

Massachusetts Institute of Technology
Organic Chemistry 5.511

November 7, 2007
Prof. Rick L. Danheiser

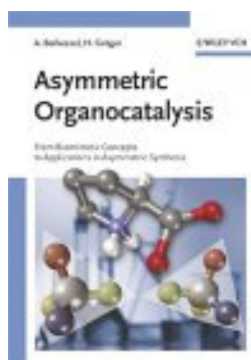
Lecture 11
Unit 3
Stereocontrolled Alkylation
and Related Electrophilic Substitution Strategies

V. Catalytic Methods

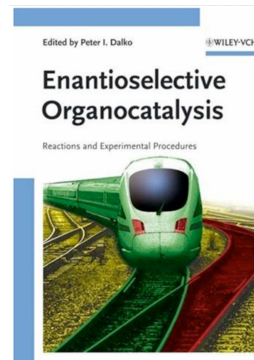
- ★ α -Oxidation of Aldehydes and Ketones (*H. Yamamoto, MacMillan, Zhong, Y. Hayashi*)
- ★ Alkylation of Imine Derivatives of α -Amino Esters (*O'Donnell, Corey, Maruoka*)
- ★ Tsuji Allylation of Ketones (*Stoltz, Trost*)
- ★ Enantioselective Allylation via "SOMO Activation" (*MacMillan*)
- ★ Enantioselective Protonation Strategies (*Fu*)



Special Issue on
Asymmetric Organocatalysis
Accts. Chem. Res. **2004**, 37, 487-631



"Asymmetric Organocatalysis"
A. Berkessel and H. Gröger
Wiley-VCH, **2005**

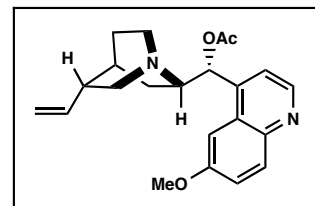
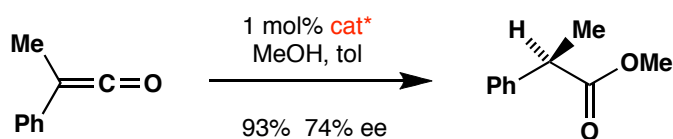


"Enantioselective
Organocatalysis"
P. I. Dalko, Ed.
Wiley-VCH, **2007**

- ★ Catalysis by Enzymes
- ★ Transition Metal Organometallic Catalysis
- ★ "Organocatalysts"

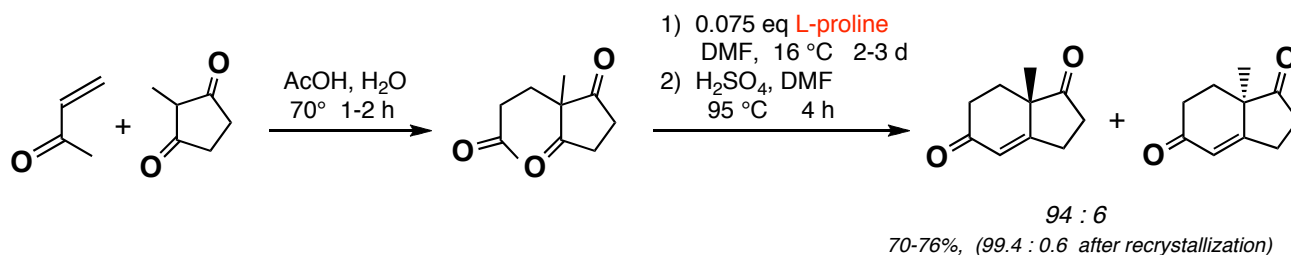
Asymmetric Organocatalysis: Early Milestones

★ H. Pracejus *Liebigs Ann. Chem.* **1960**, 634, 9; *J. Prakt. Chem.* **1964**, 24, 195

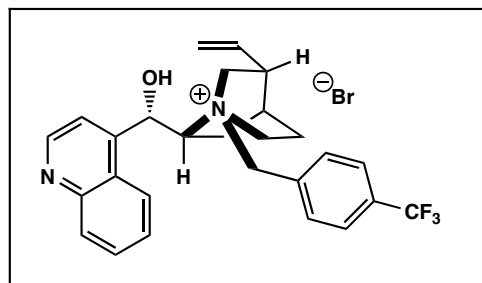
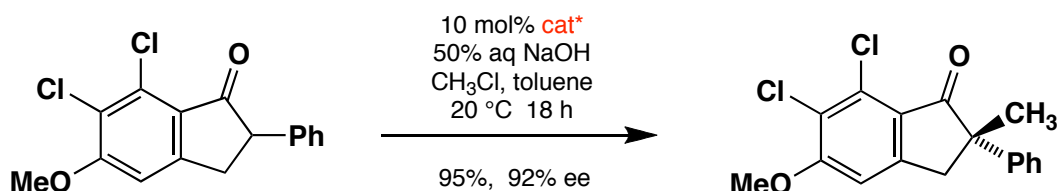


*cat** is O-acetyl quinine

★ Z. G. Hajos, D. R. Parrish *J. Org. Chem.* **1974**, 39, 1615; also U. Eder, G. Sauer, and R. Wiechert . . . see *Org. Synth.* **1985**, 63, 26 and 37



★ E. J. J. Grabowski et al. *J. Am. Chem. Soc.* **1984**, 106, 446; *J. Org. Chem.* **1987**, 52, 4745



*cat**
cinchoninium bromide
derivative

Review

"Recent Advances in Asymmetric Phase-Transfer Catalysis"
Ooi, T.; Maruoka, K. *Angew. Chem. Int. Ed.* **2007**, 46, 4222

Enantioselective Organocatalytic Oxidation of Aldehydes with Nitrosobenzene



Hisashi Yamamoto
University of Chicago

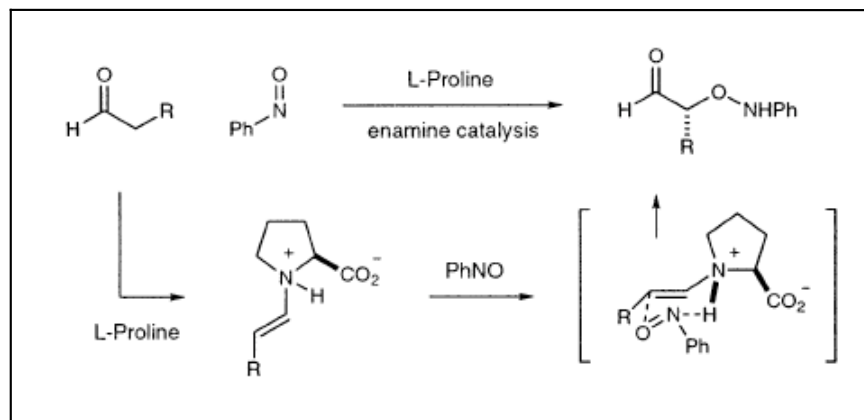
Review

Yamamoto, H.; Momiyama N.
Chem. Commun. **2005**, 3514

Brown, S. P.; Brochu, M. P.; Sinz, C. J.; MacMillan, D. W. C.
J. Am. Chem. Soc. **2003**, *125*, 10,808



David MacMillan
Princeton University



See also work of
G. Zhong and Y. Hayashi

Reviews on Catalytic, Enantioselective "Heterofunctionalization" of Carbonyl Compounds

Janey, J. M. *Angew. Chem. Int. Ed.* **2005**, *44*, 4292

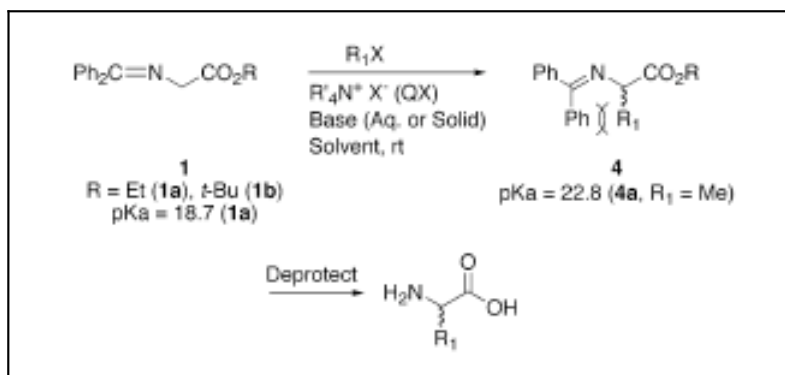
Guillena, G.; Ramon, D. J. *Tetrahedron: Asymmetry* **2006**, *17*, 1465

Marigo, M; Jorgensen, K. A. *Chem. Commun.* **2006**, 2001

Alkylation of Imine Derivatives of α -Amino Esters



Martin J. O'Donnell
IUIPUI



Enantioselective Tsuji Allylation

Minireview

You, S.-L.; Dai, L.-X. . *Angew. Chem. Int. Ed.* **2006**, 45, 5246

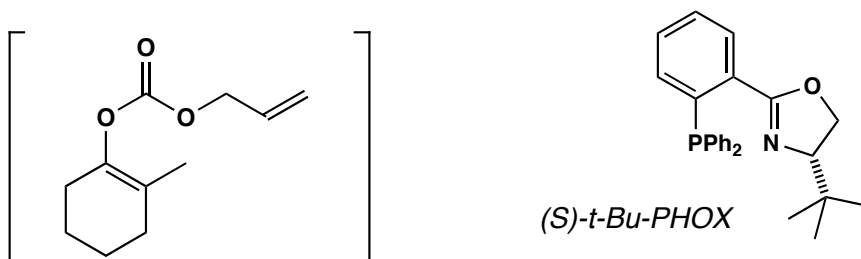
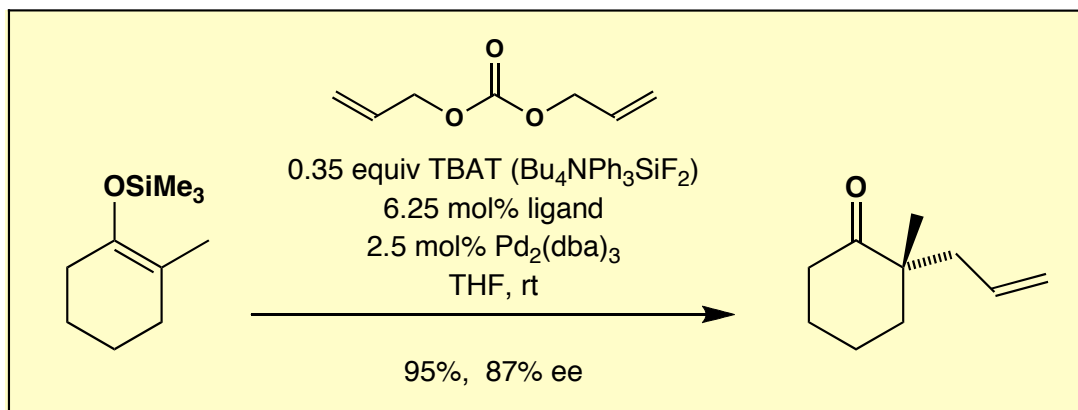
Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, 126, 15,044

Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, 127, 2846

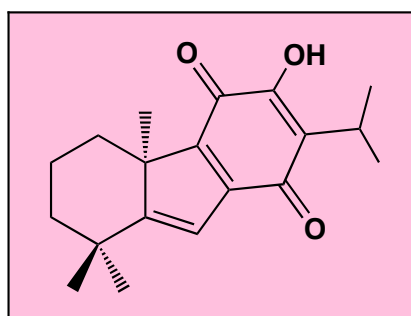
Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, 127, 17180

Trost, B. M. Bream, R. N.; Xu, J. *Angew. Chem. Int. Ed.* **2006**, 45, 3109

Braun, M.; Meier, T. *Angew. Chem. Int. Ed.* **2006**, 45, 6952

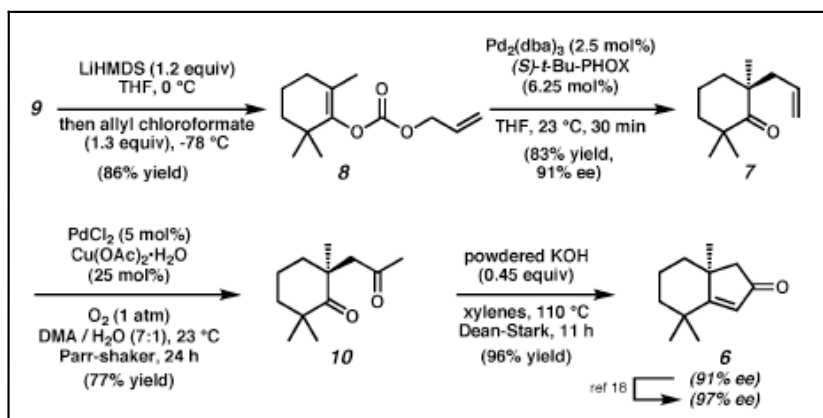


Application

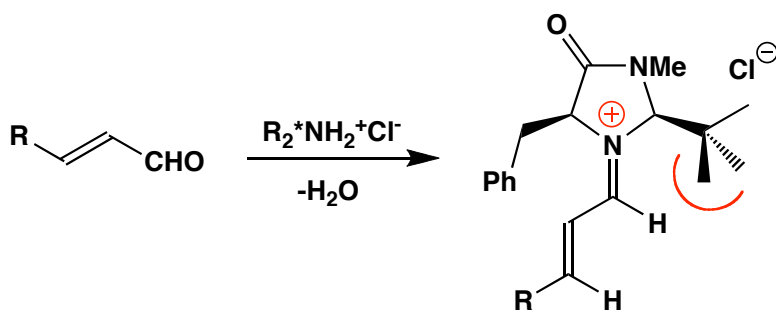


$(+)$ -Dichroanone

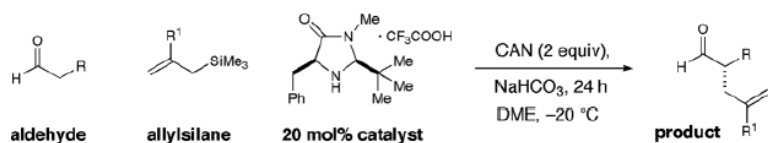
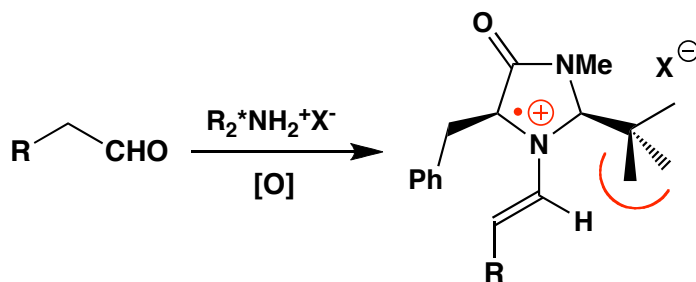
McFadden, R. M.; Stoltz, B. M.
J. Am. Chem. Soc. **2006**, 128, 7738



Enantioselective Allylation via "SOMO Activation"



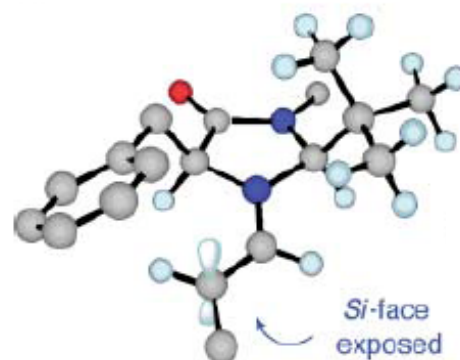
Enamine-Derived Radical Cation
"SOMO Activation"



entry	aldehyde	product*	entry	aldehyde	product*
1			4		
	81% yield, 91% ee			72% yield, 87% ee	
2			5		
	75% yield, 92% ee			75% yield†, 94% ee	
3			6		
	72% yield, 95% ee			70% yield, 93% ee	
entry	allylsilane	product†	entry	allylsilane	product†
7			9		
	88% yield, 91% ee			77% yield, 88% ee	
8			10		
	87% yield, 90% ee			81% yield, 90% ee	

Beeson, T. D.; Mastracchio, A.; Hong, J.-B.; Ashton, K.; MacMillan, D. W. C. *Science* **2007**, 316, 582

See also Sibi, M. P.; Hasegawa, M. *J. Am. Chem. Soc.* **2007**, 129, 4124 and Jang, H.-Y.; Hong, J.-B.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2007**, 129, 7004



Enantioselective Protonation Strategies

Review: J.-C. Plaquevent *Tetrahedron Asymmetry* **2004**, *15*, 3653

Enantioselective Addition of Amines to Ketenes Catalyzed by a Planar-Chiral Derivative

B. L. Hodous; G. C. Fu *J. Am. Chem. Soc.* **2002**, *124*, 10,006

See also Wiskur, S. L.; Fu, G. C. *J. Am. Chem. Soc.* **2005**, *127*, 6176

