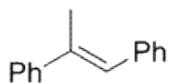


# Mechanistic Study Based on Calculations

a



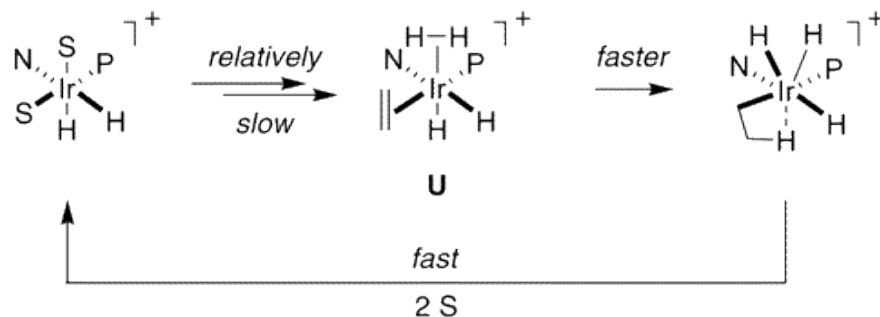
+ substrates like



Enantioselectivity would then be determined by a combination of two factors: the face selectivity of the alkene complexation and the relative rates of the migratory insertion step.

Ir(III) → Ir(V)

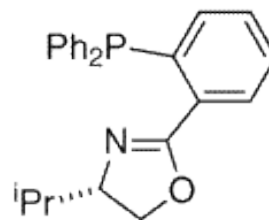
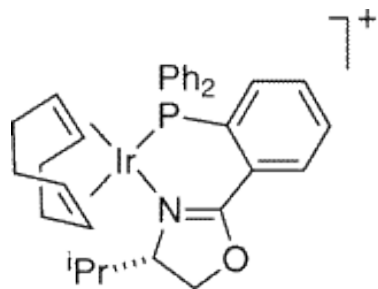
b



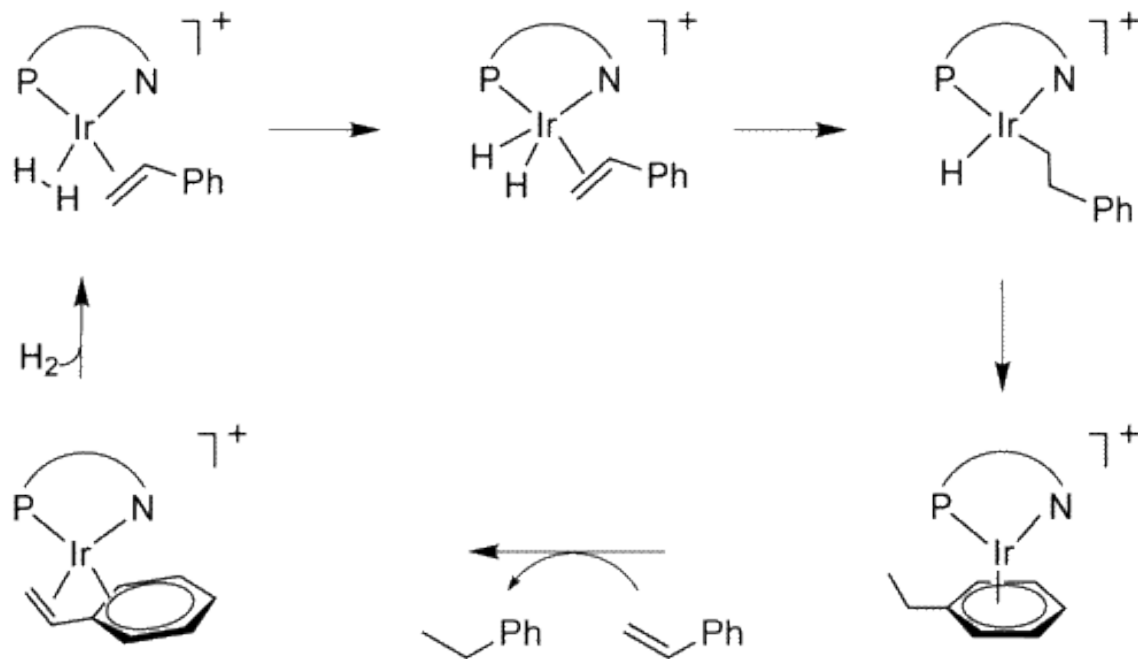
S = solvent, CH<sub>2</sub>Cl<sub>2</sub>

Brandt *CEJ* 2003 339  
Hall *JACS* 2004 16688

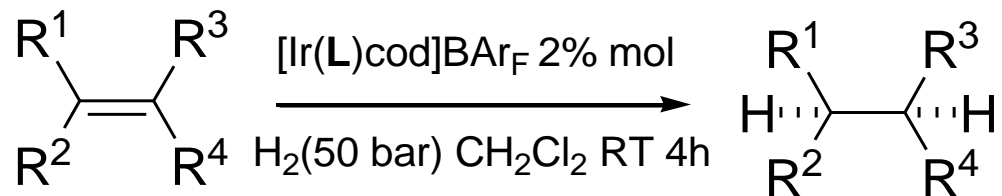
# Mechanistic Study Based on MS



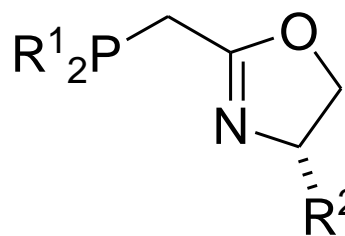
Still no widely-accepted theory  
Ir(I) → Ir(III)



# Hydrogenation of Tetrasubstituted Olefins



generate two steric adjacent centers in a single step



a  $\text{R}^1 = \text{Cy}$ ;  $\text{R}^2 = i\text{-Pr}$

b  $\text{R}^1 = \text{Cy}$ ;  $\text{R}^2 = t\text{-Bu}$

c  $\text{R}^1 = \text{Cy}$ ;  $\text{R}^2 = \text{CH}_2 t\text{-Bu}$

d  $\text{R}^1 = \text{Cy}$ ;  $\text{R}^2 = \text{Ph}$

e  $\text{R}^1 = \text{Cy}$ ;  $\text{R}^2 = \text{Bn}$

f  $\text{R}^1 = t\text{-Bu}$ ;  $\text{R}^2 = \text{Bn}$

g  $\text{R}^1 = t\text{-Bu}$ ;  $\text{R}^2 = t\text{-Bu}$

h  $\text{R}^1 = t\text{-Bu}$ ;  $\text{R}^2 = \text{CH}_2 t\text{-Bu}$

i  $\text{R}^1 = t\text{-Bu}$ ;  $\text{R}^2 = \text{Ph}$

j  $\text{R}^1 = t\text{-Bu}$ ;  $\text{R}^2 = \text{Bn}$

k  $\text{R}^1 = \text{Ph}$ ;  $\text{R}^2 = i\text{-Pr}$

l  $\text{R}^1 = \text{Ph}$ ;  $\text{R}^2 = t\text{-Bu}$

m  $\text{R}^1 = \text{Ph}$ ;  $\text{R}^2 = \text{CH}_2 t\text{-Bu}$

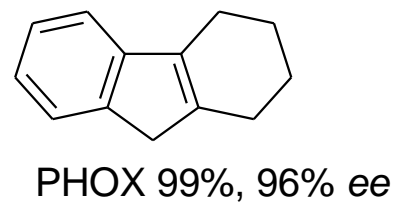
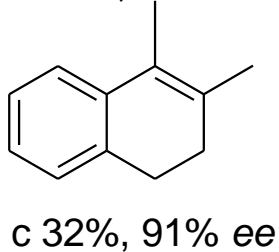
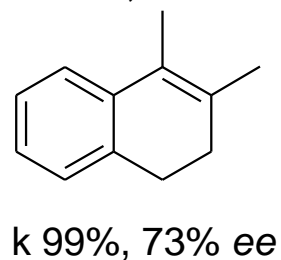
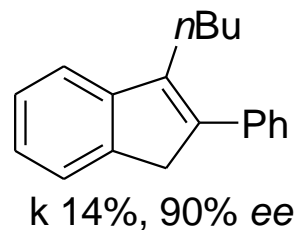
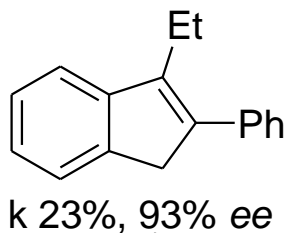
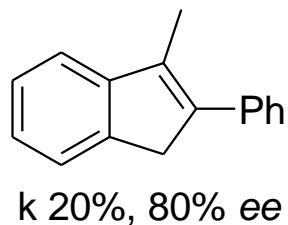
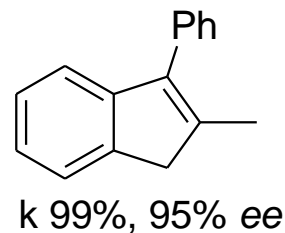
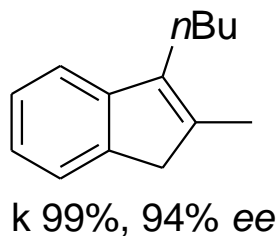
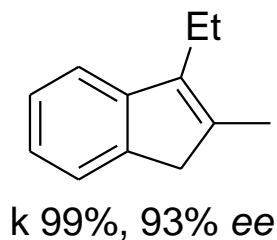
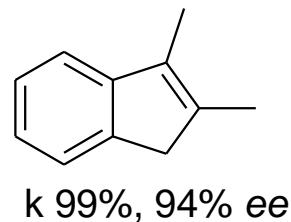
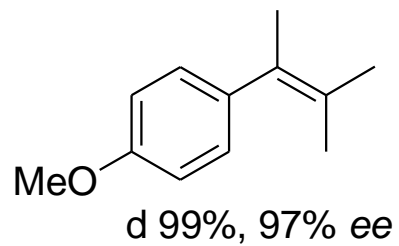
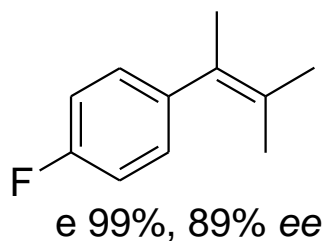
n  $\text{R}^1 = \text{Ph}$ ;  $\text{R}^2 = \text{Ph}$

o  $\text{R}^1 = \text{Ph}$ ;  $\text{R}^2 = \text{Bn}$

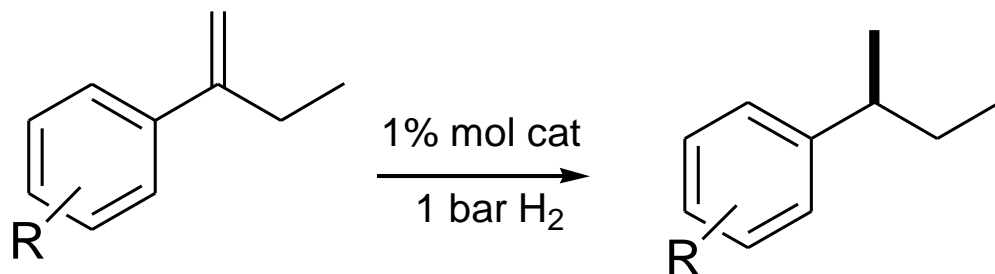
p  $\text{R}^1 = o\text{-Tol}$ ;  $\text{R}^2 = i\text{-Pr}$

q  $\text{R}^1 = o\text{-Tol}$ ;  $\text{R}^2 = \text{Bn}$

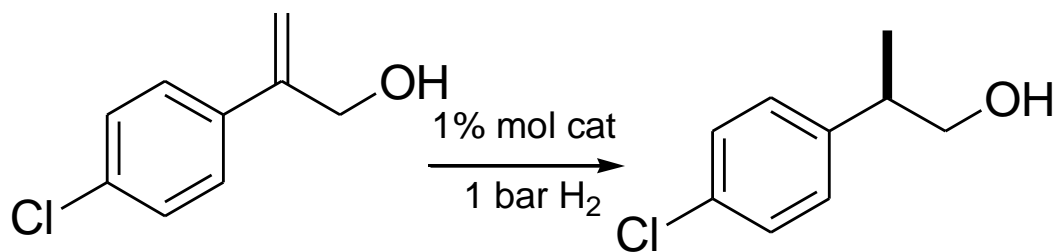
# Hydrogenation of Tetrasubstituted Olefins



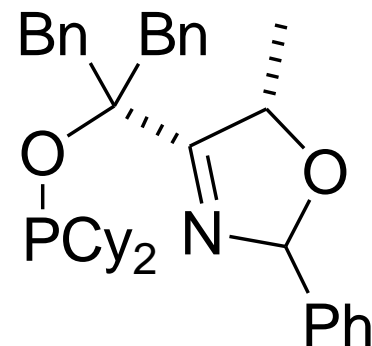
# Hydrogenation of 1,1-Disubstituted Olefins



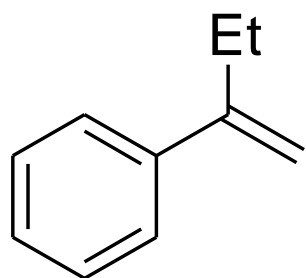
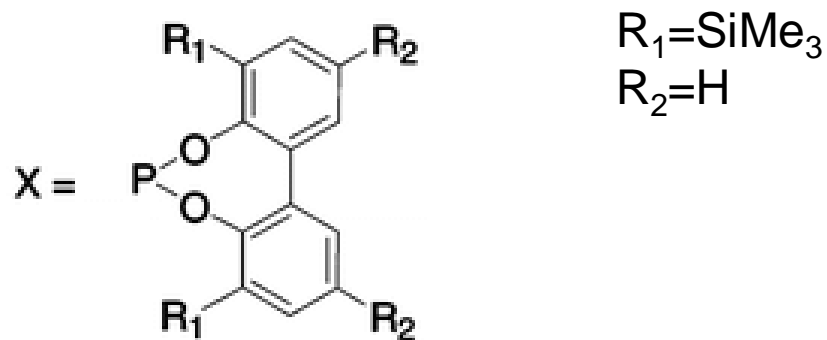
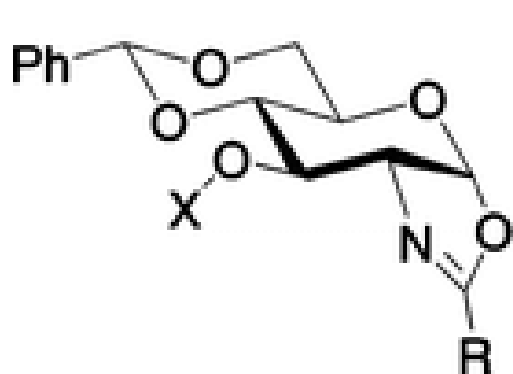
up to 94% ee



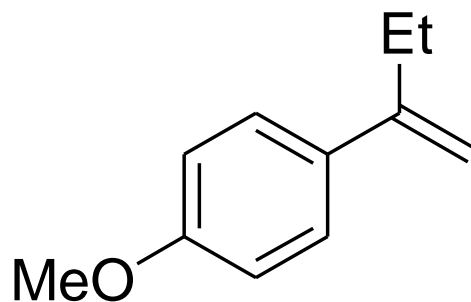
up to 88% ee



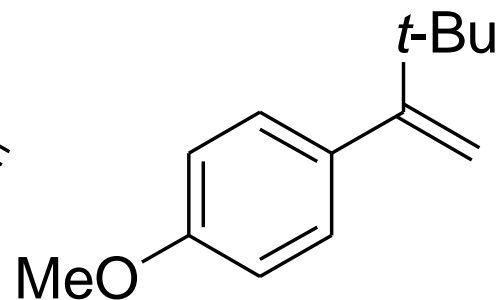
# Hydrogenation of 1,1-Disubstituted Olefins



100% 99% ee

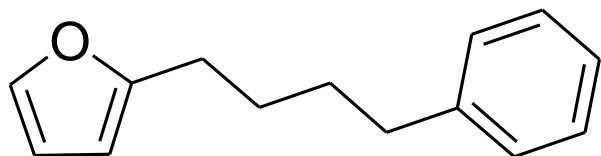


100% >99% ee

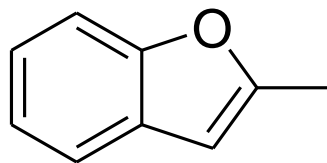


100% 97% ee

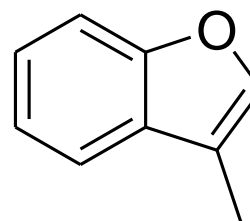
# Hydrogenation of Furan Derivatives



84% 78% ee

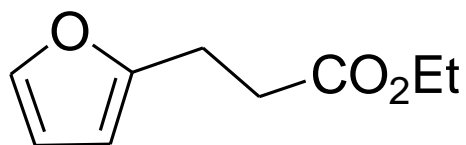


93% 98% ee

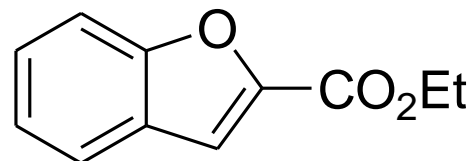


>99% 92% ee

1 mol% cat 50 bar H<sub>2</sub> 24 h 40°C

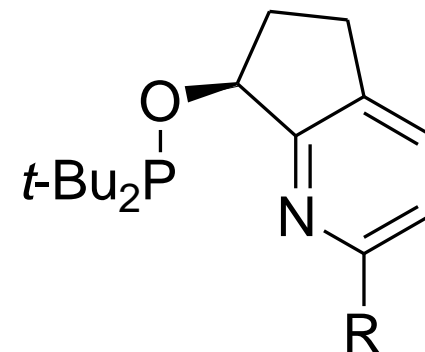


>99% 93% ee

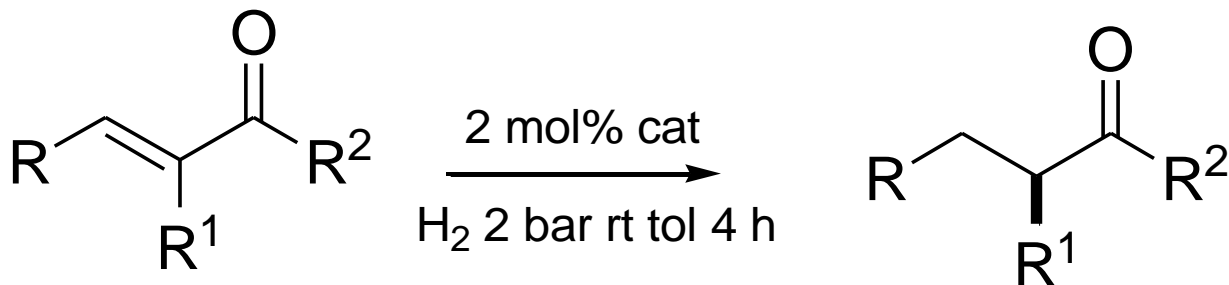


47% >99% ee

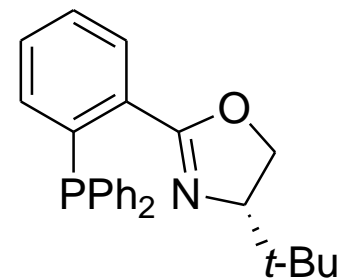
2 mol% cat 100 bar H<sub>2</sub> 24 h 40°C



# Hydrogenation of Ketenes



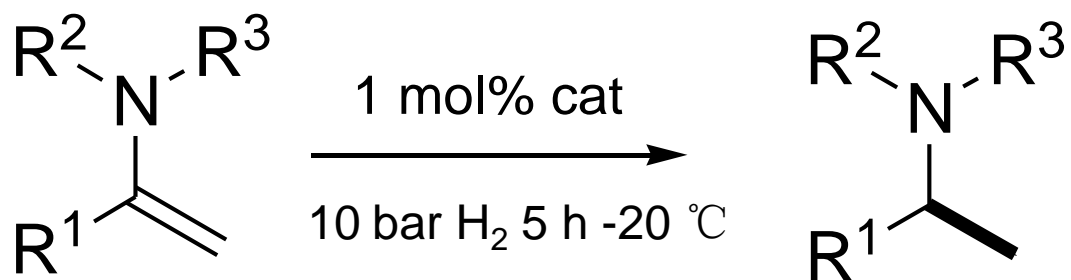
up to 99% ee



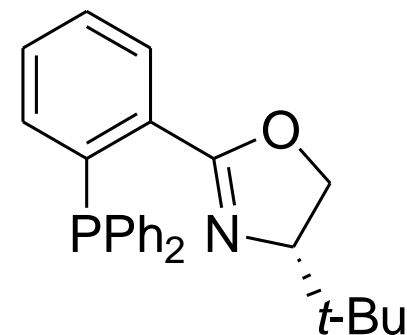
Bolm *ACIE* **2008** 8290



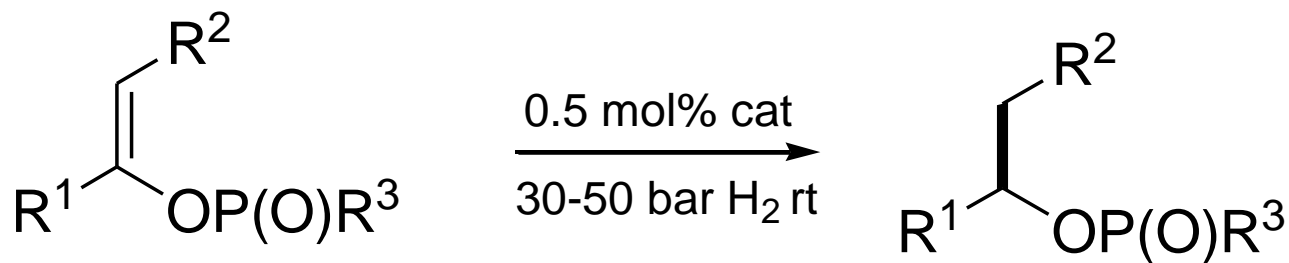
# Hydrogenation of Enamines



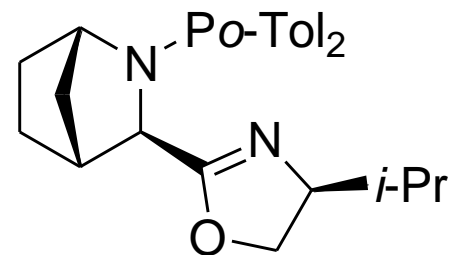
up to 91% ee



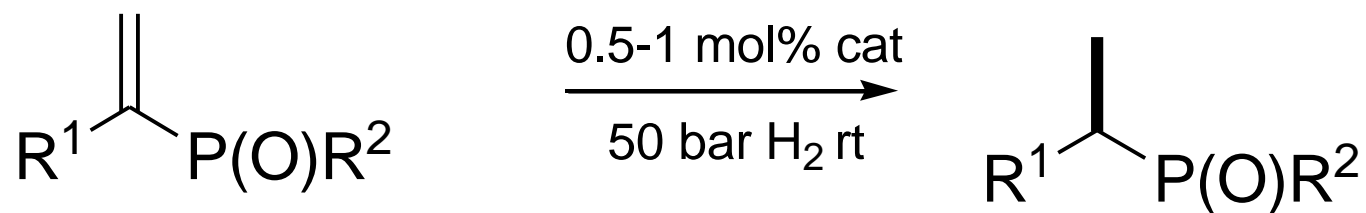
# Hydrogenation of Vinylphosphinates



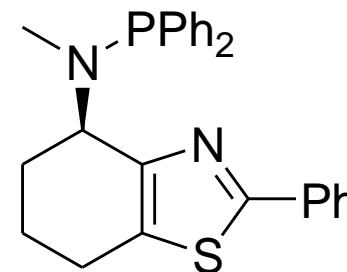
up to 99% ee



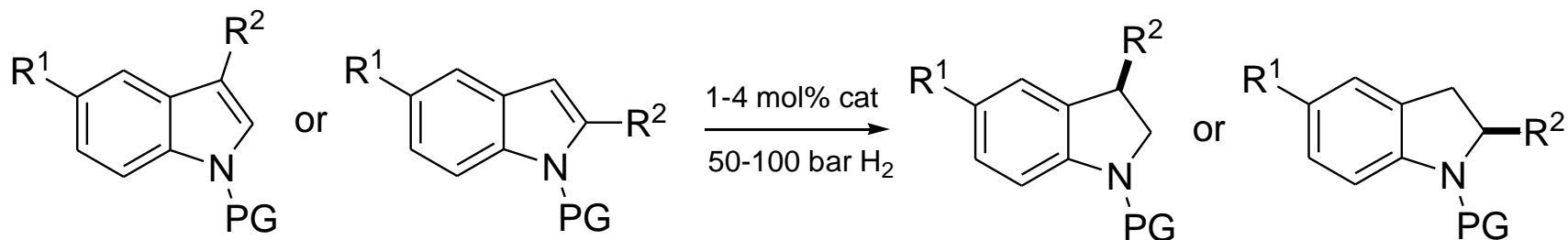
# Hydrogenation of Vinylphosphonates



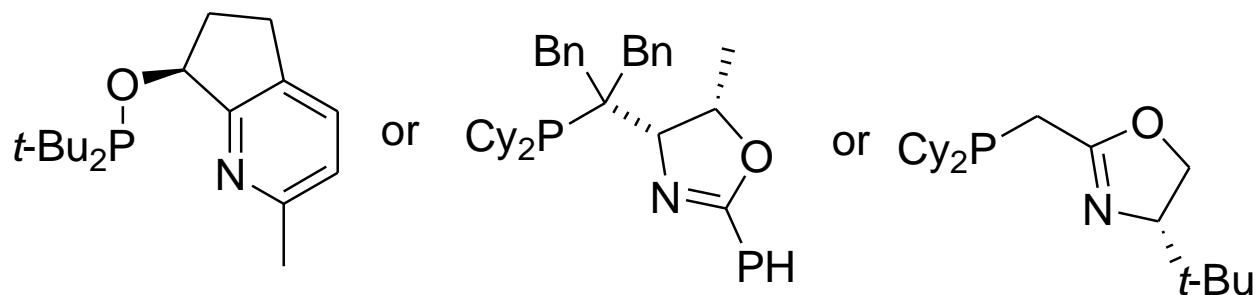
up to 99% ee



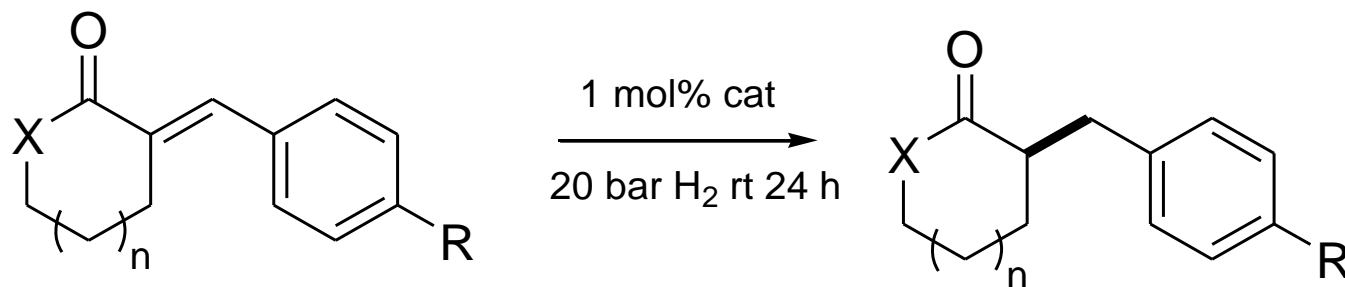
# Hydrogenation of N-Protected Indoles



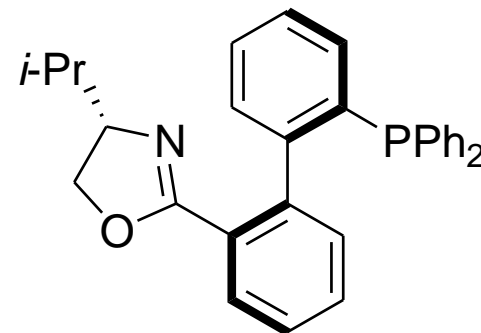
up to 99% ee



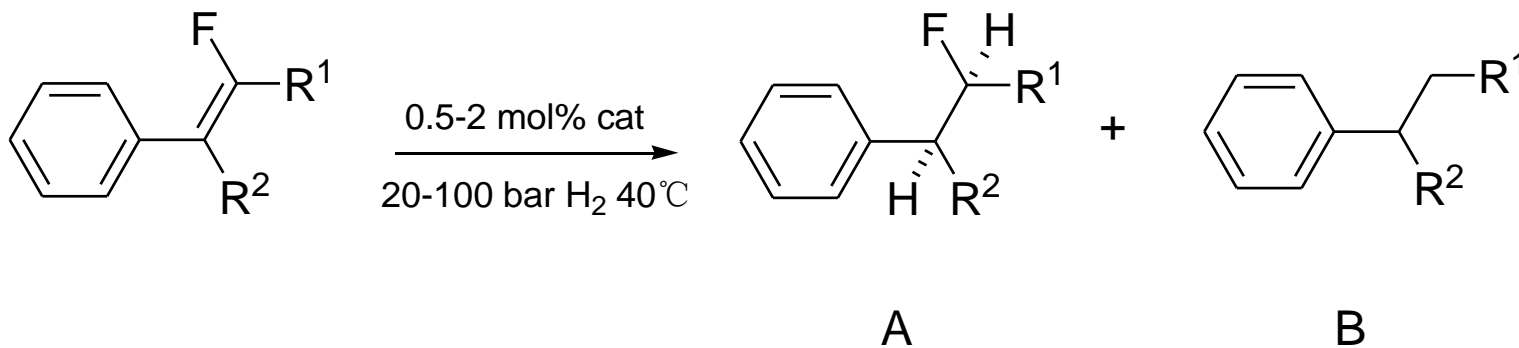
# Hydrogenation of $\alpha,\beta$ -Unsaturated Lactones and Lactams



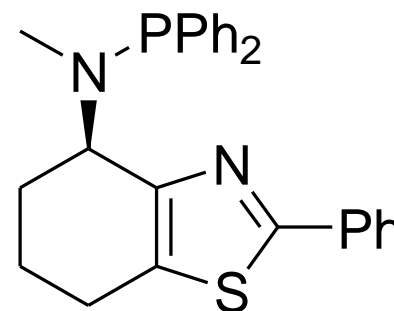
up to 98% ee



# Hydrogenation of Fluorinated Olefins

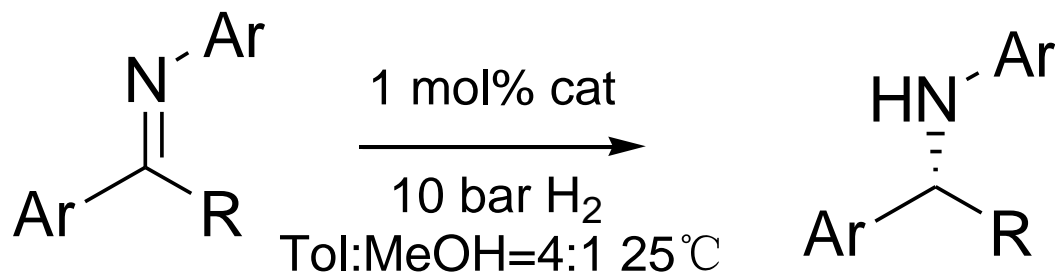


up to 100:0 A:B ratio 99% ee

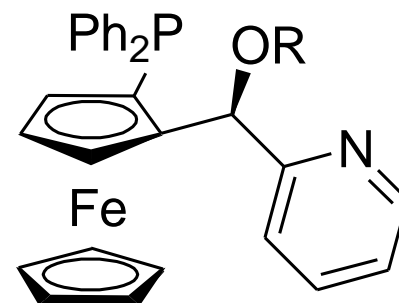


# Hydrogenation of C=N Bonds

## Hydrogenation of Imines



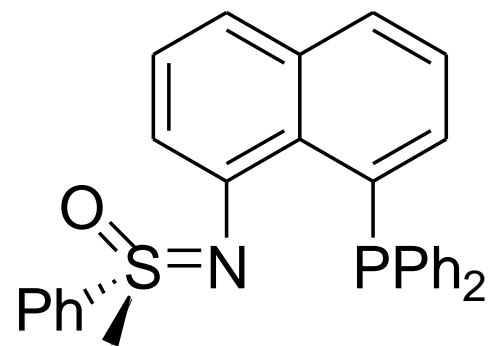
up to 98% ee



# Hydrogenation of Quinolines

n1

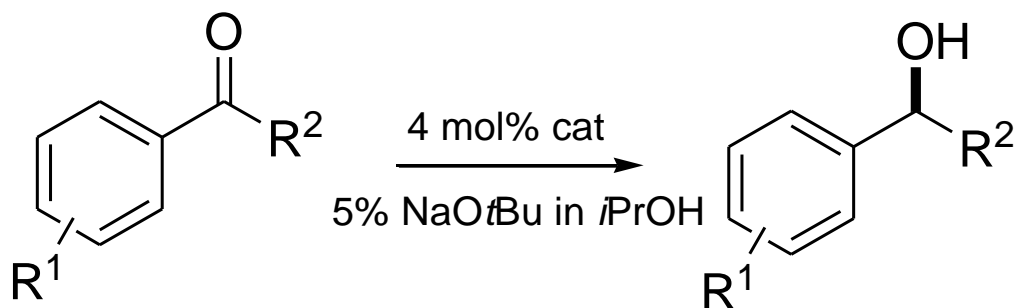
up to 87% ee





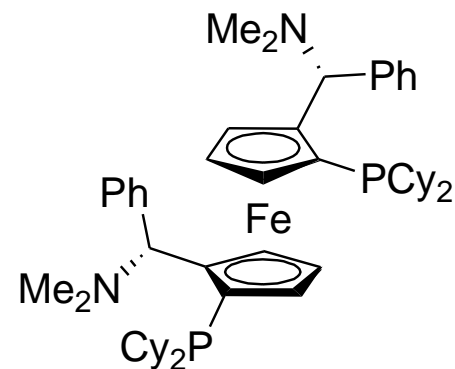
# Hydrogenation of C=O Bonds

## Transfer Hydrogenation of Ketones

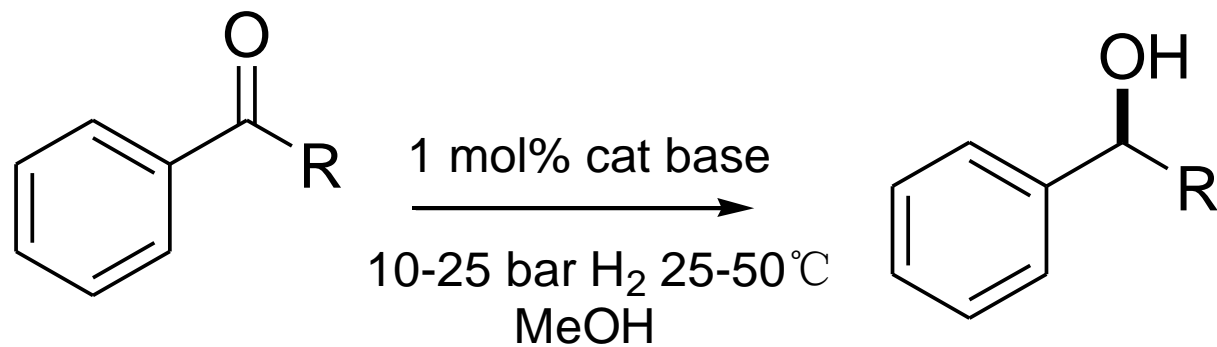


up to 95% ee

Ir:L=1:1 anion PF<sub>6</sub><sup>-</sup>

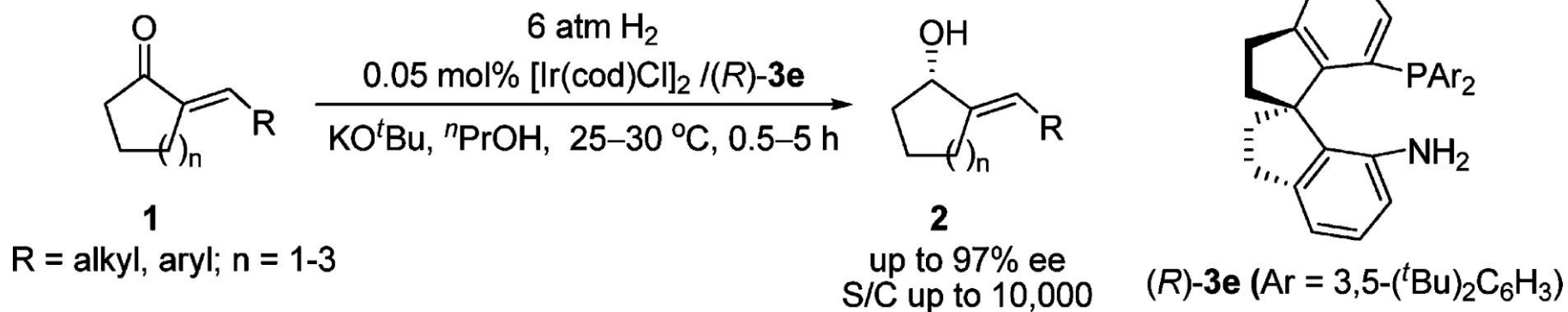


# Hydrogenation of Ketones



up to 68% ee

# Hydrogenation of Ketones



# Conclusion

- Relatively stable to air and moisture
- Broadening the scope of substrates
- Effective but facile ligands

**Thanks For Attention**