

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

贾佳

# Outline

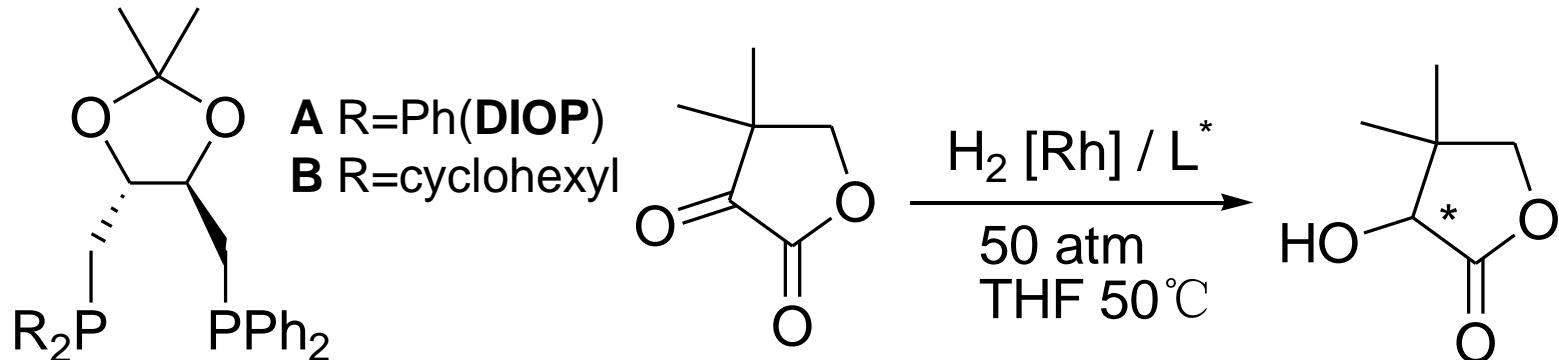
- Brief Introduction
- Hydrogenation of C=C Bonds
- Hydrogenation of C=N Bonds
- Hydrogenation of C=O Bonds
- Conclusion

# Brief Introduction

## First example of Iridium catalyst :

[Ir(cod)L<sub>2</sub>]PF<sub>6</sub> or [Ir(cod)(py)L]PF<sub>6</sub> 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

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

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

↓ does not necessarily guarantee the performance

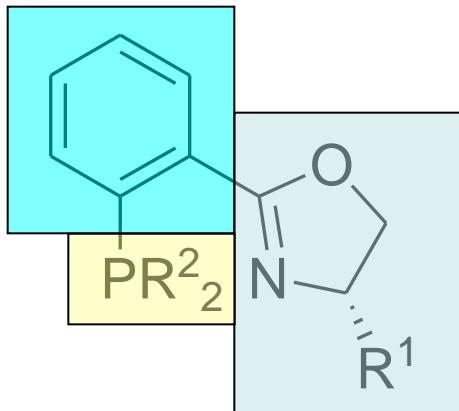
## A Mixed Donor P,N Ligands

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

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

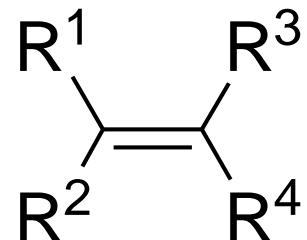
Pfaltz *PNAS* 2004 5723

# Hydrogenation of C=C Bonds

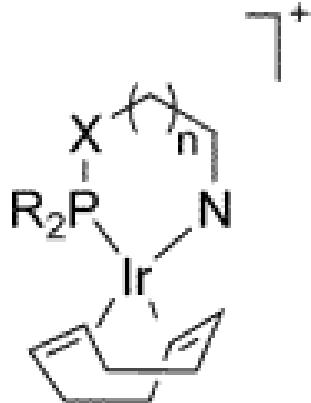


PHOX Pfaltz AC/E 1998 2897

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



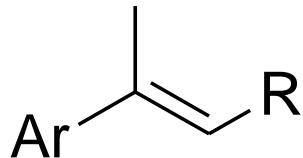
unfunctional olefins



$\text{BARF}^-$  generalized catalyst

# Hydrogenation of Trisubstituted Olefins

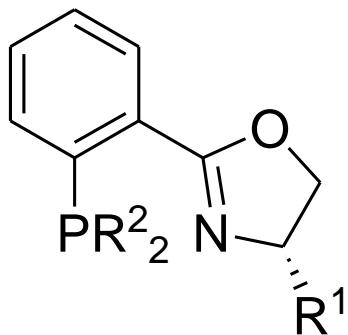
A modular process of Iridium-P,N Ligands catalytic system *limited substrate scope*



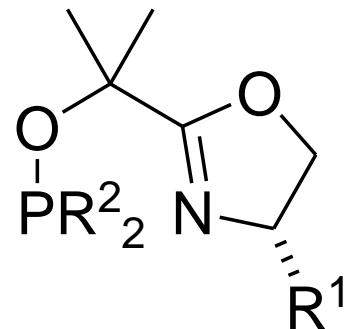
high ee especially R=Ar or Heteroaromatic  
0.02-2% catalyst loading usually 50 bar H<sub>2</sub> 2 h

## Represented Ligands *based on P atoms*

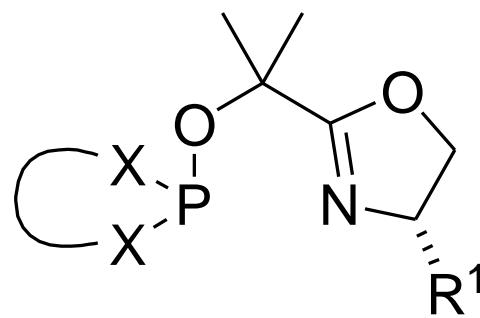
Phosphine



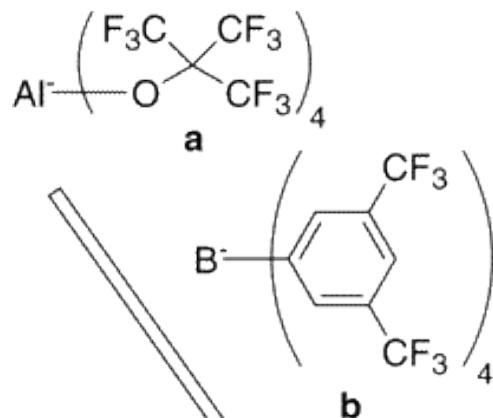
Phosphinite



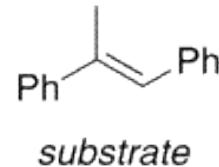
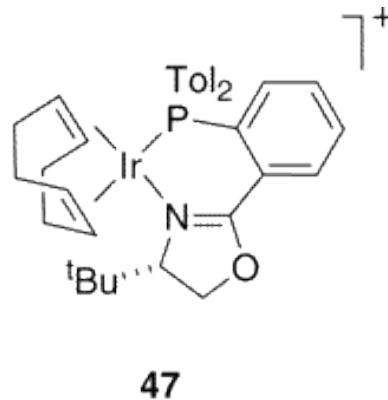
Phosphite



# Unexpected Anion Effect



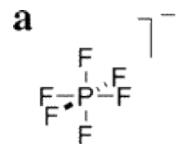
decreasing  
reaction rate



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

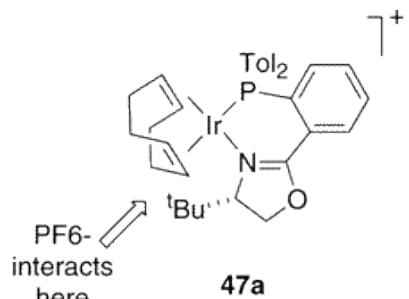
**b is less sensitive to water and to adventitious oxygen.**

# Unexpected Anion Effect

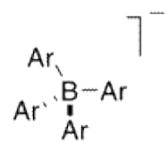


moves faster  
than Ir cation

13.78(6)

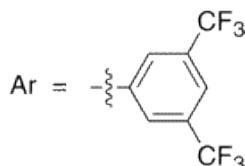


9.92(6) as  $\text{PF}_6^-$  salt  
9.73(6) as BARF salt

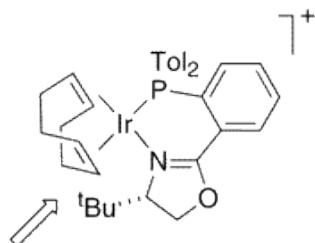


diffuses at about  
same rate as  
the Ir cation

8.90(6)



b



alkene and  
PF<sub>6</sub>- compete  
to interact  
here

**PF<sub>6</sub><sup>-</sup> Complex**

slower hydrogenation  
relative to catalyst deactivation

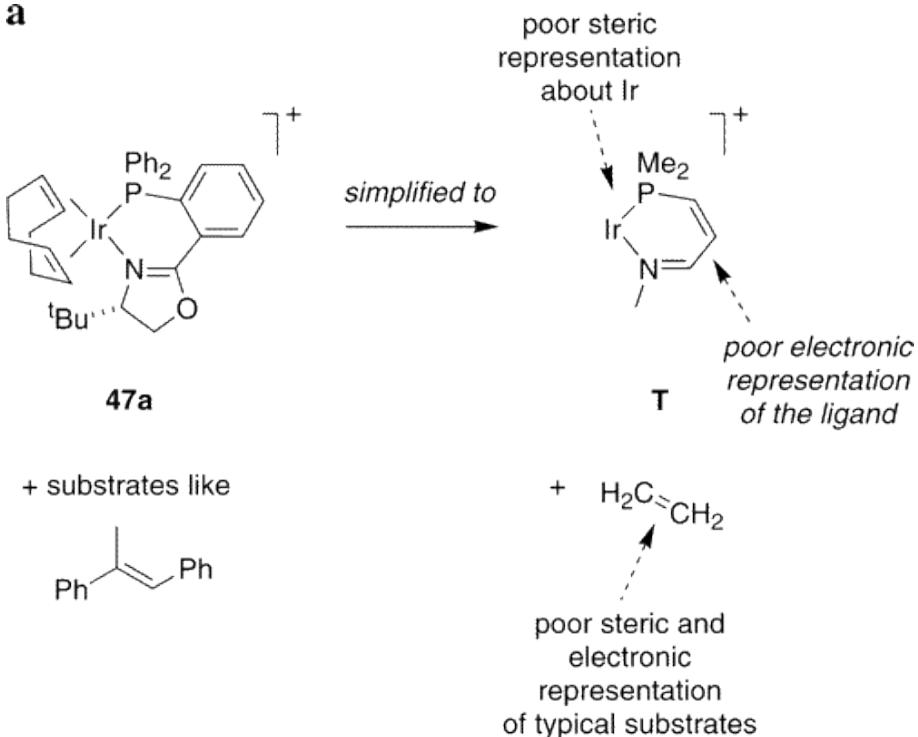
**BARF Complex**

non-specific  
contacts with  
cation,  
does not compete  
with the alkene  
alkene coordination  
stabilizes complex and  
accelerates hydrogenation

**PF<sub>6</sub><sup>-</sup> anion is less strongly  
associated with the metal than the  
BARF<sup>-</sup> but the interactions it does  
have are more specific.**

# Mechanistic Study Based on Calculations

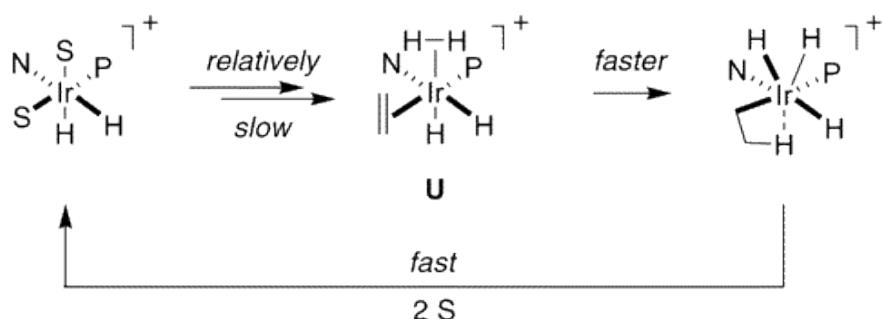
a



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.

$\text{Ir(III)} \rightarrow \text{Ir(V)}$

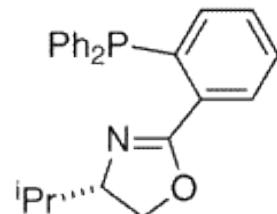
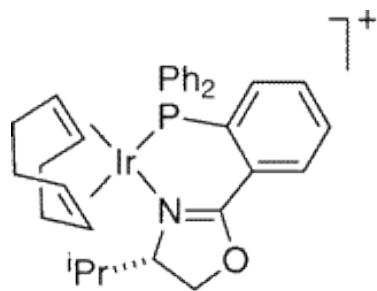
b



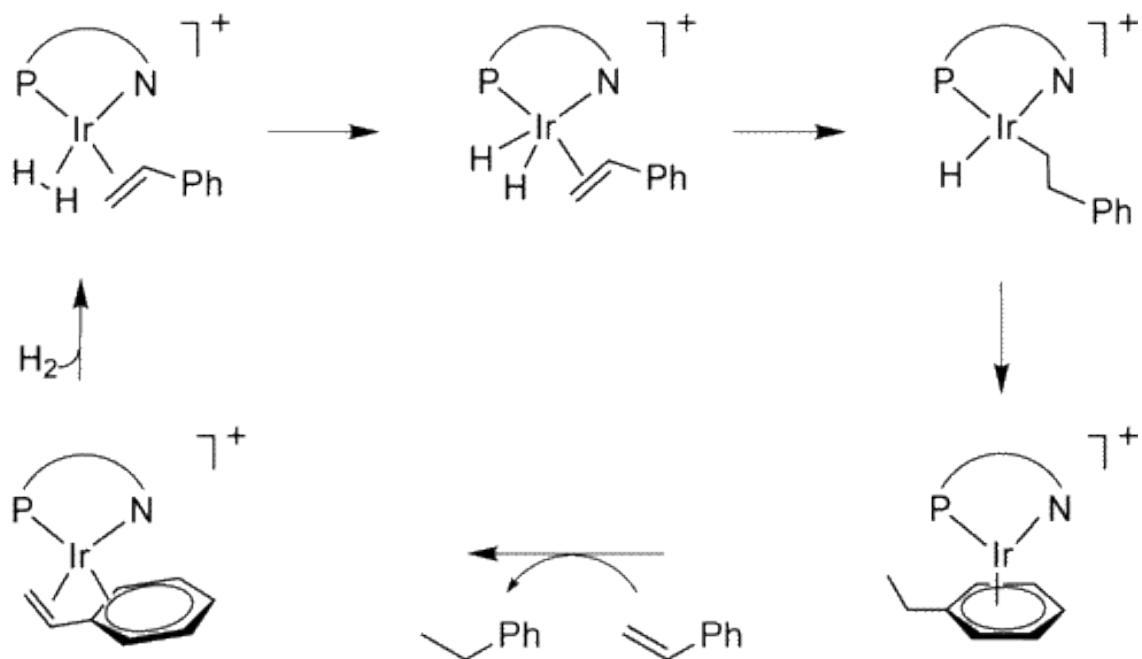
S = solvent,  $\text{CH}_2\text{Cl}_2$

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

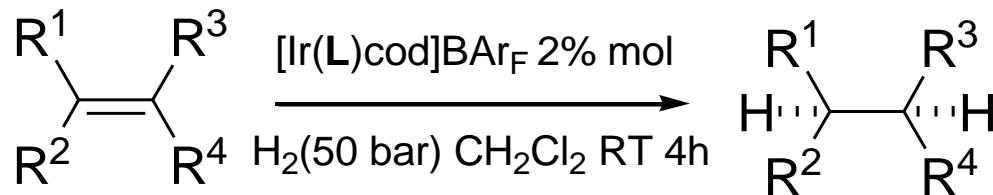
# Mechanistic Study Based on MS



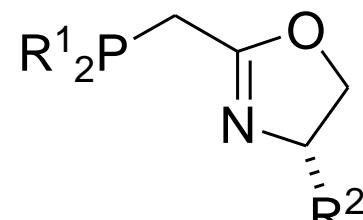
Still no widely-accepted theory  
Ir(I) → Ir(III)



# Hydrogenation of Tetrasubstituted Olefins



generate two steric adjacent centers in a single step



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

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

c  $R^1=Cy; R^2=CH_2t\text{-Bu}$

d  $R^1=Cy; R^2=Ph$

e  $R^1=Cy; R^2=Bn$

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

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

h  $R^1=t\text{-Bu}; R^2=CH_2t\text{-Bu}$

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

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

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

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

m  $R^1=Ph; R^2=CH_2t\text{-Bu}$

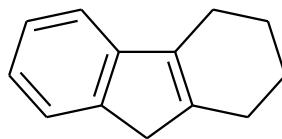
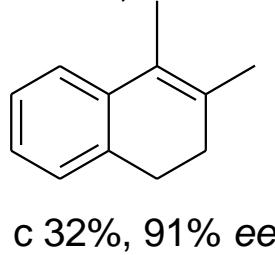
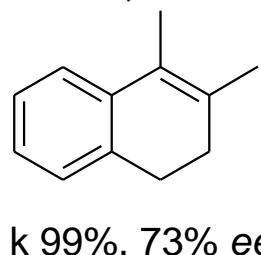
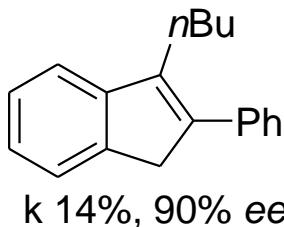
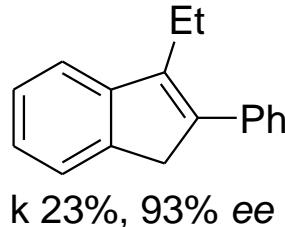
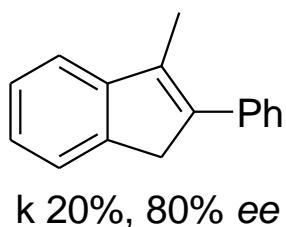
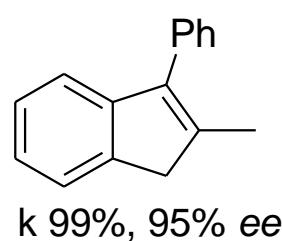
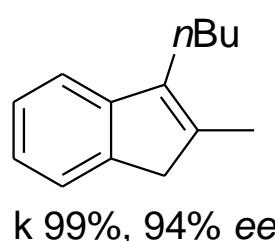
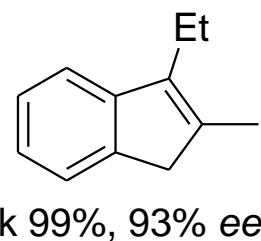
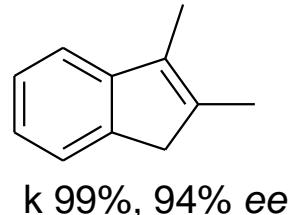
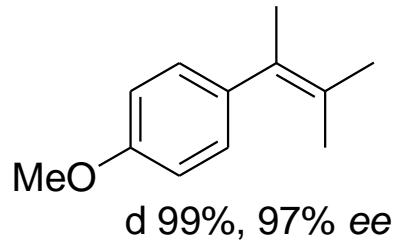
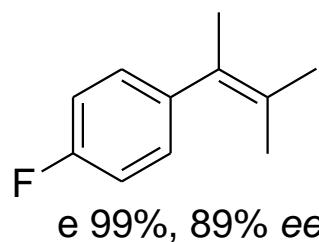
n  $R^1=Ph; R^2=Ph$

o  $R^1=Ph; R^2=Bn$

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

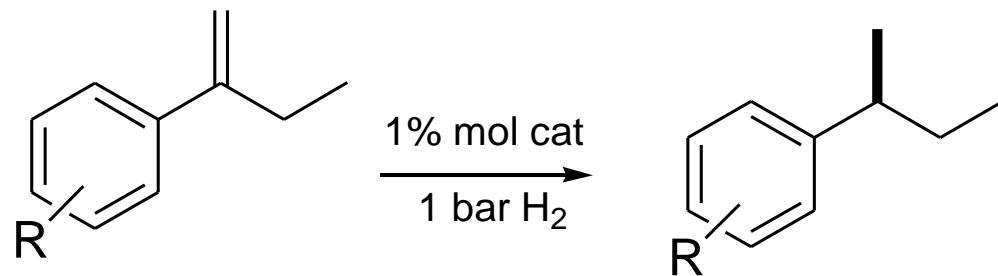
q  $R^1=o\text{-Tol}; R^2=Bn$

# Hydrogenation of Tetrasubstituted Olefins

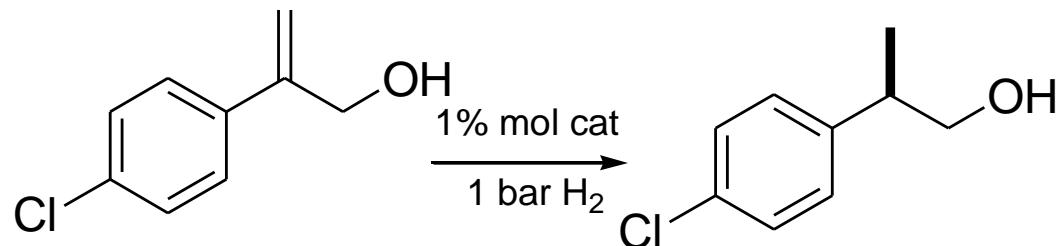
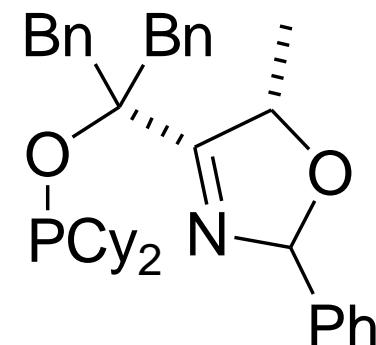


PHOX 99%, 96% ee

# Hydrogenation of 1,1-Disubstituted Olefins



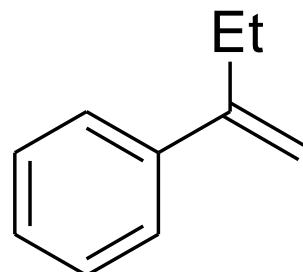
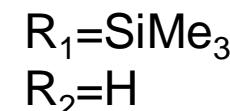
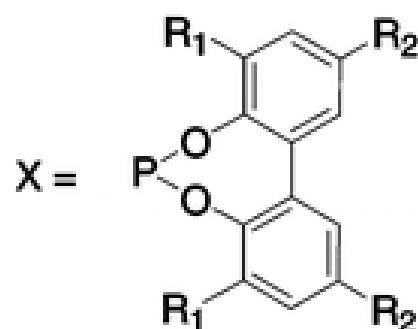
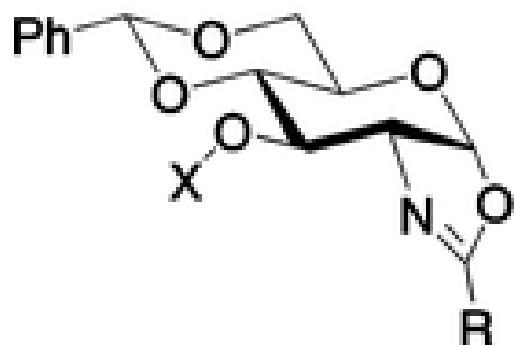
up to 94% ee



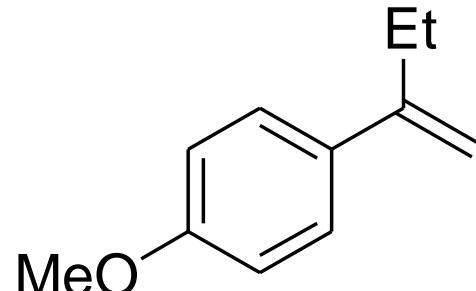
up to 88% ee

Pfaltz ASC 2005 282

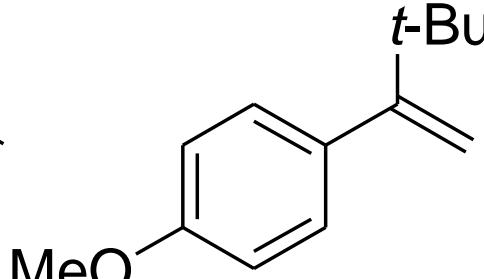
# Hydrogenation of 1,1-Disubstituted Olefins



100% 99% ee

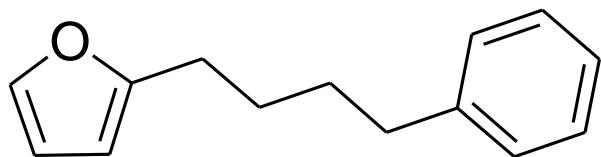


100% >99% ee

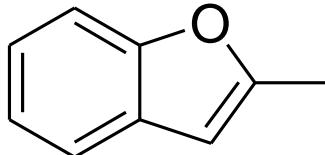


100% 97% ee

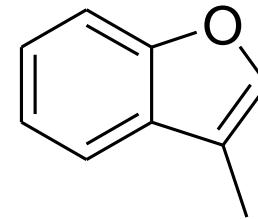
# Hydrogenation of Furan Derivatives



84% 78% ee

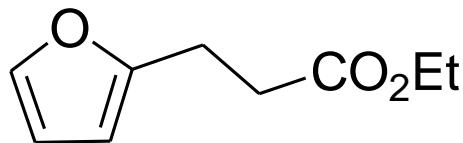


93% 98% ee

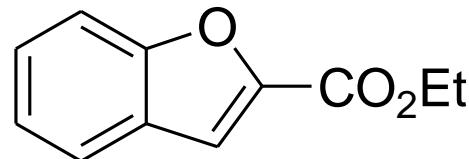


>99% 92% ee

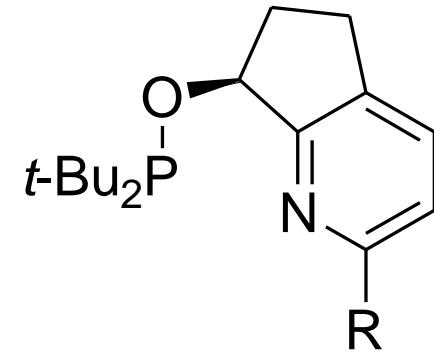
1 mol% cat 50 bar H<sub>2</sub> 24 h 40°C



>99% 93% ee

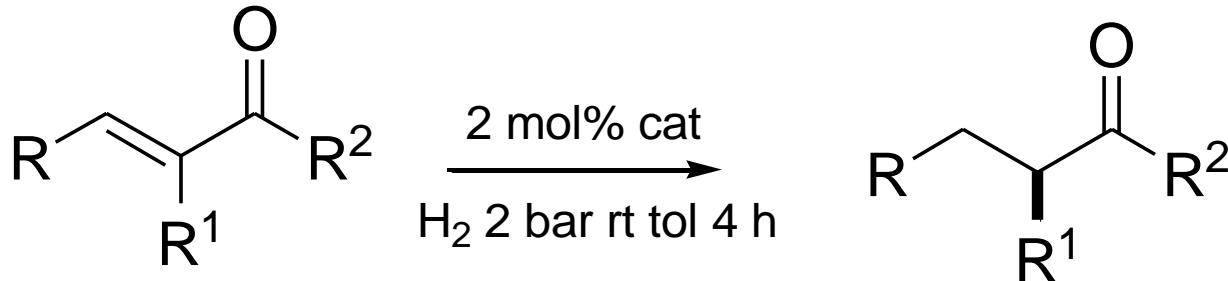


47% >99% ee

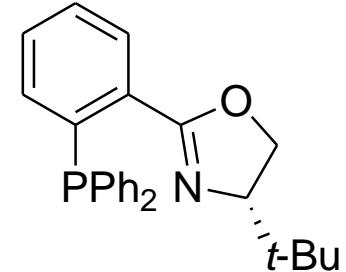


2 mol% cat 100 bar H<sub>2</sub> 24 h 40°C

# Hydrogenation of Ketenes

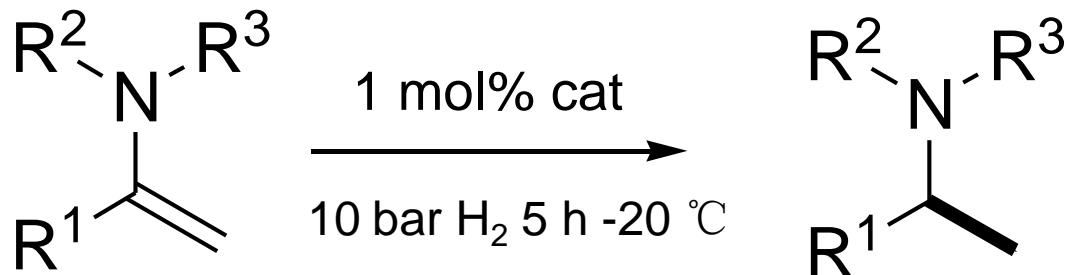


up to 99% ee

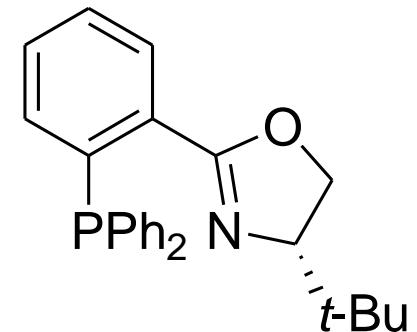


Bolm *ACIE* **2008** 8290

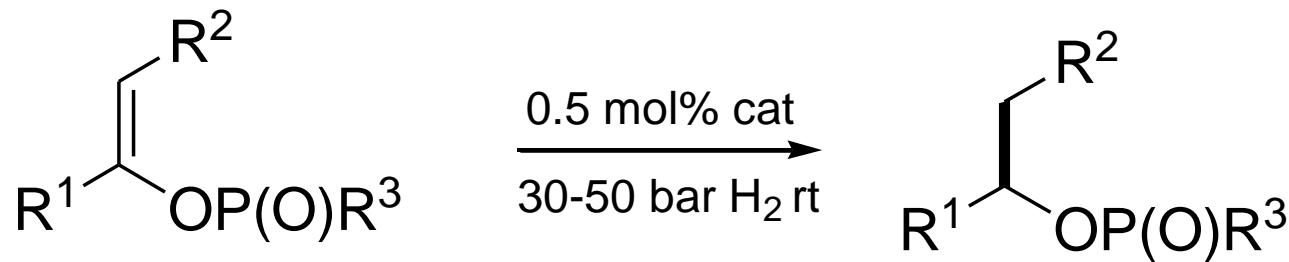
# Hydrogenation of Enamines



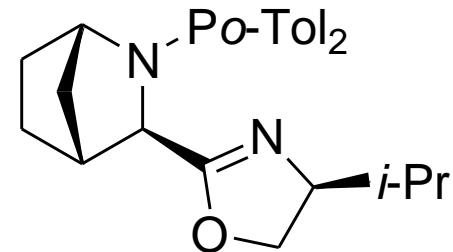
up to 91% ee



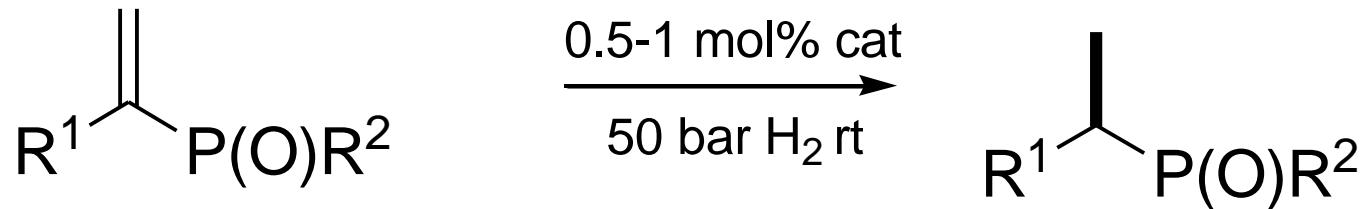
# Hydrogenation of Vinylphosphinates



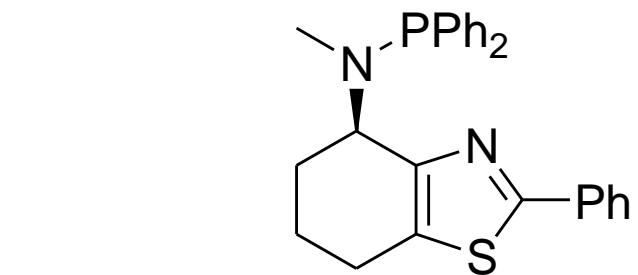
up to 99% ee



# Hydrogenation of Vinylphosphonates

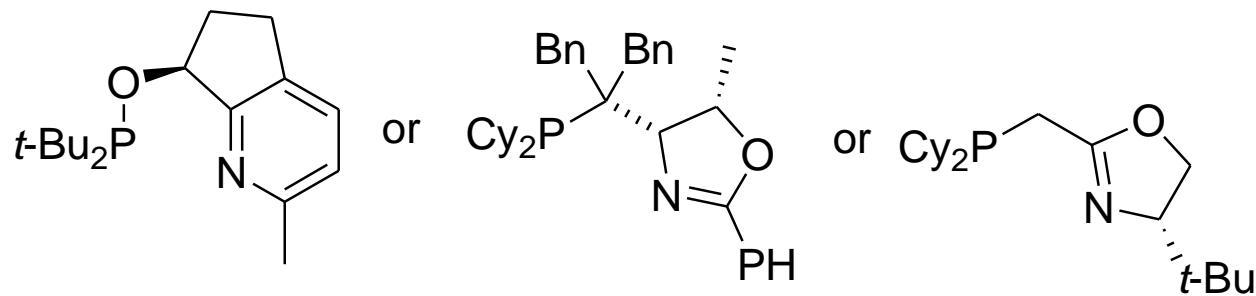
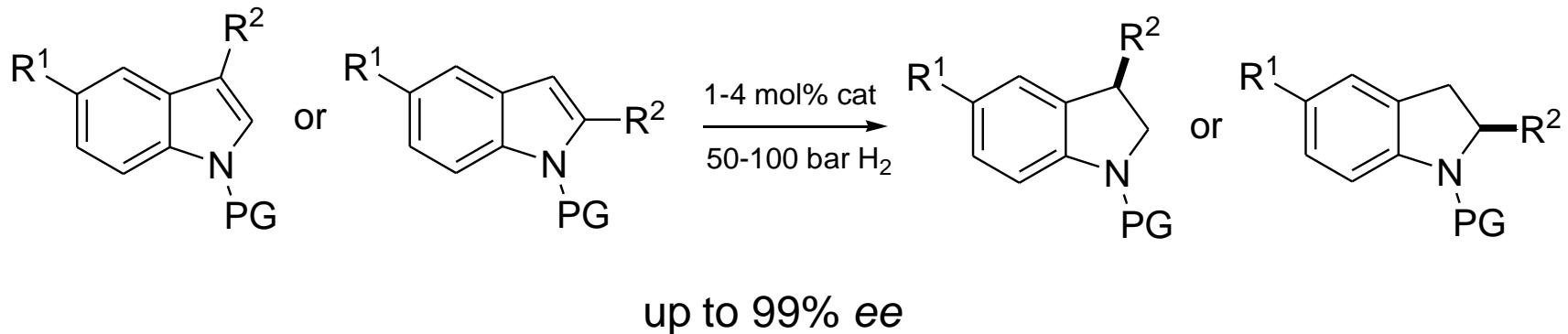


up to 99% ee

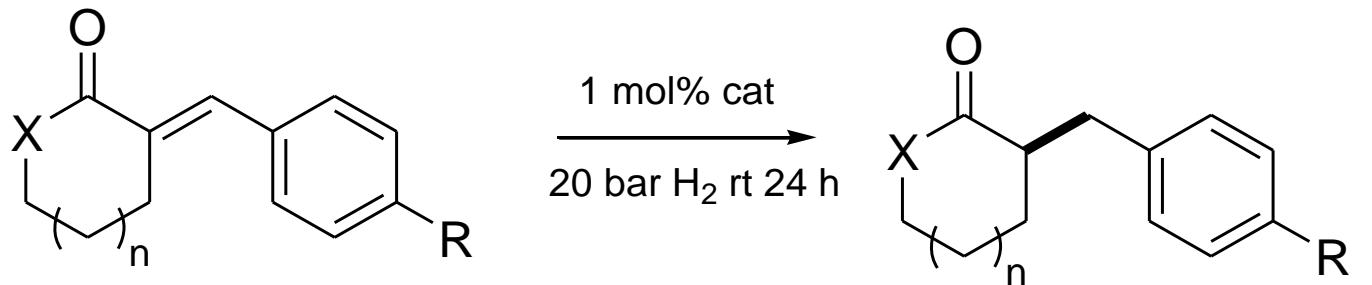


Andersson JACS 2009 8285

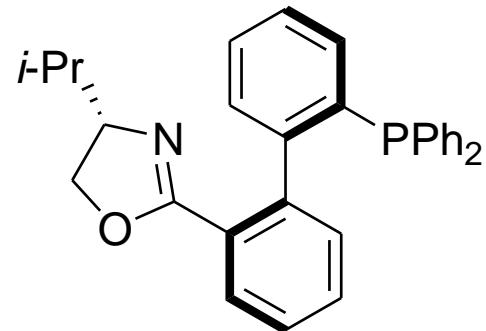
# Hydrogenation of N-Protected Indoles



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

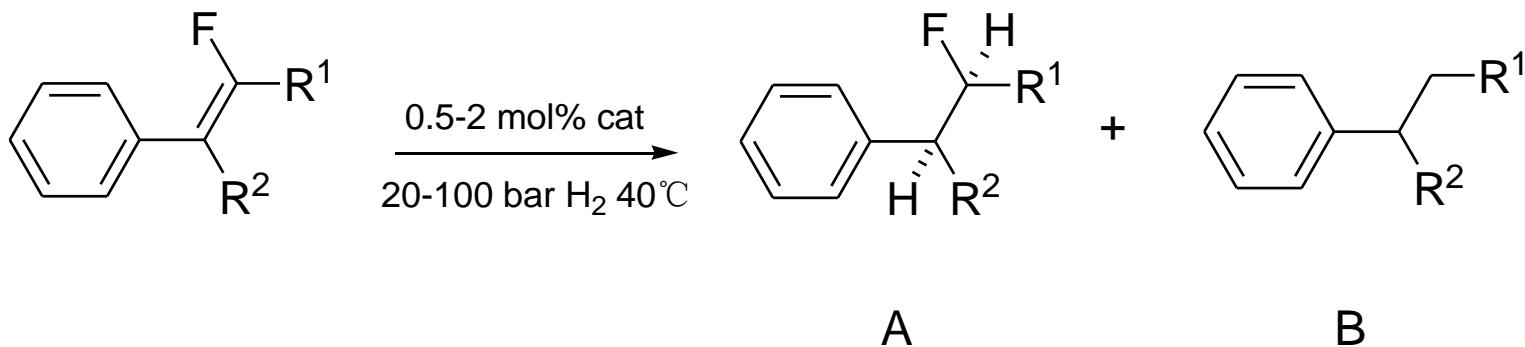


up to 98% ee

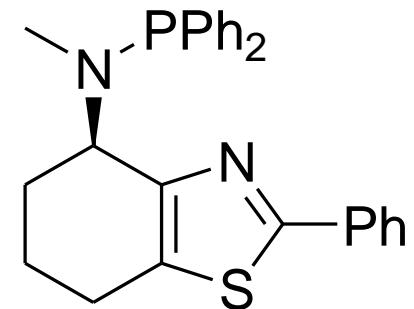


Zhang W-B ASC 2010 1841

# Hydrogenation of Fluorinated Olefins



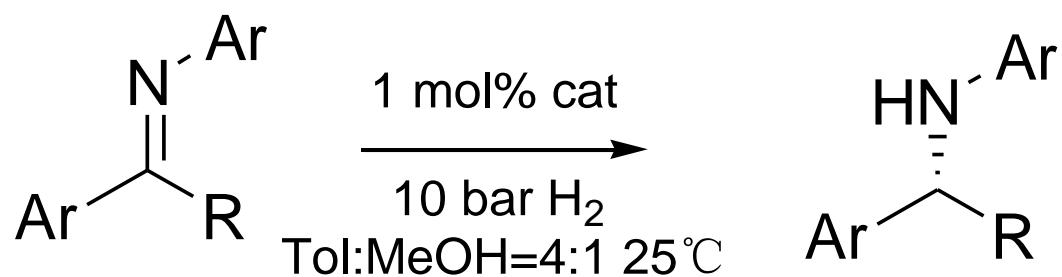
up to 100:0 A:B ratio 99% ee



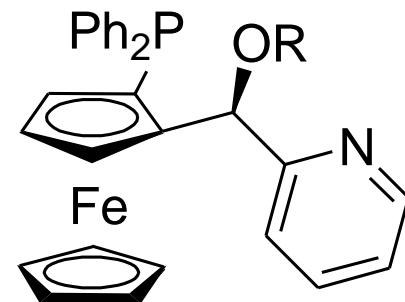
Andersson JACS 2007 4536

# Hydrogenation of C=N Bonds

## Hydrogenation of Imines



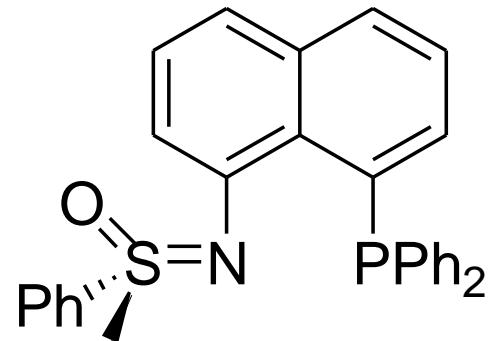
up to 98% ee



# Hydrogenation of Quinolines

21

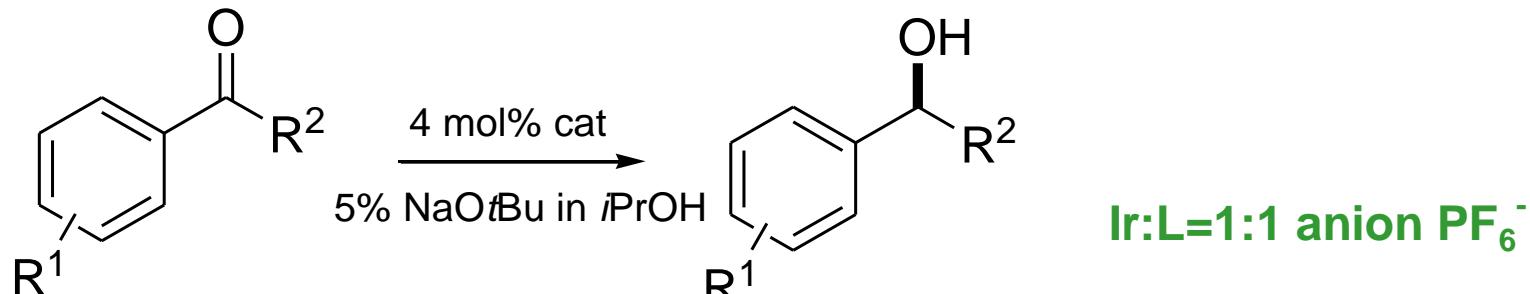
up to 87% ee



Bolm *ASC* 2008 1101

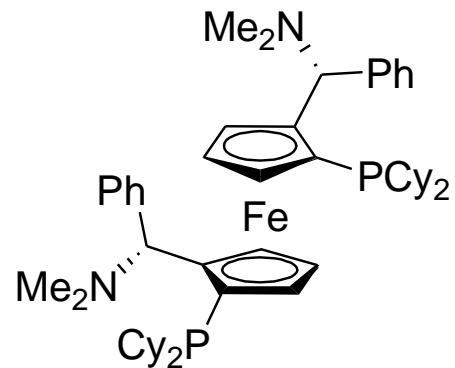
# Hydrogenation of C=O Bonds

## Transfer Hydrogenation of Ketones

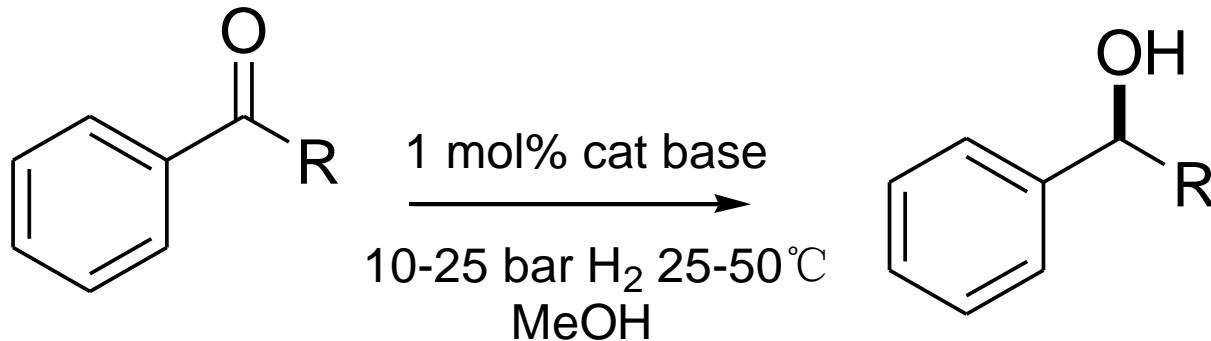


up to 95% ee

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

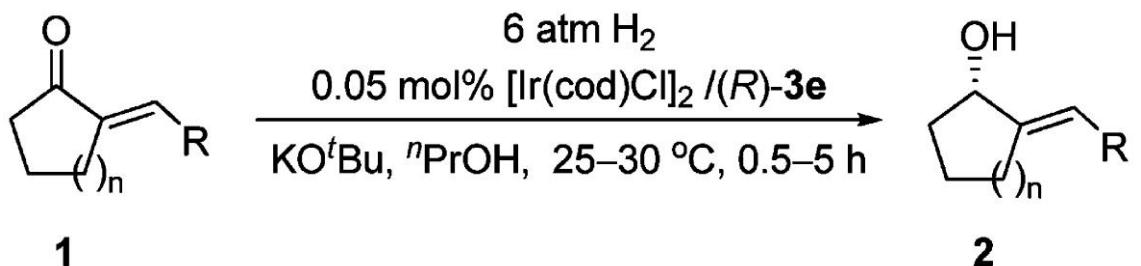


# Hydrogenation of Ketones

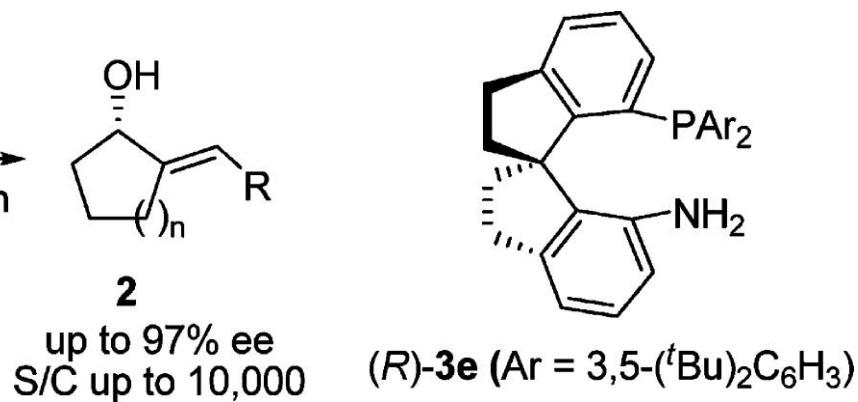


up to 68% ee

# Hydrogenation of Ketones



R = alkyl, aryl; n = 1-3



# Conclusion

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

**Thanks For Attention**