

Recent Advances on Asymmetric Addition (C=N & C=C)

陈加荣

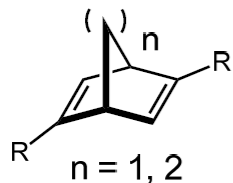
化学学院

2016年03月23日 (第6次课)

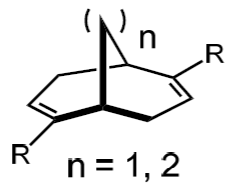
Office:731

E-mail: chenjiarong@mail.ccnu.edu.cn

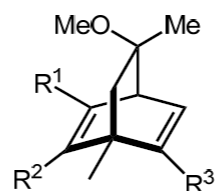
Selected diene ligands

Rh-Catalyzed Arylation: Lin, G.-Q. *ACS Catal.* **12**, 2, 95

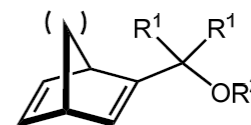
Hayashi 2003



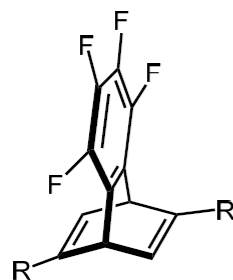
Hayashi 2005



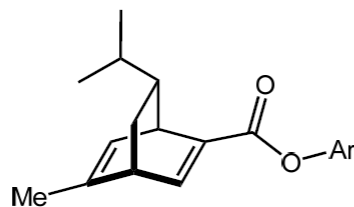
Carreira 2004



Corey 2010



Hayashi 2008



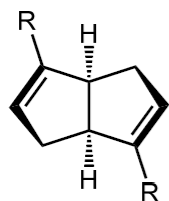
Hayashi 2008



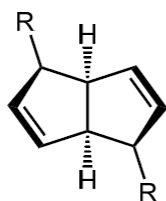
Carnell 2010



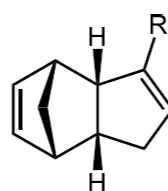
Wu 2011



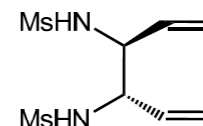
Xu & Lin 2007



Xu & Lin 2008



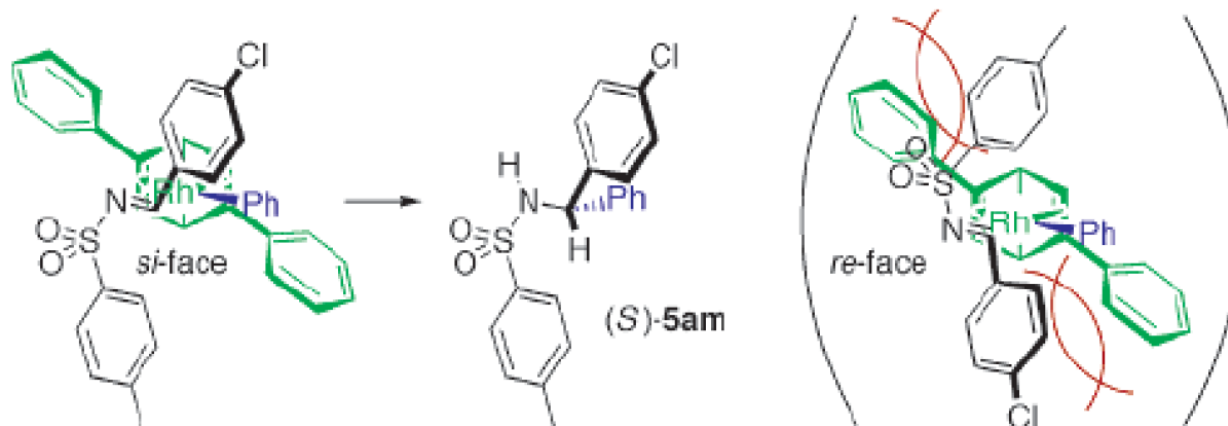
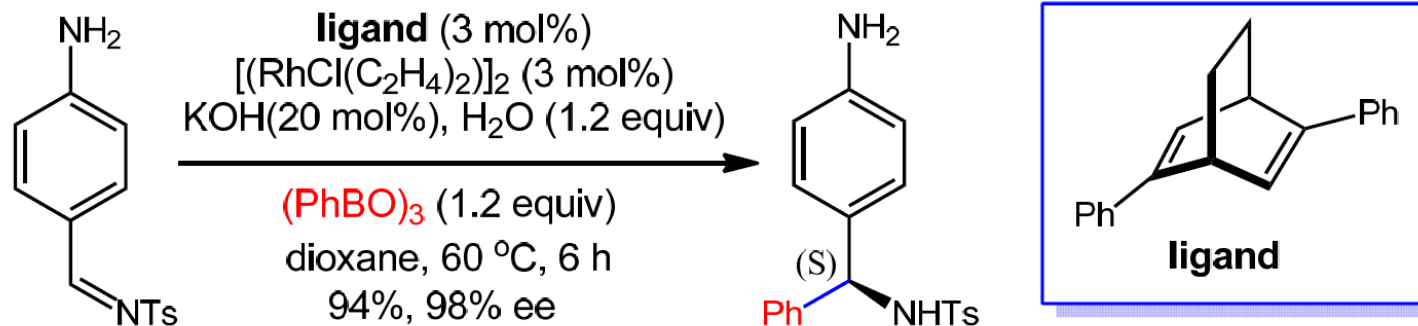
Lin 2010



Du 2010

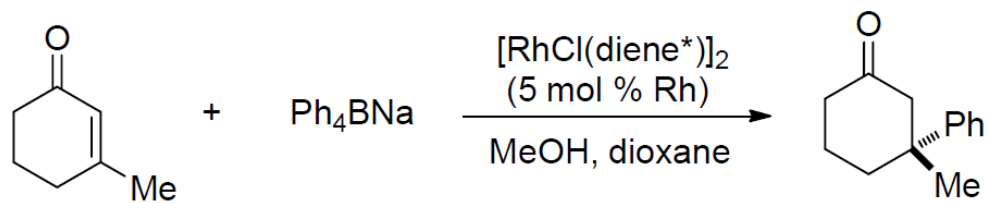
主要为Rh-catalyzed 芳基化反应

Arylation of Imines Utilizing Arylorganometallic Reagents (Sn, Ti, B)



The coordination with the other face is much less favorable due to the steric repulsions caused by both of two phenyl groups on the diene ligand.

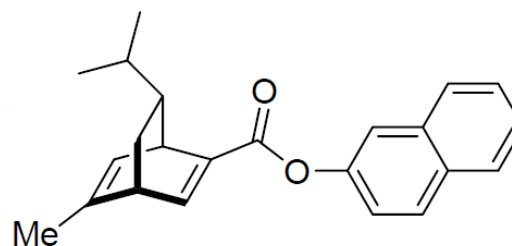
Hayashi, T. *JACS* **04**, 13584.



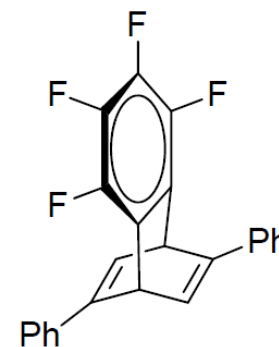
65% yield
98% ee



48% yield
99% ee



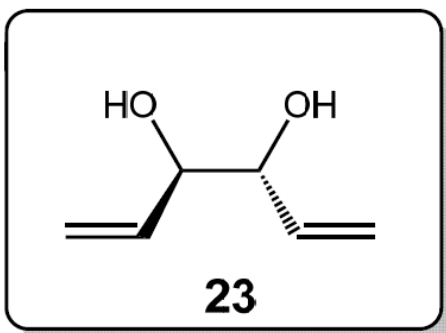
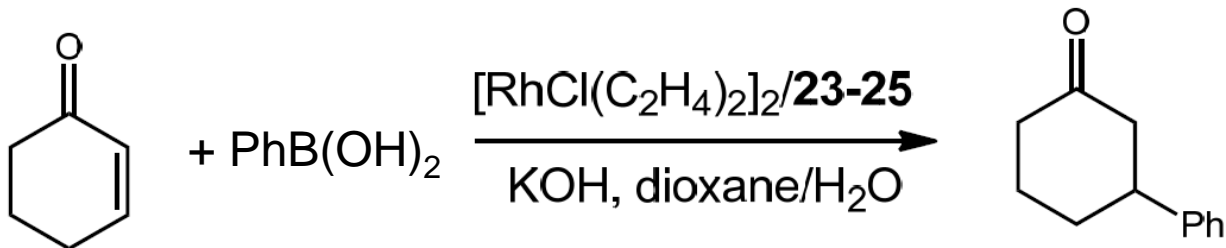
85% yield
98% ee



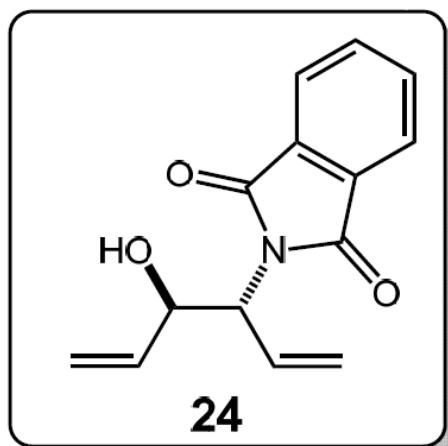
99% yield
99% ee

Hayashi, T. *JACS* **09**, 131, 13588; *ACIE* **10**, 49, 3969.

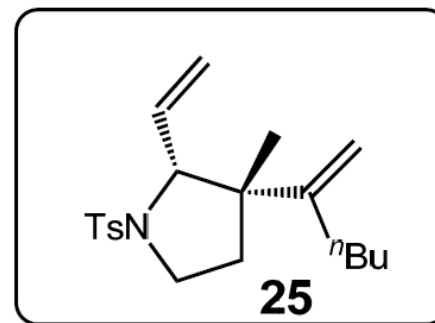
手性双烯配体



98%yield, 82% ee



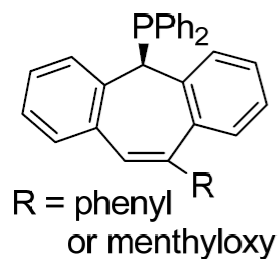
90%yield, 91% ee



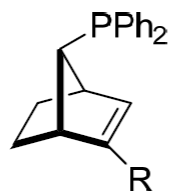
89%yield, 91% ee

Du, H. *OL* **09**, *11*, 4744; Yu, Z.-X. *OL* **11**, *13*, 1122; Trost, B. M. *OL* **11**, *13*, 4566.

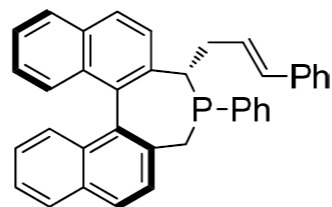
手性膦烯配体



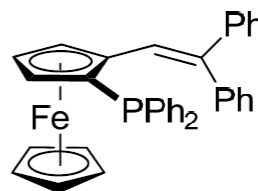
Grützmacher, 2003



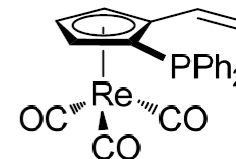
Hayashi, 2005



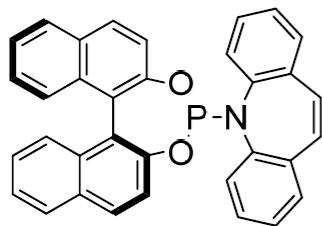
Widhalm, 2006



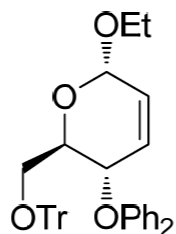
Štěpnička, 2006



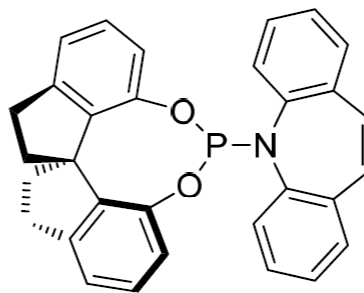
Bolm, 2007



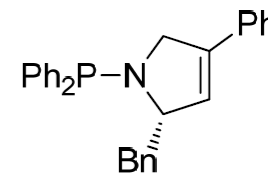
Carreira, 2007



Boysen, 2009



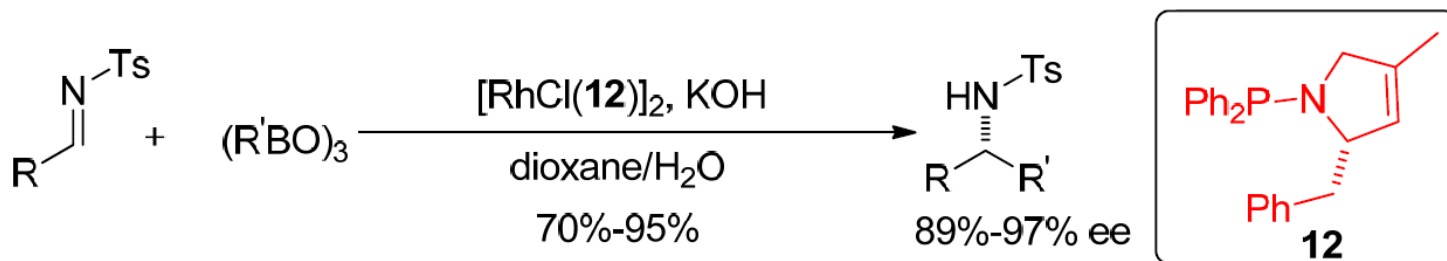
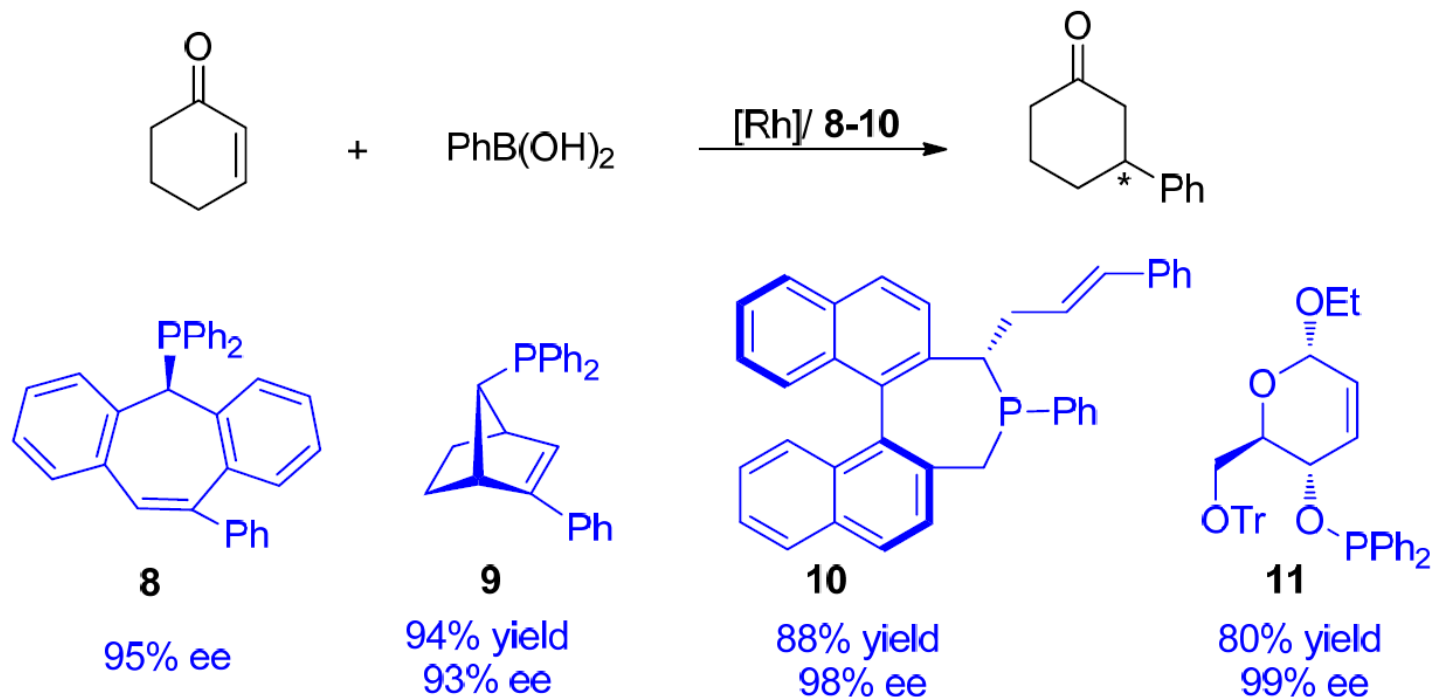
Carreira, 2011



Hayashi, 2011

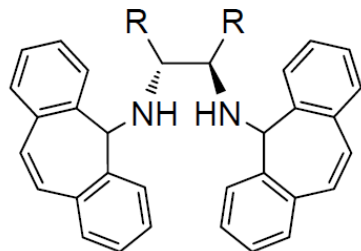
Grützmacher, H. *CEJ* **04**, 10, 4198; Hayashi, T. *ACIE* **05**, 44, 4611; Widhalm, M. *TA* **06**, 17, 3084; Štěpnička, P. *Inorg. Chem.* **06**, 45, 8785; Bolm, C. *Synlett* **07**, 9, 1365; Carreira, E. M. *ACIE* **07**, 46, 3139; Boysen, M. M. K. *OL* **09**, 11, 4212; Hayashi, T. *CC* **11**, 47, 6123.

手性膦烯配体

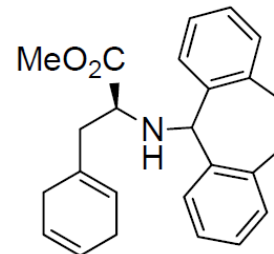


Hayashi, T. *ACIE* **05**, 44, 4611; Widhalm, M. *TA* **06**, 17, 3084; Boysen, M. M. K. *OL* **09**, 11, 4212;
Hayashi, T. *CC* **11**, 47, 6123.

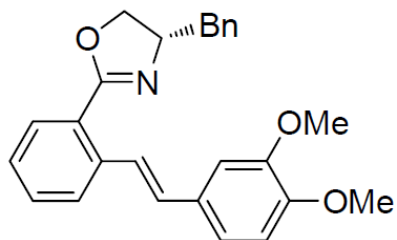
手性氮烯配体



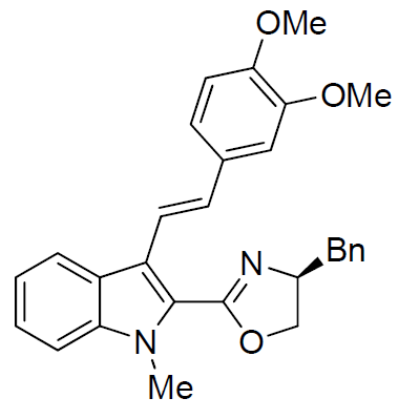
Grützmacher, 2005



Grützmacher, 2006



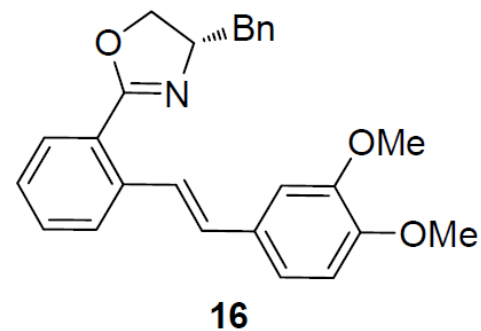
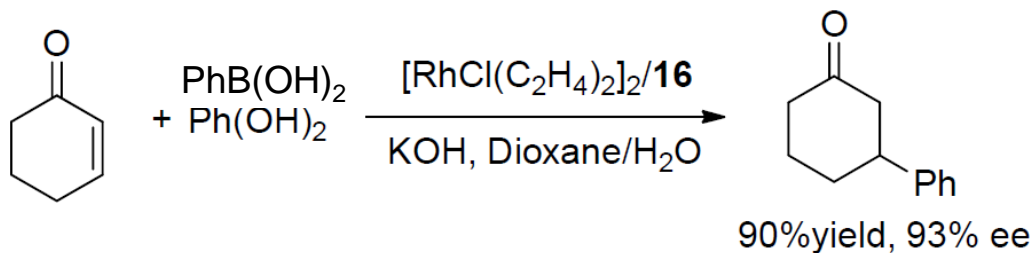
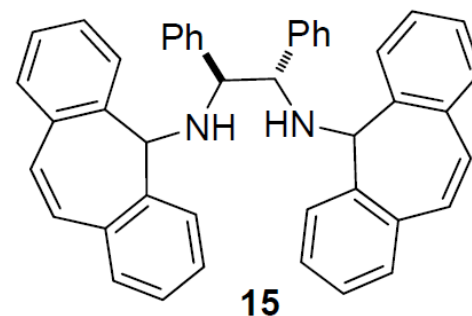
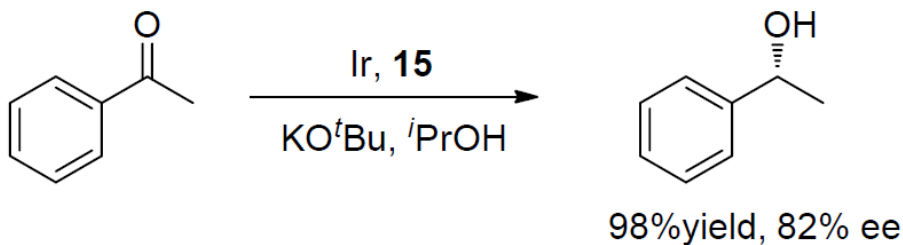
Glorius, 2010



Franzén 2011

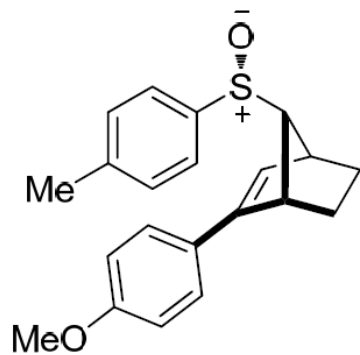
Grützmacher, H. *OM* **05**, 24, 3207; Glorius, F. *ACIE* **10**, 49, 1143; Franzén, R. *TA* **11**, 22, 468.

手性氮烯配体

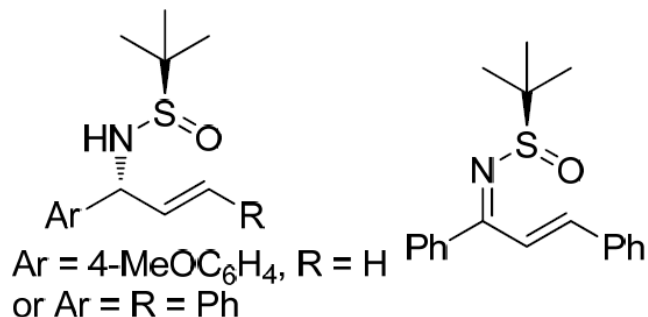


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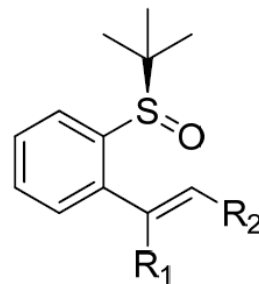
手性硫烯配体



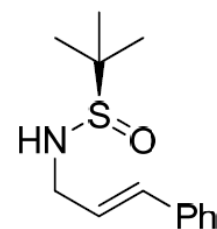
Knochel, P, 2011



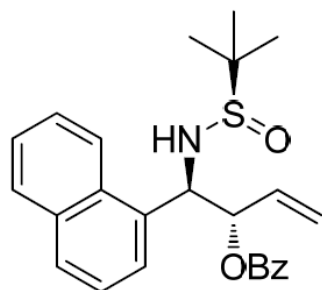
Du, 2011



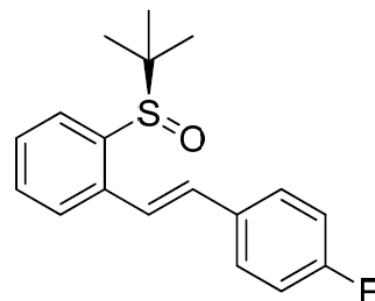
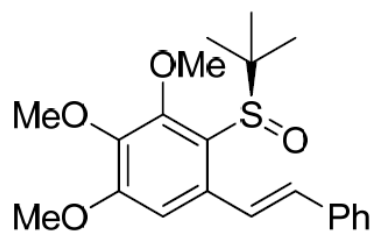
Liao, J, 2011



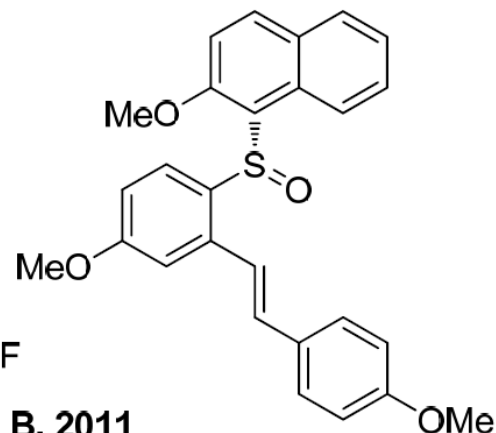
2011
Xu, M.-H
Fernández, I.



Xu, M.-H, 2011

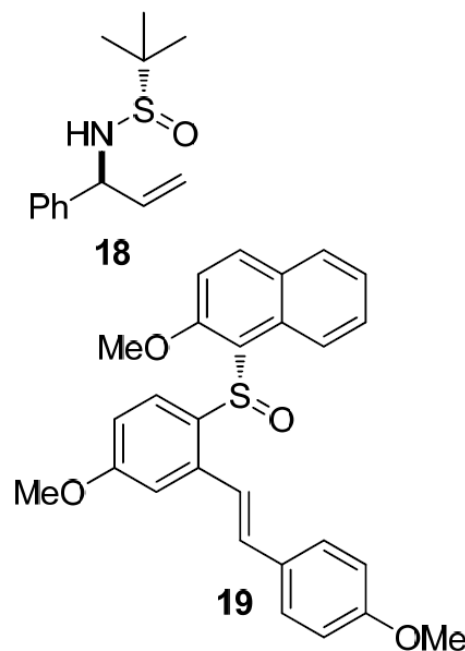
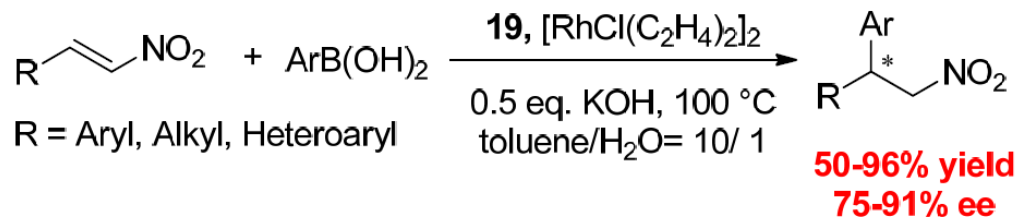
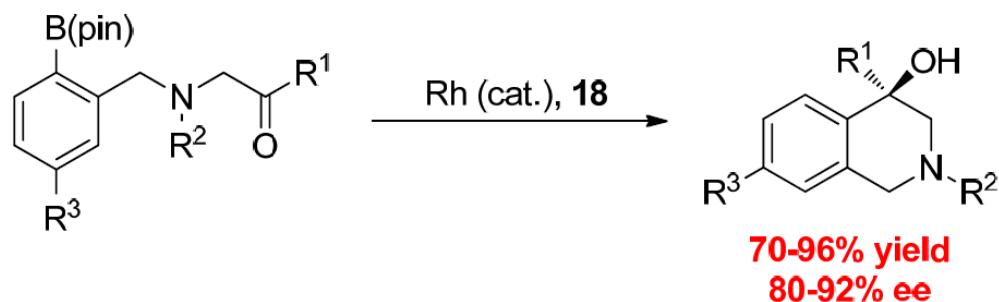
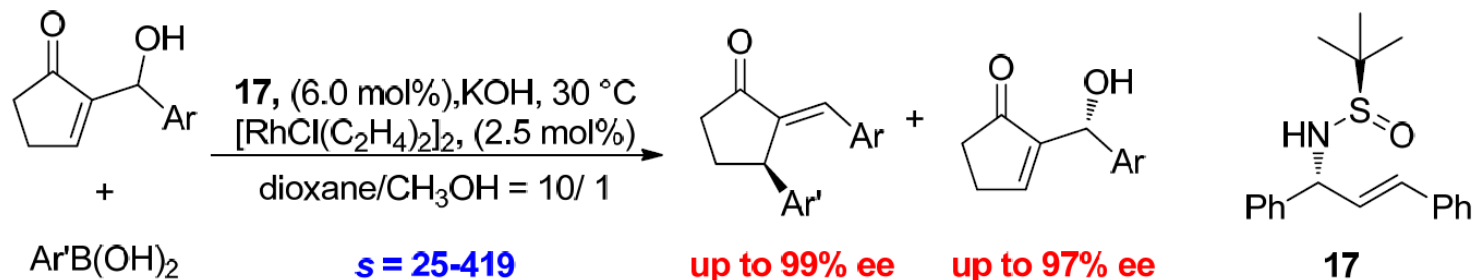


Wan, B, 2011



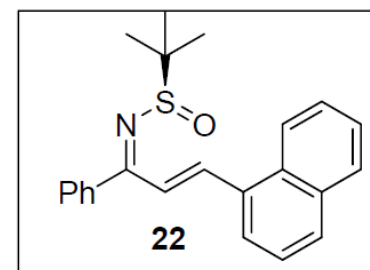
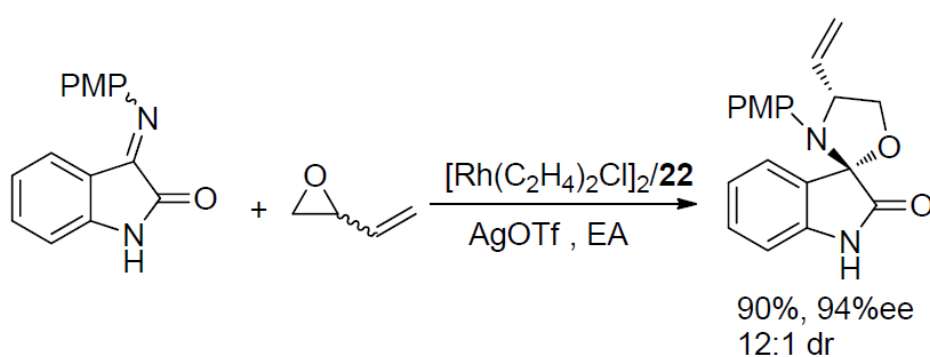
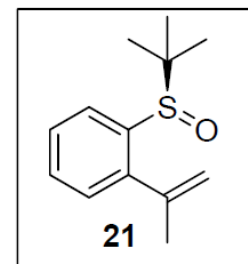
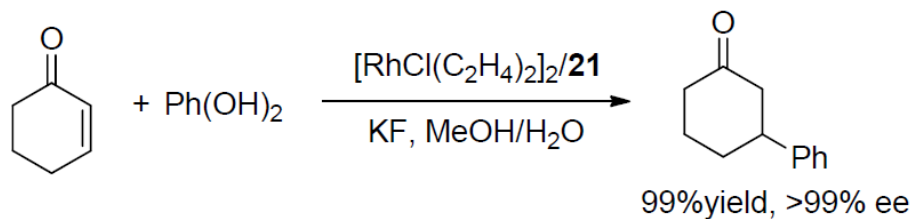
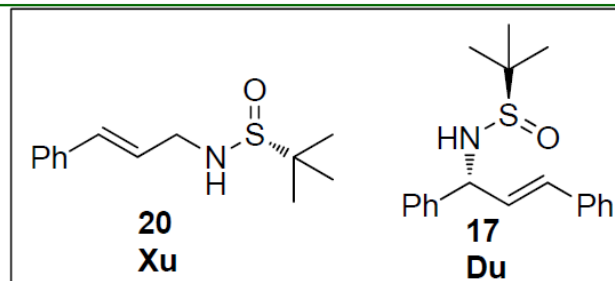
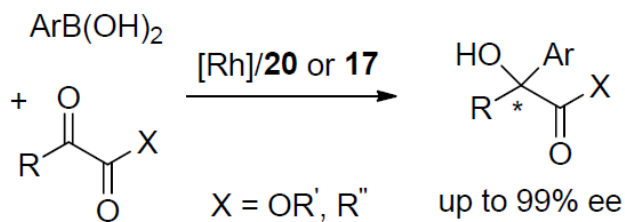
Knochel, P. *OL* **11**, *13*, 3182; Du, H. *OL* **11**, *13*, 3300 & *OBC* **11**, *9*, 5927;
Xu, M.-H. *CC* **11**, *47*, 7230 & *OL* **11**, *13*, 3410 & *ACIE* **12**, *51*, 780; Liao, J. *ACIE* **11**, *50*,
7681 & *T.* **12**, *68*, 3220; Wan, B. *JOC* **11**, *76*, 7256.

手性硫烯配体



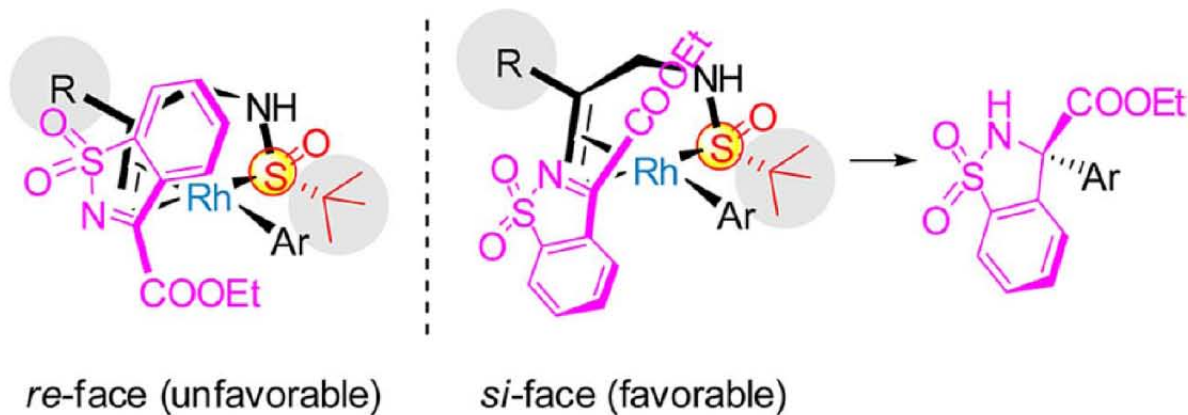
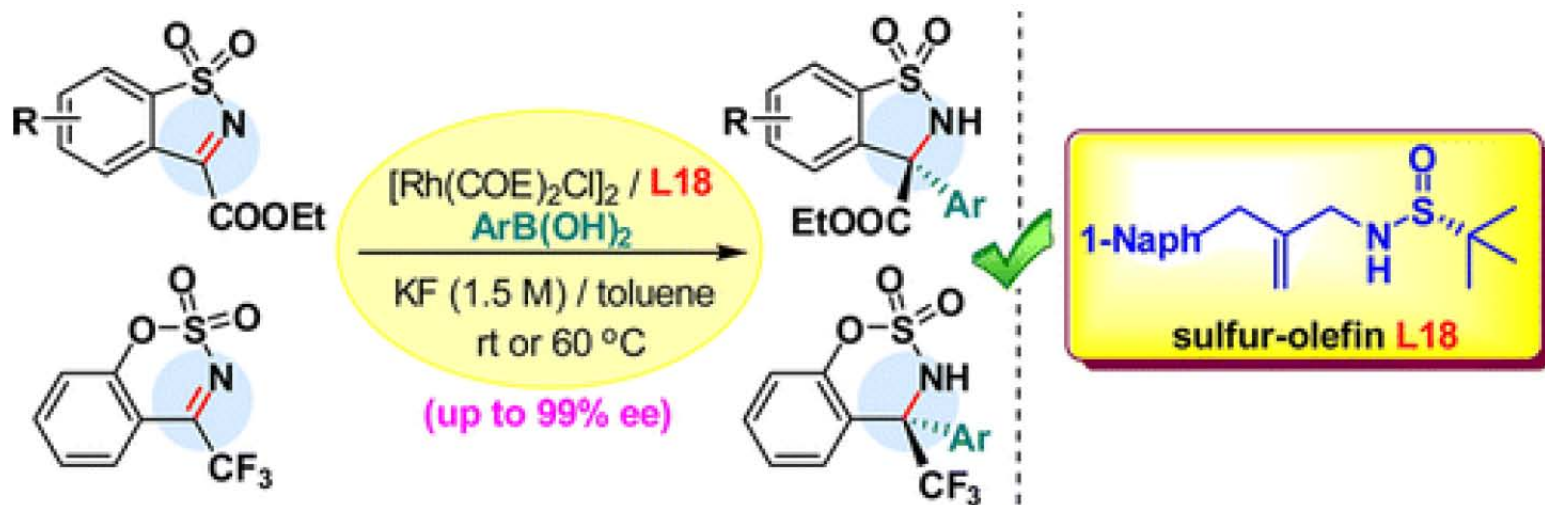
Du, H. *OL* **11**, 13, 4954; Lam, H. W. *OL* **12**, 14, 2548; Wan, B. *JOC* **12**, 77, 3071.

手性硫烯配体



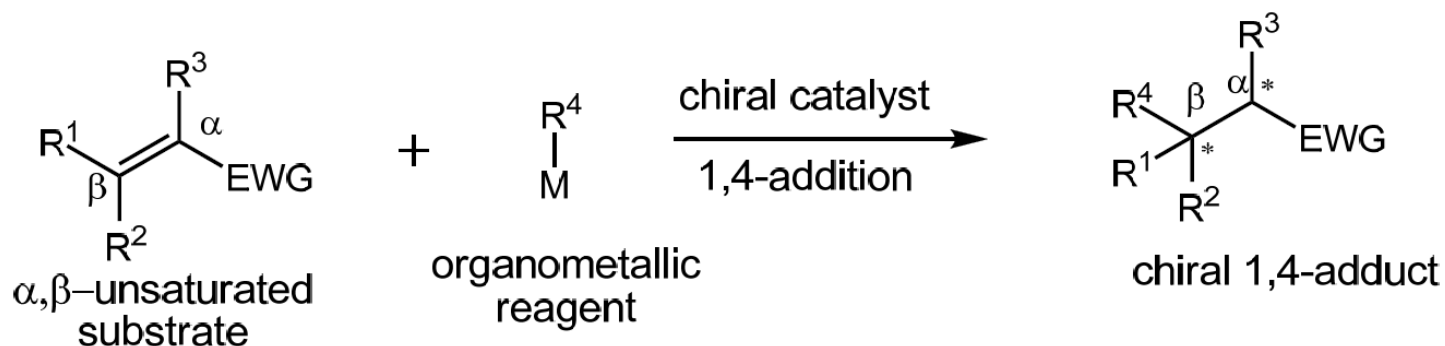
Xu, M.-H. *ACIE* **12**, 51, 780; Du, H. *OL* **12**, *14*, 624 & **11**, *13*, 3300; Lam, H. W. *OL* **12**, *14*, 2548.

手性硫烯配体



Xu, M-H. *JACS*, **13**, 971.

Metal-catalyzed Michael addition



M = Li, Mg, Cu, Al, Zn, B

EWG = COR, CHO, CO₂R, CONHR, COSR, CN, SO₂R, NO₂

Review:

Feringa, et al, *ACR* **2007**, 40, 179

Christoffers, et al, *S* **2007**, 1279

Feringa, et al, *CR* **2008**, 108, 2824

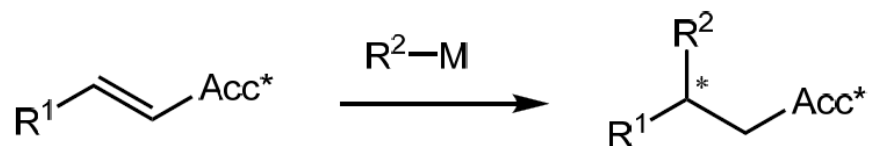
Feringa, et al, *CSR* **2009**, 38, 1039

Shibashaki, et al, *ACR* **2009**, 42, 1117

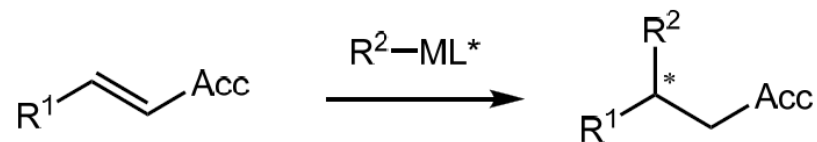
Frost, et al, *CSR* **2010**, 39, 2093

手性控制三种策略

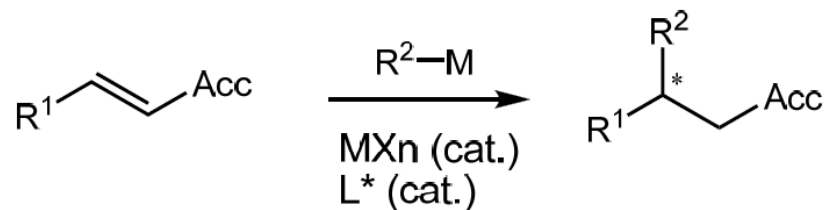
Diastereoselective Michael Addition:



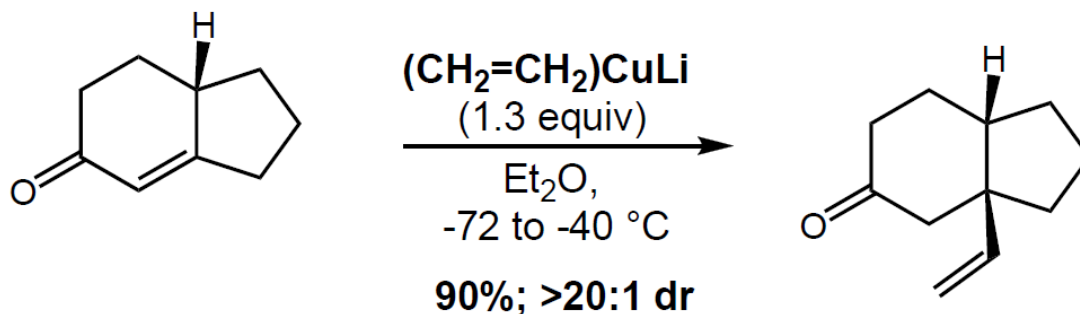
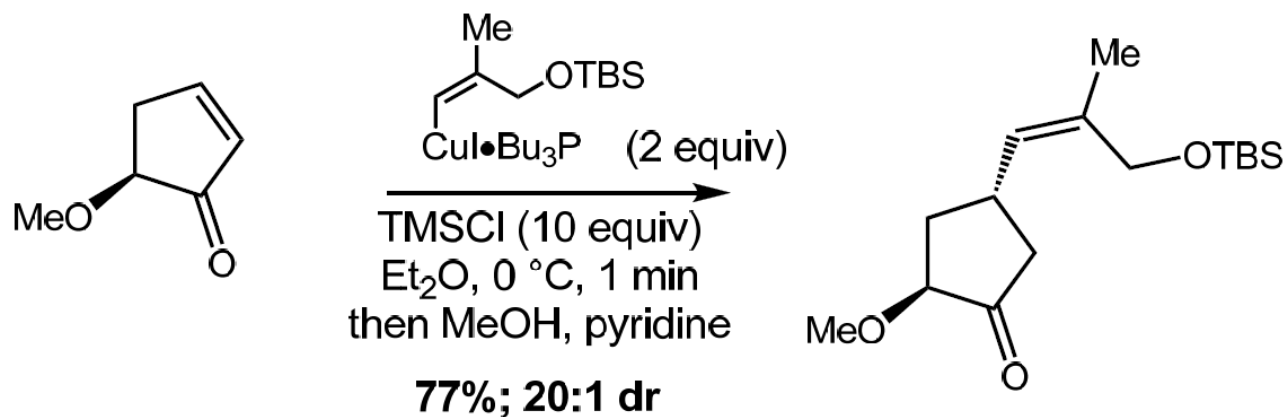
Enantioselective Michael Addition:



Catalytic Enantioselective Michael Addition:

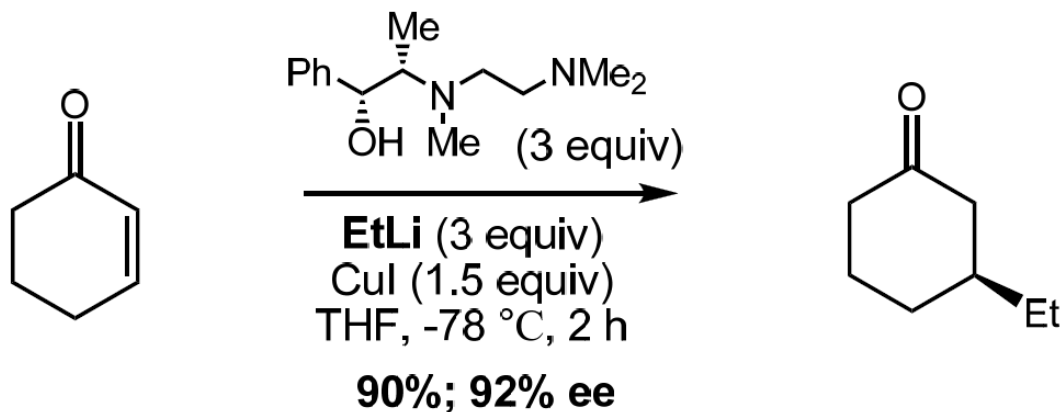


Diastereoselective Michael Addition

Corey, et al, *JACS* **1971**, 93, 7318Smith, et al, *JACS* **1992**, 114, 8008

Enantioselective Michael Addition

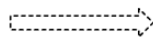
First report: two decades ago



Corey, *JACS* **1986**, *108*, 7114

Challenge:

background reactions,
alkoxide impurities
stoichiometric loading
high substrate specificity;



Metal cuprates in current use are derived from dialkylzinc, Grignard or trialkylaluminum reagents

Catalytic enantioselective Michael Addition

Catalyst:

copper with binaphthalene, TADDOL, oxazoline or others as ligands.

rhodium with diphosphane, active olefins or other as ligands

solely Lewis acidic M(II) and M(III) compounds:

such as magnesium, zinc, boron, aluminum, and lanthanoid catalysts

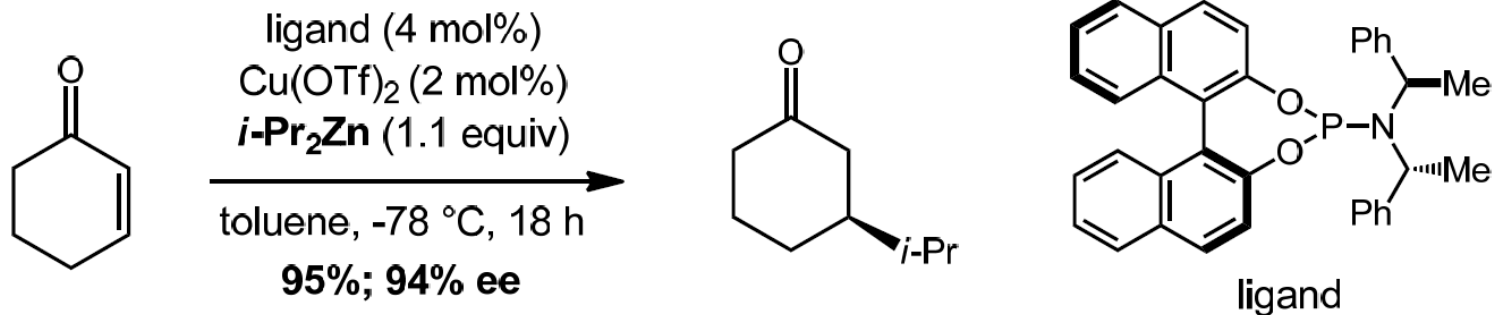
transition metal catalysts:

such as ruthenium, iridium, nickel, and palladium.

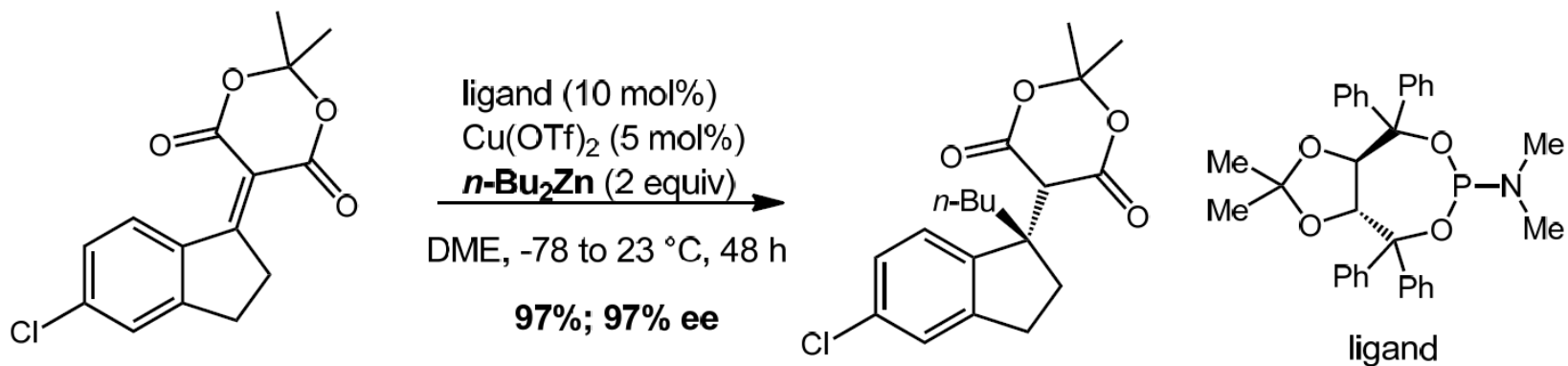
NOTE:

The catalysis with rhodium and copper complexes are the most flourishing fields.

copper

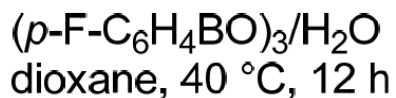
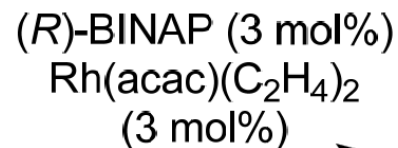
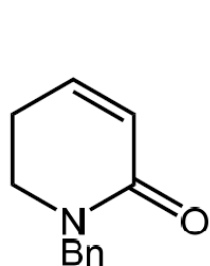


Feringa, *ACIE* **1997**, 36, 2620

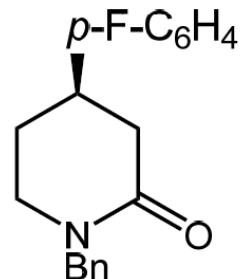


Fillion, *JACS* **2006**, 128, 2774

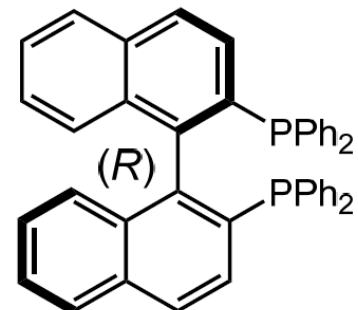
rhodium



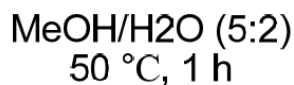
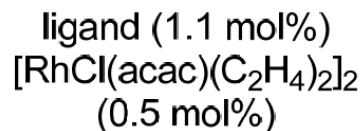
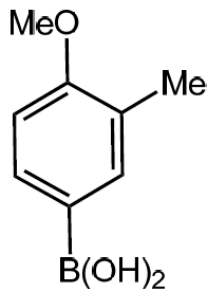
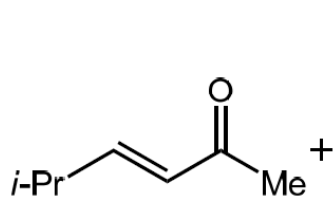
74%; 96% ee



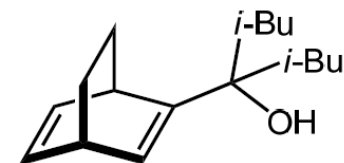
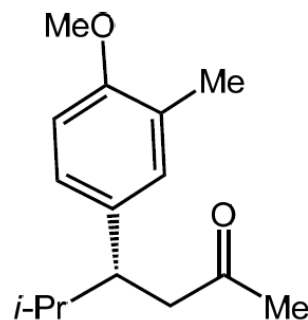
Hayashi, *JOC* **2001**, 66, 6852



(*R*)-BINAP



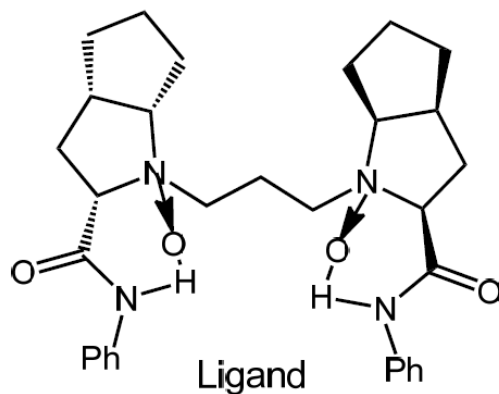
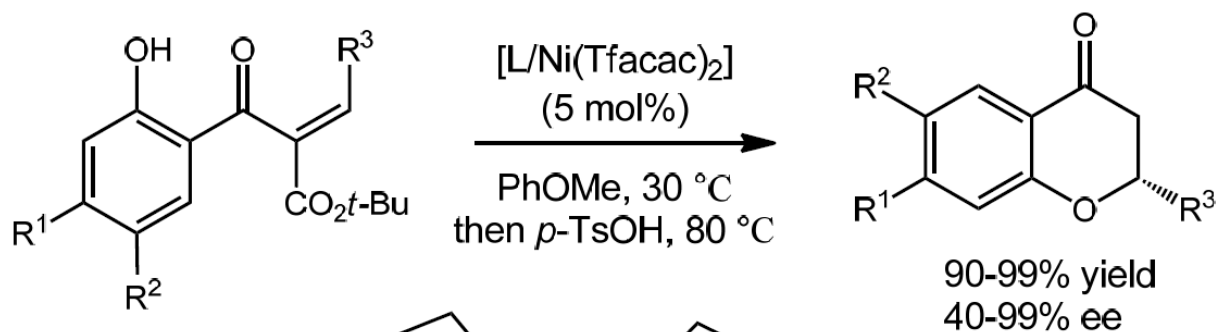
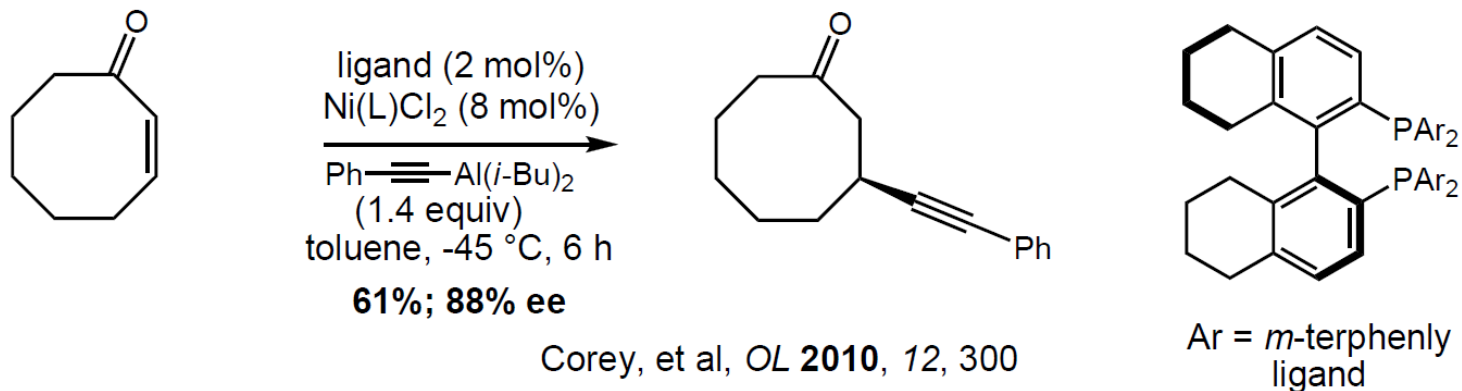
75%; 87% ee



ligand

Corey, *OL* **2009**, 12, 172

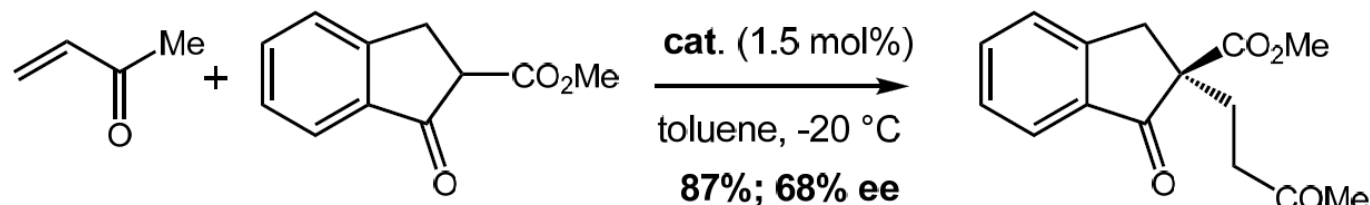
nickel



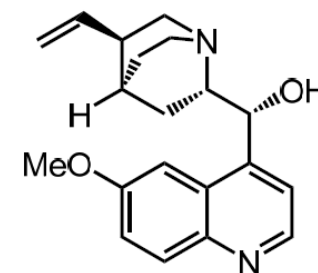
Feng, X. *ACIE* **08**, *47*, 8670.

Organocatalysts catalyzed conjugate addition:

Early report:



Wynberg, *TL* **1975**, 4057



catalyst

Reviews:

Tsogoeva, *EJOC* **2007**, 1701

Najera, *TA* **2007**, 18, 299

List, et al, *CR* **2007**, 107, 5471

Krishna, et al, *T* **2009**, 65, 9657

Enders, et al, *C-EJ* **2009**, 15, 11058

Wang, et al, *Catal. Sci. Technol.* **2012**, 2, 42

Organocatalysts and their catalytic mechanisms:

Organocatalyst:

proline and its derivatives,
chiral imidazolidinone derivatives,
chiral (thio) urea,
cinchona alkaloids and so on

Compared to metal based catalysts:

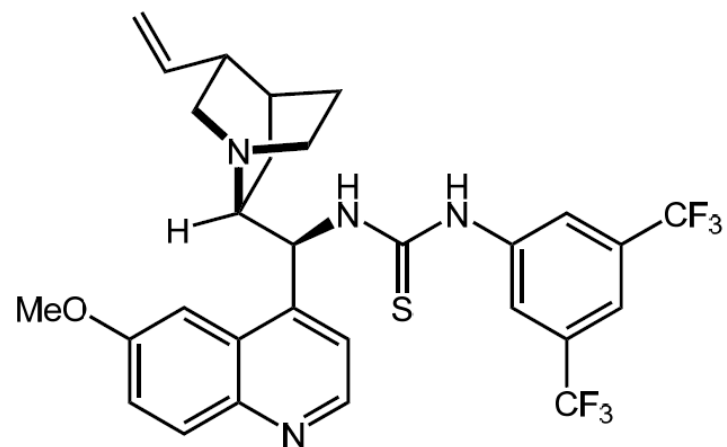
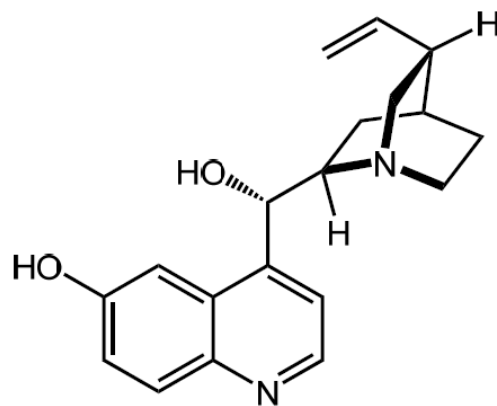
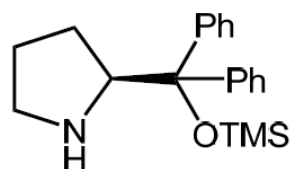
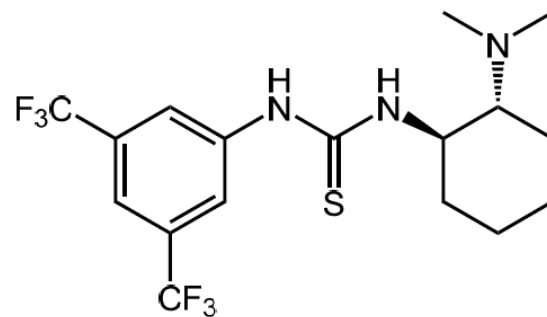
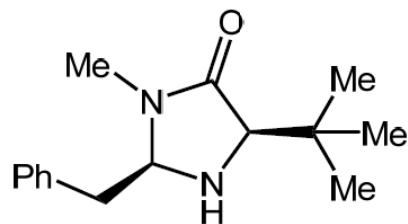
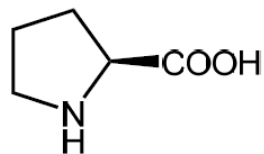
Inexpensive

Environmentally Benign

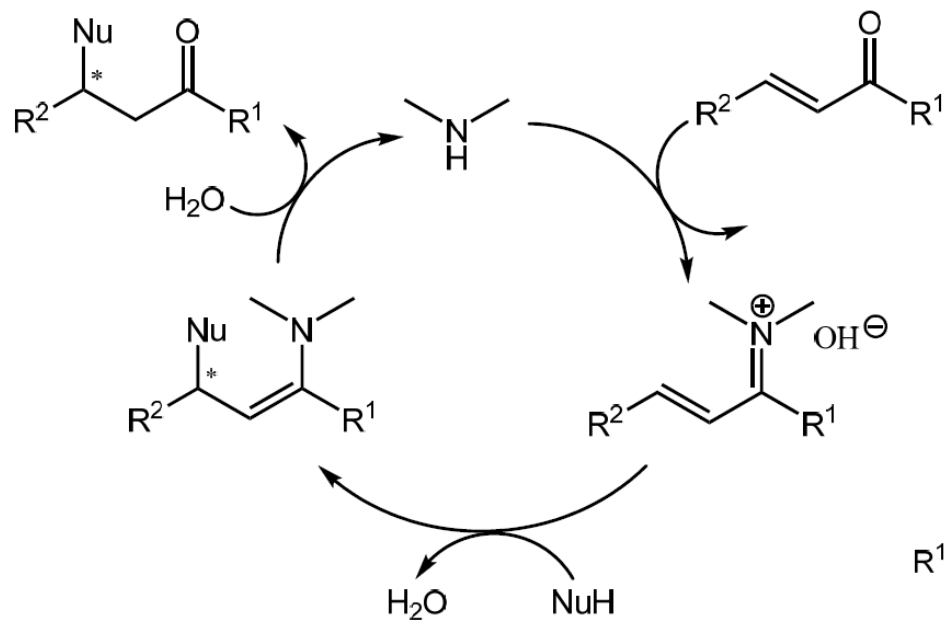
Relatively Mild Conditions

Biomimetic - Induce cascade reactions

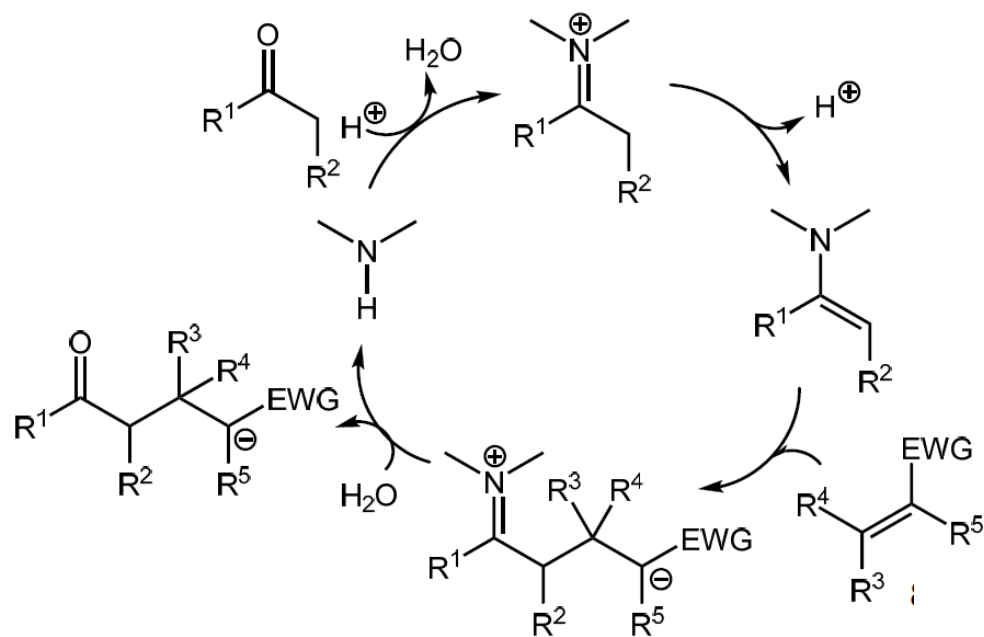
Selected examples:



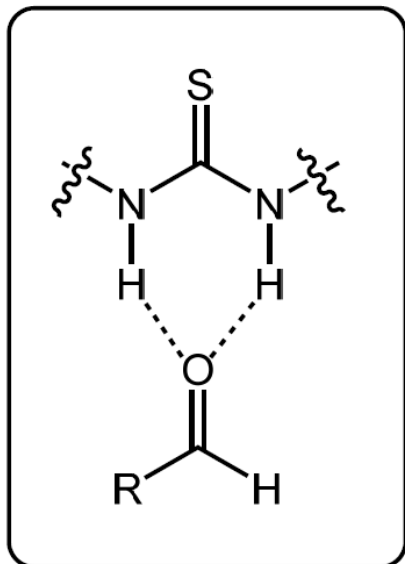
Iminium-catalytic Michael additions



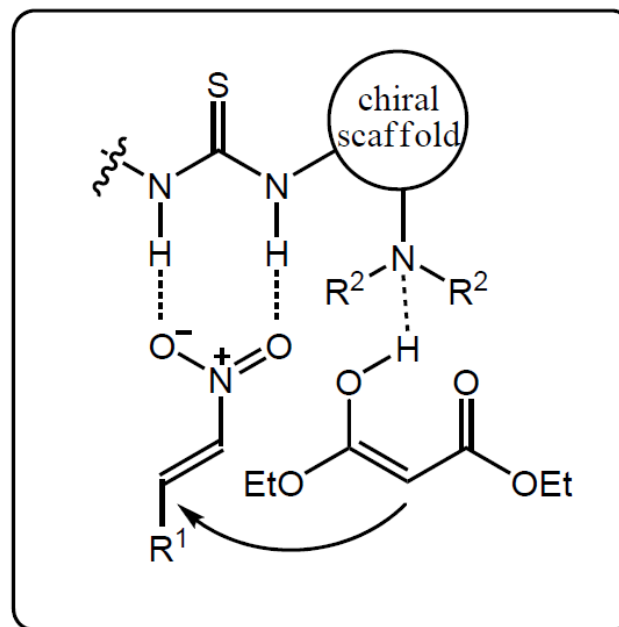
Enamine-catalytic Michael additions



Noncovalent catalyst: H-bond catalysis

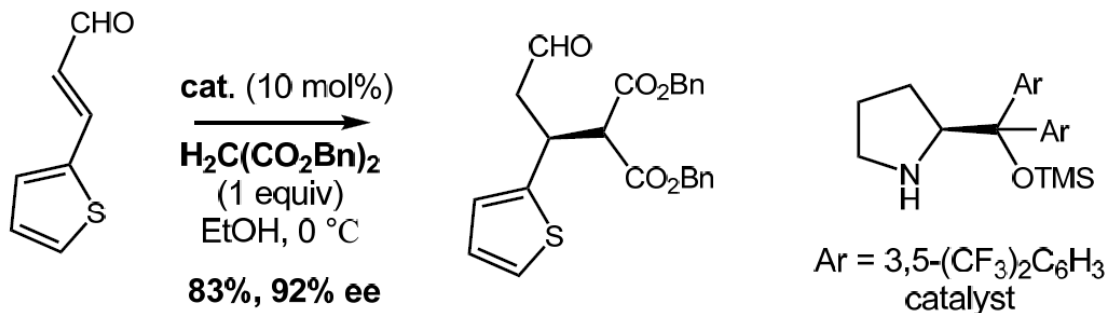


Bifunctional example

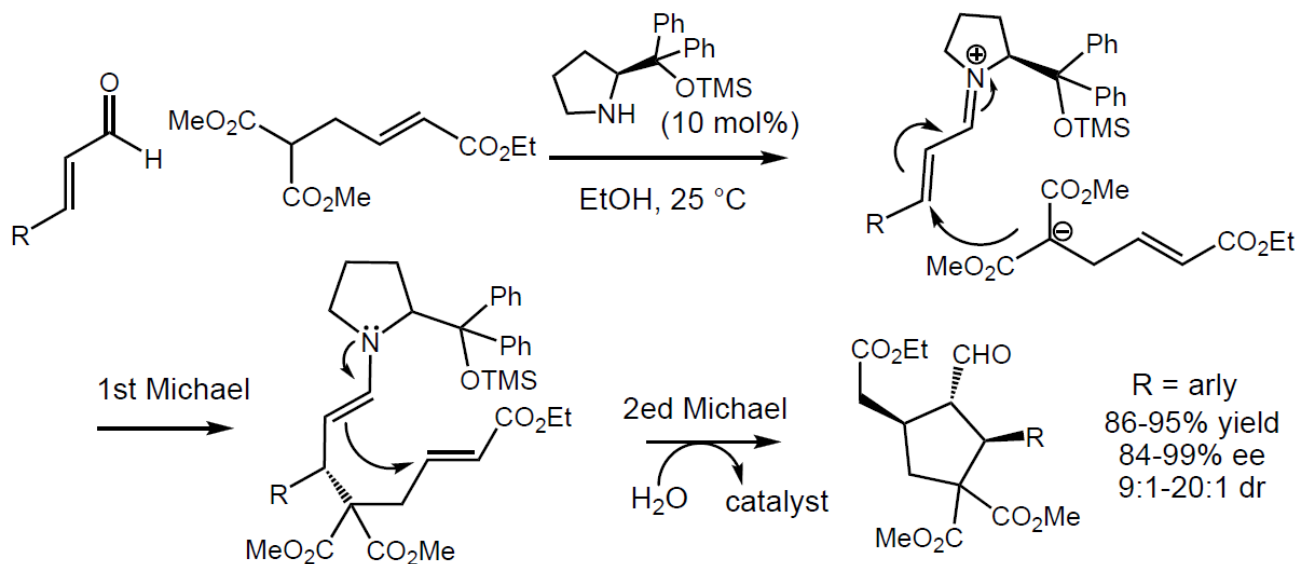


Conjugate addition of stabilized C-anions

Enal:

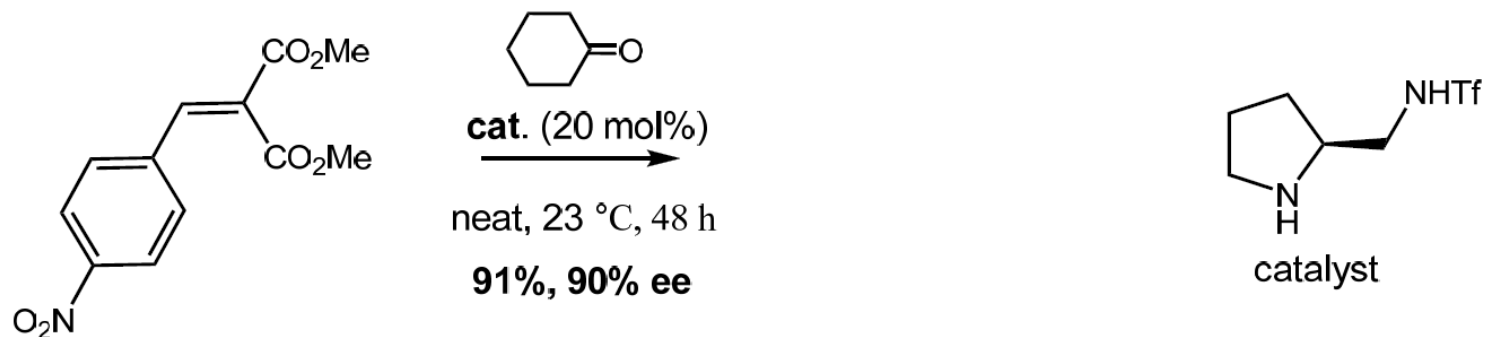


Jorgensen, et al, *ACIE* **2006**, 45, 4305



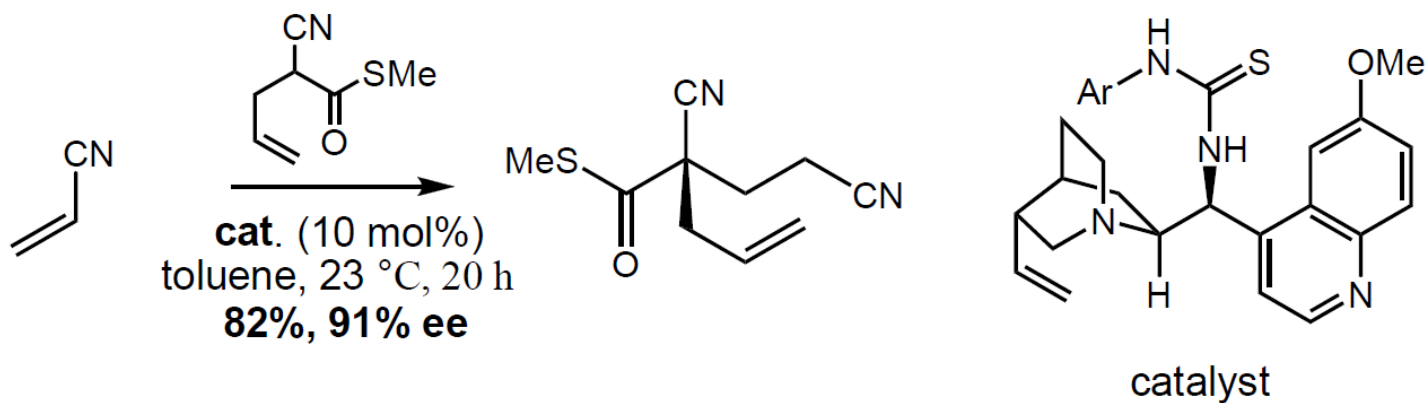
Wang, et.al. *ACIE* **2007**, 46, 3732

Unsaturated carboxylic acid derivatives

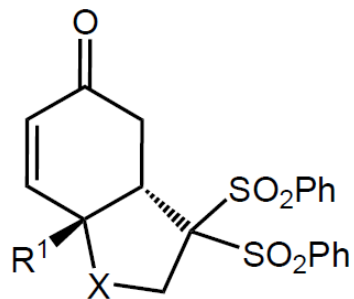
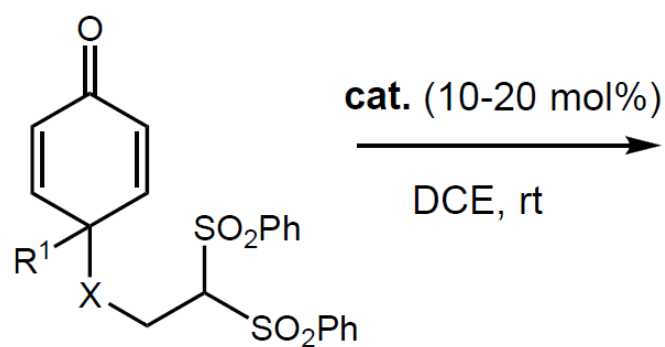


syn:anti > 13:1

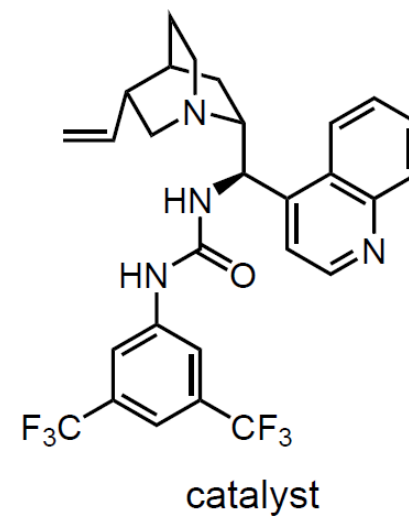
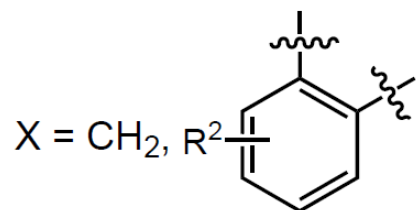
Tang, et al, *JOC* **2007**, 72, 4073



Deng, et al, *JACS* **2007**, 129, 768

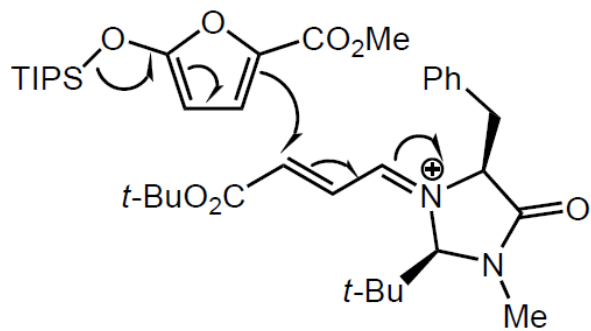
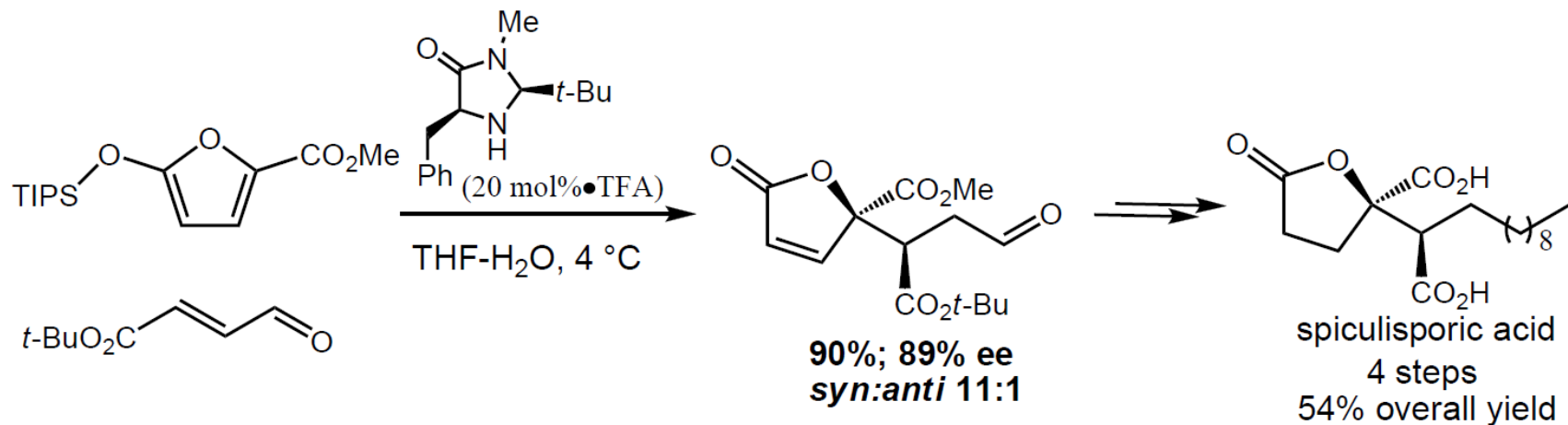


82-97% yield
84-91% ee



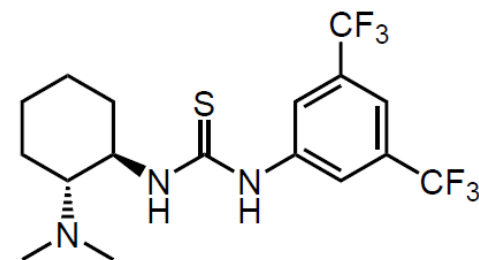
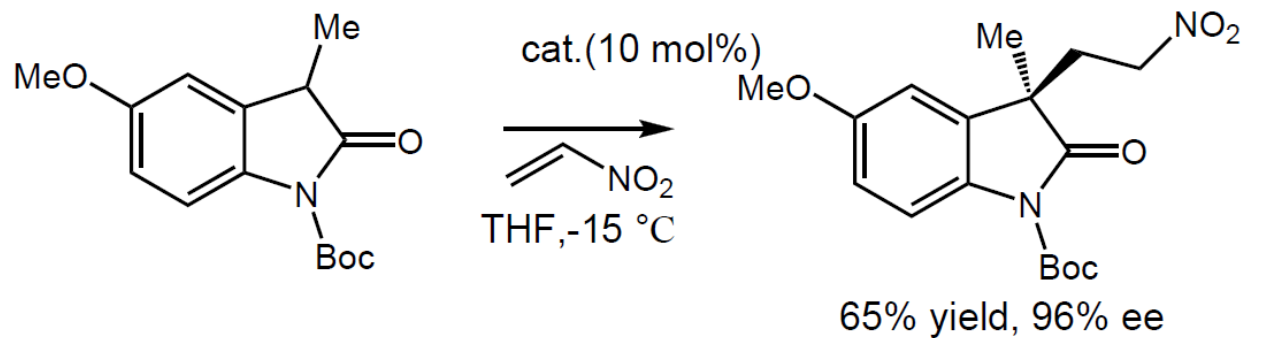
You, et al, *OL* **2011**, 13, 5192

Conjugate addition with neutral nucleophile

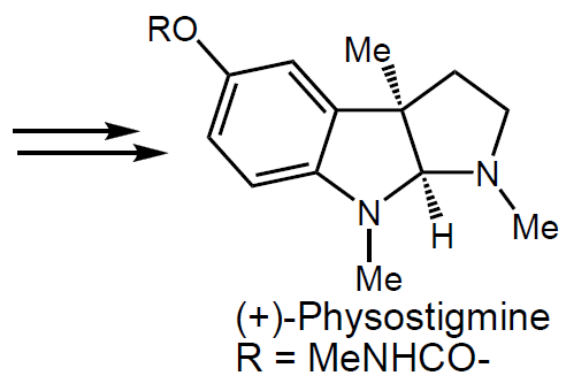
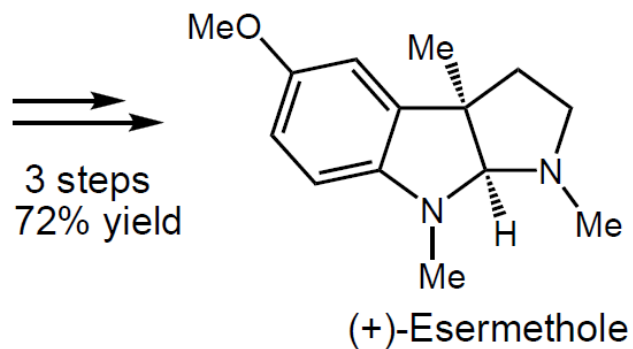


MacMillan, et.al. *JACS* **2003**, *125*, 1192

(+)-Esermethole



catalyst



Barbas, et al, *JACS* **2009**, *131*, 8758

The Intramolecular Friedel-Crafts Reaction

—*Synthesis of Tetrahydro(iso)quinolines and Chromans*

Xiao, et al. *Org. Lett.* **2007**, *9*, 1847.

The Intramolecular Friedel-Crafts Reaction

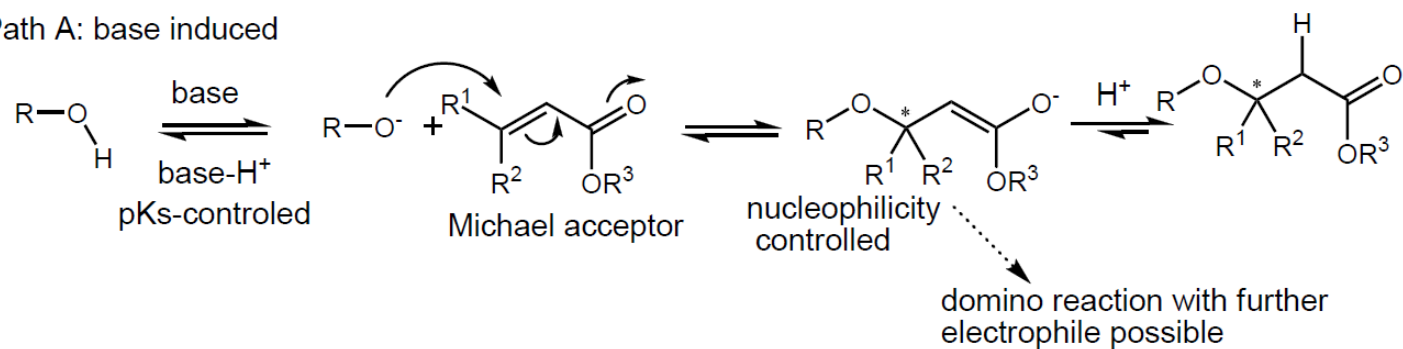
—*Synthesis of Tetrahydro(iso)quinolines and Chromans*



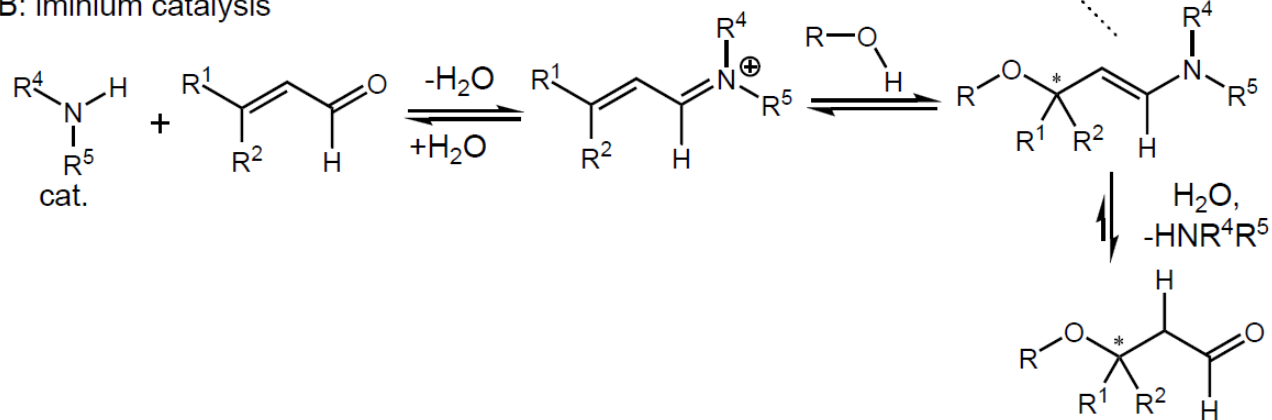
Oxa-Michael addition

Common oxa-Michael reaction pathways.

Path A: base induced



Path B: iminium catalysis

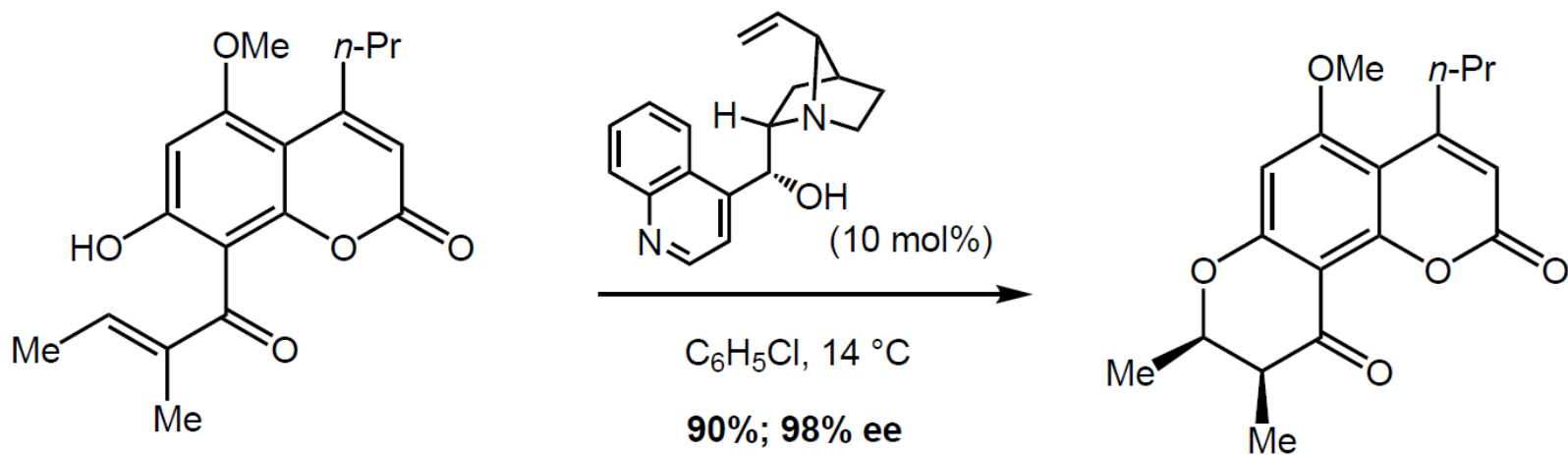


Reviews: Nising, et al, *CSR* **2008**, 37, 1218.
Nising, et al, *CSR* **2012**, 41, 988.

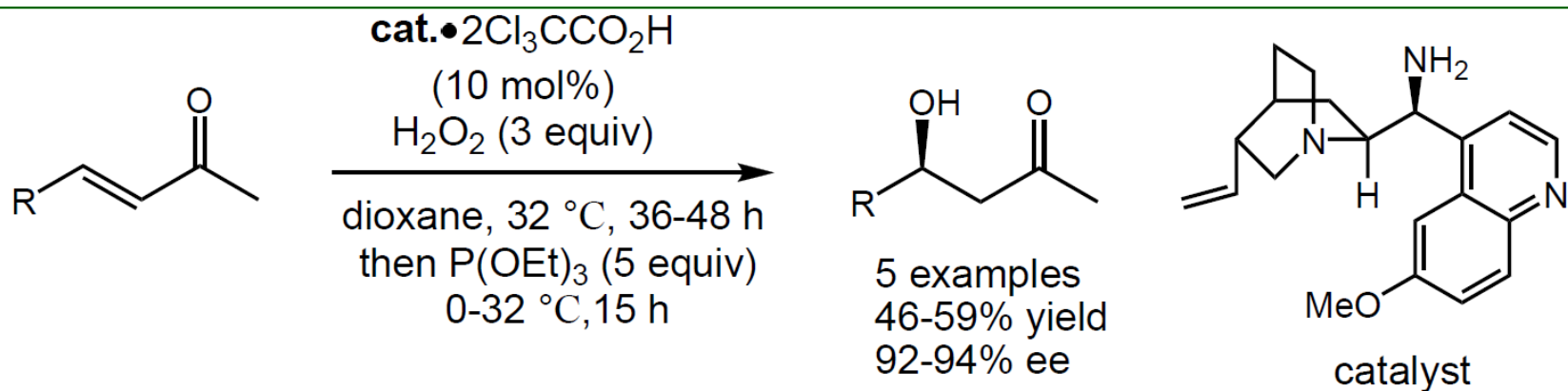
Challenge: reversibility of the alcohol addition step
relatively poor nucleophilicity

Potential: product available are valuable intermediates in organic synthesis
grant efficient access to oxygen-containing heterocycles

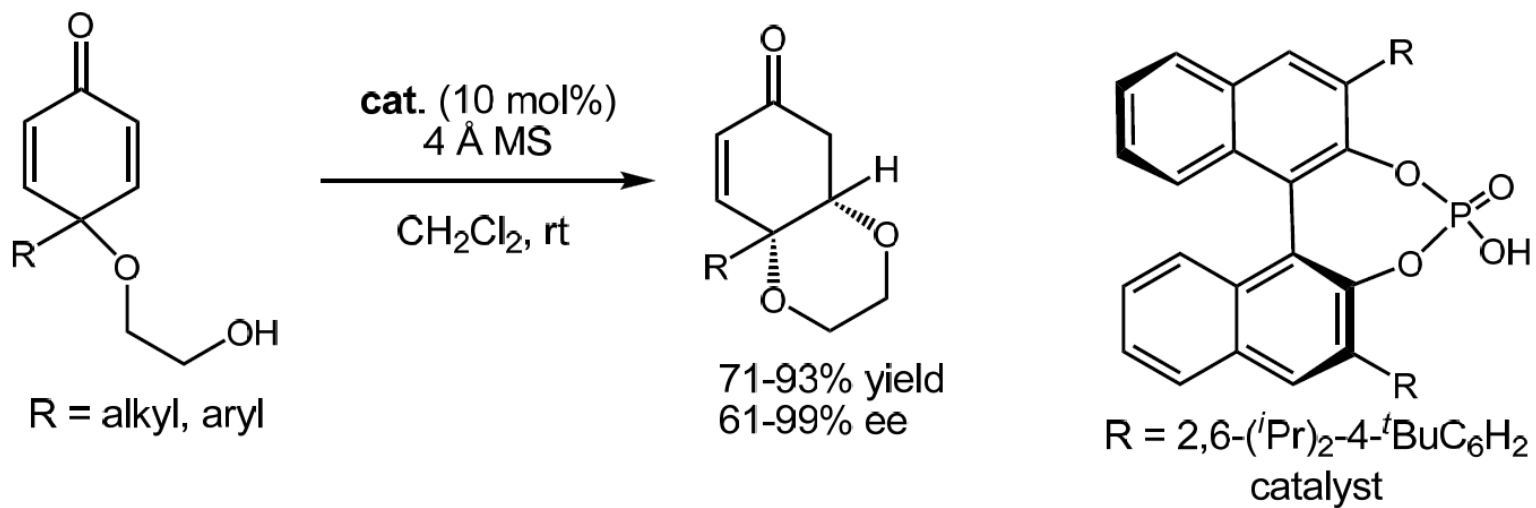
First catalytic and highly enantioselective example



Ishikawa, *TA* **2000**, *11*, 4633



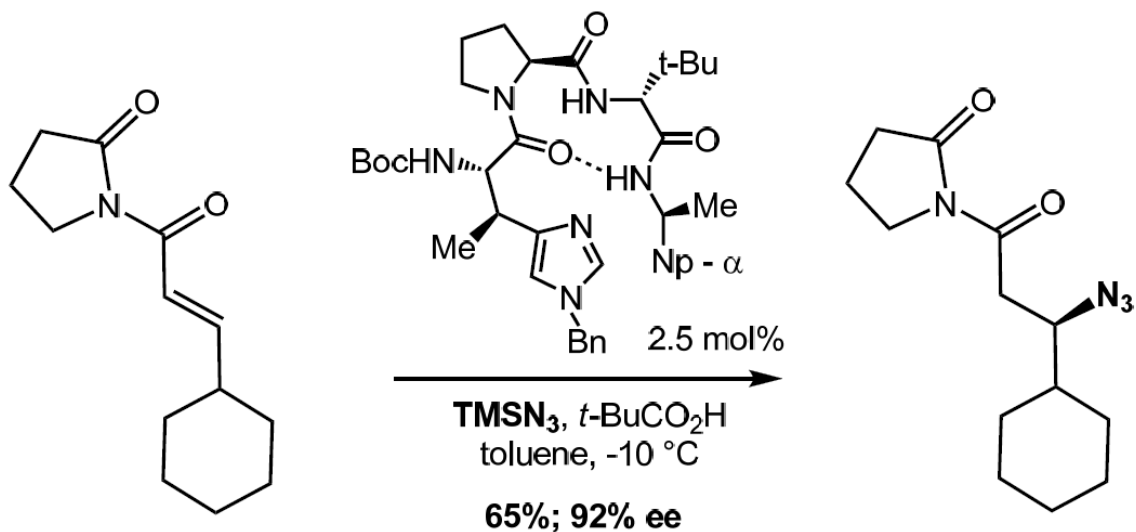
List, et al, *ACIE* **2008**, 47, 8112.



You, et al, *JACS* **2010**, 132, 4056.

aza-Michael addition

First catalytic and highly enantioselective example of aza-Michael addition

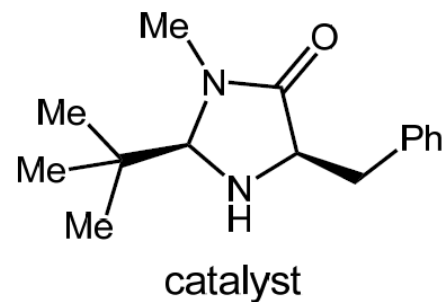
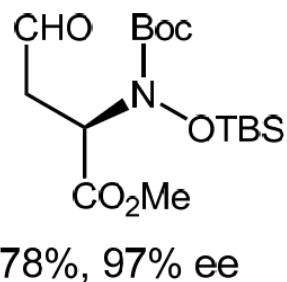
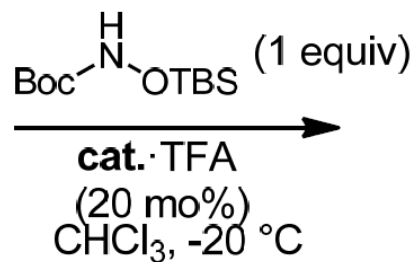
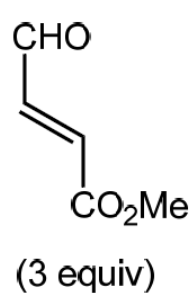


Miller, *JACS* **2002**, *124*, 2134

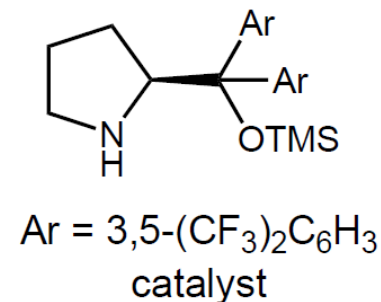
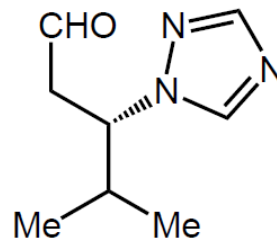
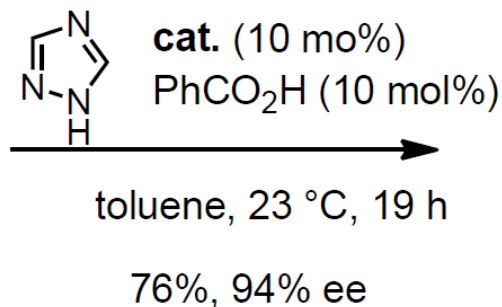
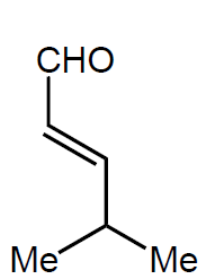
Review: Carrillo, *Synthesis* **2007**, 2065;
Krishna, et al, *T* **2009**, *65*, 9657
Enders, et al, *C-EJ* **2009**, *15*, 11058

Nitrogen nucleophiles:

hydroxylamine derivatives, imides, azides, benzotriazoles, tetrazoles, imidazoles, anilines.....

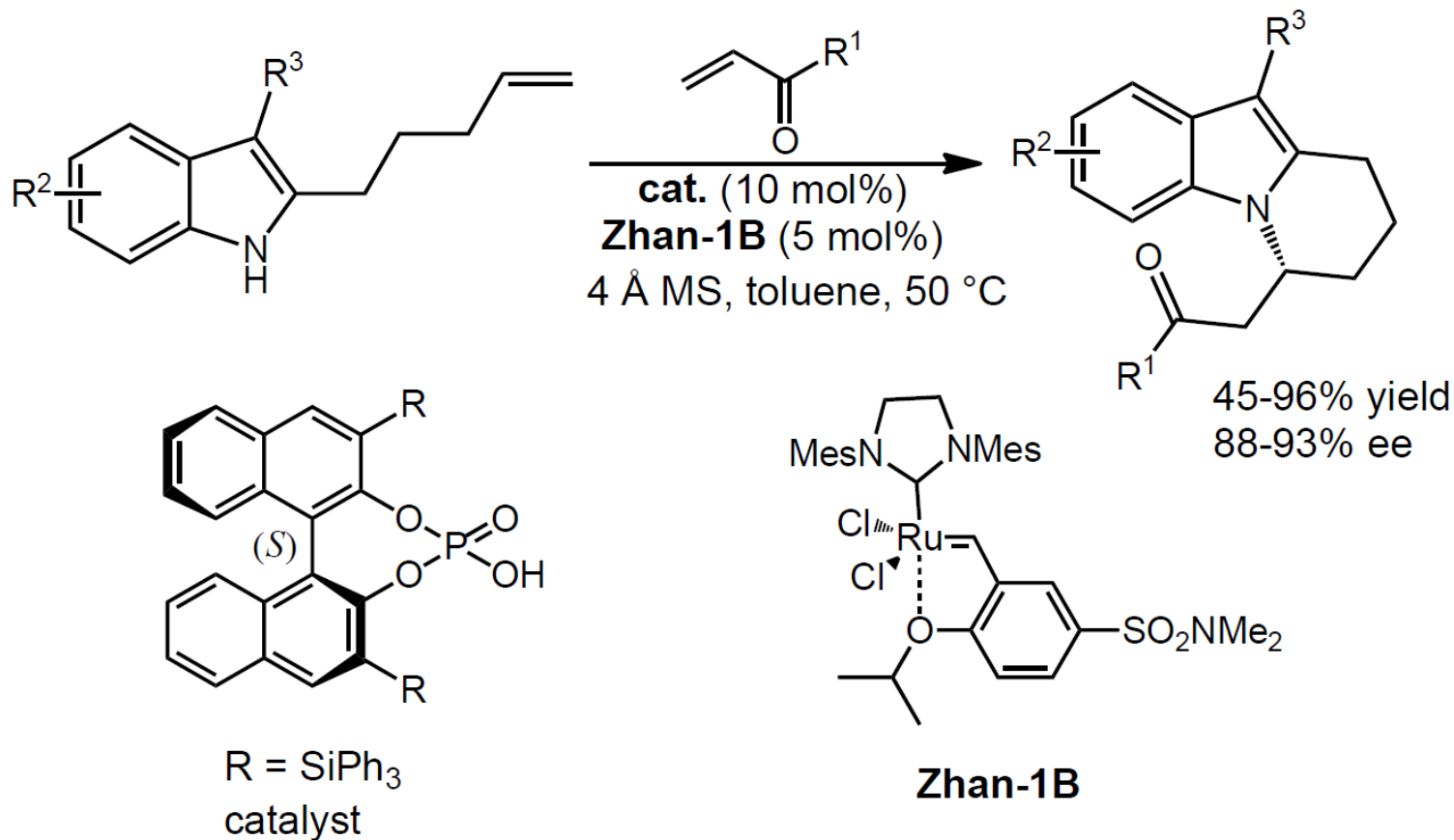


MacMillan, *JACS* **2006**, 128, 9328



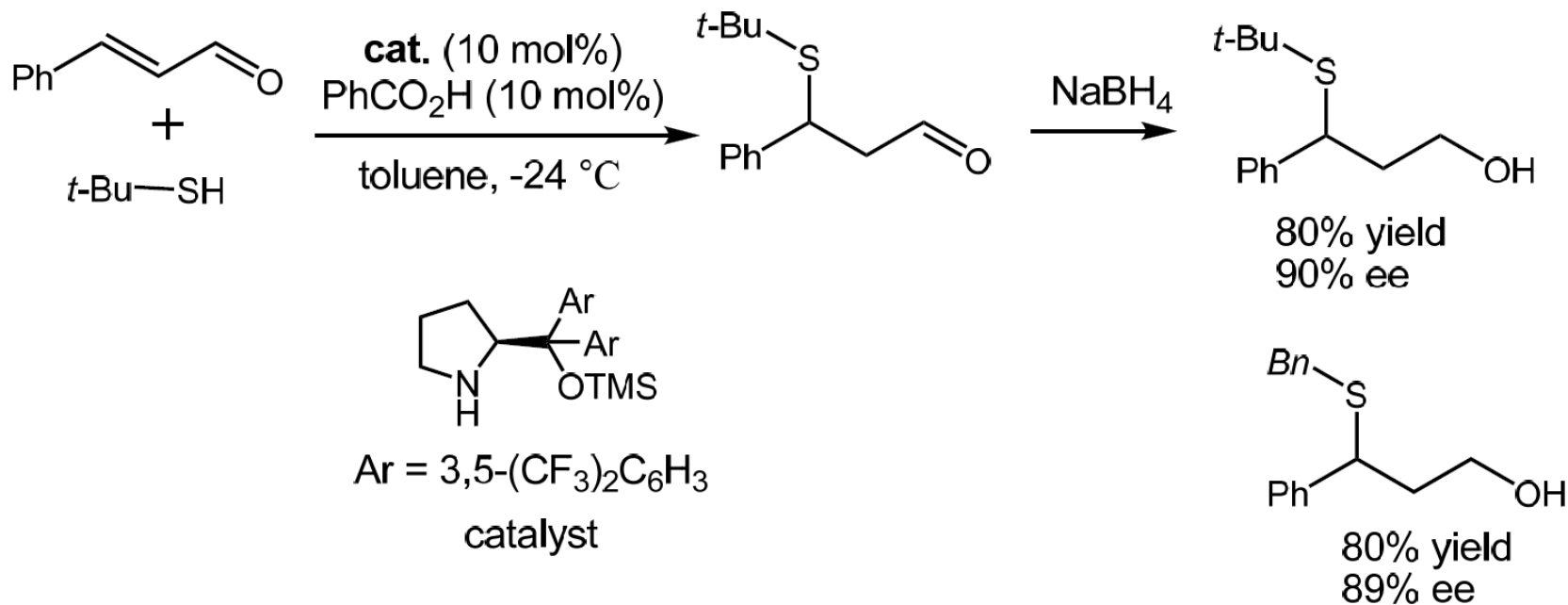
Jørgensen, *ACIE* **2007**, 46, 1983

Asymmetric olefin cross-metathesis/aza-Michael reaction



You, S.-L. *ACIE* **10**, 49, 8666

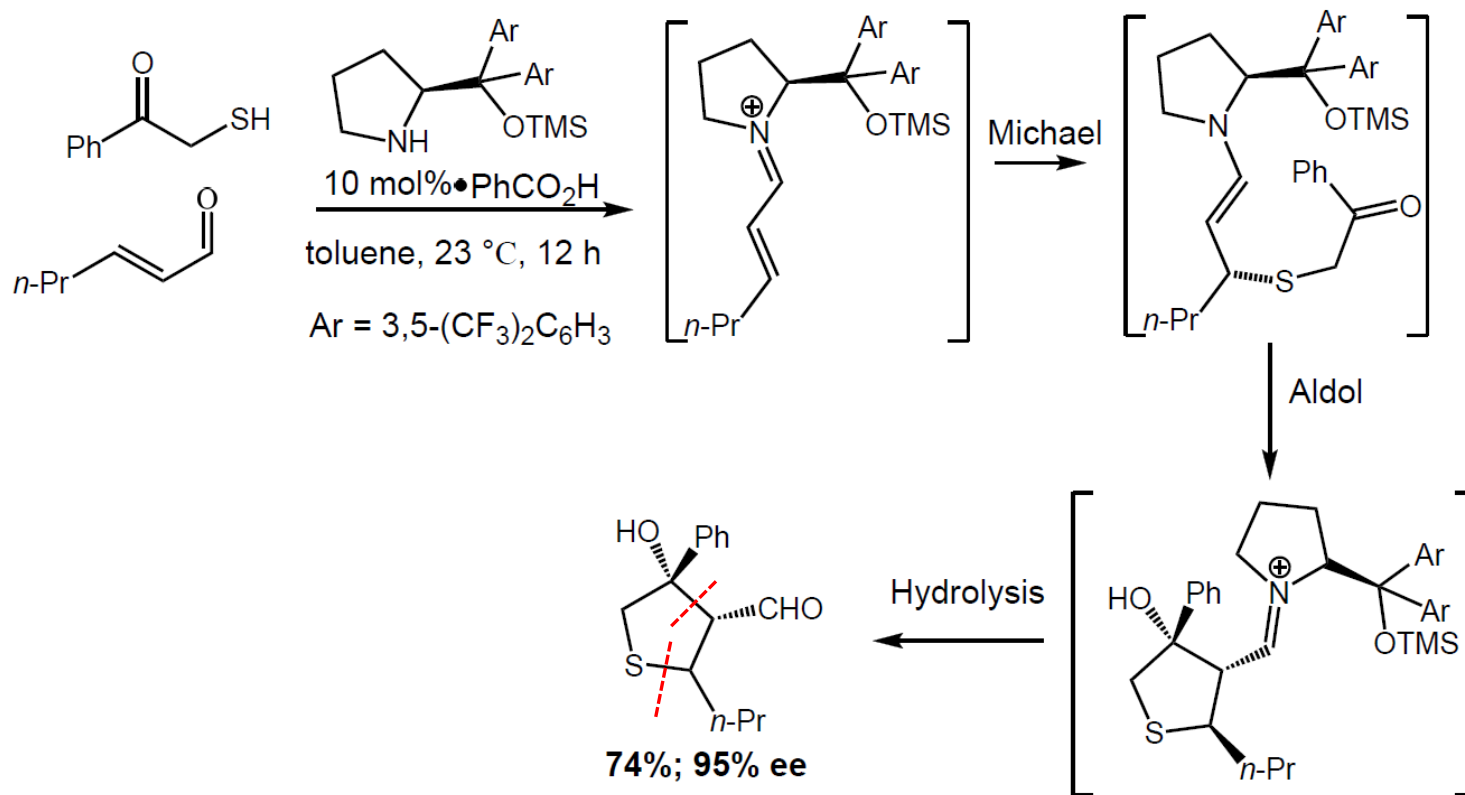
Sulfa-Michael addition



Jorgensen, et al, *JASC* **2005**, 127, 15710

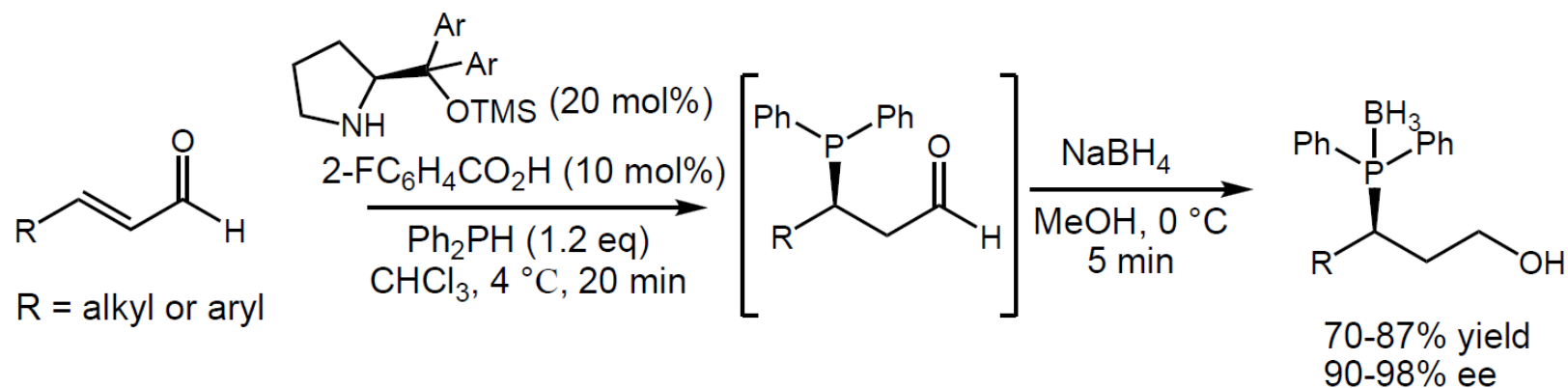
- Reduce *in situ* prevent retro-Michael
- Easily removable Protecting groups

Tetrahydrothiophenes



Jorgensen, et al, *JACS* **2006**, *128*, 14986

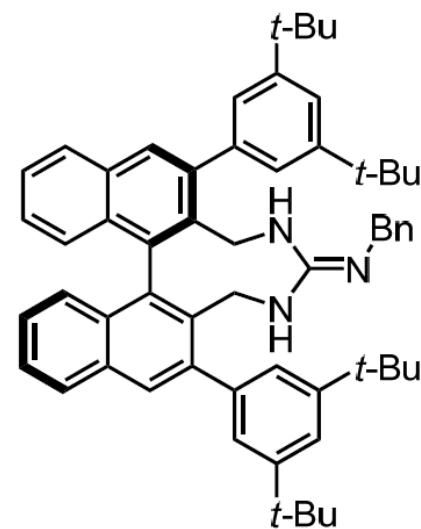
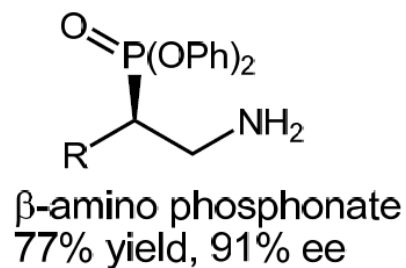
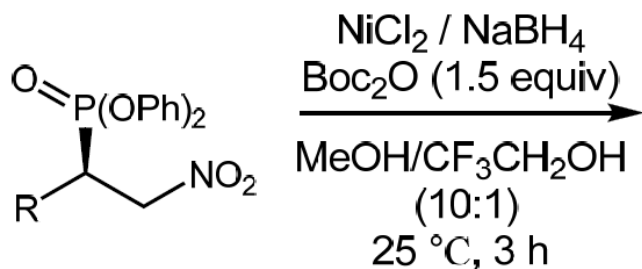
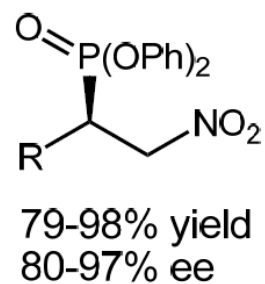
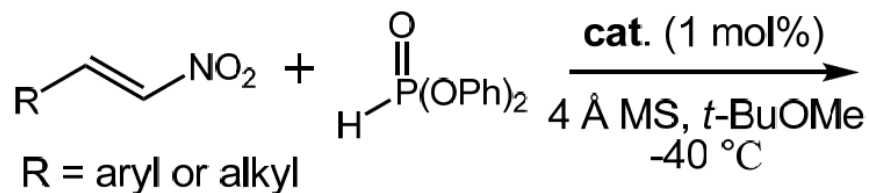
— *Org. Lett.* **2009**, *11*, 3946-3949. (Featured by List, B. *Synfacts*, **2009**, *10*, 1164)



Cordova, et al, *ACIE* **2007**, 46, 4507

- Phospine-Borates easily purified
- Metal-based catalyst not effective due to Phoshine coordination
- Chiral phosphine generally prepared by resolution

β -Amino Phosphonates



Axially chiral guanidine

Terada, et al, *JACS* **2007**, *129*, 14112