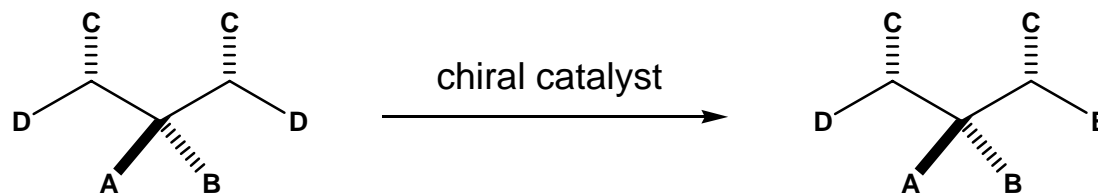


# Recent Advances in Catalytic Enantioselective Desymmetrization Reactions

November 30, 2007

Torsak Luanphaisarnnont



## Leading References:

- 1) Rovis, *New Frontiers in Asymmetric Catalysis*, Wiley, **2007**, 275.
- 2) Willis, *J. Chem. Soc. Perkin Trans 1* **1999**, 1765.
- 3) Magnuson, *Tetrahedron* **1995**, 2167.
- 4) Trotter, *DAE Group Meeting* **1997**.

DAE Group Meeting

# Contents

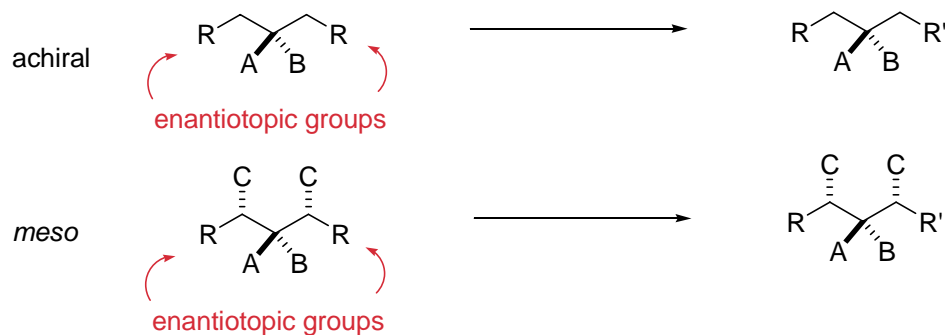
- I. Introduction
- II. Allylic Substitution
- III. Ring Opening
- IV. Deprotonation
- V. Monoprotection
- VI. Oxidation
- VII. Other Reactions

(not covered in this seminar: Catalytic Enantioselective Methathesis;  
see: Young, *DAE Group Meeting 2004*.)

# I. Introduction

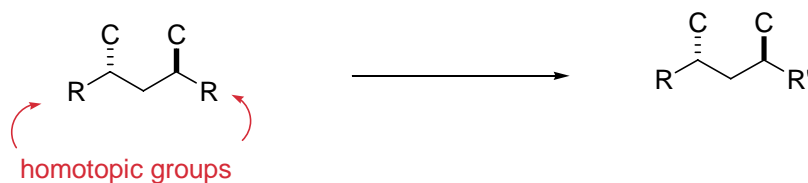
## Desymmetrization of Symmetric Compounds

- Achiral and *meso* compounds



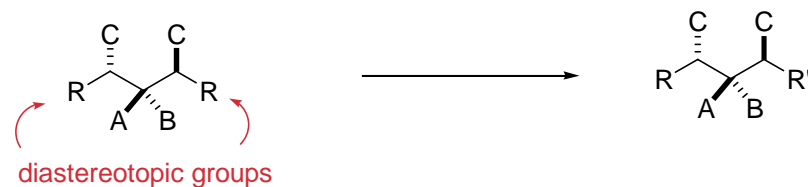
enantiotopic group selection

- achiral  $C_2$  symmetric compounds



monofunctionalization

- chiral pseudo  $C_2$  symmetric compounds



diastereotopic group selection

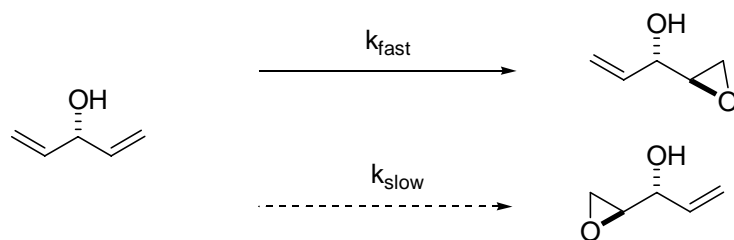
(This seminar will focus on the desymmetrization of *meso* compounds.  
Only selected desymmetrization of achiral compounds will be covered.)

Magnuson, *Tet* **1995**, 2167.

## Enantioselective Desymmetrization and Kinetic Resolution

### Enantioselective Desymmetrization

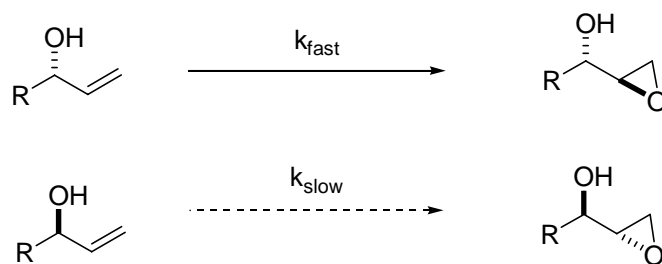
Chiral reagents/catalysts react with each of the enantiotopic groups in the same molecule at different rates.



A sufficient rate difference allows reaction at single enantiotopic groups to give an asymmetric product. Theoretical yield = 100%

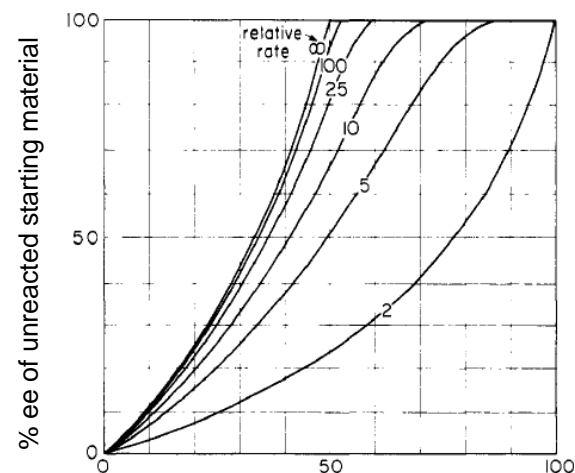
### Kinetic Resolution

Chiral reagents/catalysts react with each of the enantiomers at different rates.



$$\text{relative rate (selectivity factor)} = k_{\text{fast}} / k_{\text{slow}}$$

A sufficient rate difference allows consumption of one enantiomer and recovery of the other. Theoretical yield = 50%.



$$s = \frac{\ln[(1-C)(1-ee)]}{\ln[(1-C)(1+ee)]}$$

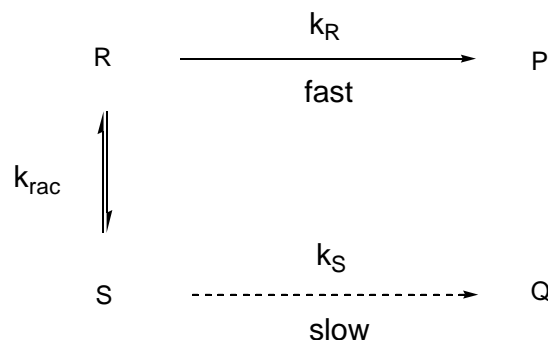
Sharpless, *JACS* **1981**, 6237.

Trotter, *DAE Group Meeting* **1997**.

## Enantioselective Desymmetrization and Kinetic Resolution (Cont.)

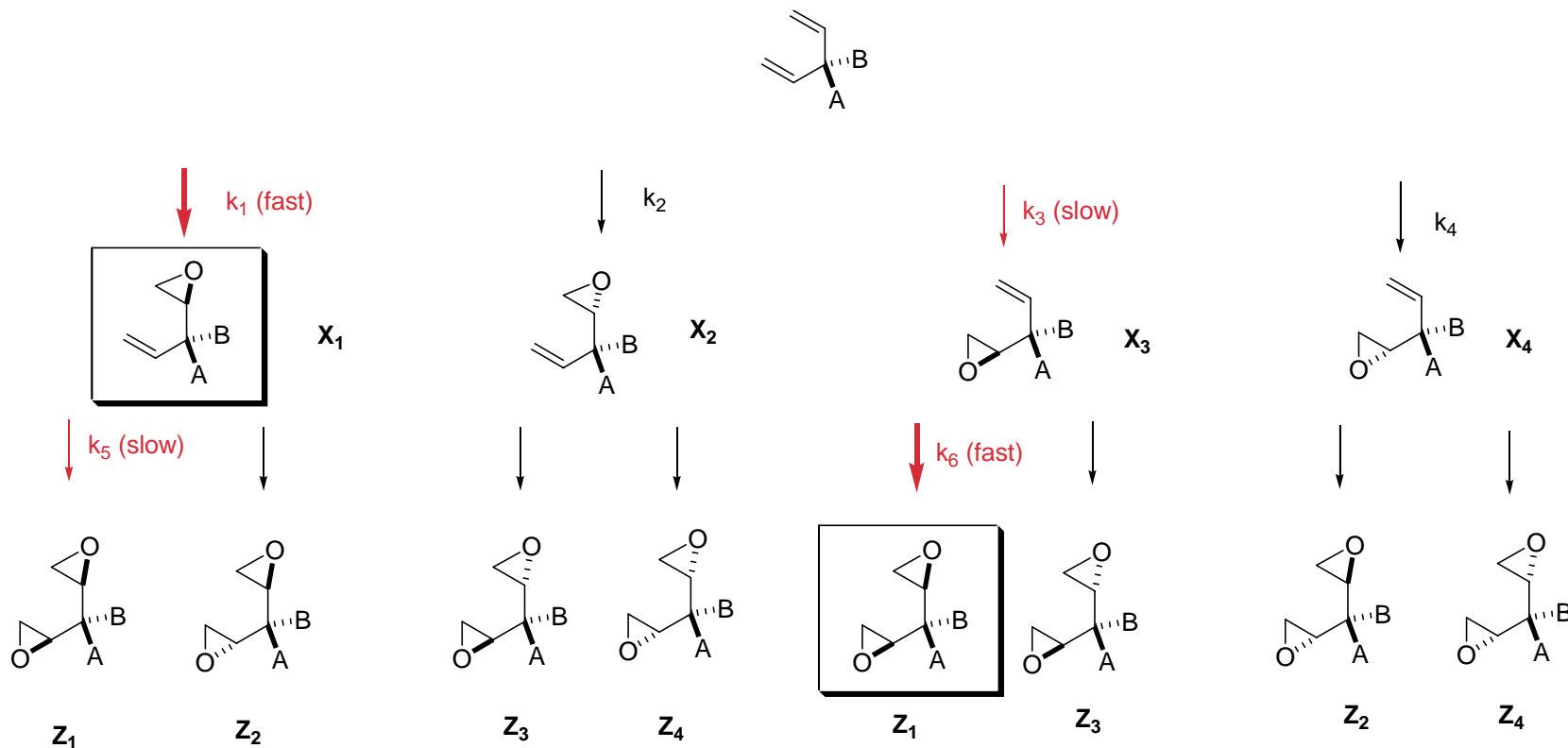
### Dynamic Kinetic Resolution

An equilibration between two enantiomers of the starting material allows for full conversion of starting material.



- 1) kinetic resolution should be irreversible to ensure high enantioselectivity.
- 2)  $k_{\text{fast}}/k_{\text{slow}}$  should be at least greater than 20.
- 3) to avoid depletion of R,  $k_{\text{rac}}$  should be at least equal to or greater than  $k_{\text{R}}$
- 4) if the selectivity is only moderate,  $k_{\text{rac}}$  should be greater than  $k_{\text{R}}$  by at least 10.
- 5) any spontaneous reaction involving substrate enantiomers as well as racemization of the product should be absent.
- 6) Dynamic resolution is generally limited to compound possessing one single stereocenter.

## Coupled Enantioselective Desymmetrization and Kinetic Resolution



- The reactions that couple a kinetic resolution to an initial asymmetric synthesis can provide primary products with enhanced levels of enantiomeric purity.

(Only selected cases of this type of desymmetrization will be covered in this seminar.)

# Enantioselective Enzymatic Desymmetrization

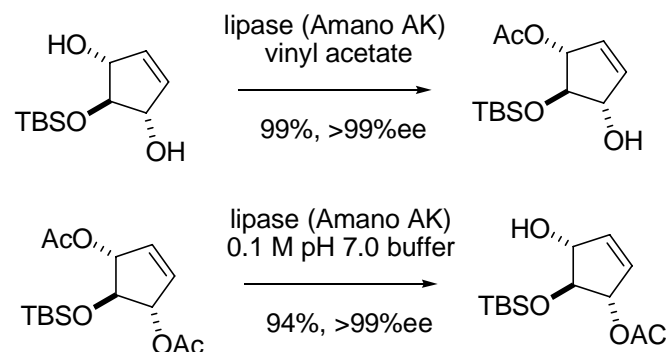
(not covered in this seminar)

## Selected reviews:

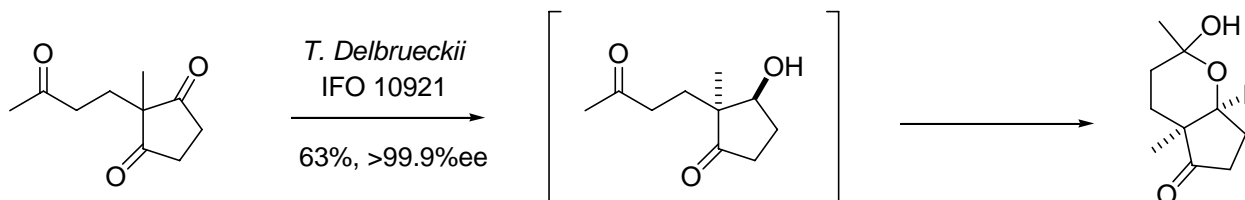
- 1) Gotor, *Chem. Rev.* **2005**, *105*, 313.
- 2) Johnson, *Tetrahedron* **1996**, *52*, 3769.

## Selected transformations:

### Hydrolyses and transesterifications of alcohols



### Reduction of ketones



Toyama, *BCSJ* **2001**, 997.

Sugai, *JOC* **2000**, 129.

**Other transformations:** C=C reduction, oxidation of alcohols, monohydroxylations, oxidation of sulfides, dihydroxylations, Baeyer-Villiger oxidations, aldol reactions, hydrocyanation

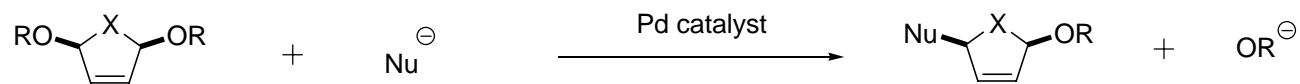
Gotor, *CR* **2005**, 313 and references therein.

## II. Allylic Substitution

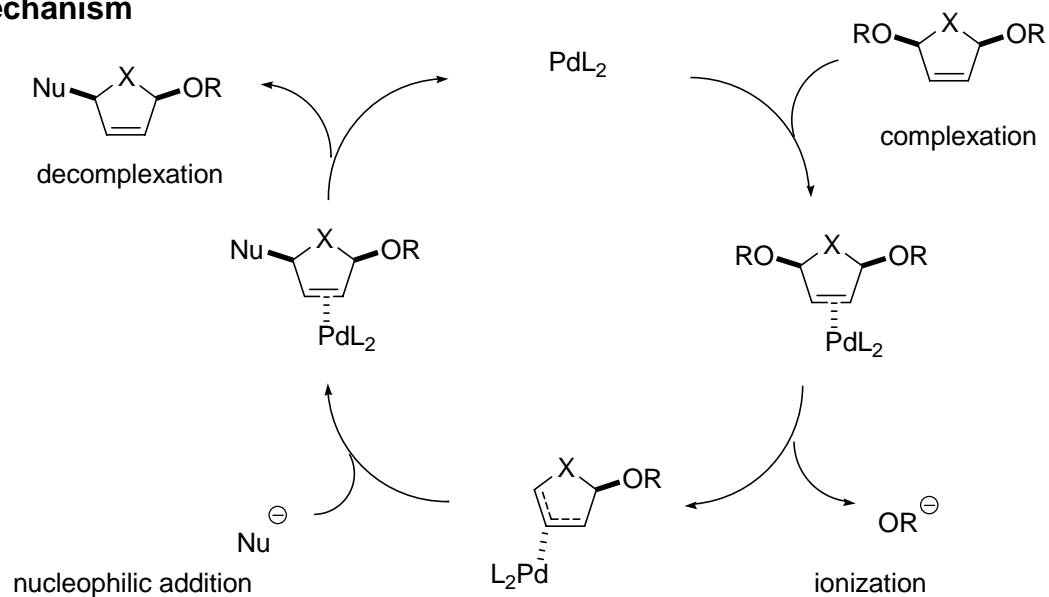
(Leading reviews: Ma, *ACIE* **2007**, Early View.)

- A) Palladium catalyzed reaction
- B) Copper catalyzed reaction
- C) Rhodium catalyzed reaction

### A) Palladium catalyzed reaction

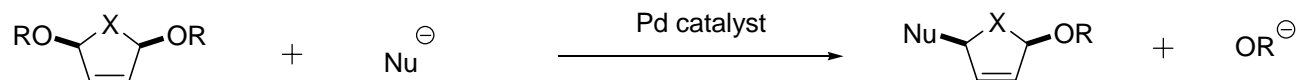


#### General mechanism

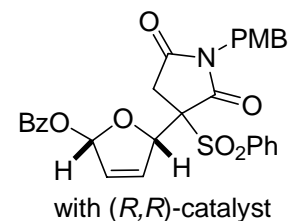
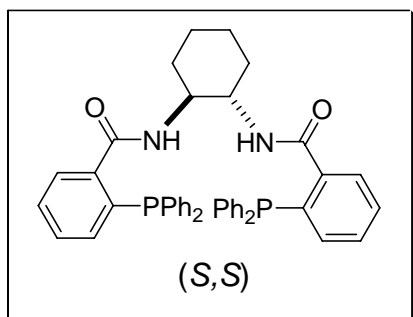




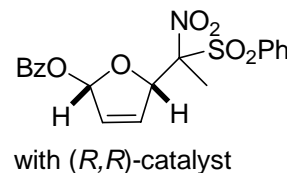
## Nucleophiles and leaving groups



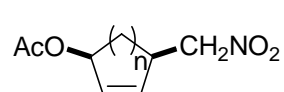
## Diphenylphosphinobenzoic-acid-based catalyst



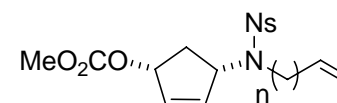
67%, 92% ee, dr 7:3

Trost, *JOC* **1999**, 5427.

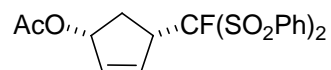
91%, 93% ee, dr 5:1

Trost, *CEJ* **2002**, 259.

n=1 75%, 99% ee  
 n=2 83%, 99% ee  
 n=3 83%, 99% ee

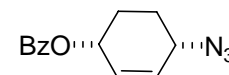
Trost, *ACIE* **2000**, 3122.

n=1 88%, 99% ee  
 n=2 89%, 98% ee

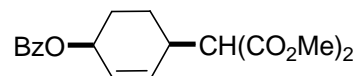
Blechert, *JACS* **2000**, 9584.

87%, 95% ee

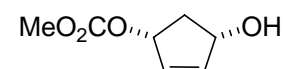
with (R,R)-catalyst

Toru, *ACIE* **2006**, 5095.

87%, 95% ee

Trost, *TL* **1996**, 7485.

68%, 95% ee

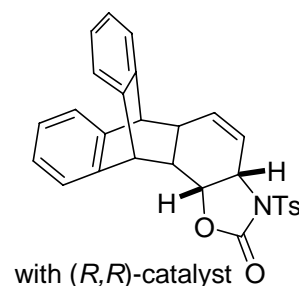
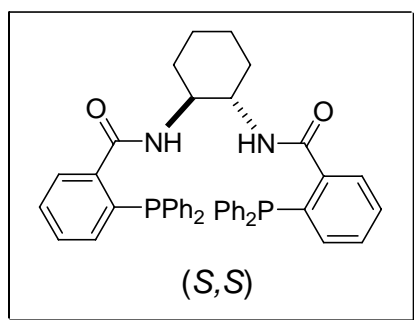
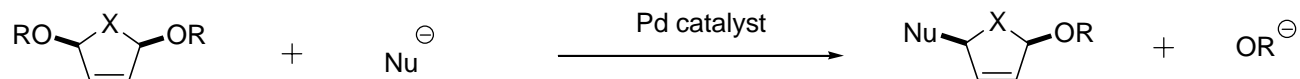
Trost, *JACS* **2006**, 2540.

87%, 96% ee

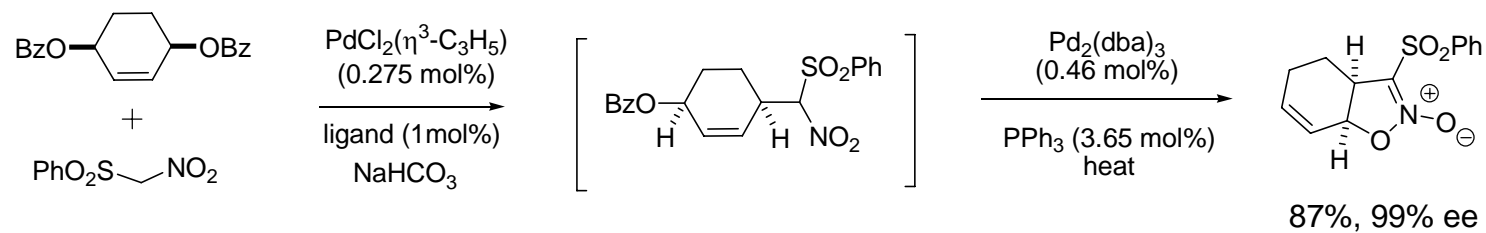
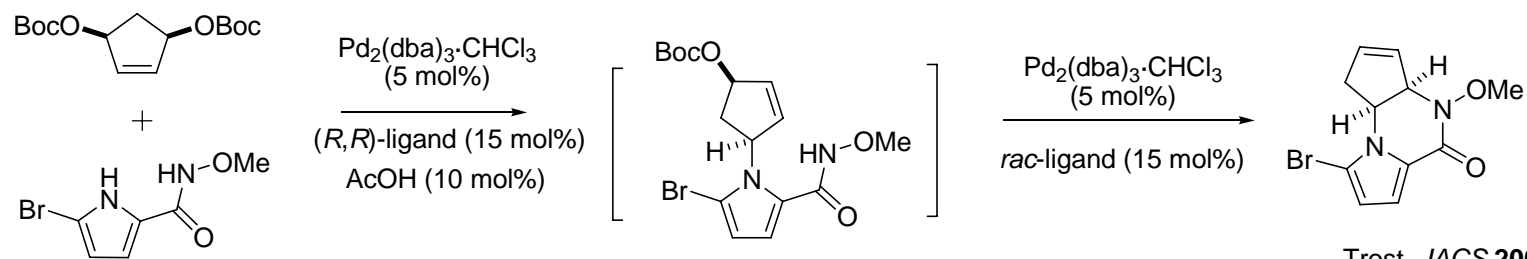
with (R,R)-catalyst

Gais, *TL* **2005**, 6279.

## Nucleophiles and leaving groups (cont.)

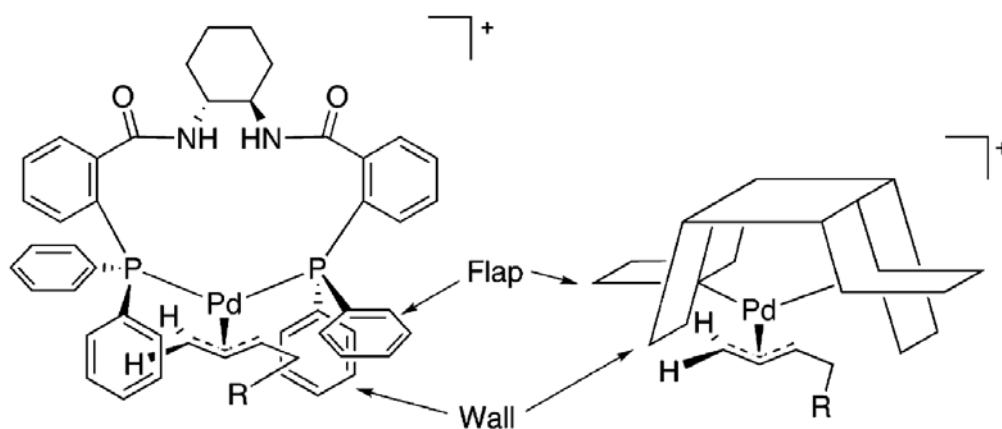


80%, 99% ee

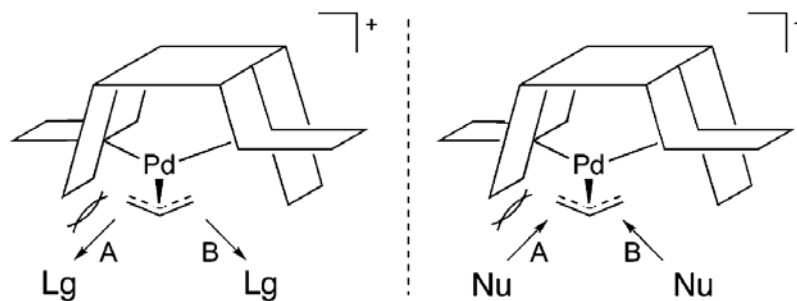
Trost, *CEJ* **1999**, 3279.Trost, *JACS* **1998**, 1732.

### Working model for enantioselective allylic substitution

- Model serves as **predictive tool** for most of diphenylphosphinobenzoic-acid-based Pd-asymmetric allylic substitution.
- Cartoon model for the Pd-ligand complex based on the ground-state energy minimized conformation. Structural data suggest that the complex are in equilibrium with oligomeric species depending on catalyst concentration and temperature.

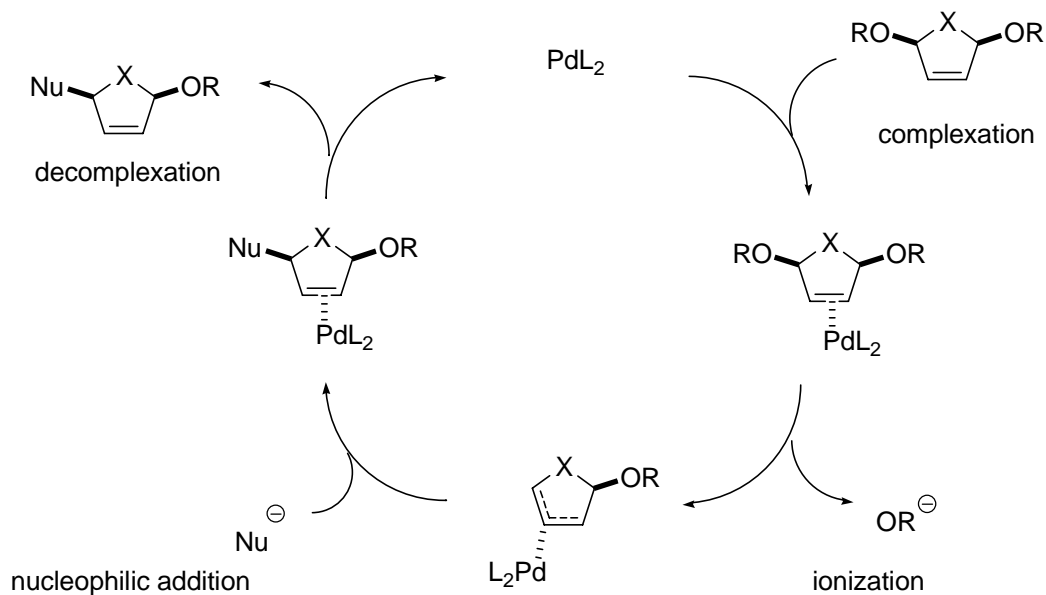


- Leaving groups/ nucleophiles follow the path that minimize steric interaction with ligands.

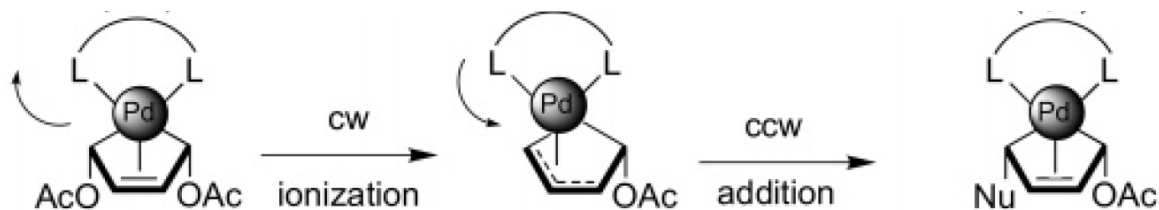


### Working model for enantioselective allylic substitution (cont.)

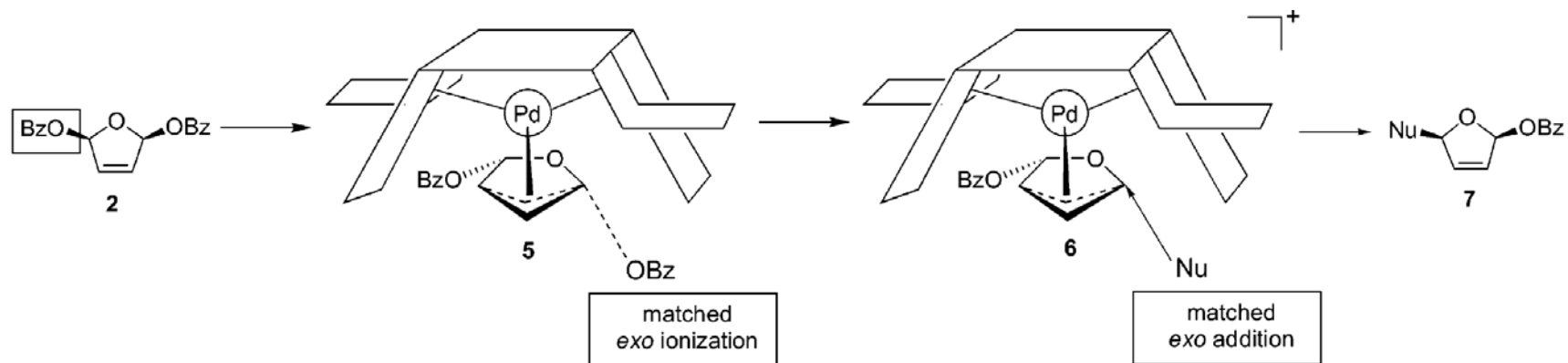
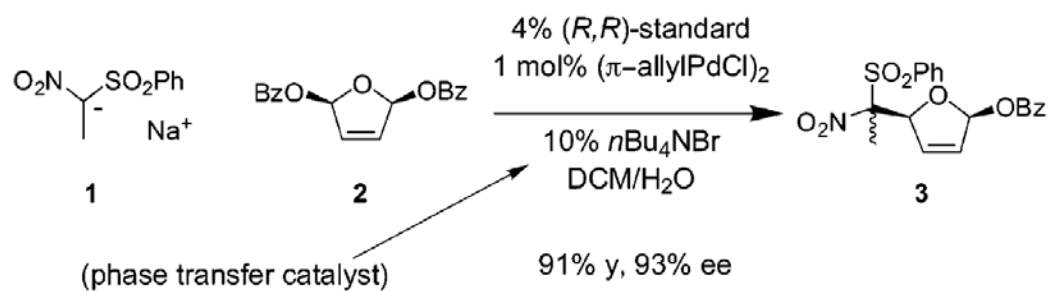
- In desymmetrization reaction, catalyst has to differentiate two enantiotopic leaving groups in the ionization step.



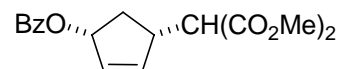
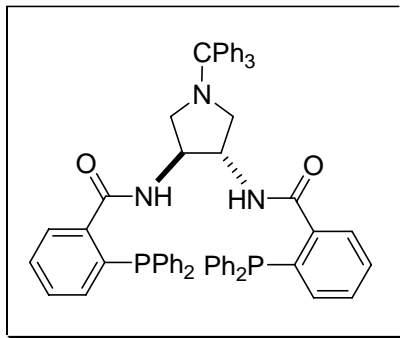
- During ionization, the catalyst is expected to move toward the leaving groups. Nucleophilic addition is the microscopic reverse of the ionization; therefore, the catalyst is expected to move away from the nucleophiles.



Working model for enantioselective allylic substitution (cont.)

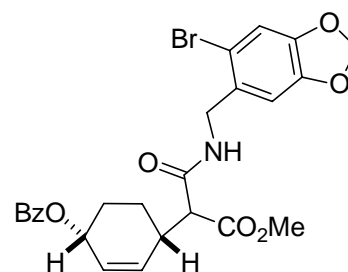
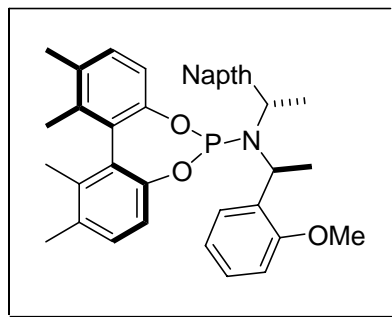


Other ligands (selected cases)



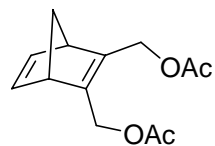
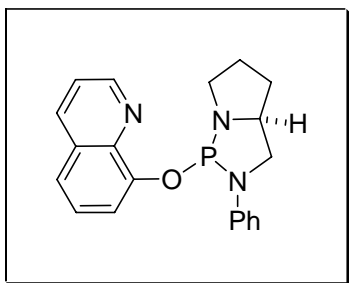
98%, 98% ee

Song, *ACIE* **2002**, 3852.

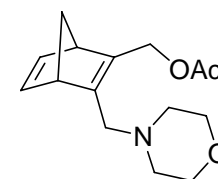
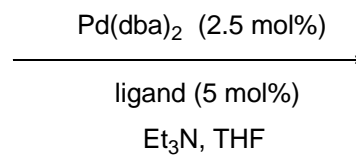
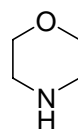


83%, 99.4% ee, dr = 54:46

Ojima, *OL* **2006**, 1395.



+



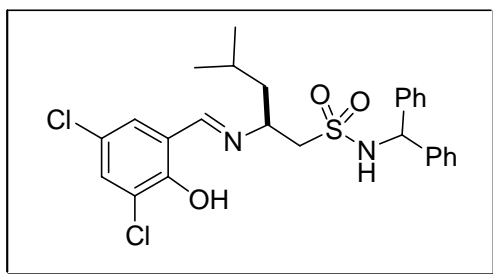
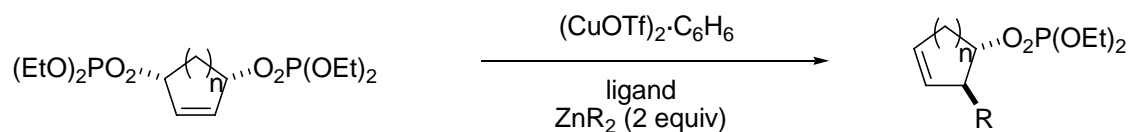
93%, 89% ee

Buono, *Tet.* **1998**, 10435.

## B) Copper catalyzed reaction

- catalytic in copper, (super)stoichiometric in alkylmetal reagents (zinc, aluminum)
- generally give  $S_N2'$  product with net inversion (unlike Palladium catalysis)
- mechanism is not well established

## Selected cases

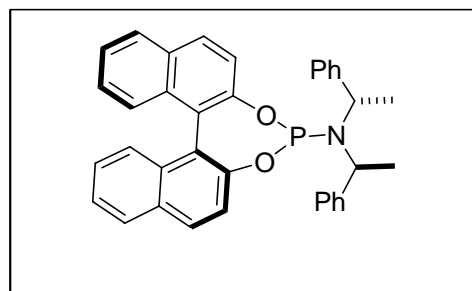


10 mol% Cu, 10 mol% ligand,  $n=1$

R=Et 47%, 88% ee

R=Me 40%, 99% ee

Piarulli, *ACIE* **2003**, 234.

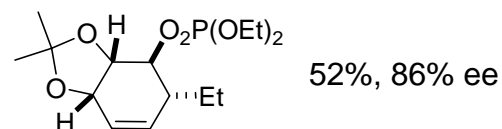


5 mol% Cu, 20 mol% ligand, R=Et  
(*ent*-product obtained)

$n=1$  98%, 87% ee

$n=2$  77%, 90% ee (87:13 inversion:retention)

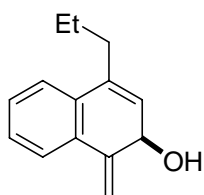
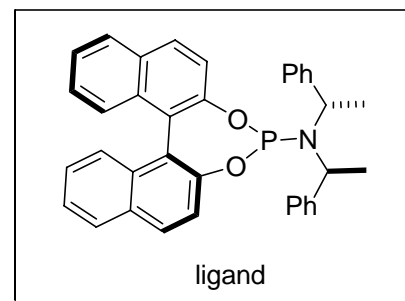
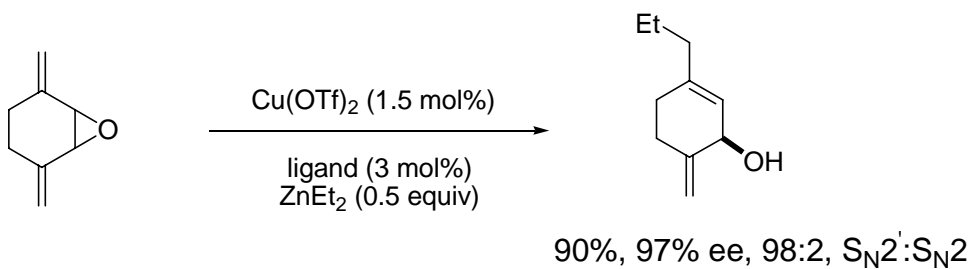
$n=3$  85%, >98% ee



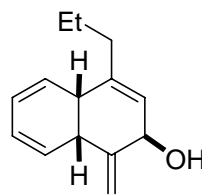
52%, 86% ee

Piarulli & Feringa, *OL* **2003**, 4493.

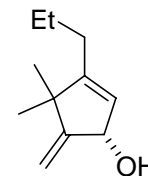
Selected cases (cont.)



92%, 66% ee, 98:2  $\text{S}_{\text{N}}2':\text{S}_{\text{N}}2$

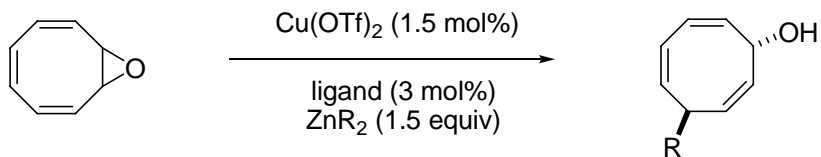


78%, 71% ee, 93:7  $\text{S}_{\text{N}}2':\text{S}_{\text{N}}2$

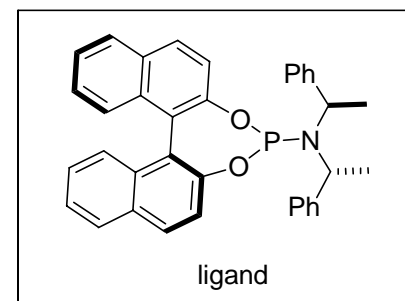


80%, 85% ee, 87:13  $\text{S}_{\text{N}}2':\text{S}_{\text{N}}2$

Pineschi & Feringa, *OL* **2000**, 933.



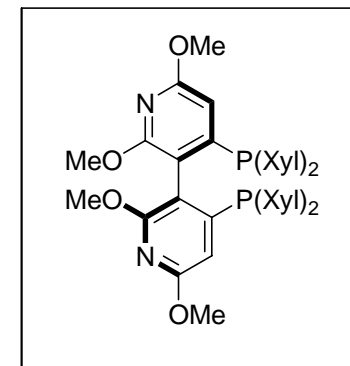
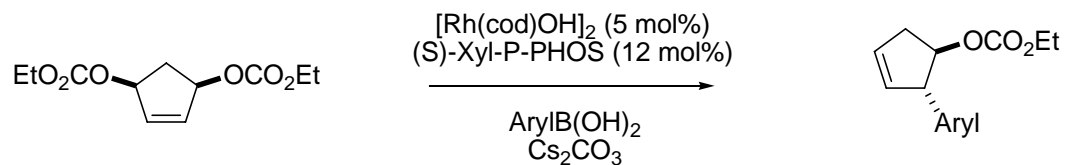
R=Me, 65%, >90% ee  
 R=Et, 90%, 86% ee  
 R=Bu, 78%, 82% ee



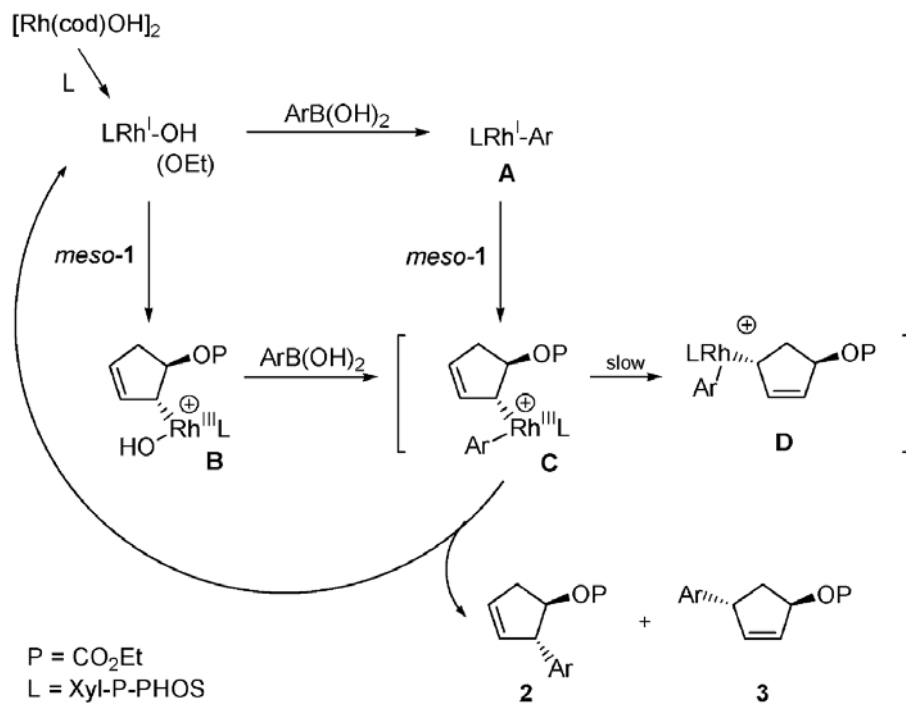
Pineschi, *OL* **2003**, 1971.



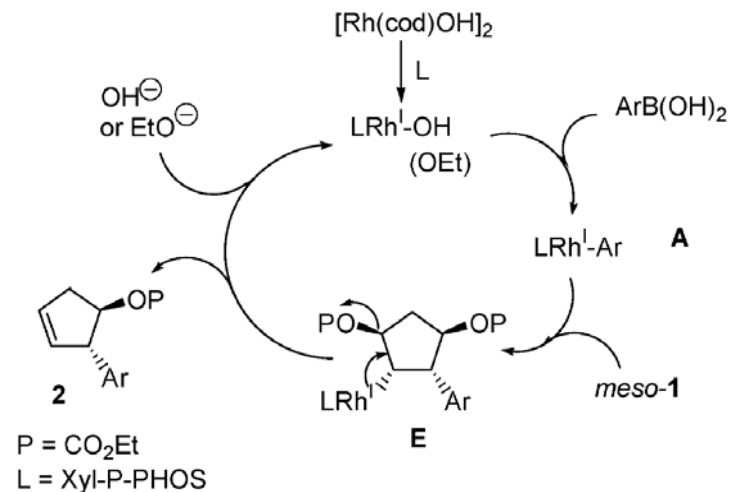
## C) Rhodium catalyzed reaction



## Proposed mechanisms

via a  $\sigma$ -intermediate

## via carboration

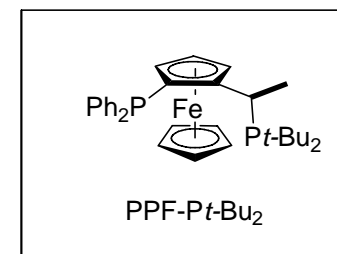
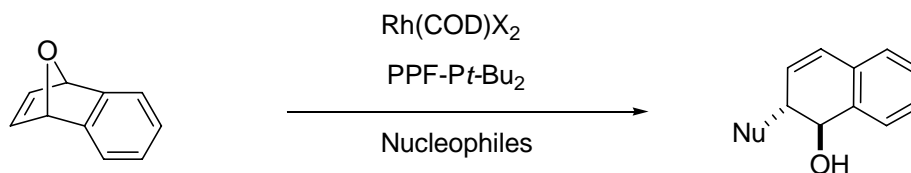


# III. Ring Opening

- A) Bridged systems
- B) Epoxides
- C) Aziridines
- D) Cyclic Anhydrides
- E) Others

## A) Bridged systems

### Rhodium catalyzed reactions



### Nucleophiles:

ROH x=Cl, R= Me, Et, *i*-Pr, allyl, benzyl, etc. 9 examples, 53-96%, 93-99% ee  
(with *ent*-ligand)

x=Cl, R= Aryl, 10 examples, 60-41%, 91-99% ee

RSH x=Cl, R= Aryl, benzyl, alkyl 14 examples, 52-92%, 90-98% ee

R<sub>2</sub>NH x= I, Nuc = activated amines (phthalamide, aniline, quinoline) 5 examples,  
71-97%, 88-98% ee (*indole gives C-alkylation*)

CH<sub>2</sub>(CO<sub>2</sub>Me)<sub>2</sub> x=I, 97%, 98%ee

Lautens, *JACS* **2000**, 5650.

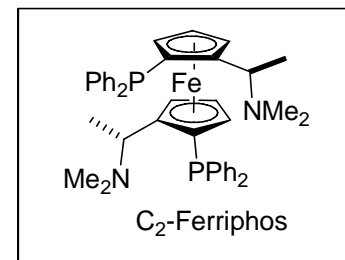
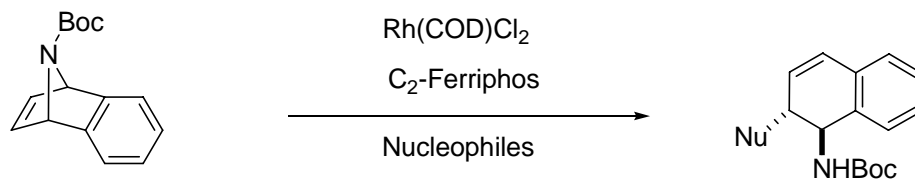
Lautens, *OL* **2000**, 1677.

Lautens, *JOC* **2004**, 2194.

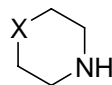
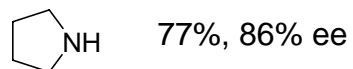
Lautens, *JACS* **2001**, 7170.

Lautens, *JACS* **2001**, 7170.

Rhodium catalyzed reactions (cont.)



Nucleophiles:



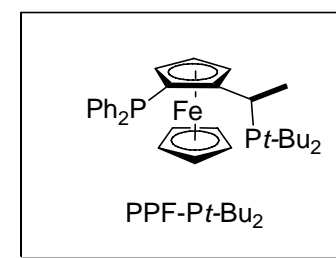
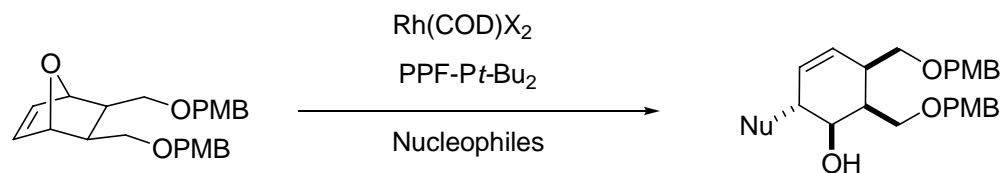
$x = \text{CH}_2$  85%, 84% ee

$x = \text{NPh}$  75%, 96% ee  
(with PPF-*t*-Bu<sub>2</sub> ligand)

$x = \text{O}$  90%, 80% ee

Bn<sub>2</sub>NH 80%, 89% ee

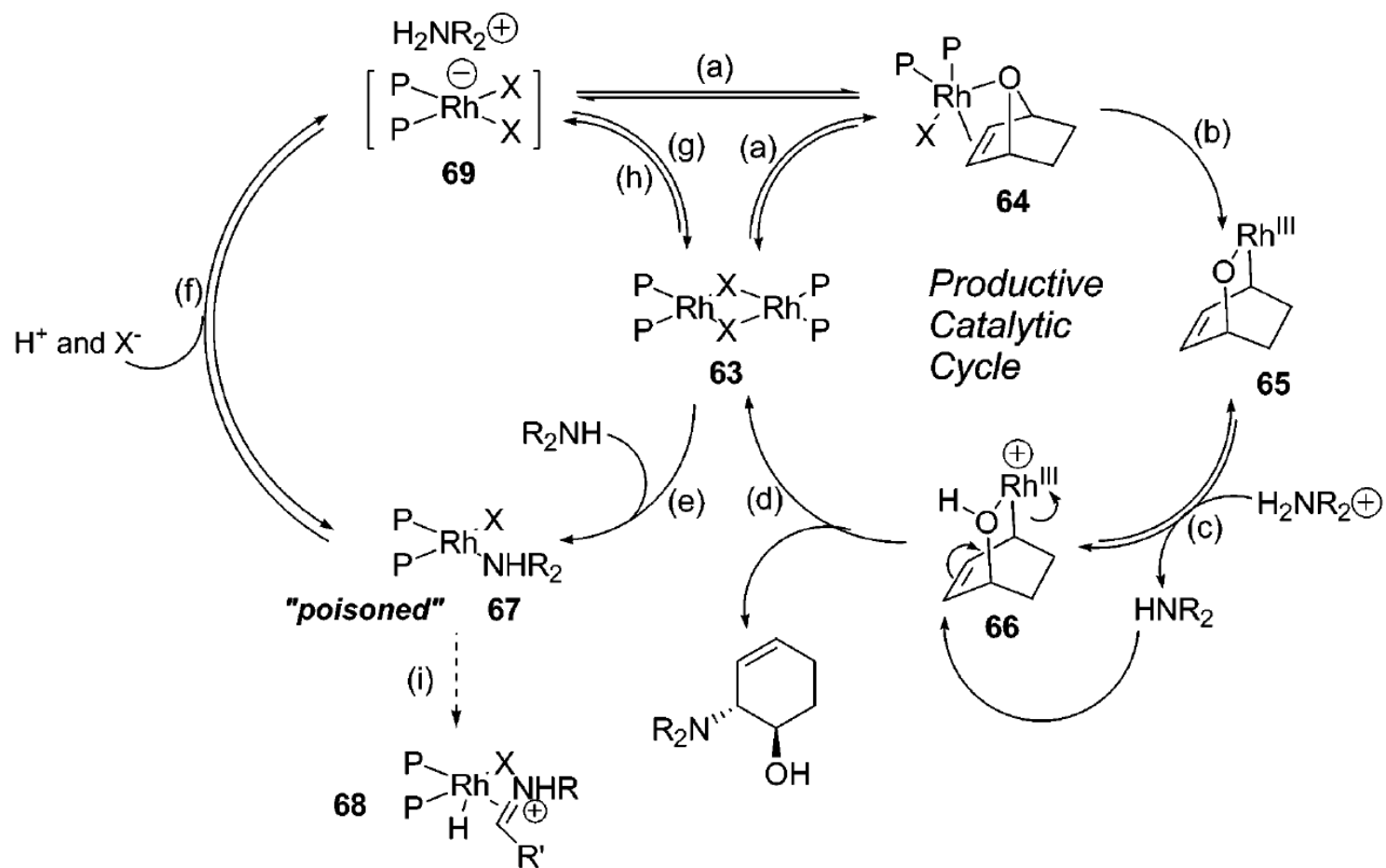
Lautens, *OL* **2002**, 3465.



nucleophiles: PhOH 84%, 93% ee  
PhNHMe 93%, 95% ee

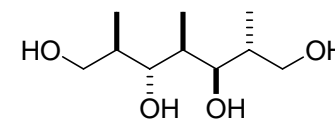
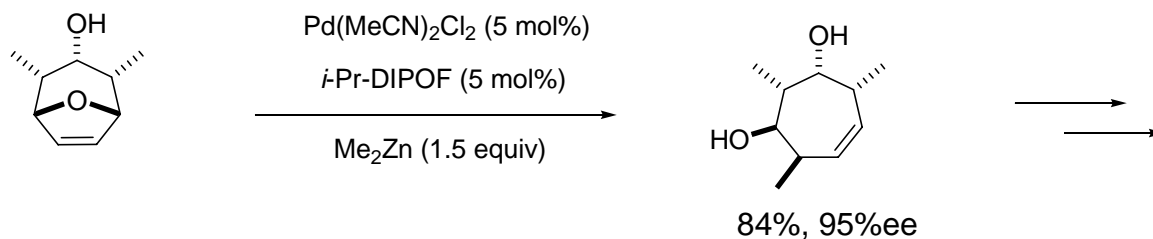
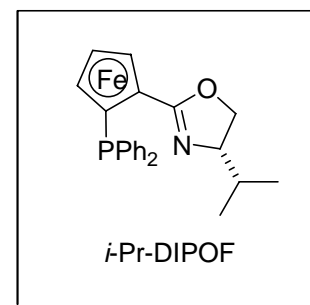
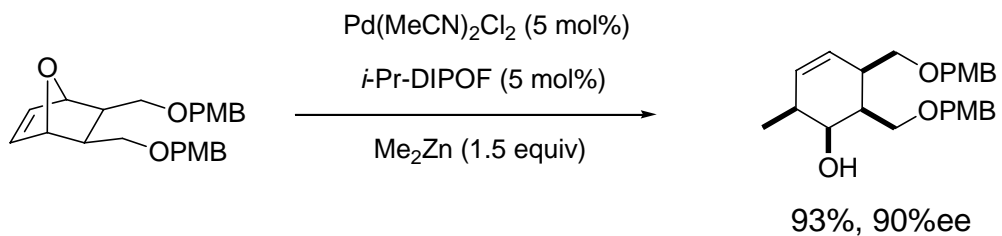
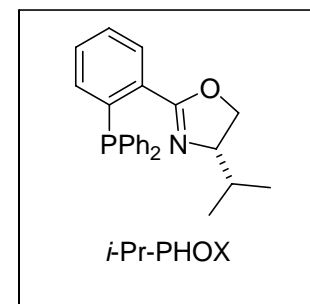
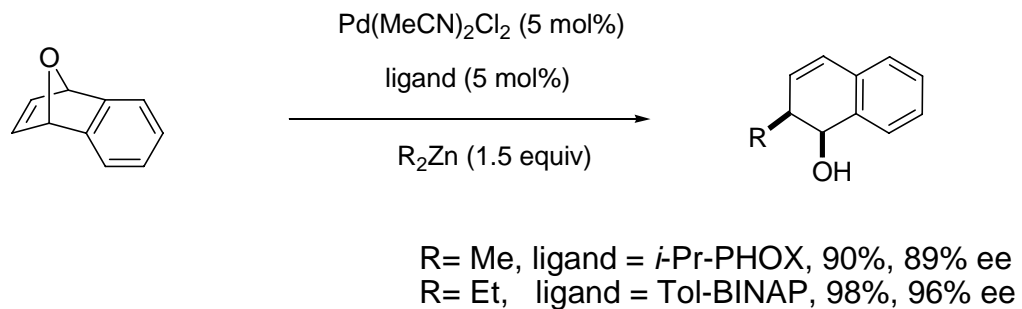
Lautens, *JACS* **2001**, 7170.

## Proposed mechanism

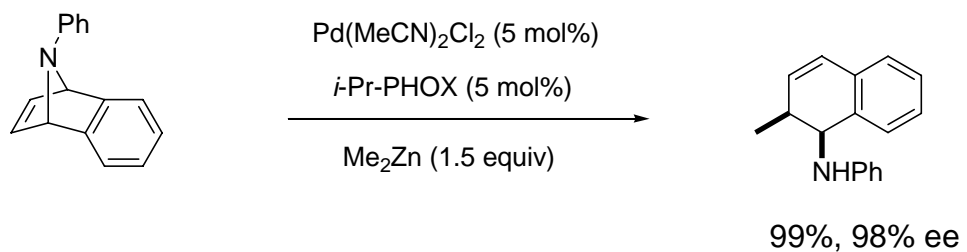


## Palladium catalyzed reactions

## Ring Opening: Bridged systems



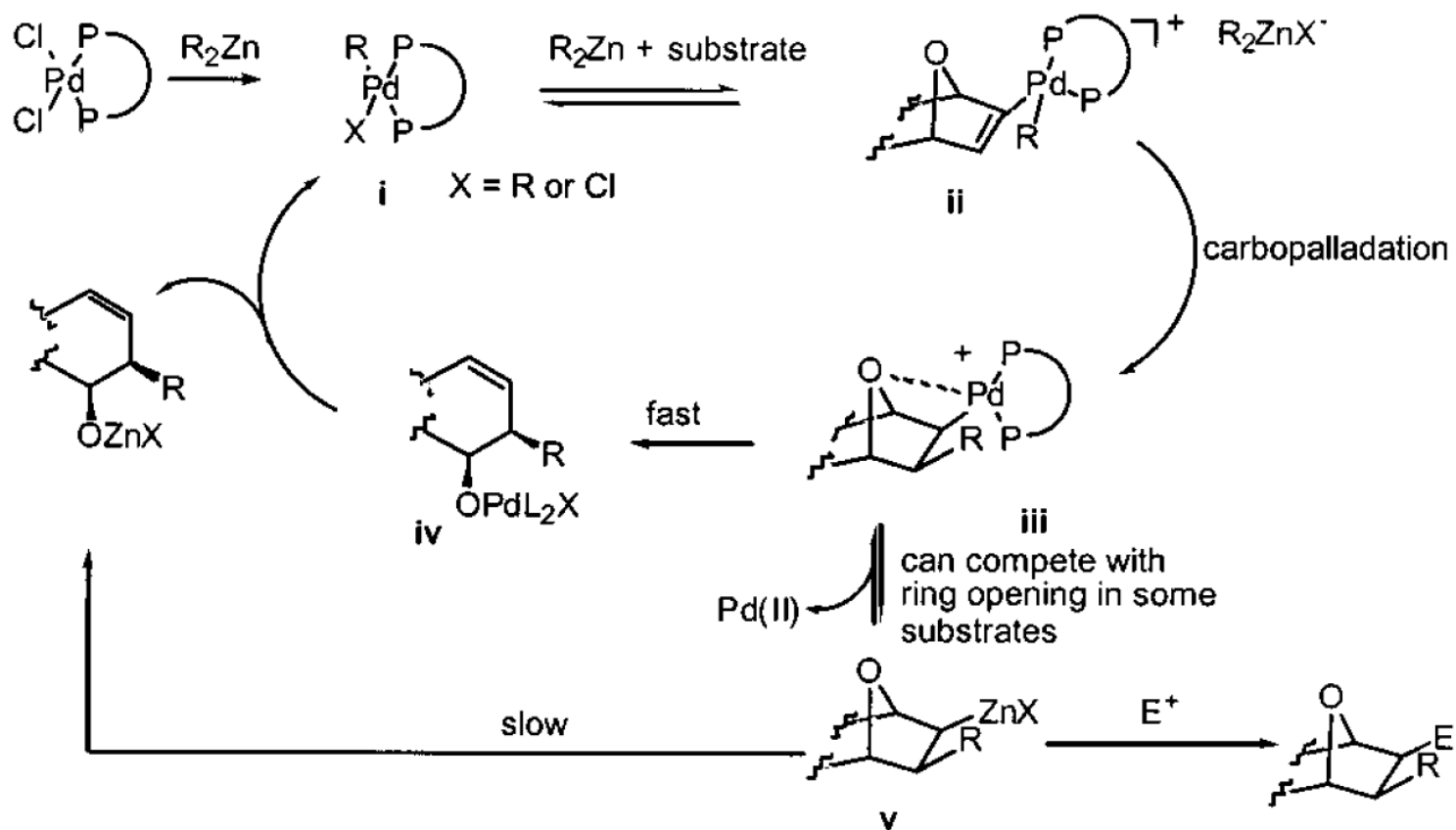
Lautens, *JACS* **2000**, 1804.



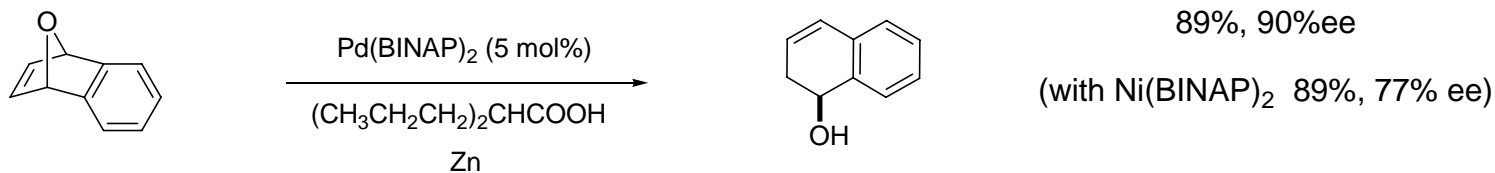
Lautens, *OL* **2000**, 1971.

## Proposed Mechanism

Mechanistic study was done using dppf as a ligand

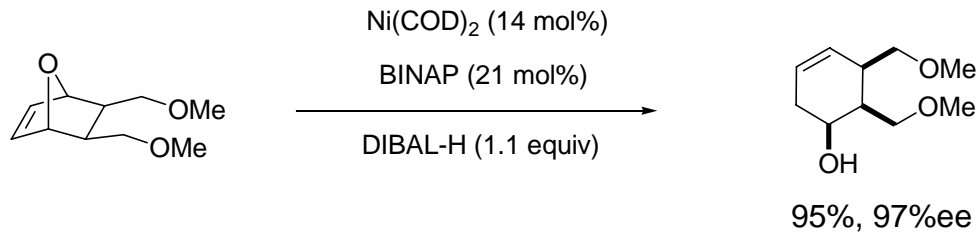


**Palladium catalyzed reactions (cont.)**

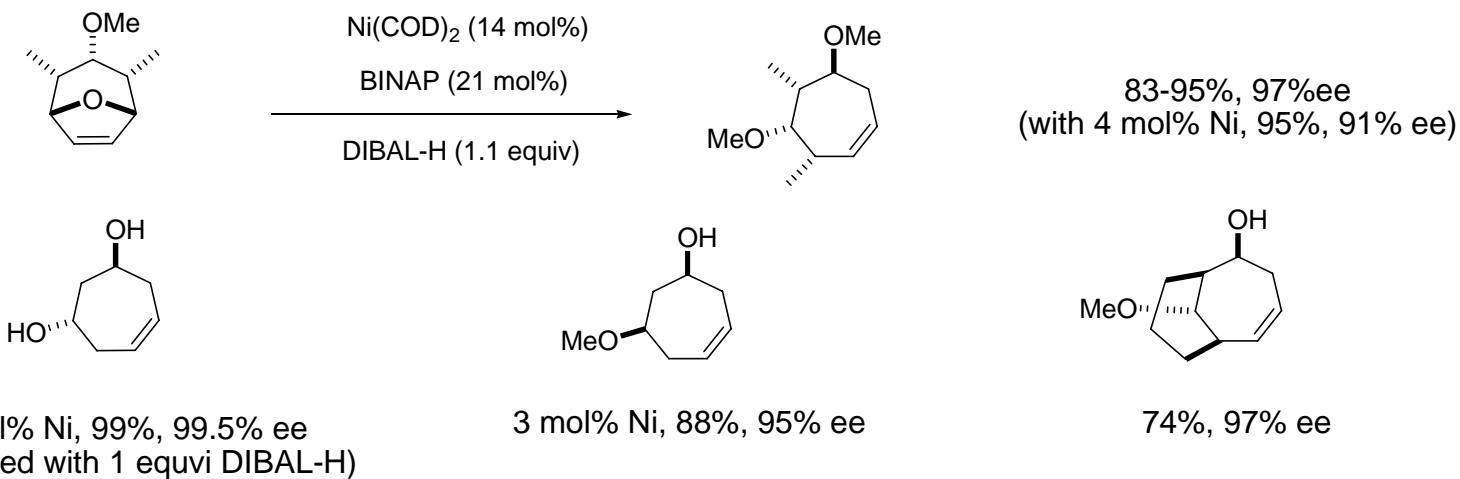


Cheng, *OL* **2003**, 1621.

**Nickel catalyzed reactions**

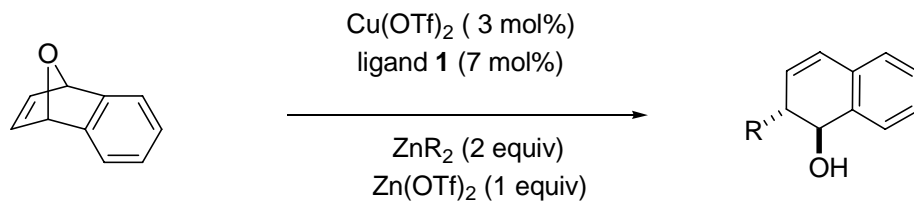


Lautens, *JACS* **1995**, 532.



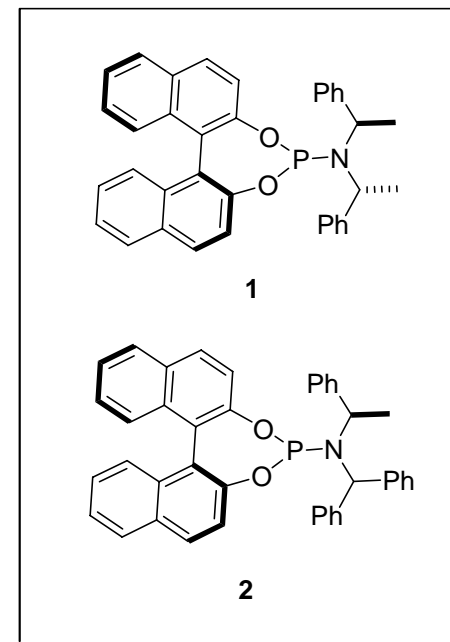
Lautens, *JACS* **1997**, 11090.

## Copper catalyzed reactions

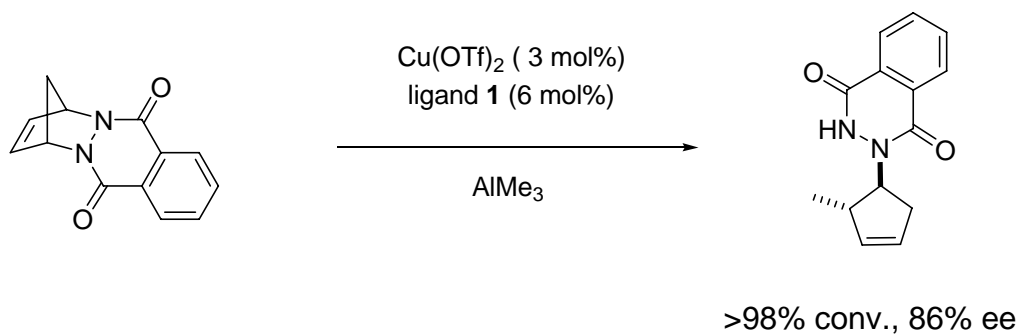


- R= Me 17%, 88% ee, 99:1 anti:syn (35% conv.)  
 R= Et 88%, 90% ee, 98:2 anti:syn  
 92%, 94% ee, 97:3 anti:syn (with ligand **2**)  
 R= *i*-Pr 55%, 91% ee, 70:30 anti:syn  
 R= *n*-Bu 95%, 92% ee, 99:1 anti:syn (with ligand **2**)

substrates with substitutions on the ring are also viable:  
 with R=Et, 5 examples, 58-90%, 80-99% ee, 83:17 to 99:1 anti:syn



Pineschi & Feringa, *OL* **2002**, 2703.



Pineschi, *OL* **2005**, 3605.



## B) Epoxides

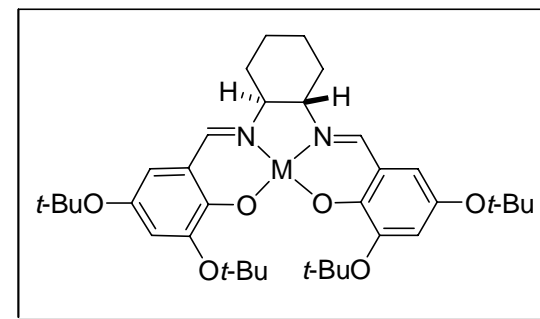
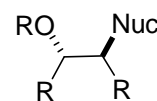
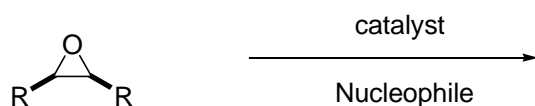
## Selected Reviews:

- 1) Jacobsen, *Comprehensive Asymmetric Catalysis* **1999**,1309.
- 2) Schneider, *Synthesis* **2006**, 3919.

(Only selected cases will be covered in this seminar)

## Salen catalysts

catalyst activates both epoxides and nucleophiles

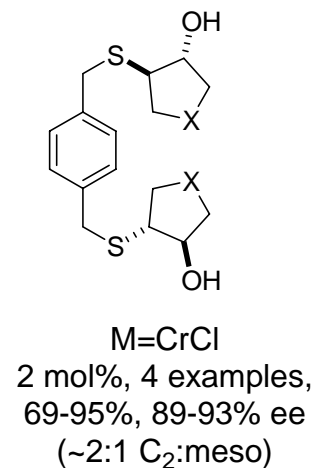


## Products:

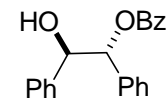


M= CrCl  
2 mol%, 7 examples,  
65-90%, 81-98% ee

Jacobsen, *JACS* **1995**, 5897.

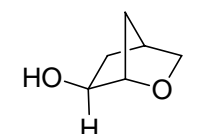


M=CrCl  
2 mol%, 4 examples,  
69-95%, 89-93% ee  
(~2:1 C<sub>2</sub>:meso)  
(BnSH gives moderate ee)  
Jacobsen, *JOC* **1998**, 5252.

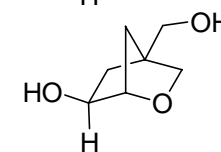


M= Co  
92%, 92%ee  
other cases: 55-77%ee

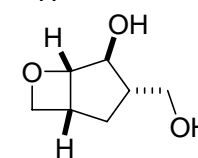
Jacobsen, *TL* **1997**, 773..



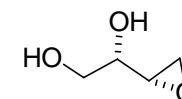
M=CoOAc  
96%, 98% ee



86%, 95% ee



45%, 99% ee

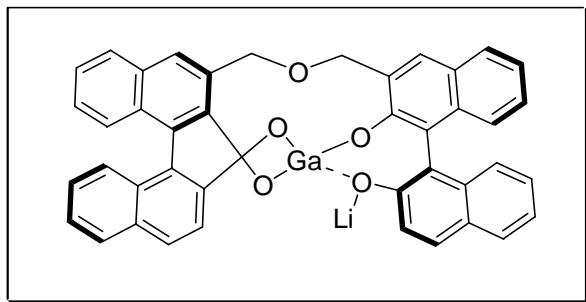
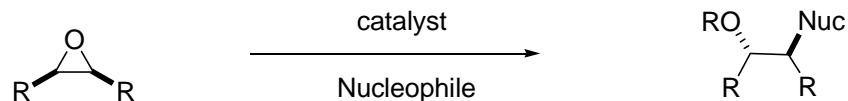


81%, 96% ee

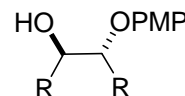
Jacobsen, *ACIE* **1999**, 2012.

## Bimetallic catalysts

## Ring Opening: Epoxides

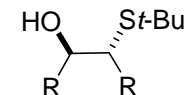


Lewis acidic gallium, Brønsted basic lithium binaphthalate



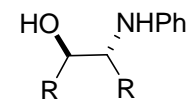
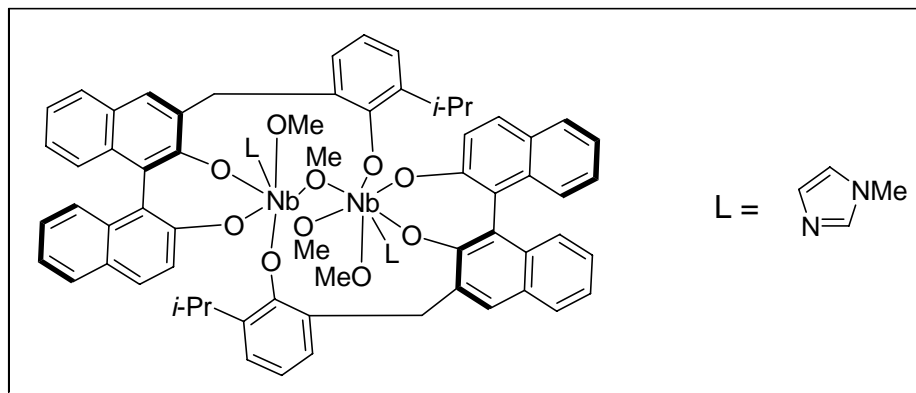
10 mol%, 9 examples,  
67-94%, 66-96% ee

Shibasaki, *JACS*, **2000**, 2252.



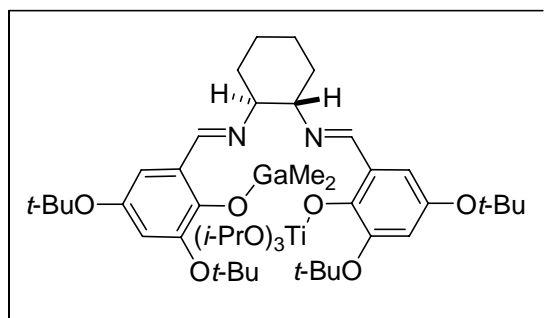
10 mol%, 7 examples,  
74-89%, 82-97% ee

Shibasaki, *JACS* **1997**, 4783.

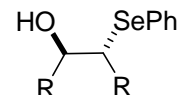


10 mol%, 12 examples,  
54-100%, 70-95% ee

Kobayashi, *JACS* **2007**, 8103..



Soft Lewis acidic gallium, hard Lewis acidic titanium

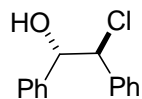
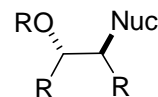
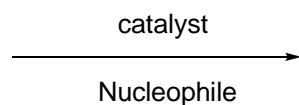
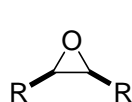


5 mol%, 8 examples,  
70-94%, 70-94% ee

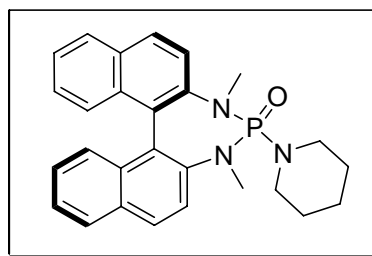
Zhu, *OL* **2005**, 1927.

## Lewis basic catalysts

## Ring Opening: Epoxides

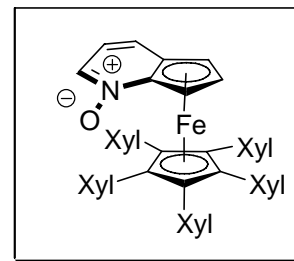


other substrates give moderate ee



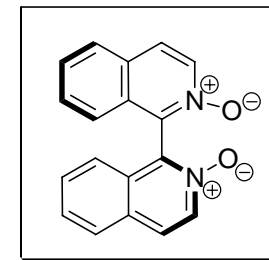
10 mol%, 94%, 87% ee

Denmark, *JOC* **1998**, 2428.



5 mol%, 88%, 94% ee

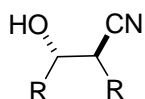
Fu, *JACS* **2001**, 353.



10 mol%, 95%, 90% ee

Nakajima, *TL* **2002**, 8827.

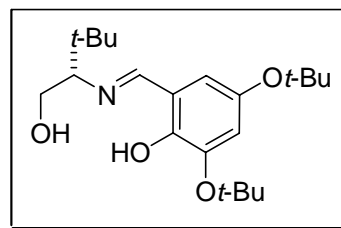
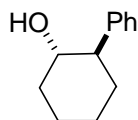
## Other catalysts



$\text{YbCl}_3(\text{Ph-pyBox})$  or  $(t\text{-Bu-pyBox})$

10 mol%, 4 examples,  
72-90%, 87-92% ee

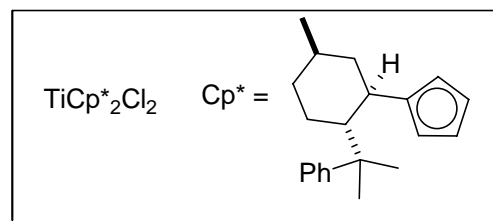
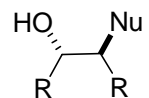
Jacobsen, *OL* **2000**, 1001.



5 mol%, 100%, 90% ee  
other substrates give lower ee

Oguni, *TL* **1998**, 9023.

## Other catalysts (cont.)



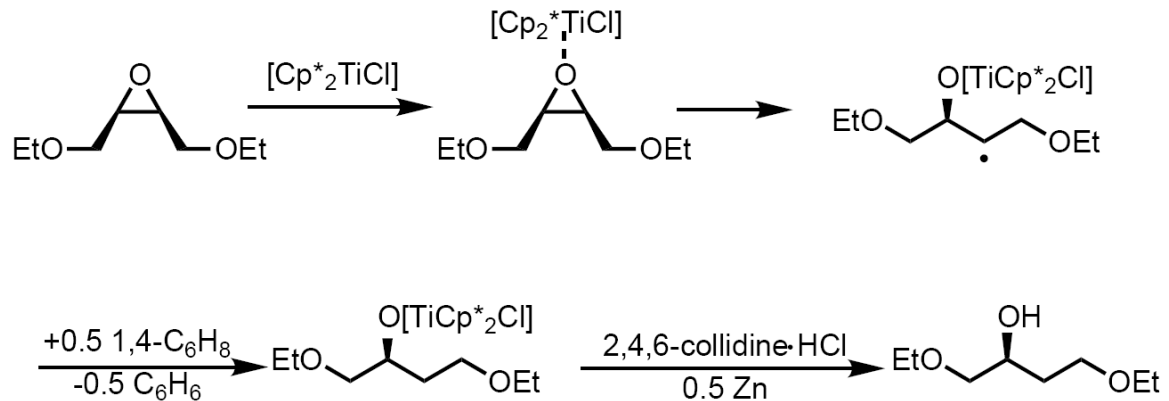
via single electron transfer

10 mol%, with Zn (1.5 equiv) and collidine·HCl

Nu= H (from 1,4 cyclohexadiene) 71%, 93% ee

Nu=  $\text{CH}_2\text{CH}_2\text{CO}_2t\text{-Bu}$ , 3 examples,  
61-72%, 81-82% ee

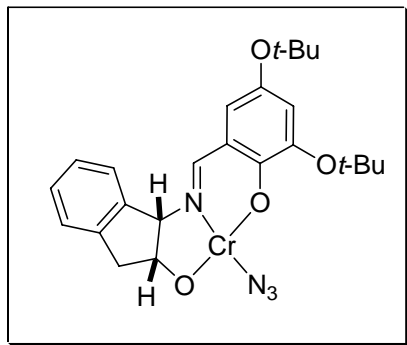
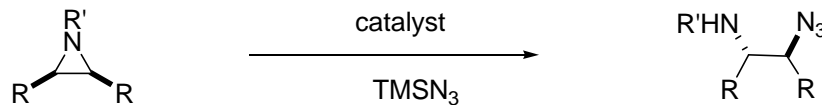
## Mechanism



Gansäuer, *ACIE* **1999**, 2909.

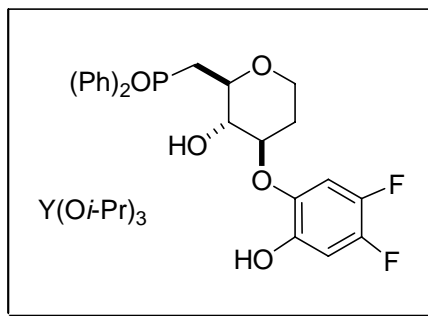
Gansäuer, *CEJ* **2003**, 531.

## B) Aziridines



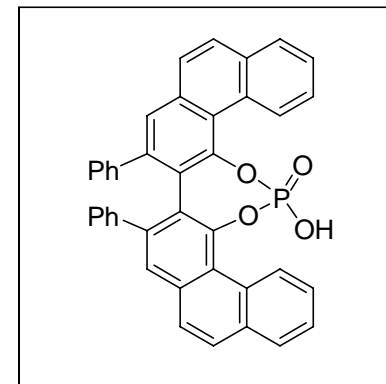
R' = 2,4-dinitrobenzyl  
10 mol%, 4 examples,  
75-95%, 83-94% ee

Jacobsen, *OL* **1999**, 1611.



R' = 2,4-dinitrobenzoyl  
metal:ligand = 1:2  
10 mol%, 10 examples,  
94-99%, 87-96% ee

Shibasaki, *JACS* **2006**, 6312.



R' = bis(3,5-trifluoromethyl)benzoyl  
10 mol%, 9 examples,  
49-97%, 70-95% ee

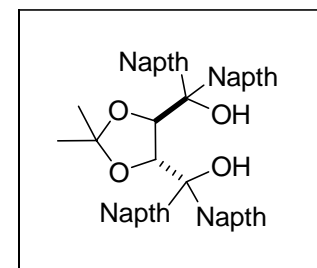
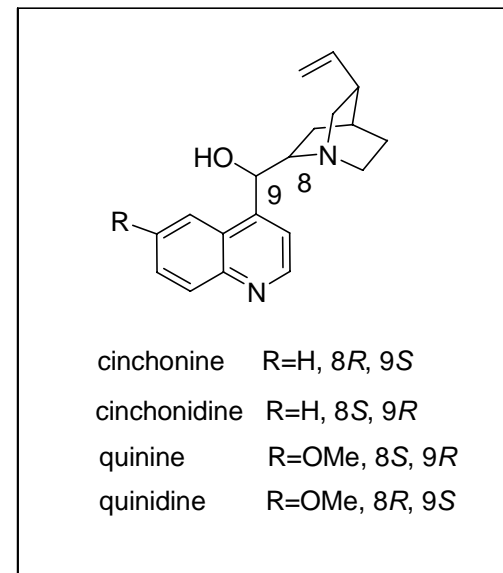
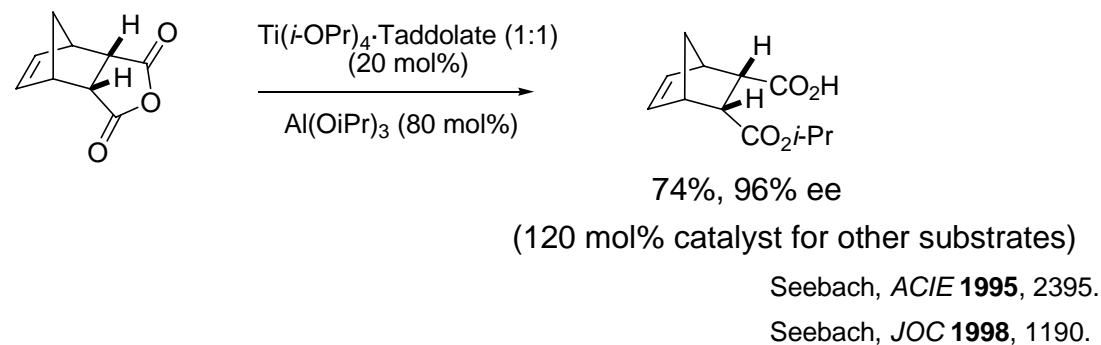
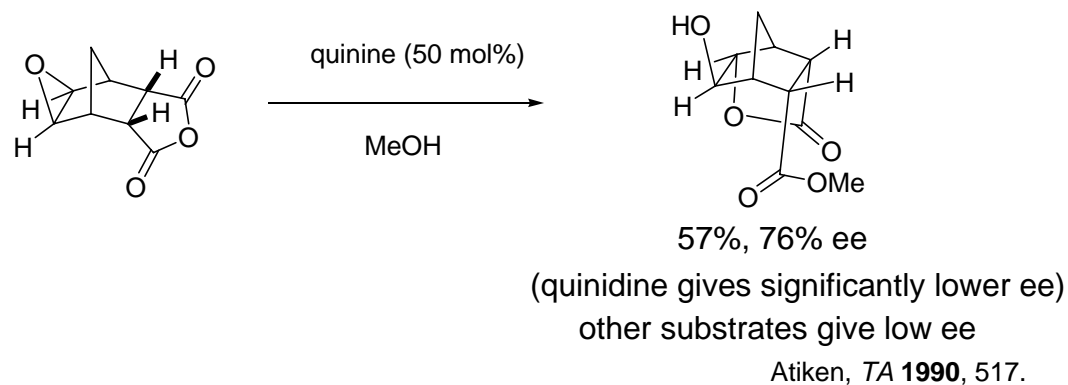
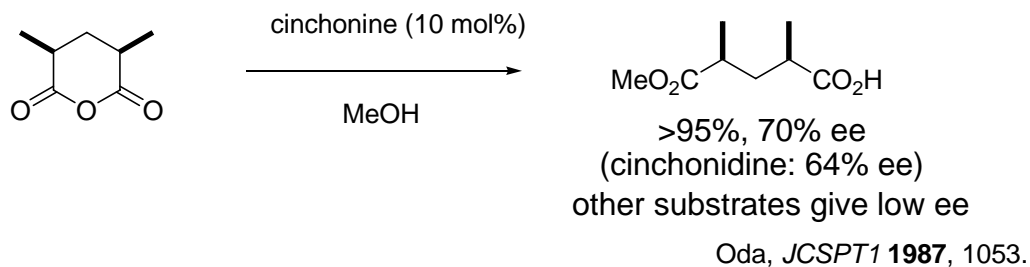
Antilla, *JACS* **2007**, 12084.

Other nucleophiles give low to moderate enantioselectivity.

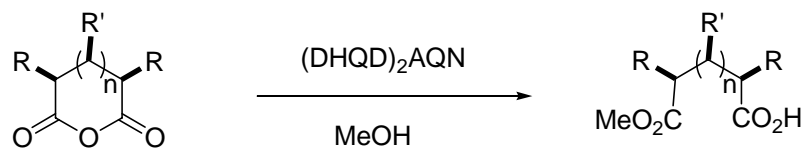
## C) Cyclic anhydrides

Selected review: Spivey, *ACIE* **2001**, 3131.

## Monoesterification



## Monoesterification (cont.)

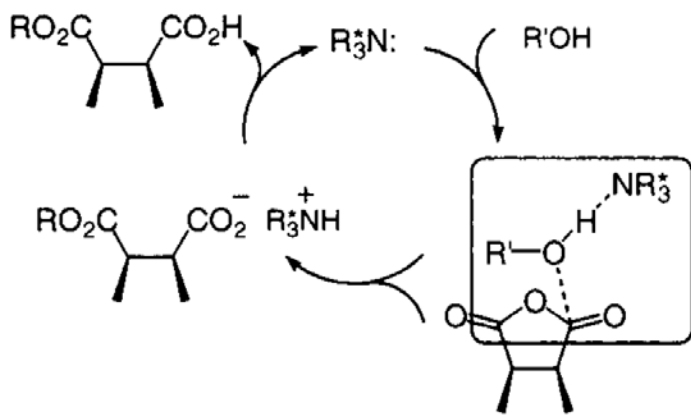


$n=0$ , 8-20 mol%, 7 examples, 74-99%, 92-98% ee

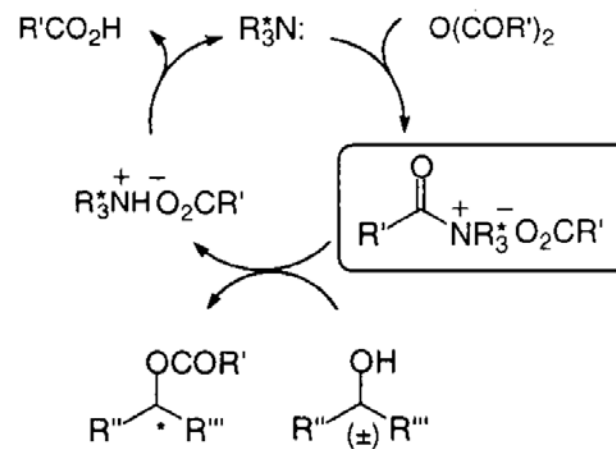
$n=1$ , 30 mol%, 2 examples, 70-72%, 90-91% ee

((DHQ)<sub>2</sub>AQN gives slightly lower yield and ee)

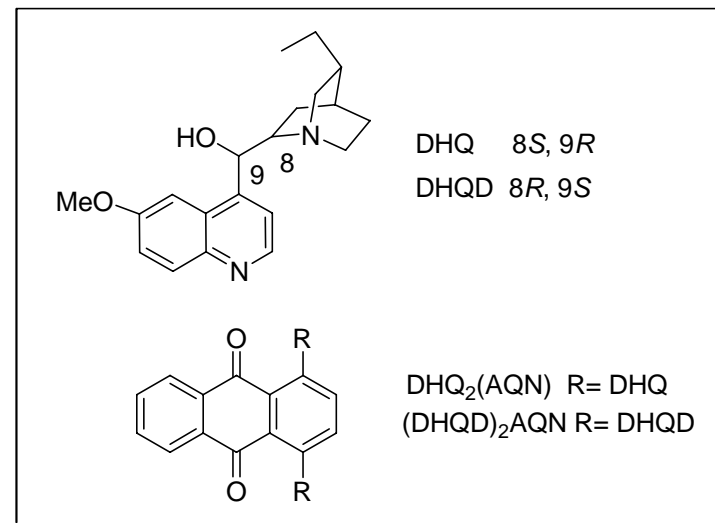
## Plausible mechanisms



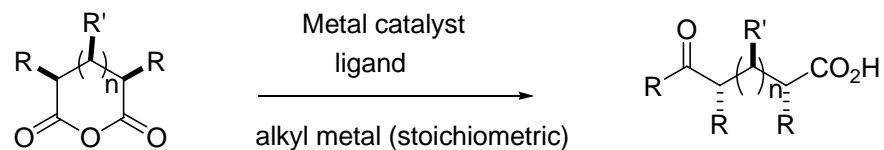
general base catalysis



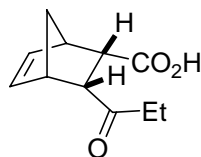
nucleophilic catalysis



## Alkylative desymmetrization



Ni(COD)<sub>2</sub> (10 mol%), *i*-Pr-PHOX, Et<sub>2</sub>Zn,



85%, 79% ee

Rovis, *JACS* **2002**, 174.

Pd(OAc)<sub>2</sub> (5 mol%), JOSIPHOS, Ph<sub>2</sub>Zn    n=1, 5 examples, 61-83%, 89-97% ee

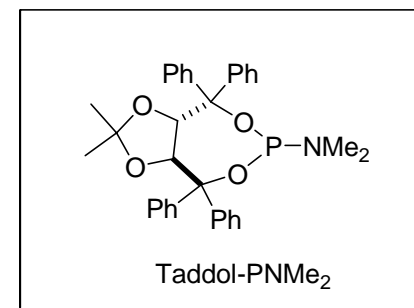
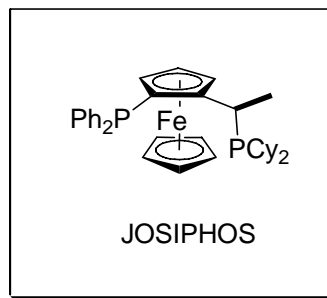
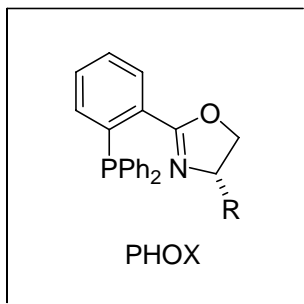
Rovis, *JACS* **2004**, 10248.

Rh(COD)<sub>2</sub>Cl<sub>2</sub> (4 mol%), Taddol-PNMe<sub>2</sub>, LiAryl, Zn(OTf)<sub>2</sub>, n=1, 13 examples, 56-88%, 76-88% ee

Rovis, *ACIE* **2007**, 4514.

Rh(COD)<sub>2</sub>Cl<sub>2</sub> (5 mol%), *t*-Bu-PHOX, (Alkyl)<sub>2</sub>Zn, n=2, 12 examples, 62-87%, 88-95% ee

Rovis, *JACS* **2007**, 9302.

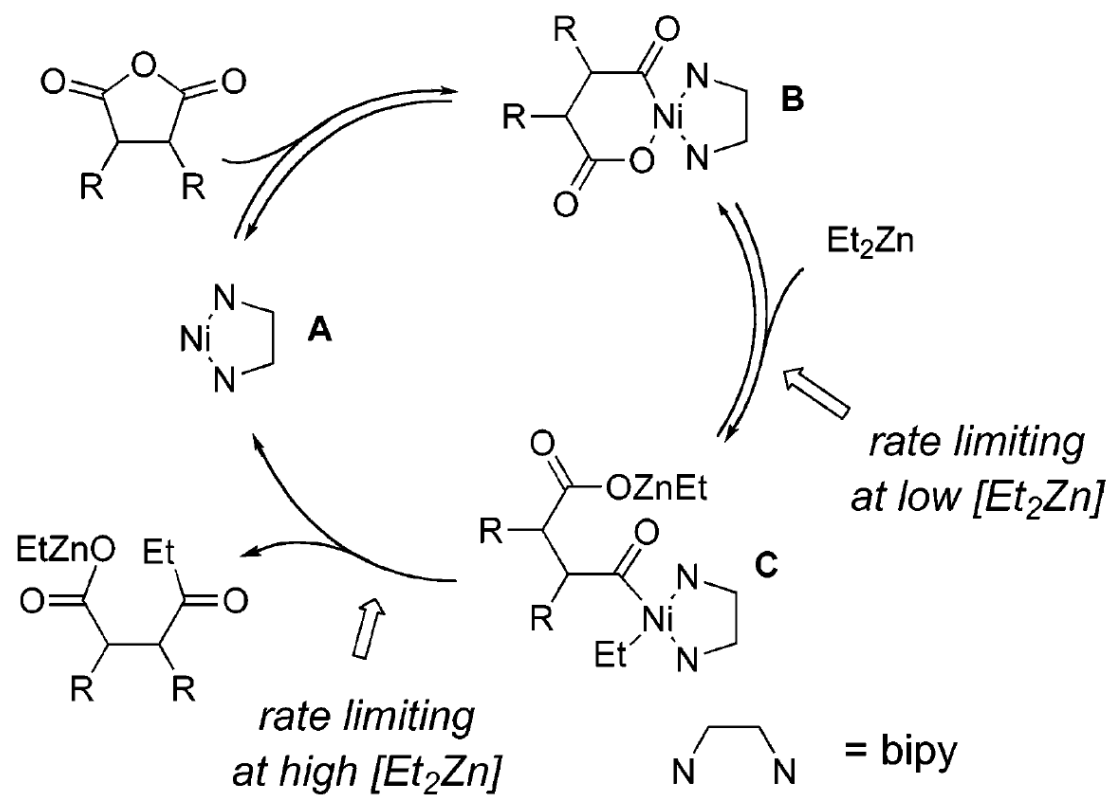




## Alkylative desymmetrization (cont.)

## Mechanism

(Mechanistic study was done using achiral bipyridine ligand.)

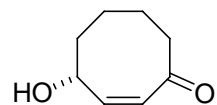
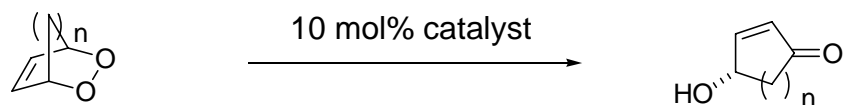


Rovis, JACS **2007**, 2718.

Rovis, JACS **2005**, 247.

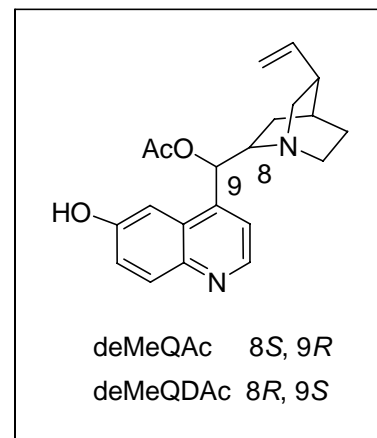
## D) Others

## Endoperoxide rearrangement (Kornblum DeLaMare rearrangement)

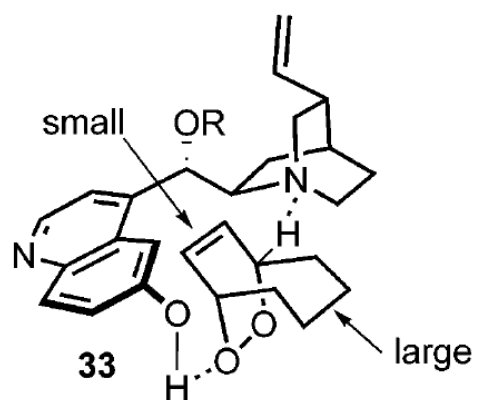


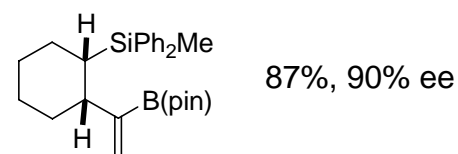
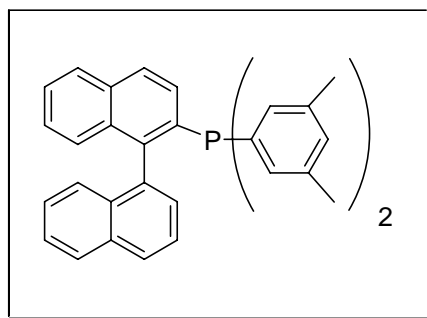
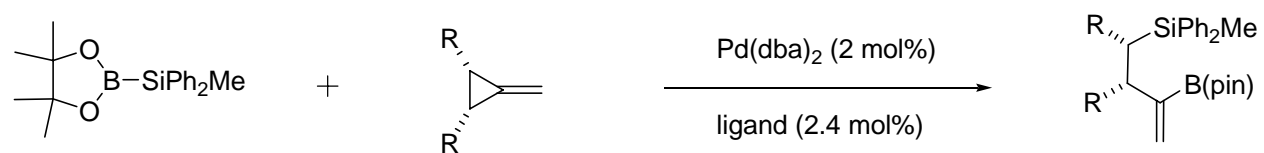
99% 97% ee with deMeQAc  
99%, -99% ee with deMeQDAc

8 other examples (n=2-4)  
76-99%, 70-99% ee



## Proposed model for enantioinduction

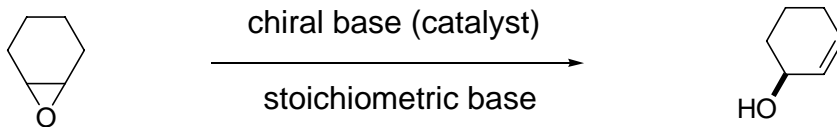


C-C cleavage of *meso*-methylenepropanes

5 other examples, 50-95%, 81-91% ee

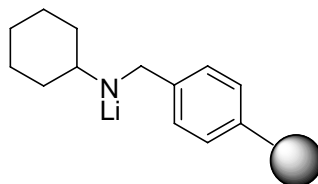
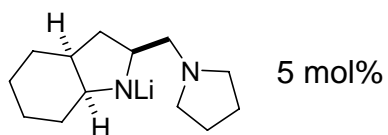
# IV. Deprotonation

- Most of the work in enantioselective deprotonation reactions involves stoichiometric amount of chiral reagent.
- Stoichiometric bases in catalytic reactions has to balances their ability to turn over the catalyst and their inefficiency to deprotonate the substrate.
- Two main approaches: 1) more effective chiral base 2) less effective sotichiometric base



**catalyst**

**stoichiometric base**



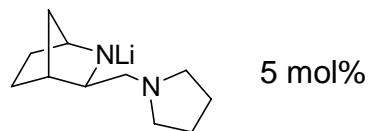
76%, 91% ee

Asami, *Tet.* **2002**, 4655.

5 other examples,  
48-90%, 52-95% ee

LDA

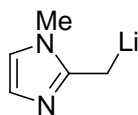
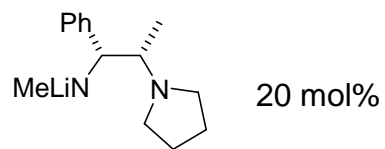
5 min addition 53% conv., 70% ee  
5 h addition 53% conv., 86% ee



LDA  
with 10 equiv DBU

5 min addition 98% conv., 95% ee  
5 h addition 95% conv., 98% ee

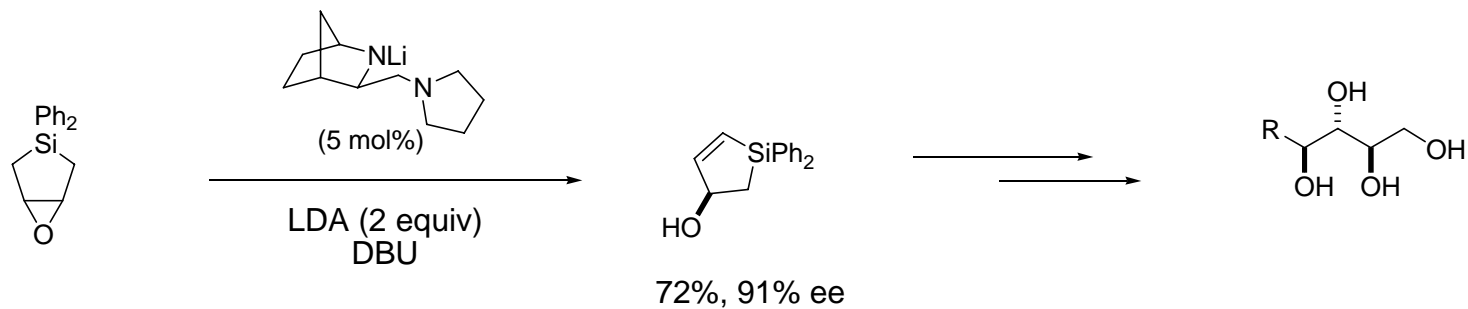
Andersson, *Tet.* **2002**, 4665.



96%, 93% ee

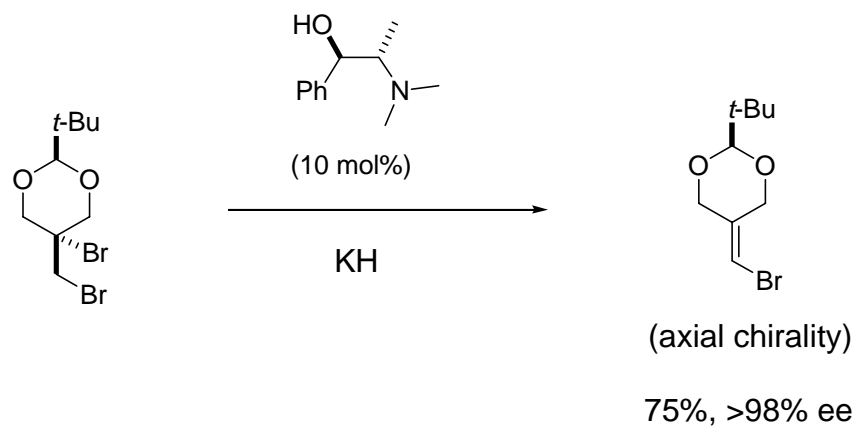
Ahlberg, *Tet.* **2002**, 4669.

**silacyclopenteneoxide**



Kozmin, *ACIE* **2001**, 4757.

**chiral alkoxides**

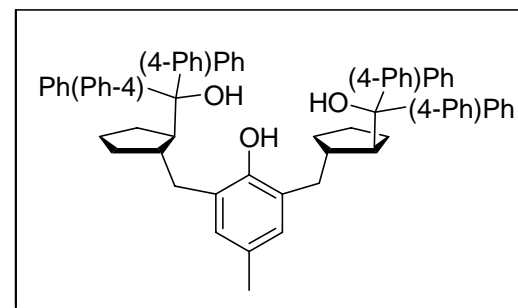
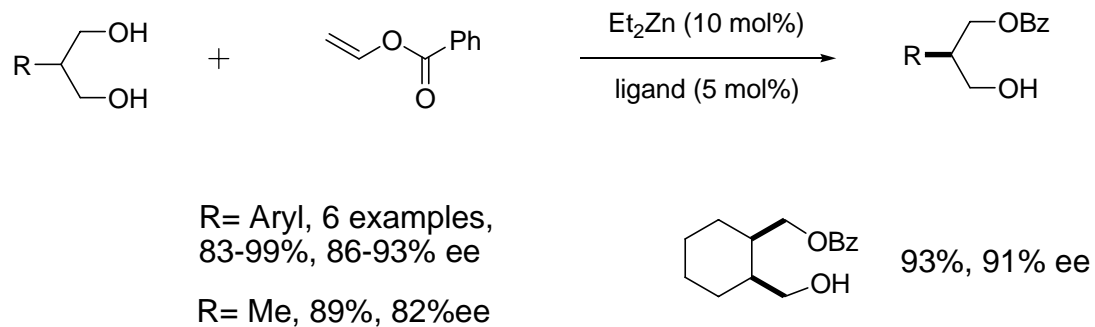


Duhamel, *JACS* **1996**, 12483.

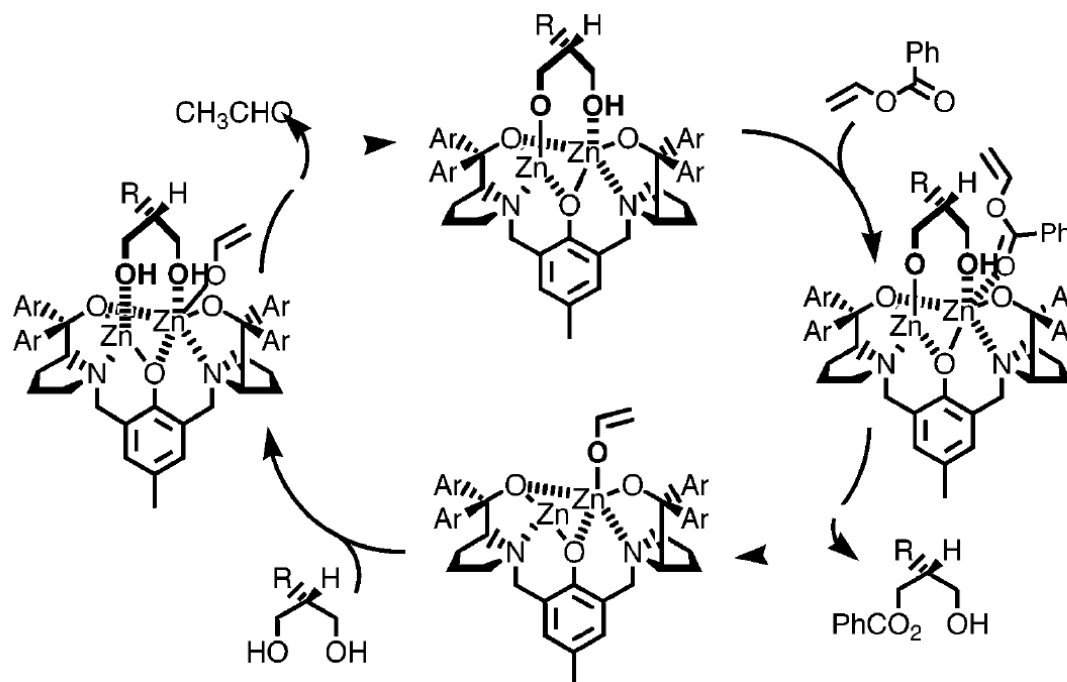
# V. Monoprotection

(only selected cases will be covered in this seminar)

## Acylation

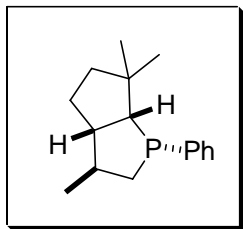
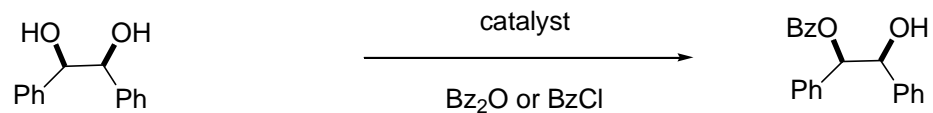


## Mechanism



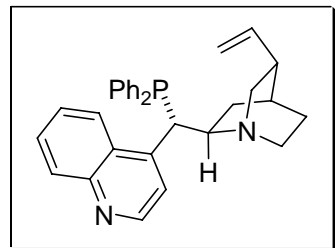
## Acylation (cont.)

Monoprotection



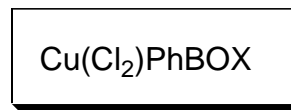
10 mol%  
73% conv, 83% ee

Vedejs, *JOC* **2004**, 1389.



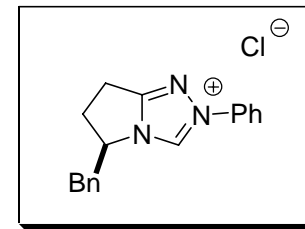
30 mol%  
98%, 91% ee

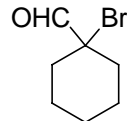
Fujimoto, *ACIE* **2003**, 3383.



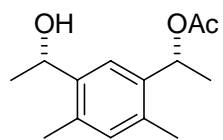
5 mol%  
79%, 94% ee

Onomura, *JACS* **2003**, 2052.



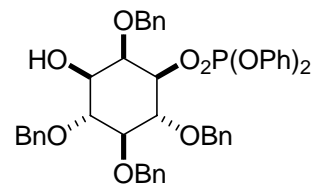
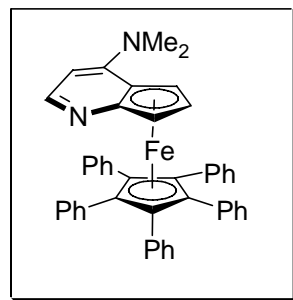
10 mol% with   
75%, 83% ee

Rovis, *JACS* **2004**, 9518.



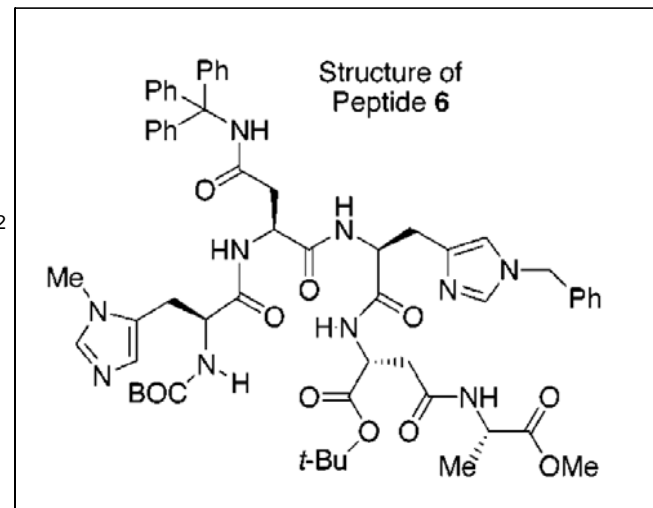
1 mol%  
91%, 99.7% ee

Fu, *JOC* **1998**, 2794.

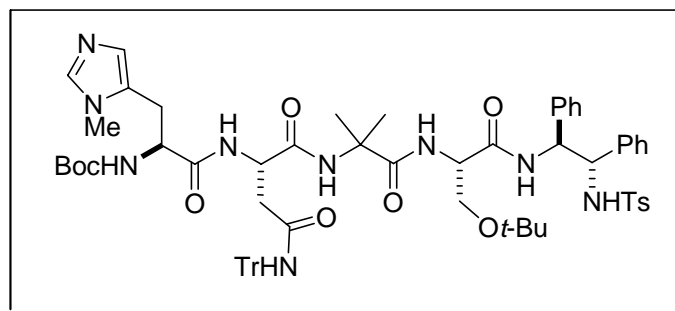
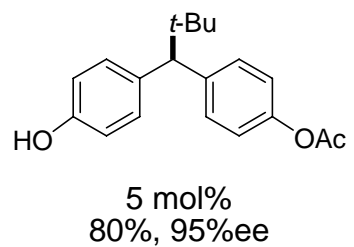


2 mol%  
65%, 98% ee

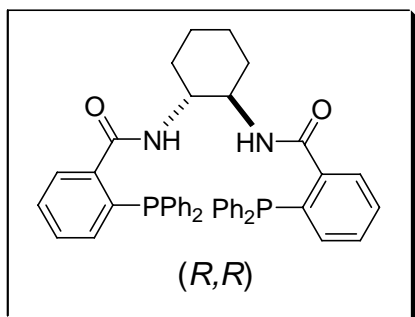
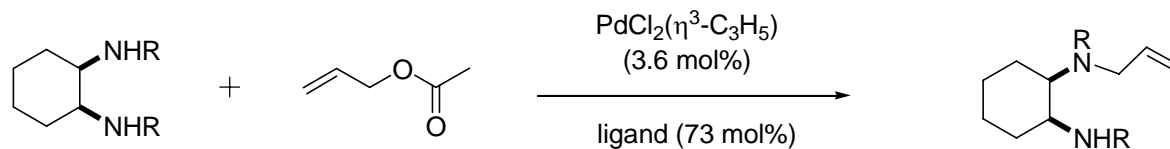
Miller, *JACS* **2001**, 10152.



## Acylation (cont.)

Miller, *JACS* **2006**, 16454.

## Allylation of diamide derivatives

*via* allylic substitution

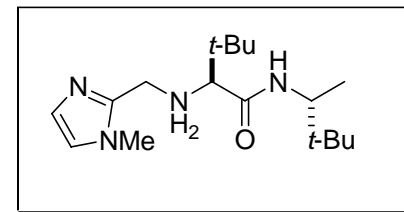
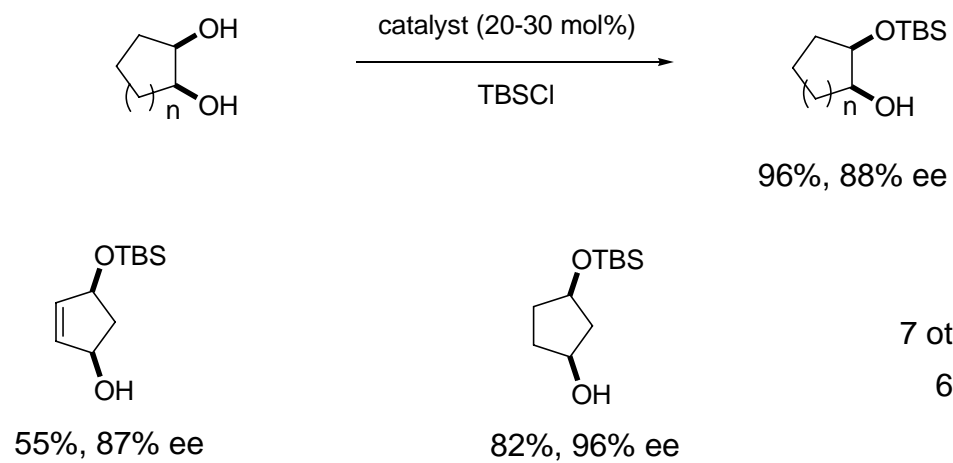
R = Trs (2,4,6-triisopropylbenzenesulfonyl)  
3 examples, 65-85%, 96-93% ee

R = Ts, ent-product, 77%, 85% ee

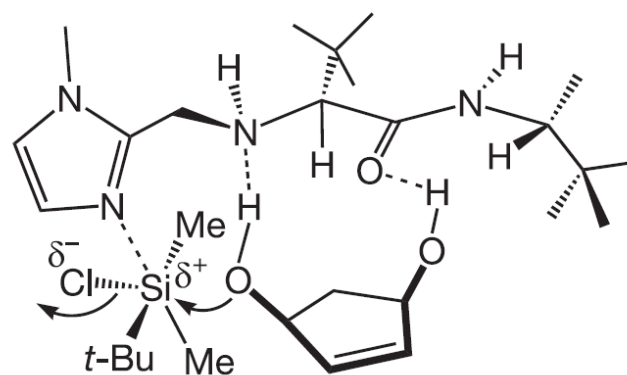
Taguchi, *JOC* **2006**, 2524.



## Silylation

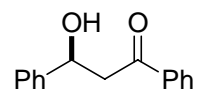
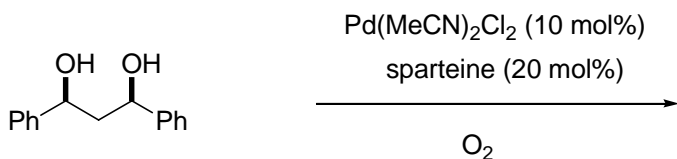


## Proposed transition state model



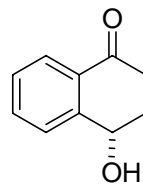
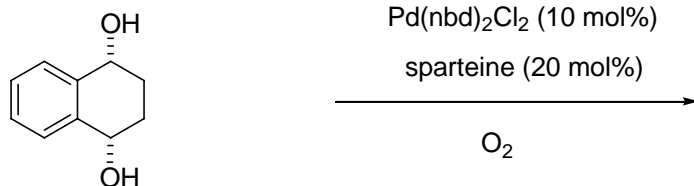
# VI. Oxidation

## Palladium catalyzed oxidation



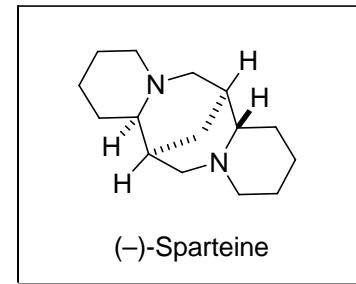
69%, 82% ee

Sigman, *JACS* **2001**, 7475.

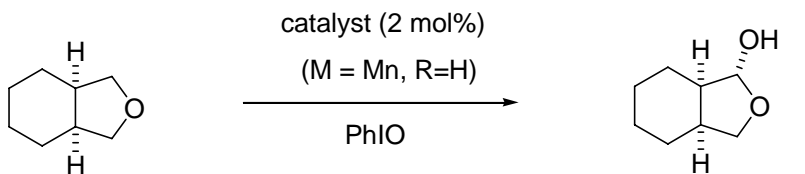


72%, 95% ee

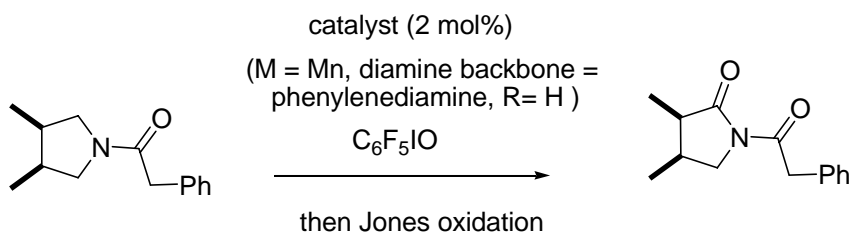
Stoltz, *JACS* **2001**, 7725.



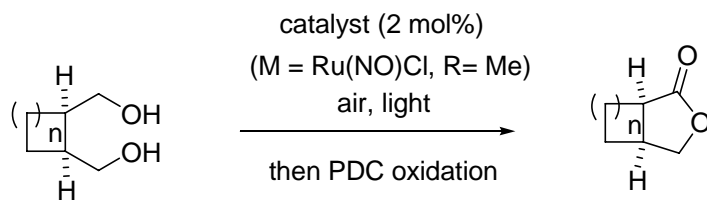
## C-H oxidation at activated positions



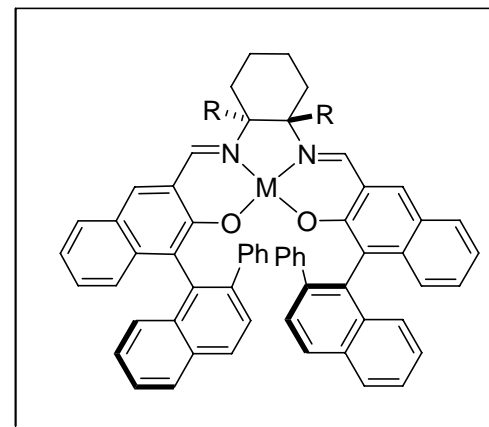
61%, 90% ee

Katsuki, *Tet* **1998**, 10339.

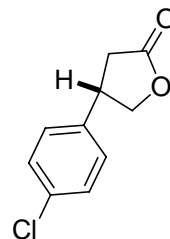
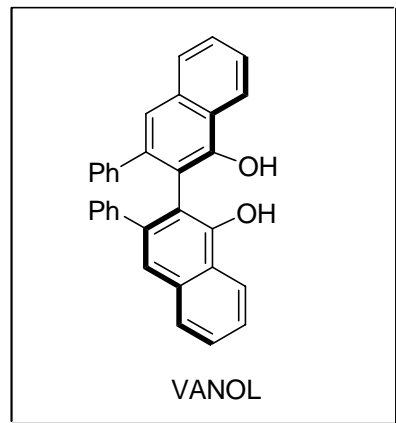
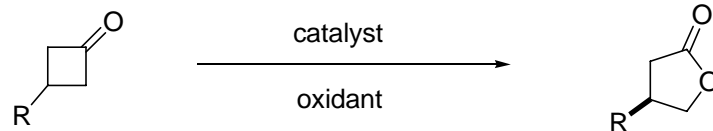
49%, 84% ee

Katsuki, *TL* **1998**, 8295.

n= 1-4, 49-66%, 59-67% ee

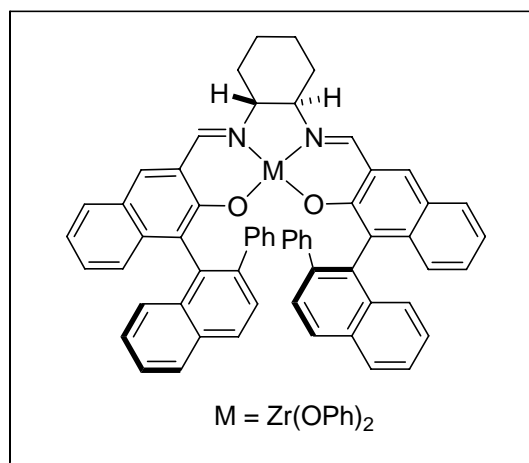
Katsuki, *CL* **2002**, 1080.

## Baeyer-Villiger Oxidation

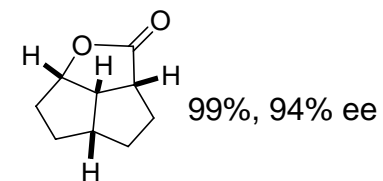


$\text{Me}_2\text{AlCl}$  (20 mol%)  
 VANOL (20 mol%)  
 CHP  
 92%, 84% ee

Bolm, *SL* **2004**, 1619

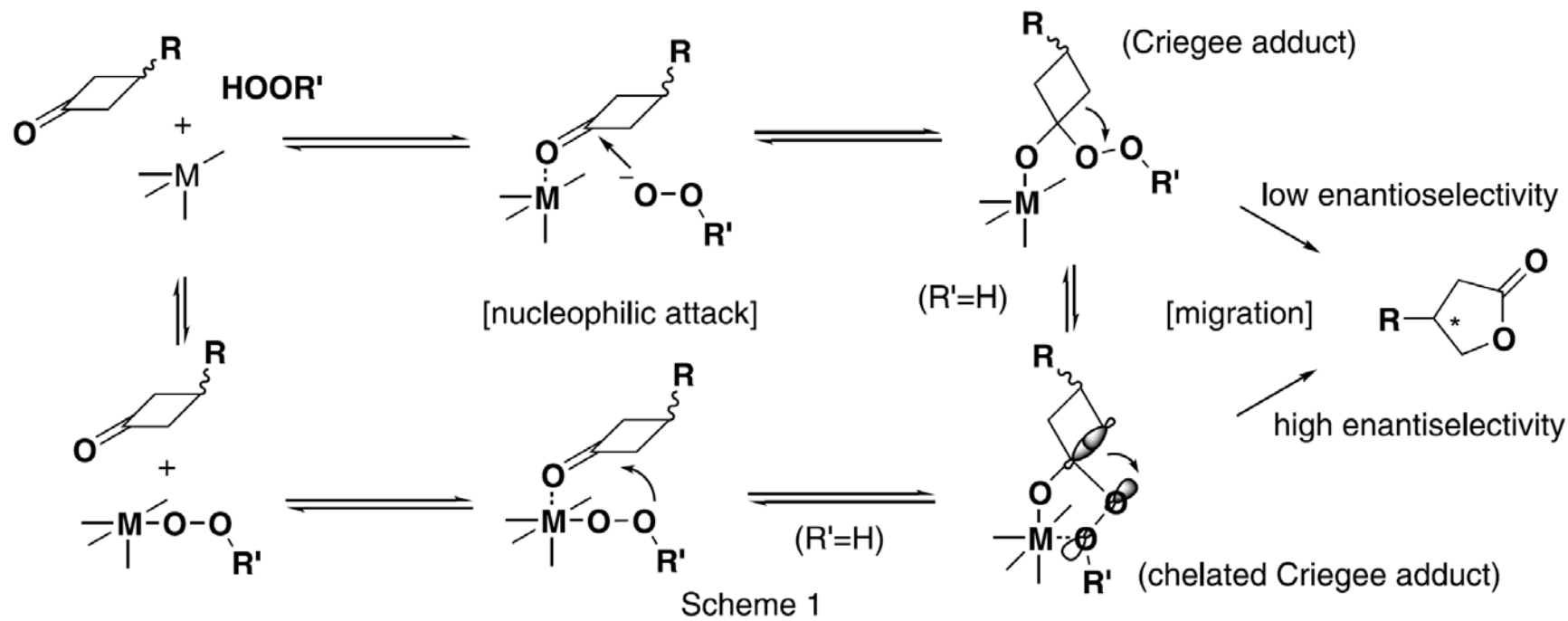


5 mol% catalyst,  
 urea·H<sub>2</sub>O<sub>2</sub>  
 R = Aryl, 4 examples,  
 43-68%, 81-87% ee

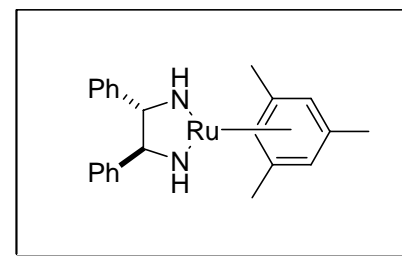
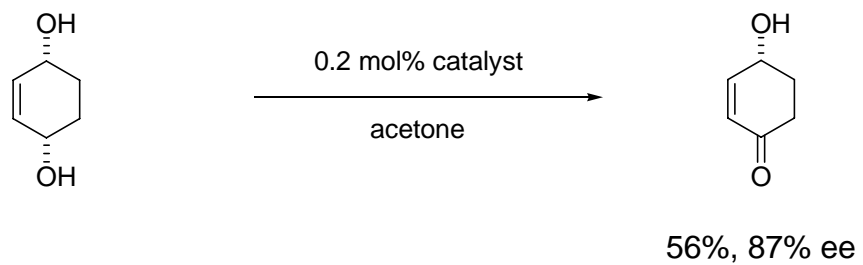
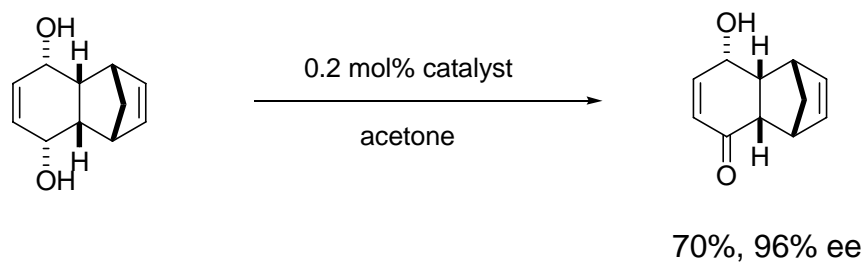


Katsuki, *TL* **2002**, 4481.

## Baeyer-Villiger Oxidation (mechanism)



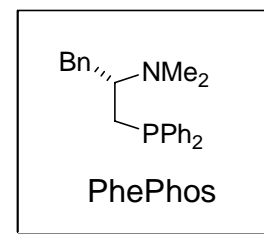
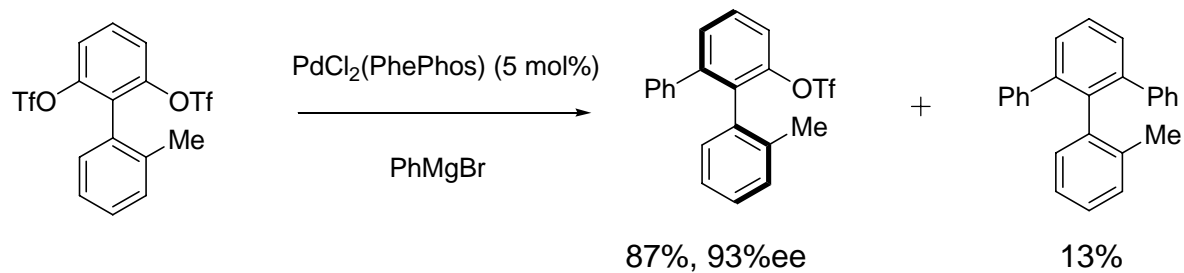
## Ruthenium catalyzed hydrogen transfer reactions



## VII. Other Reactions

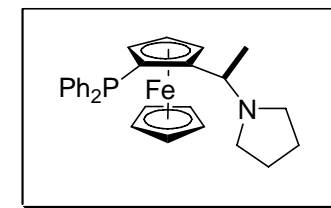
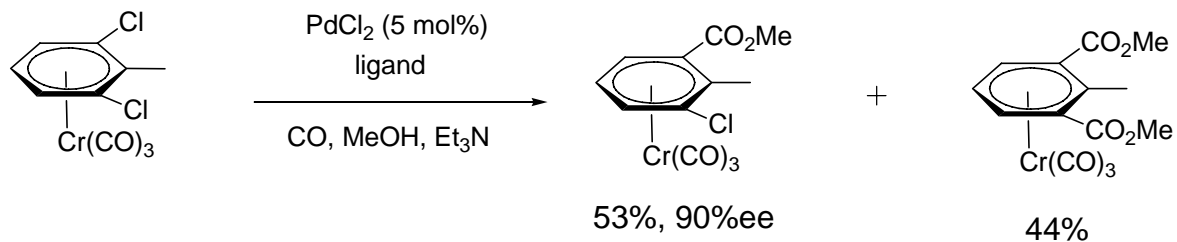
Desymmetrization approach to axial and planar chirality

### Axial chirality



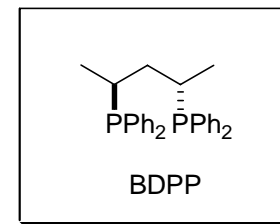
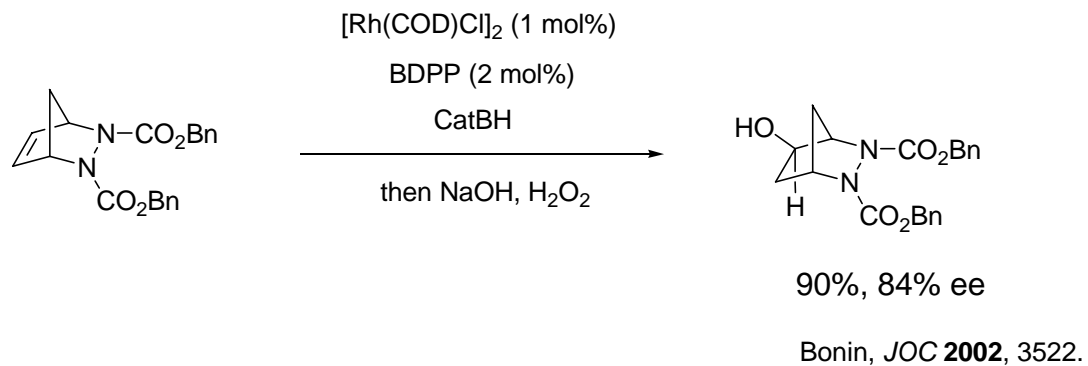
Hayashi, *JACS* **1995**, 9101.

### Planar chirality

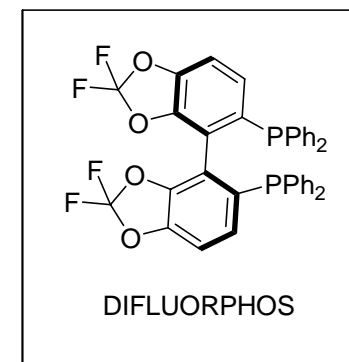
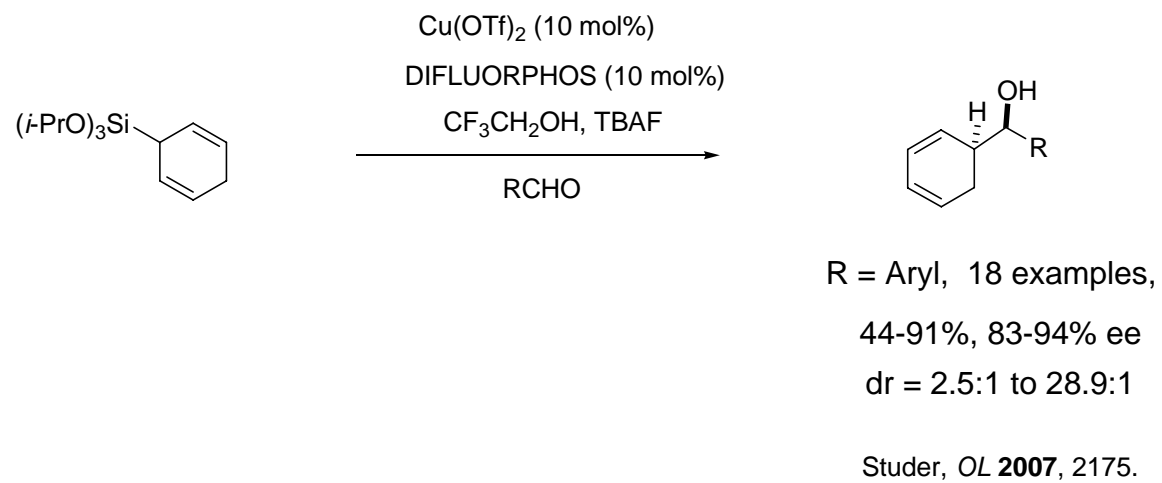


Schmalz, *SL* **2003**, 1595.

## Hydroboration-oxidation

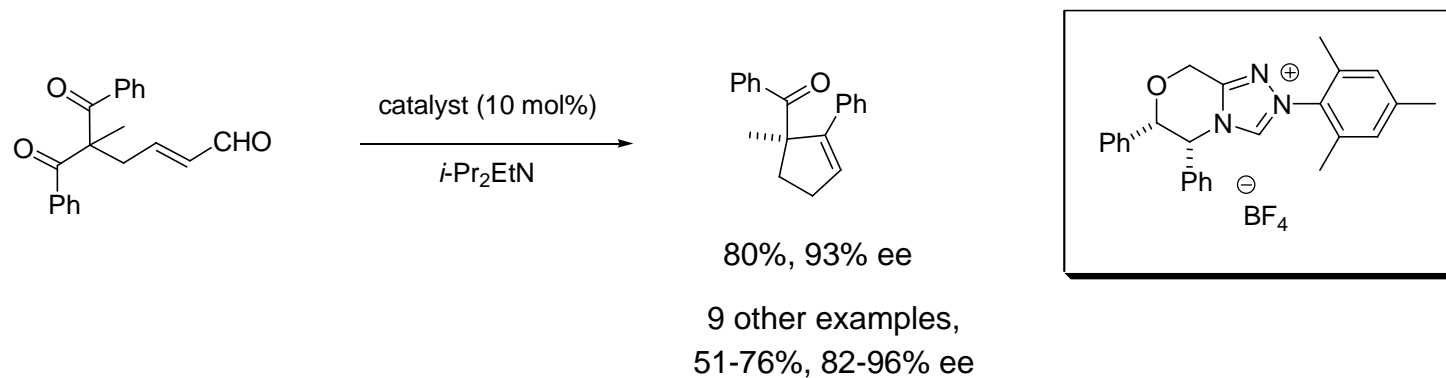


## Desymmetrization of 1,4-cyclohexadiene derivatives





## NHC-catalyzed desymmetrization of 1,3-Diketones



## Mechanism

