

Massachusetts Institute of Technology  
Organic Chemistry 5.512

April 4, 2007  
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Unit 4

Stereocontrolled 1,2-Addition to Carbonyl Groups

★ Addition of "Unstabilized" Carbon Nucleophiles

- ★ Reagent Control: Organozinc and Related Addition Reactions  
Alkyl, Alkenyl, and Alkynyl Metal Compounds

General Reviews on Organozinc Chemistry

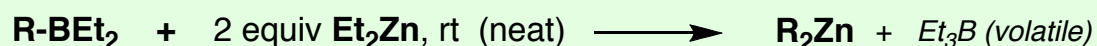
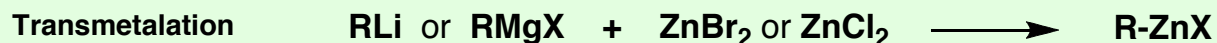
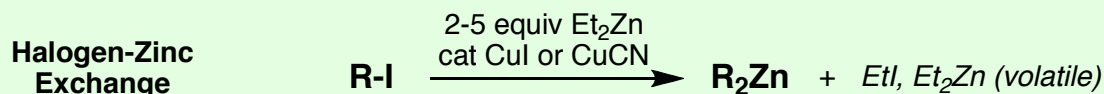
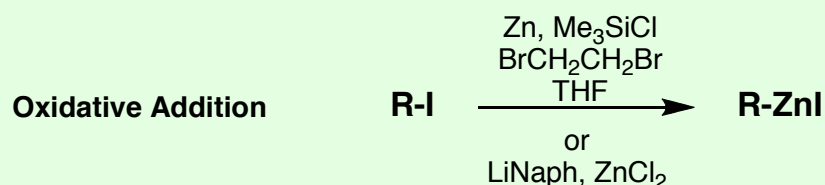
"Preparation and Applications of Functionalized Organozinc Compounds"

Knochel, P.; Millot, N.; Rodriguez, A. L.; Tucker, C. E. *Organic Reactions* **2001**, 58, 417-731

"Organozinc Reagents: A Practical Approach" Knochel, P.; Jones, P.; Oxford, 1999

"Polyfunctional Zinc Organometallics for Organic Synthesis" In *Handbook of Functionalized Organometallics*, Knochel, P., Ed.; Wiley-VCH, Vol. 1, 2005, pp 251-346

General Methods for the Preparation of Organozinc Compounds



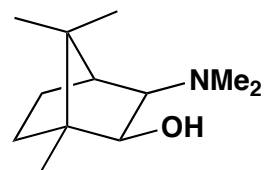
## Asymmetric Addition of Dialkylzinc Compounds to Aldehydes

**Review:** "Catalytic Asymmetric Organozinc Additions to Carbonyl Compounds"

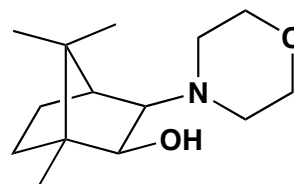
Pu, L.; Yu, H.-B. *Chem. Rev.* **2001**, *101*, 757



Ryoji Noyori in Stockholm (2001)



**DAIB**



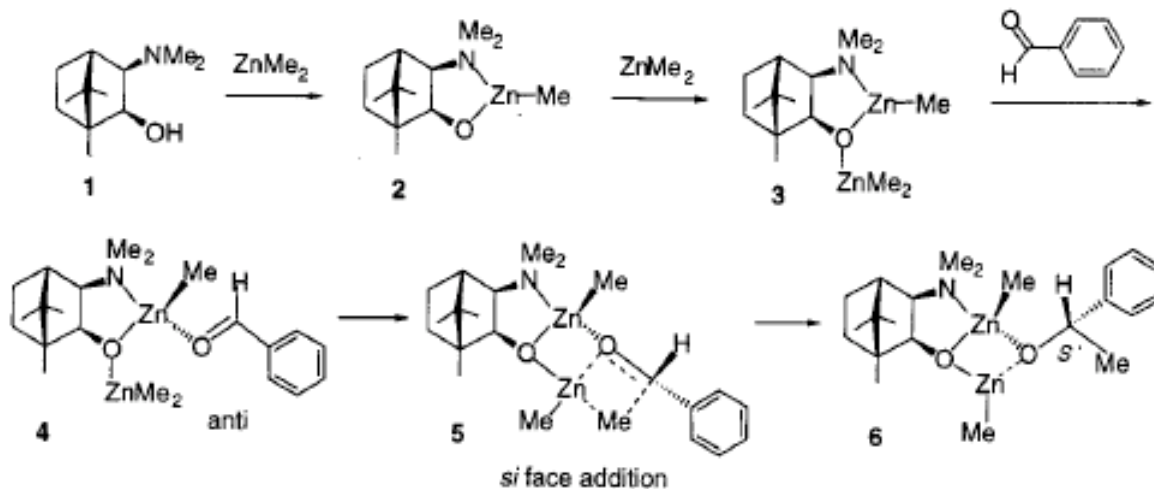
**MIB**

W. A. Nugent

*Chem. Commun.* **1999**, 1369

*Org. Synth.* **2005**, *82*, 87

### Proposed Mechanism for the Catalytic Dimethylzinc Addition to Benzaldehyde



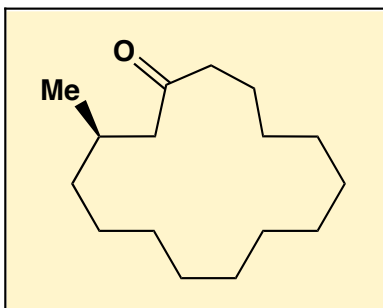
# Asymmetric Addition of Alkenylmetal Compounds to Aldehydes

## ★ Alkenylzinc Additions

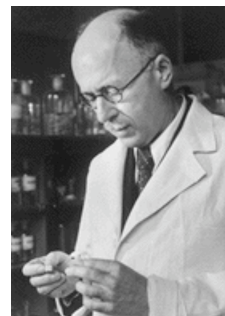
### Case Studies

#### (1) Synthesis of (*R*)-(-)-Muscone

Oppolzer, W.; Radinov, R. N. *J. Am. Chem. Soc.* **1993**, *115*, 1593



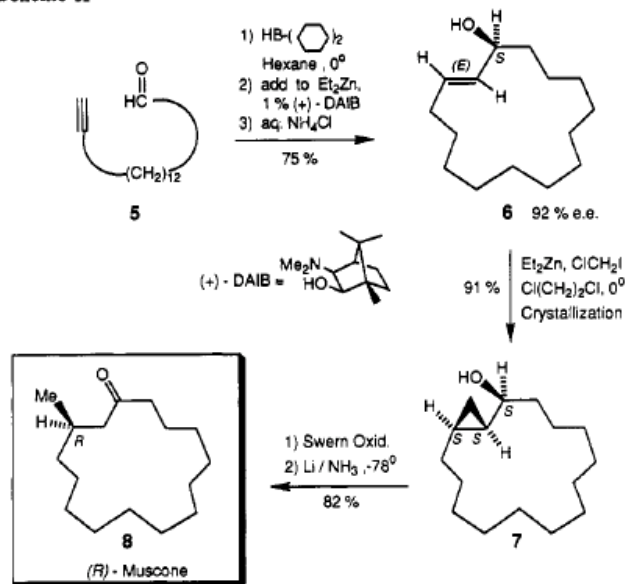
**Leopold Ruzicka**  
(1887-1976)  
Nobel Prize 1939



*Moschus moschiferus*

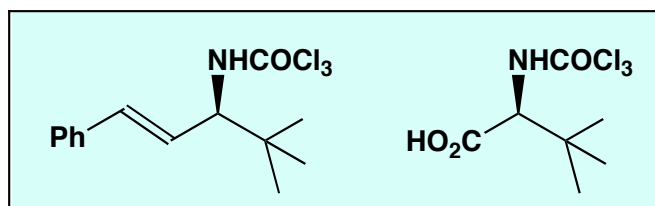
"To obtain the perfume from a musk deer, the animal is killed and the gland completely removed and dried, either in the sun, on a hot stone, or by immersion in hot oil. It appears in commerce as "musk in pod" (i.e. the glands are entire) or as "musk in grain" (in which the perfume has been extracted from its receptacle). Since obtaining natural musk requires killing the endangered animal, nearly all muscone used in perfumery today is synthetic."

**Scheme II**



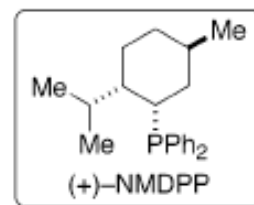
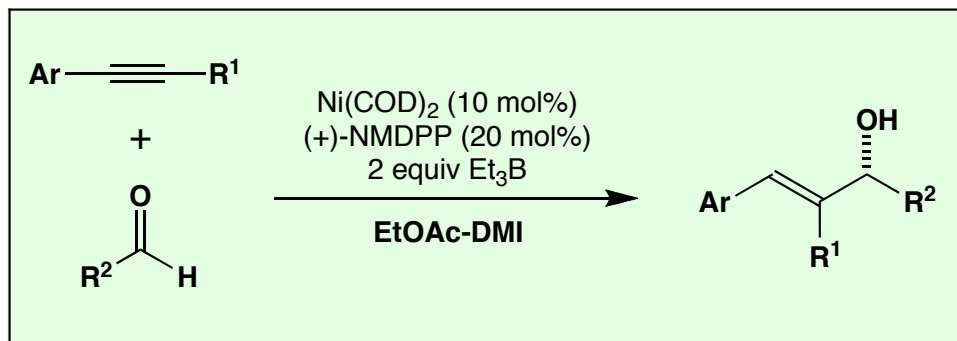
#### (2) Synthesis of Allylic Amines and Amino Acids

Chen, Y. K.; Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 12,225



### ★ Jamison Vinylation

Miller, K. M.; Huang, W.-S.; Jamison, T. F. *J. Am. Chem. Soc.* **2003**, 125, 3442



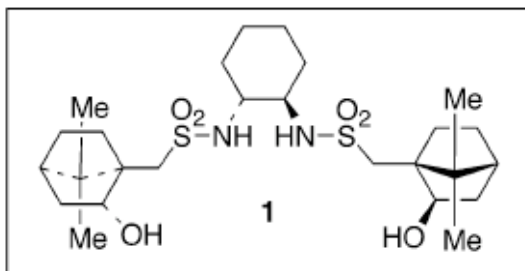
*J. D. Morrison ligand*

### ★ Asymmetric Addition of Alkenylmetal Compounds to Aldehydes

#### ★ Frontier: Asymmetric Vinylation of Ketones

P. J. Walsh *J. Am. Chem. Soc.* **2004**, 126, 6538, *J. Org. Chem.* **2005**, 70, 448,  
*J. Am. Chem. Soc.* **2005**, 127, 8355

*modified Yoshioka ligand*



#### ★ Frontier: Enantioselective NHK (Nozaki-Hiyama-Kishi) Reactions

Y. Kishi et al. *J. Am. Chem. Soc.* **2004**, 126, 12248, *Org. Lett.* **2004**, 6, 5031