Massachusetts Institute of Technology

Organic Chemistry 5.512

April 21, 2006
Prof. Rick L. Danheiser

Unit 4

Stereocontrolled 1,2-Addition to Carbonyl Groups

★ **General Principles**

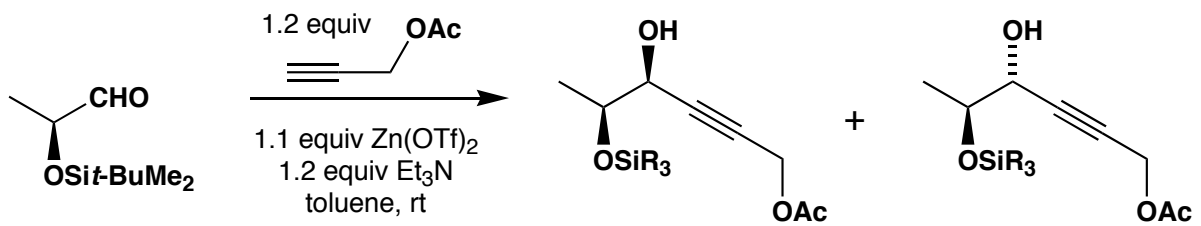
- ★ Substrate Control: 1,2-Induction by Molecular Framework
- ★ Substrate Control: 1,3-Induction by Molecular Framework
- ★ Reagent Control: Organozinc and Related Addition Reactions

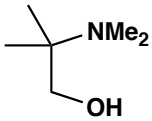
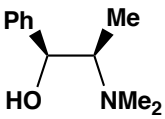
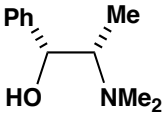
Addition of Alkyl, Aryl, Alkenyl, and Alkynyl Metal Compounds

★ Asymmetric Addition of Alkynylzinc Compounds to Aldehydes

Double Asymmetric Synthesis: Carreira Alkynylation

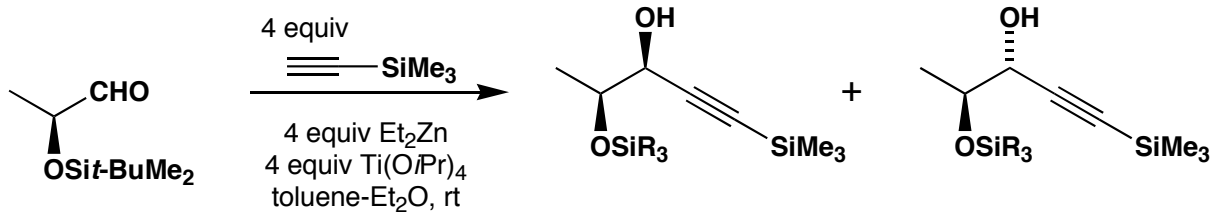
E. M. Carreira et al. *J. Am. Chem. Soc.* **2001**, *123*, 9687, *Org. Lett.* **2001**, *3*, 3017



1.2 equiv			80	20
		70%	96	4
		69%	9	91

Double Asymmetric Synthesis: Chan-Pu Alkynylation

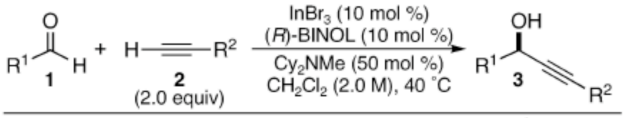
L. Pu et al. *PNAS* **2004**, *101*, 5417; J. A. Marshall et al. *Org. Lett.* **2003**, *5*, 3197
Also see J. A. Baldwin et al. *Tetrahedron* **2005**, *61*, 7219



	no ligand	45%	85	15
0.4 equiv	(S)-BINOL	55%	45	55
0.4 equiv	(R)-BINOL	60%	92	8
	Carreira method	0%		

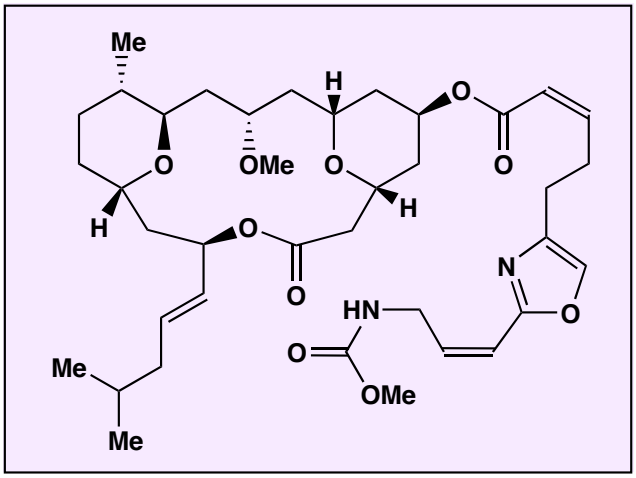
Frontiers in Asymmetric Alkynylation

M. Shibasaki et al. *J. Am. Chem. Soc.* **2005**, *127*, 13760



entry	aldehyde	alkyne	time (h)	yield (%)	ee (%)
1	CHO **1a**	H—≡—Ph **2a**	9	95	98
2		H—≡—(CH$_2$)$_2$Ph **2b**	36	77	>99
3	CHO **1b**	H—≡—Ph **2a**	25	85	96
4		H—≡—(CH$_2$)$_2$Ph	48	46	98

Case Study

Fettes, A.; Carreira, E. M.
J. Org. Chem. **2003**, *68*, 9274

leucascandrolide A