

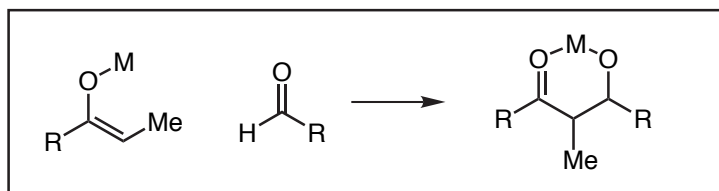
<http://www.courses.fas.harvard.edu/~chem206/>

Chemistry 206

Advanced Organic Chemistry

Lecture Number 26

### The Aldol Reaction-2



- (E) & (Z) Enolates: Felkin Selectivity
- Double Stereodifferentiating Aldol Reactions
- The Mukaiyama Aldol Reaction Variant
- Allylmetal Nucleophiles as Enolate Synthons

#### ■ Reading Assignment for this Week:

Carey & Sundberg: **Part A**; Chapter 7  
*Carbanions & Other Nucleophilic Carbon Species*

Carey & Sundberg: **Part B**; Chapter 2  
*Reactions of Carbon Nucleophiles with Carbonyl Compounds*

D. A. Evans

Monday,  
November 17, 2002

#### ■ Assigned Reading

Lithium Diisopropylamide-Mediated Lithiations of Imines: Insights into highly Structure -Dependent Rates and Selectivities. D. Colum, *JACS* **2003**, *125*, ASAP (**handout**)

W. R. Roush, *J. Org. Chem.* **1991**, *56*, 4151-4157. (**handout**)

#### ■ Other Useful References

Evans, D. A., J. V. Nelson, et al. (**1982**). "Stereoselective Aldol Condensations." *Top. Stereochem.* **13**: 1.

Heathcock, C. H. (**1984**). The Aldol Addition Reaction. *Asymmetric Synthesis. Stereodifferentiating Reactions, Part B.* J. D. Morrison. New York, AP. **3**: 111.

Oppolzer, W. (**1987**). "Camphor Derivatives as Chiral Auxiliaries in Asymmetric Synthesis." *Tetrahedron* **43**: 1969.

Heathcock, C. H. (**1991**). The Aldol Reaction: Acid and General Base Catalysis. *Comprehensive Organic Synthesis.* B. M. Trost and I. Fleming. Oxford, Pergamon Press. **2**: 133.

Heathcock, C. H. (**1991**). The Aldol Reaction: Group I and Group II Enolates. *Comprehensive Organic Synthesis.* B. M. Trost and I. Fleming. Oxford, Pergamon Press. **2**: 181.

Kim, B. M., S. F. Williams, et al. (**1991**). The Aldol Reaction: Group III Enolates. *Comprehensive Organic Synthesis.* B. M. Trost and I. Fleming. Oxford, Pergamon Press. **2**: 239.

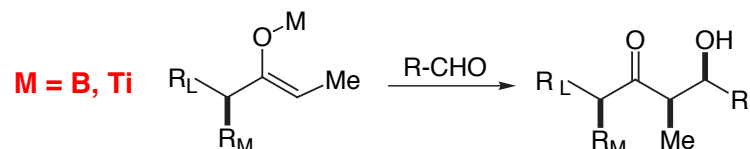
Franklin, A. S. and I. Paterson (**1994**). "Recent Developments in Asymmetric Aldol Methodology." *Contemporary Organic Synthesis* **1**: 317-338.

Cowden, C. J. and I. Paterson (**1997**). "Asymmetric aldol reactions using boron enolates." *Org. React. (N.Y.)* **51**: 1-200.

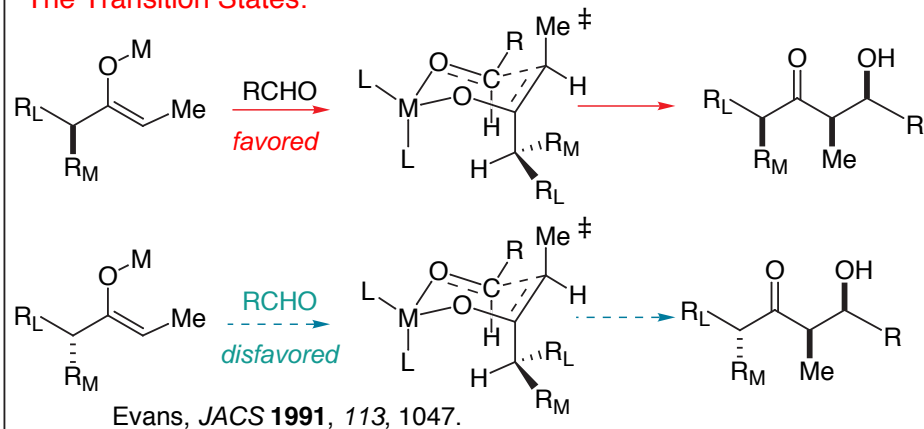
Nelson, S. G. (**1998**). "Catalyzed enantioselective aldol additions of latent enolate equivalents." *Tetrahedron: Asymmetry* **9**(3): 357-389.

Mahrwald, R. (**1999**). "Diastereoselection in Lewis-acid-mediated aldol additions." *Chem. Rev.* **99**(5): 1095-1120.

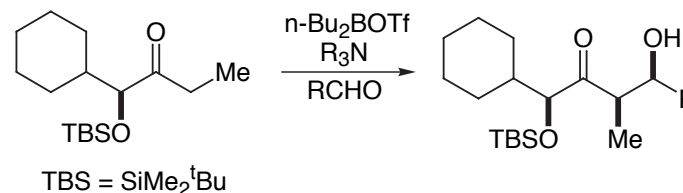
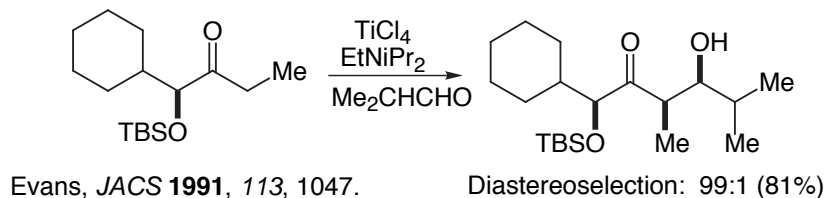
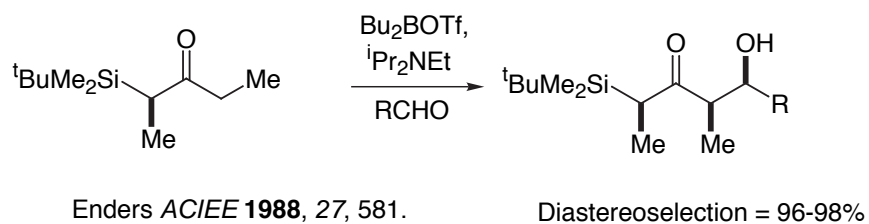
## General Reaction for Syn Aldols: M = B, Ti



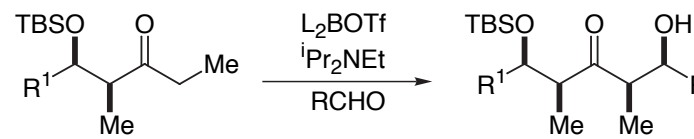
## The Transition States:



## Examples:

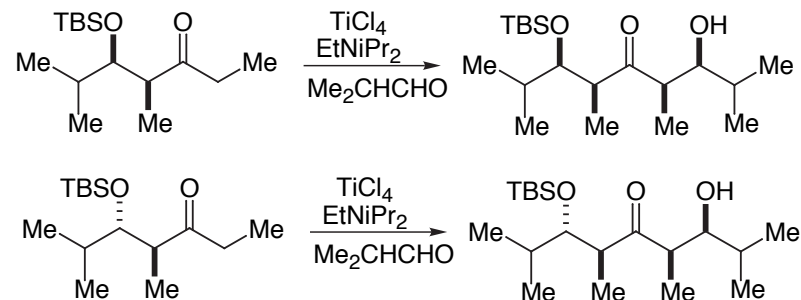


R	Diastereoselection
Ph	97:3
Et	98:2
BnOCH <sub>2</sub> CH <sub>2</sub>	96:4
Me <sub>2</sub> CH	>99:<1

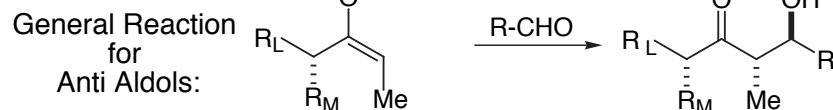
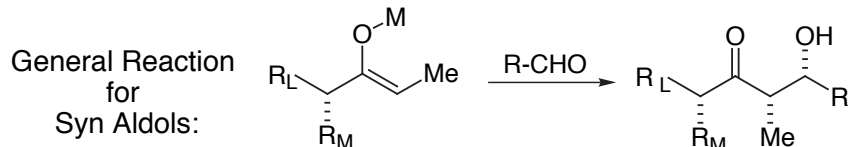
Masamune, *JACS* **1981**, 103, 1566.

L	Diastereoselection
Bu	63:37 - 84:16
9-BBN	83:17 - 85:15
(-)-Ipc	72:28
(+)-Ipc	91:9 - 94:6

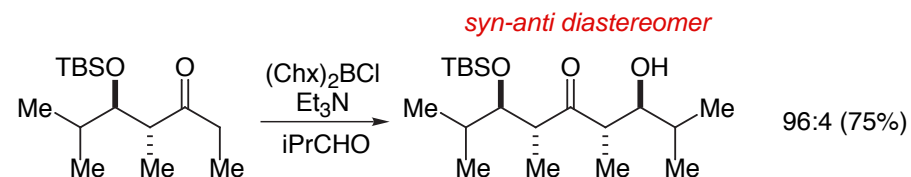
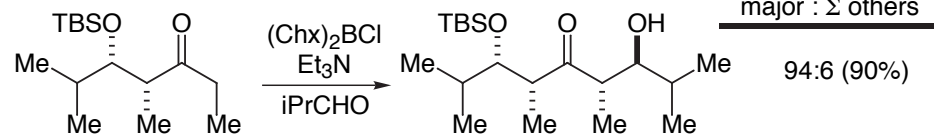
This system does not give a completely clean (Z) enolate

Paterson, McClure, *Tet.Lett.* **1987**, 28, 1229.Evans, *JACS* **1991**, 113, 1047.

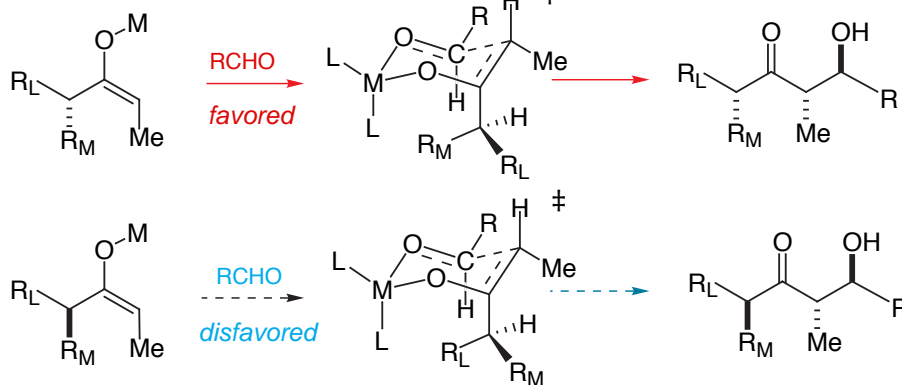
Diastereoselection: 95:5 (80-90%)



## Examples:

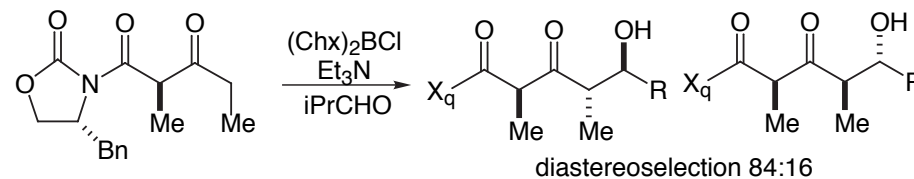
*syn-anti diastereomer*

## The Transition States:

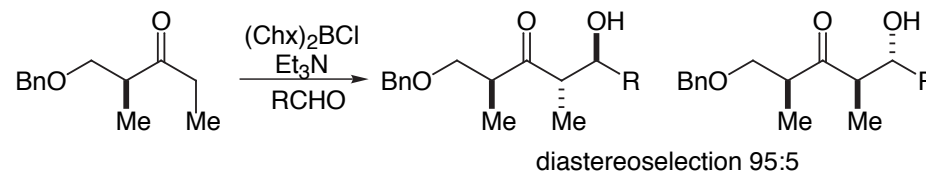


Evans, JACS 1991, 113, 1047.

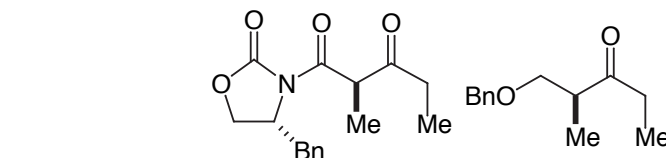
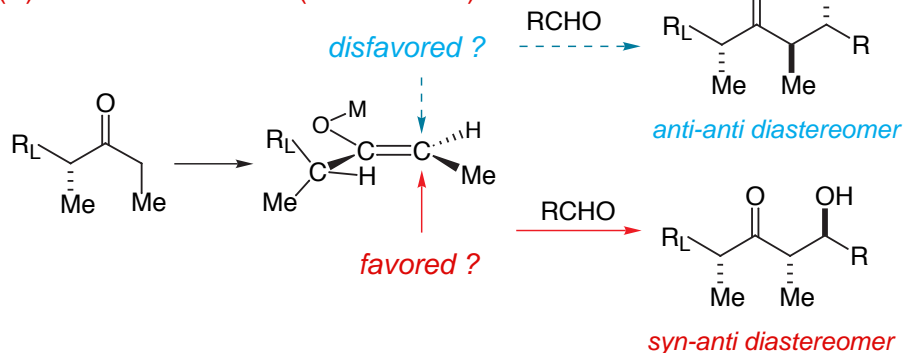
## However, the preceding precedent does not extend to these systems:

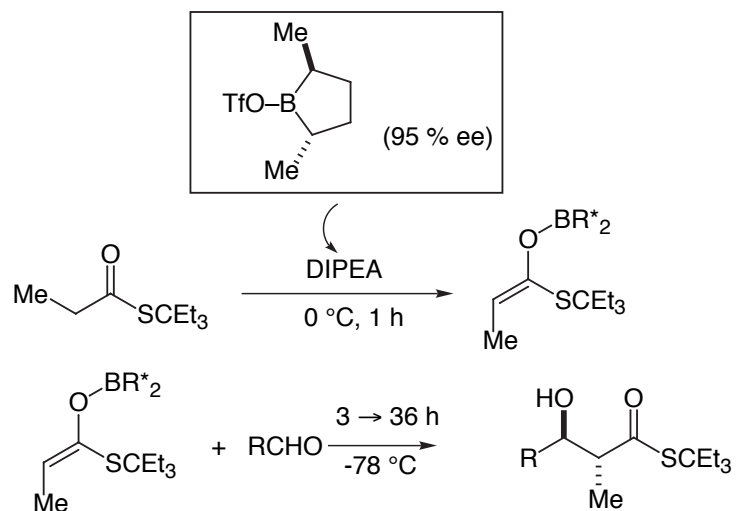
D. A. Evans, H. P. Ng, J. S. Clark, D. L. Rieger *Tetrahedron*, 1992, 48, 2127-2

## An analogous case:

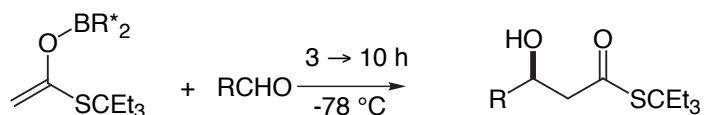
I. Patterson, J. M. Goodman, M. Isaka *Tetrahedron Lett.* 1989, 30, 7121-7

## (E) Enolate Facial Bias (Steric Model)

These enolates do not comply with steric analysis:  $\rightarrow$  electronic effects?*Tetrahedron*, 1992, 48, 2127-2142.

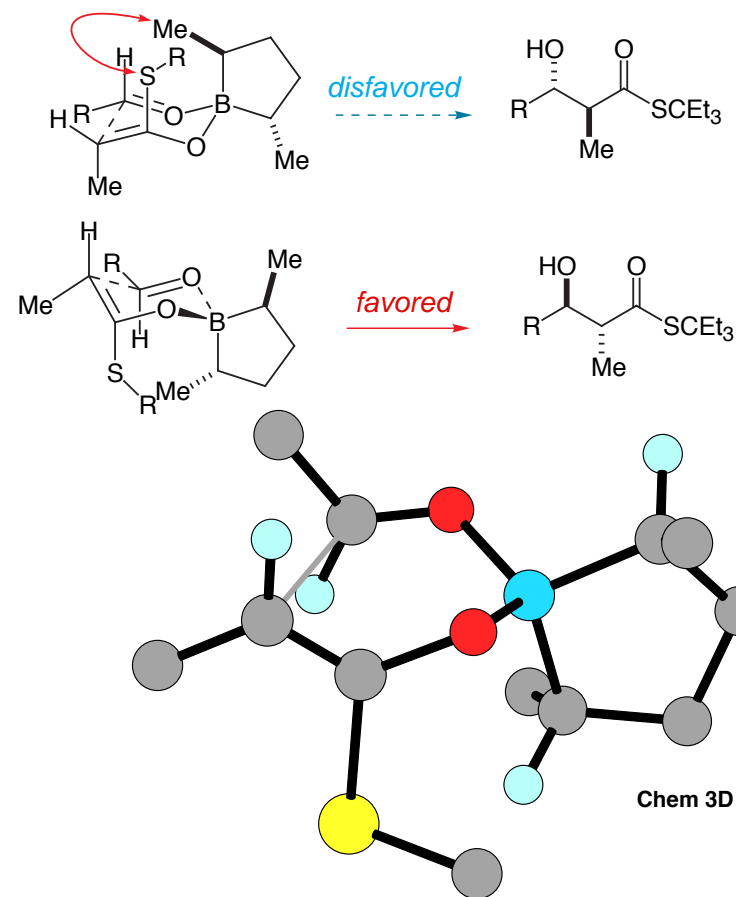
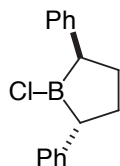
Masamune, Sato, Kim, Wollmann *J. Am. Chem. Soc.* **1986**, *108*, 8279-8281.

RCHO	Yield, %	anti/syn	ee % (corrected)
n-PrCHO	91	33:1	93 (98)
i-PrCHO	85	30:1	95 (99)
t-BuCHO	95	30:1	96 (99.9)
c-C <sub>6</sub> H <sub>11</sub> CHO	82	32:1	93 (98)
PhCHO	(71)	33:1	96 (99.8)

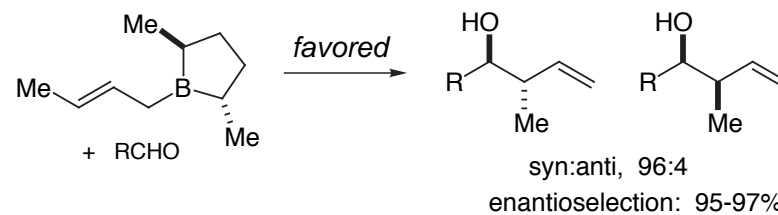


RCHO	Yield, %	ee % (corrected)
n-PrCHO	82	87 (91)
i-PrCHO	81	87 (92)
t-BuCHO	71	94 (98)
c-C <sub>6</sub> H <sub>11</sub> CHO	95	86 (90)
PhCHO	78	88 (92)

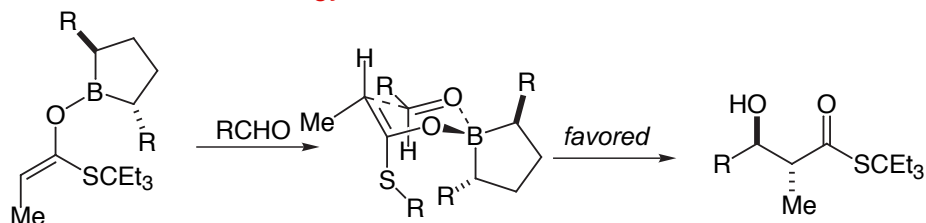
See analogous study by Reetz

Reetz *Tetrahedron Lett.* **1986**, 4721

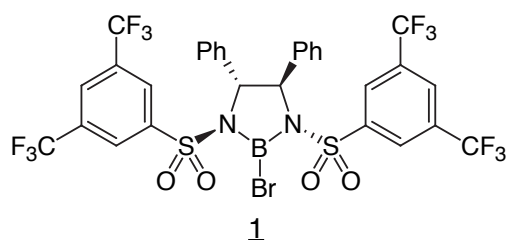
## Analogous Carbonyl Allylation

Masamune, Sato, Kim, Wollmann *J. Org. Chem.* **1987**, *52*, 4831

## Masamune-Reetz Analogy:



## ■ Metal-Based Chiral Auxilliary:



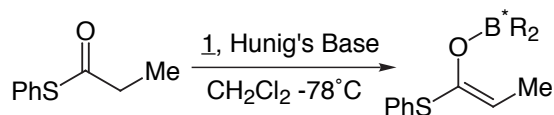
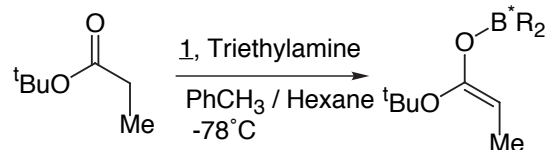
## References:

(Corey) *JACS*. **1989**, *111*, 5494  
 (Corey) *JACS*. **1990**, *112*, 4977  
 (Corey) *TL*. **1991**, *32*, 2857  
 (Corey) *TL*. **1993**, *34*, 1737.

Does this reagent perform in accord with the Masamune-Reetz analogy?  
 Note: The sulfonamide nitrogens are pseudo-tetrahedral

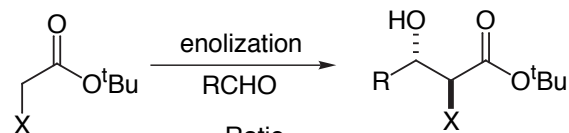
## ■ Enolization:

Either enolate geometry possible with proper choice of base, solvent, and substrate.



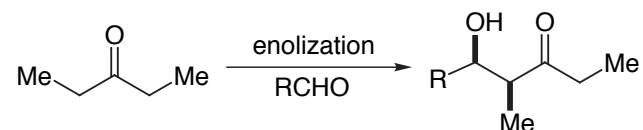
A mechanistic proposal for enolization control is presented in paper

(Corey) *JACS*. **1989**, *111*, 5494

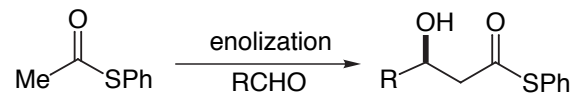
■ Chiral Anti Aldol Reaction: *JACS* **1990**, *112*, 4977; *TL* **1991**, *32*, 2857.

(R)	(X)	Ratio syn:anti	% ee	Yield
Ph-	Me	2 : 98	94	93 %
chex-	Me	6 : 94	75	82 %

(R)	(X)	Ratio syn:anti	% ee	Yield
Ph-	Br	2 : 98	96	86 %
chex-	Br	2 : 98	91	65 %

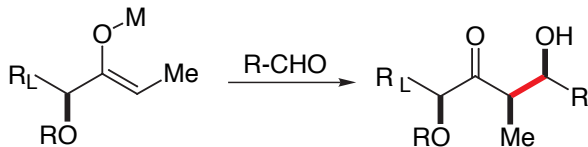
■ Chiral Syn Aldol Reaction *JACS* **1989**, *111*, 5494.

(R)	Ratio syn:anti	% ee	Yield
Ph-	94 : 6	97	86 %
Me <sub>2</sub> CH-	98 : 2	95	91 %
MeCH <sub>2</sub> -	>98 : 2	>98	68 %

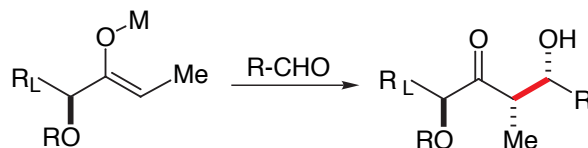
■ Chiral Acetate Aldol Reaction *JACS* **1989**, *111*, 5494.

(R)	% ee	Yield
Ph-	91	84 %
Me <sub>2</sub> CH-	83	82 %

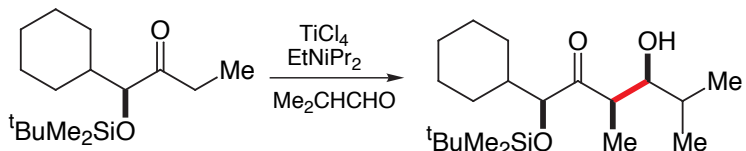
## Reference Rxn



## Chelate-Organized Variant

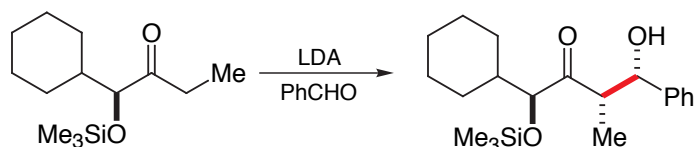


## Nonchelate Reaction

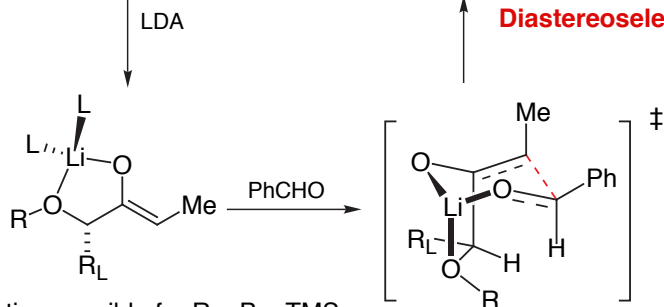


Masamune, *JACS* **1981**, 103, 1566 (boron enolate)  
Evans, *JACS* **1991**, 113, 1047 (titanium enolate)

Diastereoselection: 99:1



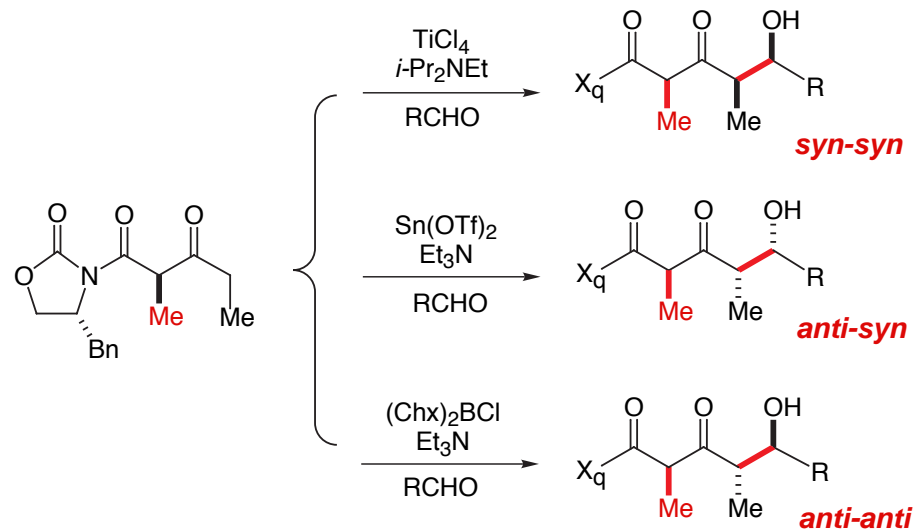
Diastereoselection: 90:10



Chelation possible for R = Bn, TMS  
but marginal for TBS

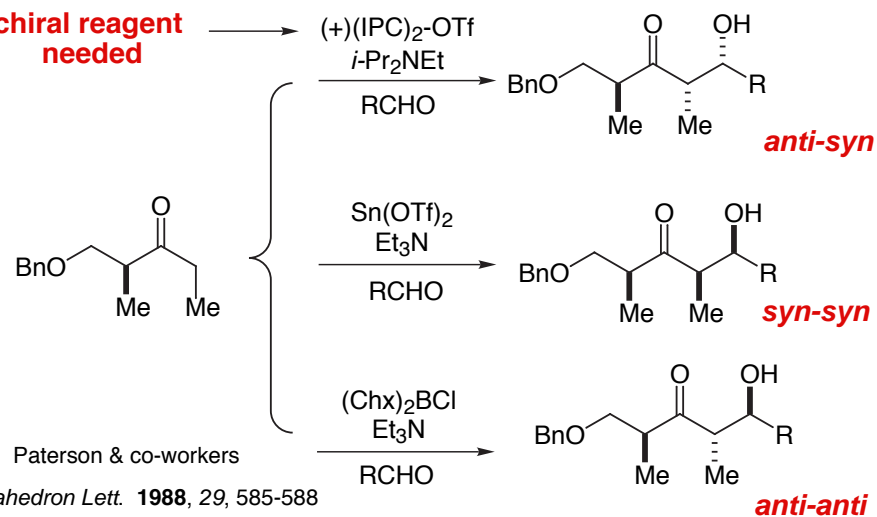
Thorton, *Tet. Let.* **1990**, 31, 6001

## Complimentary aldol reactions may be obtained by changing metal as well as enolate geometry



*JACS*, **1990**, 112, 866; *Tetrahedron*, **1992**, 48, 2127-2142.

## chiral reagent needed

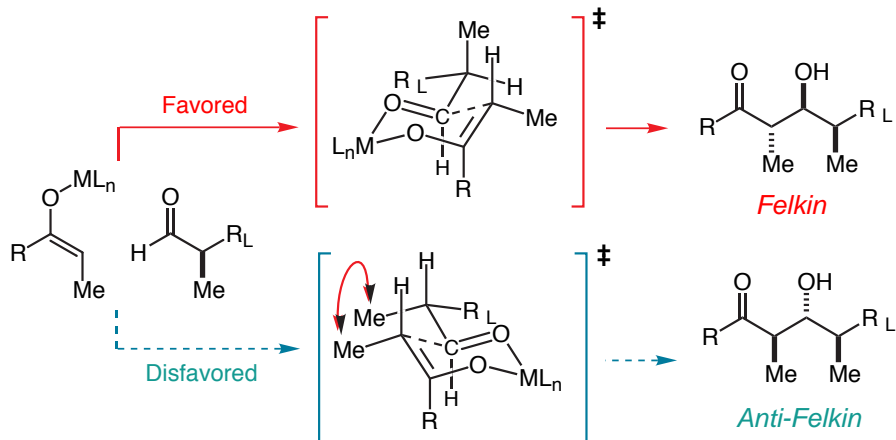


Paterson & co-workers

*Tetrahedron Lett.* **1988**, 29, 585-588

*Tetrahedron Lett.* **1989**, 30, 7121-7124

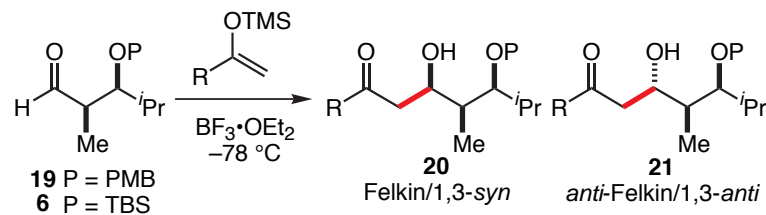
*Tetrahedron Lett.* **1992**, 33, 4233-4236

**(E) Enolates Exhibit Felkin Aldehyde Diastereoface Selection**

■ The illustrated syn-pentane interaction disfavors the anti-Felkin pathway.

Evans, Nelson, Taber, *Topics in Stereochemistry* **1982**, 13, 1-115.

W. R. Roush, *J. Org. Chem.* **1991**, 56, 4151-4157.

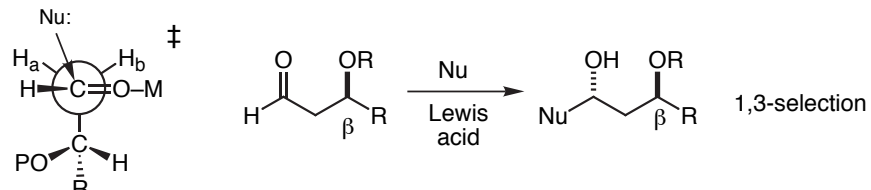
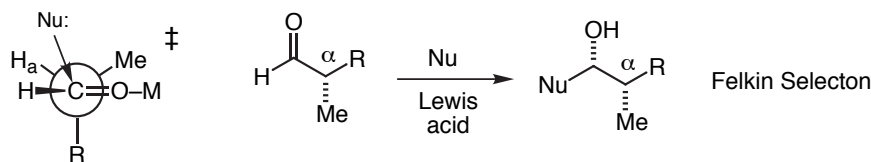
**The Non-Reinforcing syn-RCHO is the most Interesting  
Dependence of the Selectivity of Felkin-controlled Reactions on Nu Size**

	P = PMB	P = TBS
R	<b>20 : 21</b>	<b>20 : 21</b>
t-Bu	96 : 04	94 : 06
i-Pr	56 : 44	75 : 25
Me	17 : 83	40 : 60

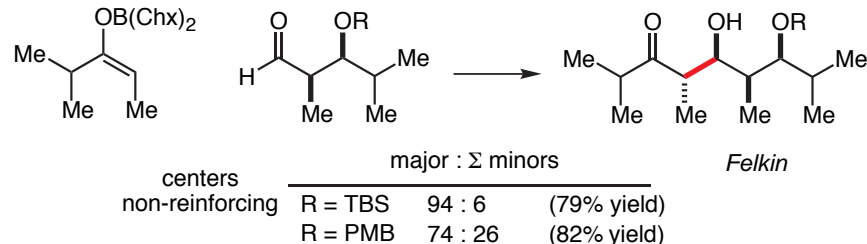
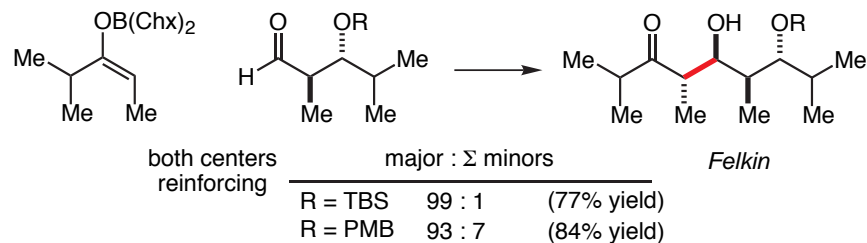
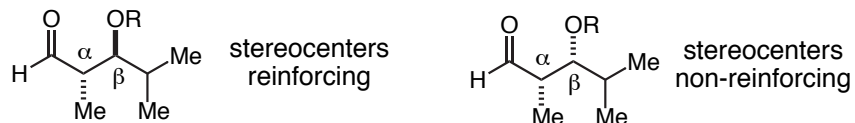
**$\alpha$ -substituent dominates for Large Nu**  
 **$\beta$ -substituent dominates for small Nu**

**Background Information: The influence of  $\beta$ -OR substituents on RCHO**

Evans, *JACS* **1996**, 118, 4322-4343

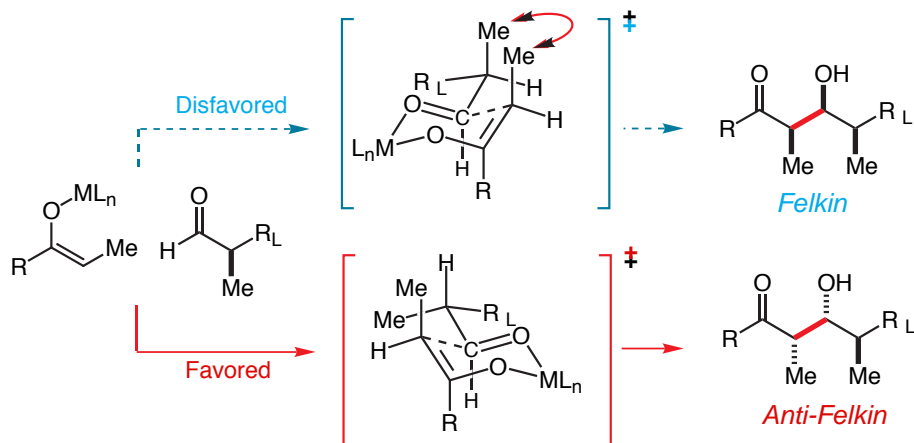


Therefore, one might conclude that:



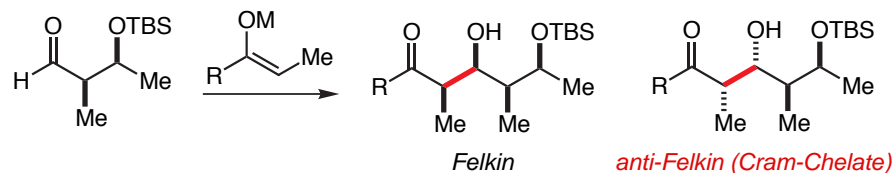
Achiral (E) enolates preferentially add to the Felkin diastereoface  
High anti:syn diastereoselectivity ( $\geq 97 : 3$ ) is observed in all cases

Evans et al. *JACS* **1995**, 117, 9073

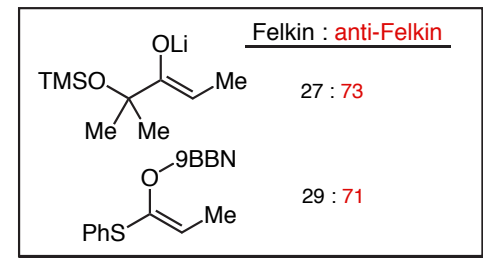
**(Z) Enolates Exhibit Anti-Felkin Aldehyde Diastereoface Selection**

The illustrated syn-pentane interaction disfavors the Felkin pathway.

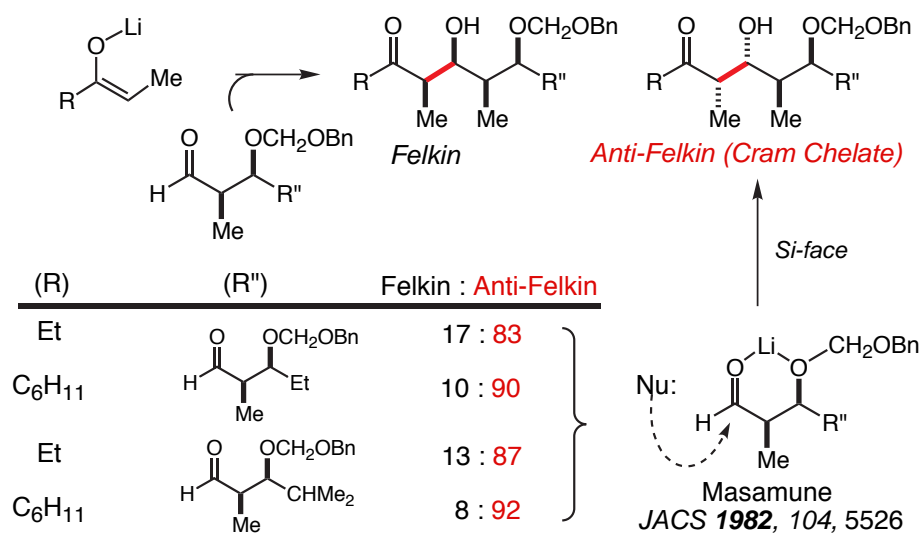
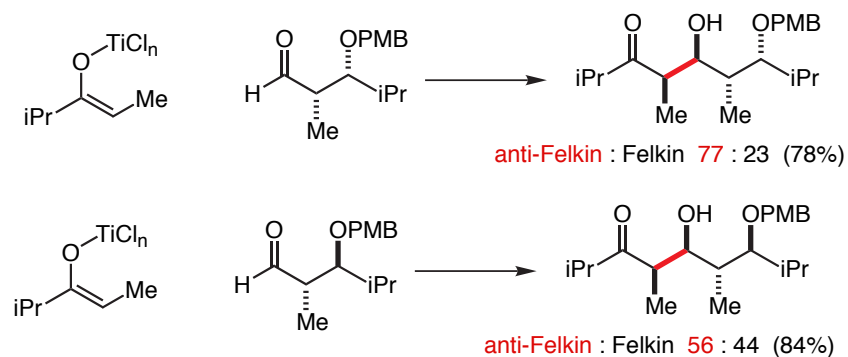
Evans, Nelson, Taber, *Topics in Stereochemistry* **1982**, 13, 1-115.  
W. R. Roush, *J. Org. Chem.* **1991**, 56, 4151-4157.



D. W. Brooks & Co-workers  
*Tetrahedron Lett.* **1982**, 23, 4991-4994.



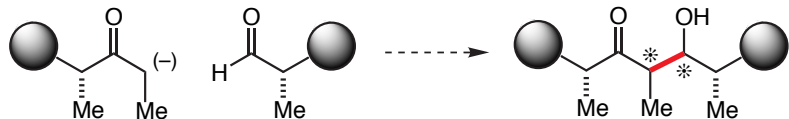
- The bulky OTBS group disfavors chelation. (see Keck, *JACS* **1986**, 108, 3847.)
- The boron and lithium enolates display nearly equal levels of anti-Felkin selectivity.

**An Early study rationalized results through chelated transition states:****Titanium enolates exhibit the same trend**

Evans et al. *JACS* **1995**, 117, 9073



### Double Stereodifferentiating Aldol Bond Constructions



#### Stereochemical Control Elements

Enolate geometry

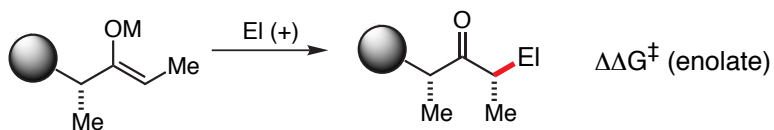
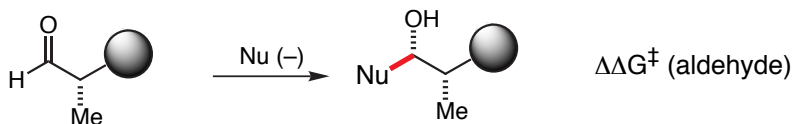


Product

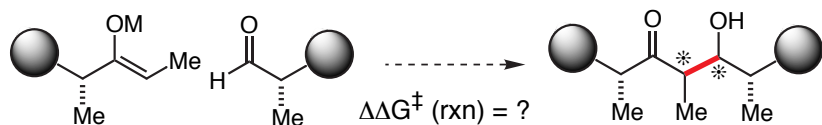
Enolate facial bias  $\rightleftharpoons$  Stereochemistry  $\leftleftharpoons$  Aldehyde facial bias

**The Issue:** Can one reliably take the diastereoselectivities of the individual reaction partners and use this information in the illustrated extrapolation:

#### The model reactions:



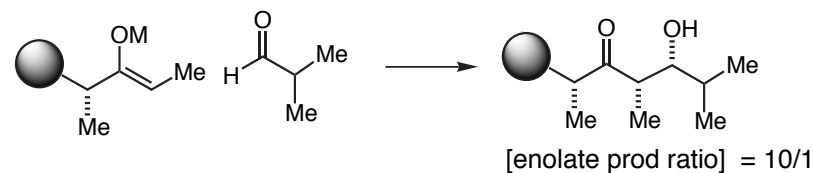
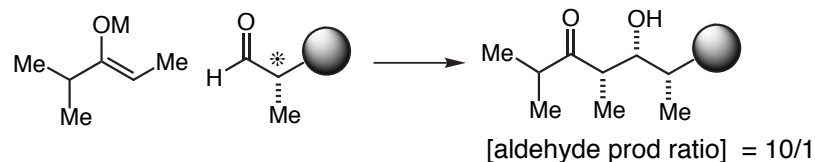
#### The extrapolation:



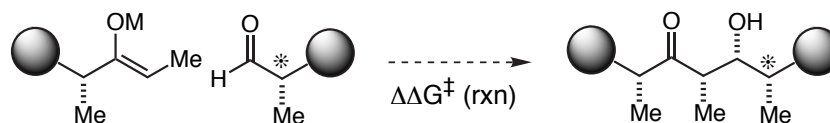
Masamune, *Angew. Chem. Int. Ed.* **1985**, 24, 1-76

### Matched reactant pair: Stereo-induction from both partners reinforcing

#### The reference reactions:



#### ■ The double stereodifferentiating situation: Stereoselectivity?



#### ■ The assumption: (Masamune, Heathcock)

It is presumed that useful information can be obtained from related achiral enolate & RCHO addition reactions and that the free energy contributions will be additive:

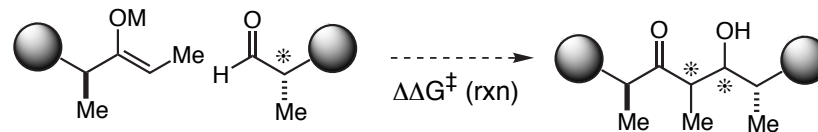
$$\Delta\Delta G^\ddagger (\text{Rxn}) \sim \Delta\Delta G^\ddagger (\text{enolate}) + \Delta\Delta G^\ddagger (\text{RCHO})$$

$$\log [\text{Product ratio}] \sim \log [\text{enolate ratio}] + \log [\text{aldehyde ratio}]$$

$$[\text{Product ratio}] \sim [\text{enolate prod ratio}] \times [\text{aldehyde prod ratio}]$$

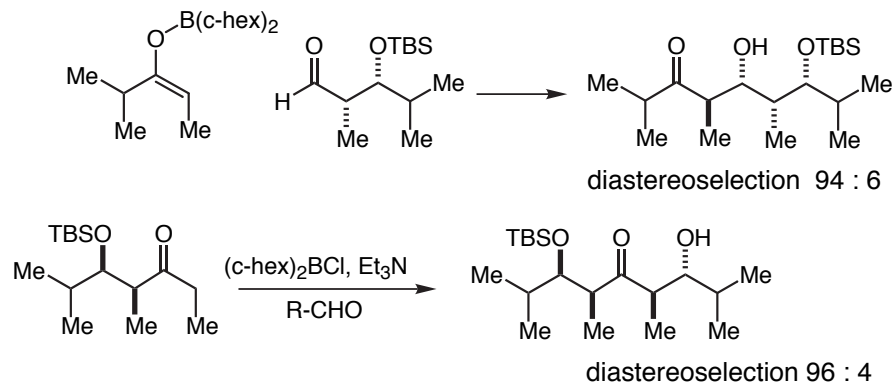
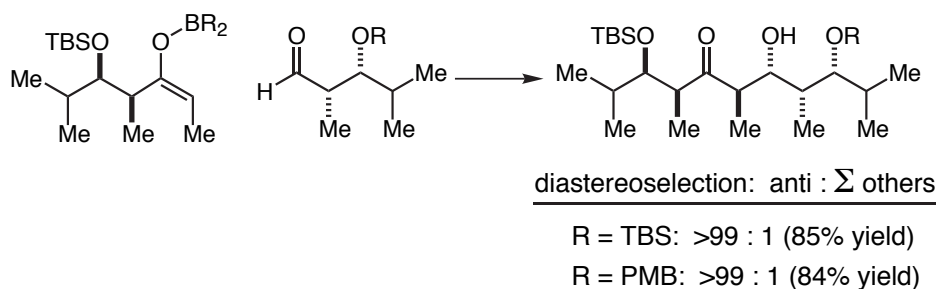
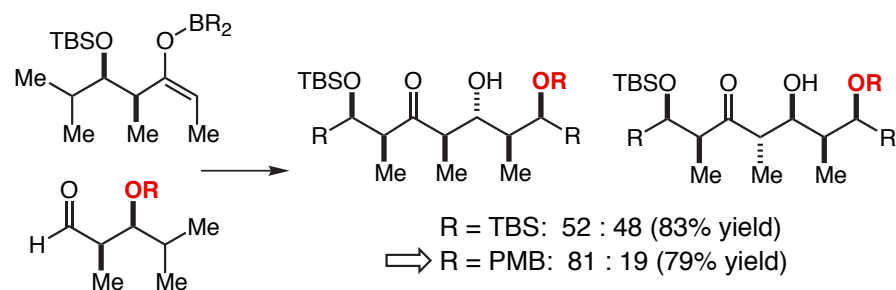
#### ■ Hence, for the case at hand: [Product ratio] $\sim$ [10] $\times$ [10] $\sim$ 100

### Mismatched reactant pair: Stereo-induction from partners nonreinforcing

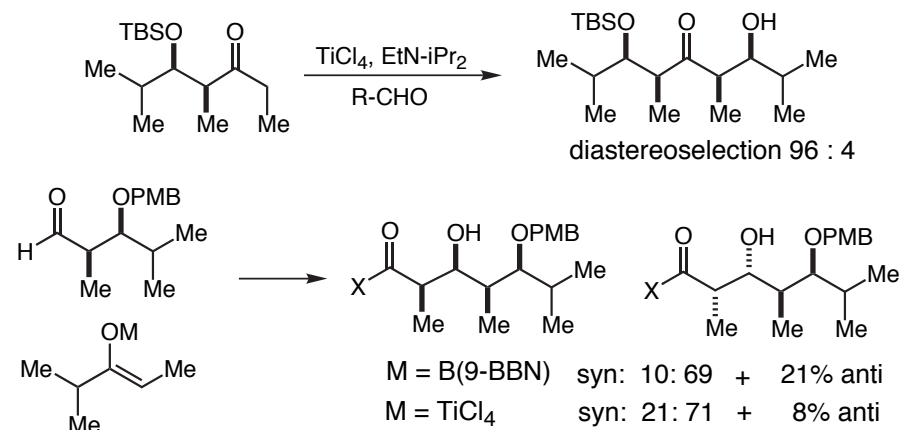
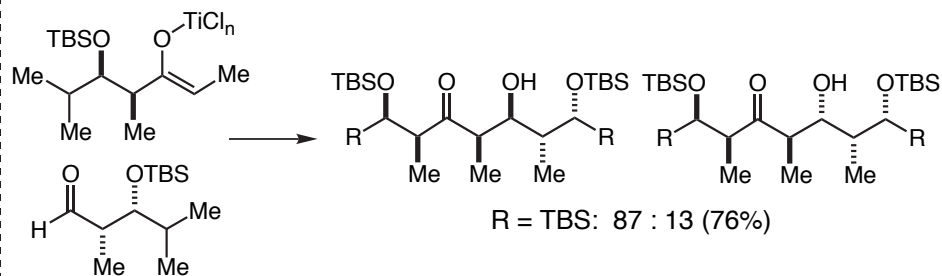
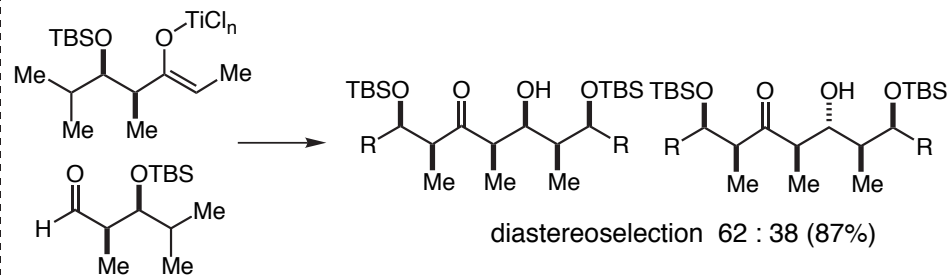


$$\Delta\Delta G^\ddagger (\text{Rxn}) \sim \Delta\Delta G^\ddagger (\text{enolate}) - \Delta\Delta G^\ddagger (\text{RCHO})$$

## The Masamune-Heathcock generalizations hold to a point:

**(E)-Boron Enolates: The reference reactions****(E)-Boron Enolates: The matched cases****(E)-Boron Enolates: The mismatched cases**

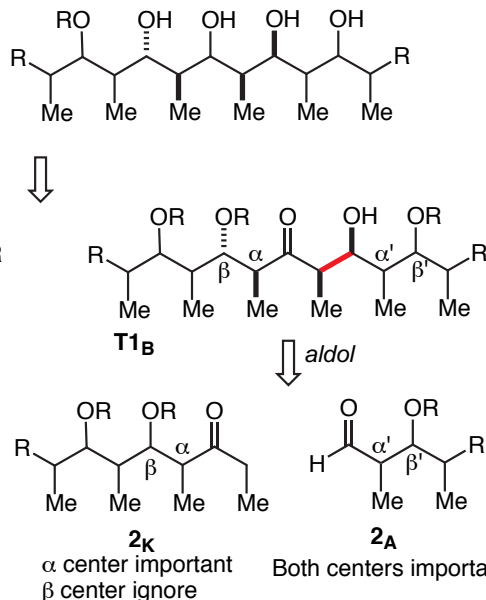
**$\beta$ -center on RCHO can play a significant role in this marginal situation**

**(Z)-Titanium Enolates: The reference reactions****(Z)-Titanium Enolates: The matched cases****(Z)-Titanium Enolates: The mismatched cases**

"Double Stereodifferentiating Aldol Reactions. The Documentation of "Partially Matched" Aldol Bond Constructions". Evans, D. A.; Dart, M. J.; Duffy, J. L.; Rieger, D. L. *JACS* **1995**, *117*, 9073-9074.

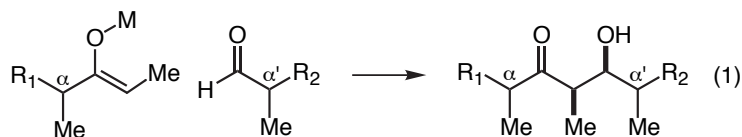
### Synthesis of Polyketide chains

Given a polypropionate chain of alternating Me & OH substituents, select a disconnection point sectioning the fragments into subunits of comparable complexity by adding C=O as illustrated.



Focusing on the =O FG, there are 2 1st-order aldol disconnections highlighted. Let's proceed forward with **T1B**. Carry out the disconnection to subunits **2K** and **2A**.

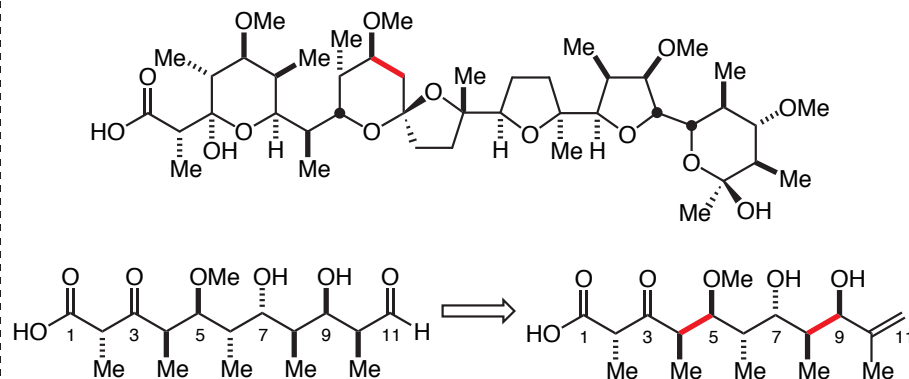
For substituted enolate and enolsilane-based processes, there are at least three identifiable **stereochemical determinants** that influence reaction diastereoselectivity (eq 1). Two of these determinants are associated with the local chirality of the individual reaction partners. For example, enolate (enolsilane) chirality influences the absolute stereochemistry of the forming methyl-bearing stereocenter, and in a similar fashion, aldehyde chirality controls the absolute stereochemical outcome of the incipient hydroxyl-bearing stereocenter. The third determinant, the pericyclic transition state, imposes a relative stereochemical relationship between the developing stereocenters. This important control element is present in the aldol reactions of metal enolates ( $M = BR_2, TiX_3, Li$ , etc.), but is absent in the Lewis acid catalyzed (Mukaiyama) enolsilanes aldol variants that proceed via open transition states.



Stereochemical Determinants	M = SiR <sub>3</sub>	
	M = BR <sub>2</sub>	M = SiR <sub>3</sub>
enolate facial bias	✓	✓
aldehyde facial bias	✓	✓
pericyclic transition state	✓	✗

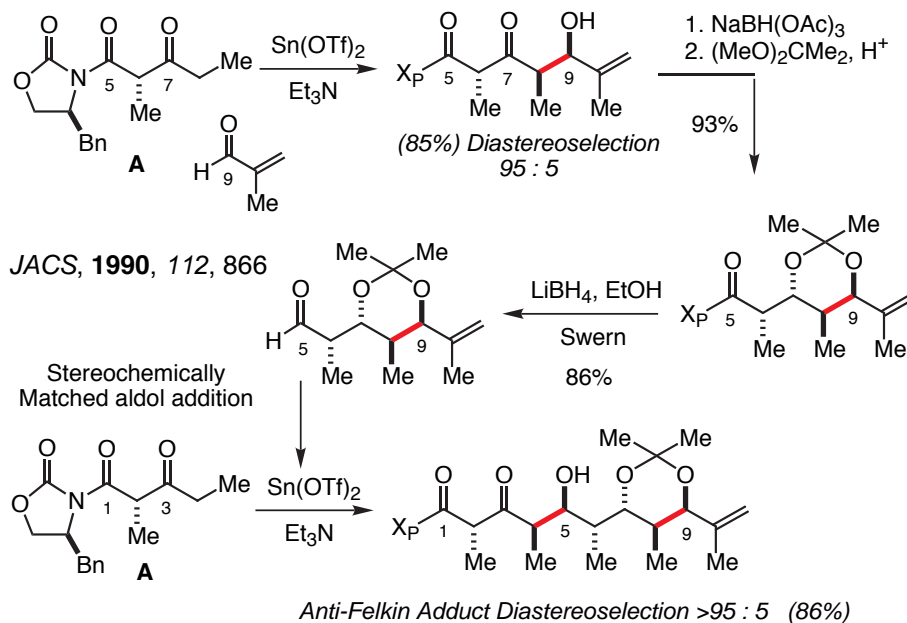
### The Lonomycin Synthesis: An example of polypropionate assemblage

Evans, Ratz, Huff, Sheppard JACS **1995**, 117, 3448

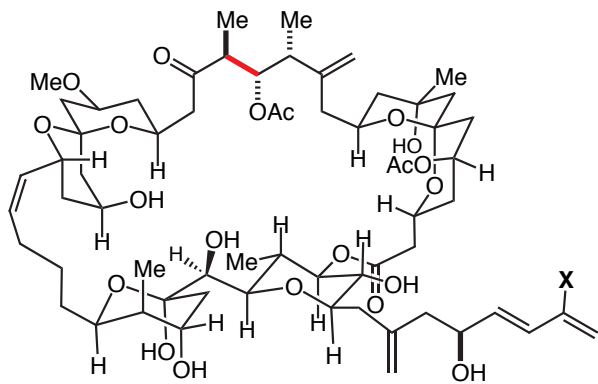


BH<sub>3</sub> Transform: See Lecture No. 8

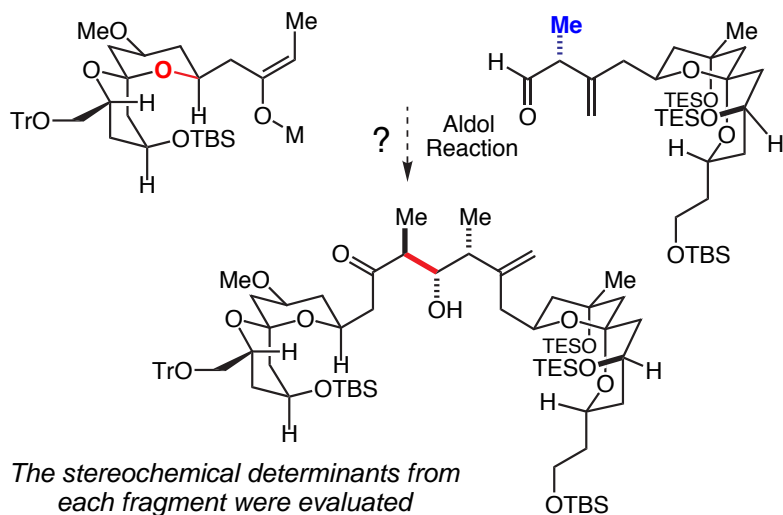
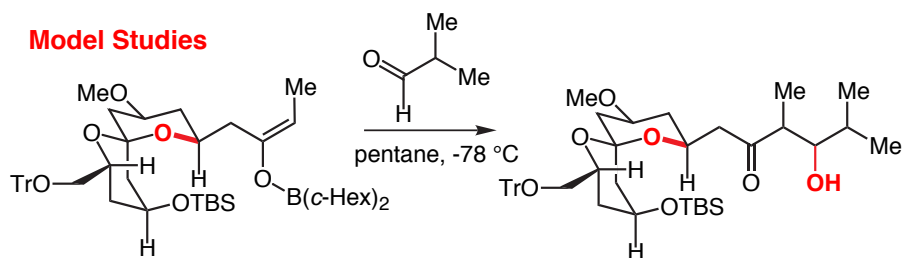
### C<sub>1</sub>-C<sub>11</sub> Assemblage



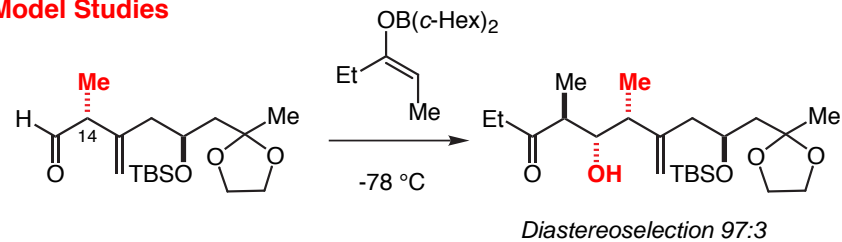
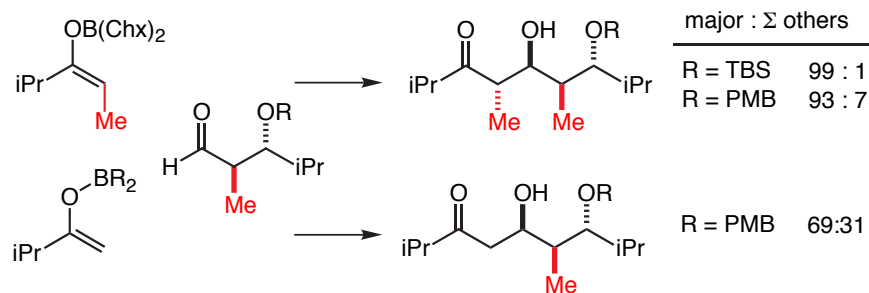
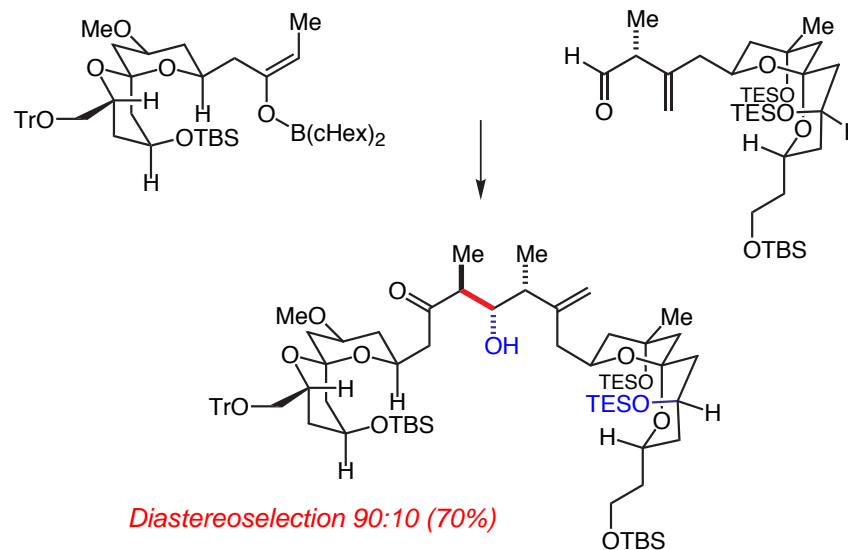
The Sn(OTf)<sub>2</sub> aldol reaction of A: see this lecture + JACS, **1990**, 112, 866

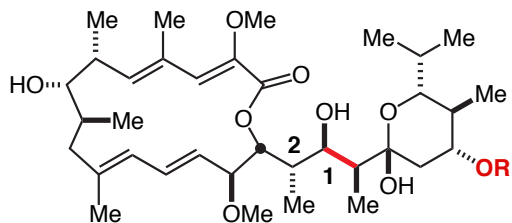
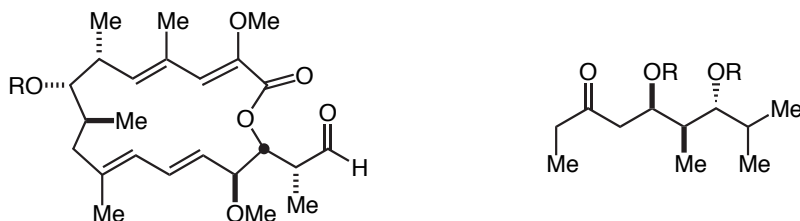
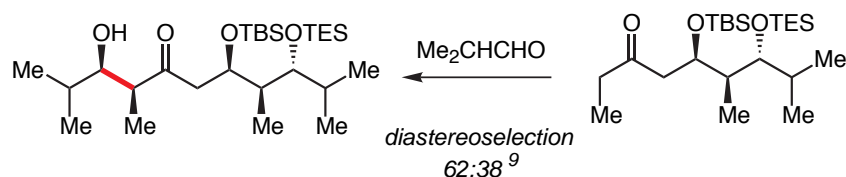
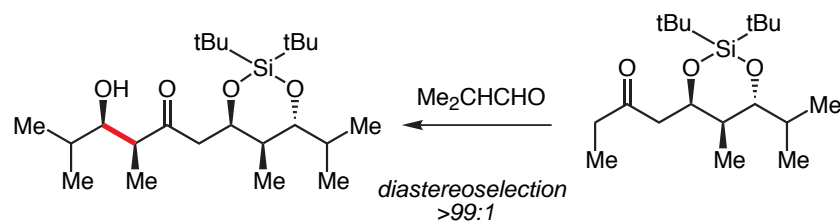
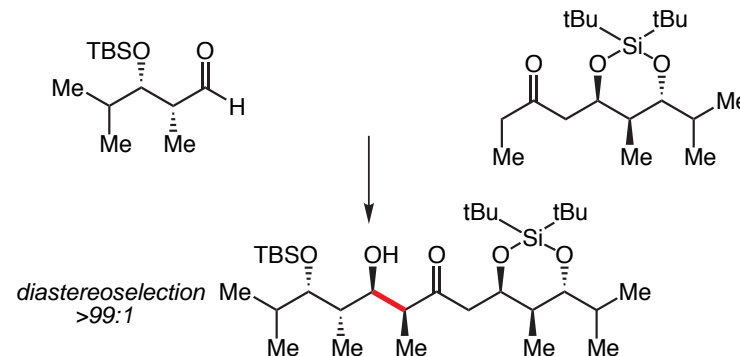
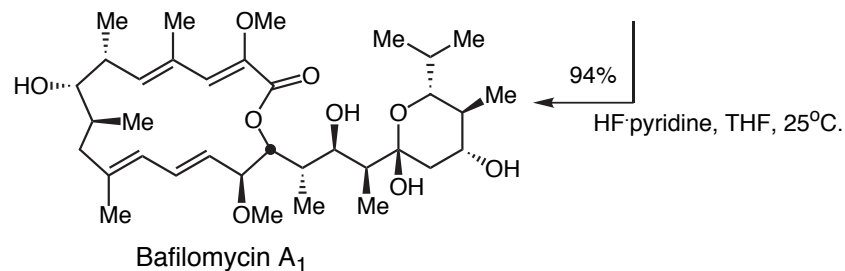
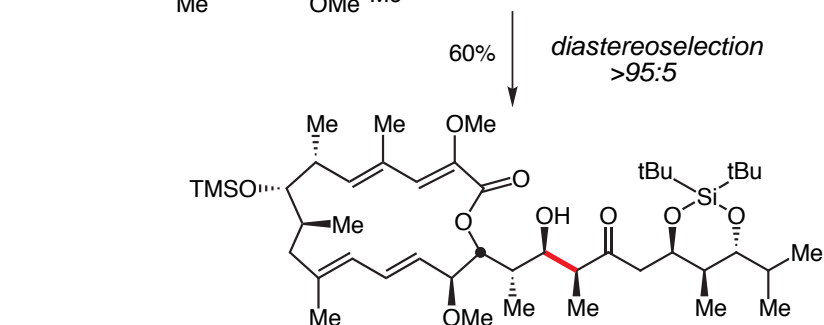
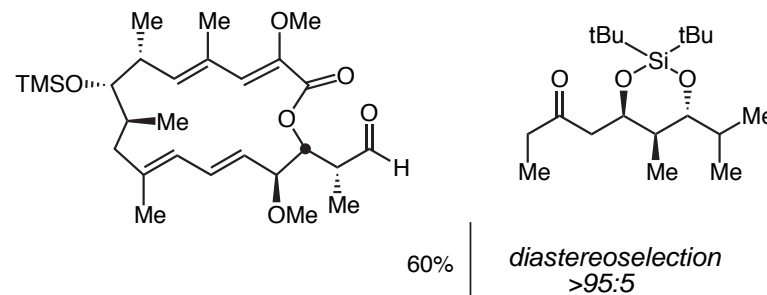
**The Althoirtin Synthesis: An example of polypropionate assemblage**

Evans, Trotter, Coleman, Côté, Dias, Rajapakse, *Tetrahedron* **1999**, *55*, 8671-8726.

**Model Studies**

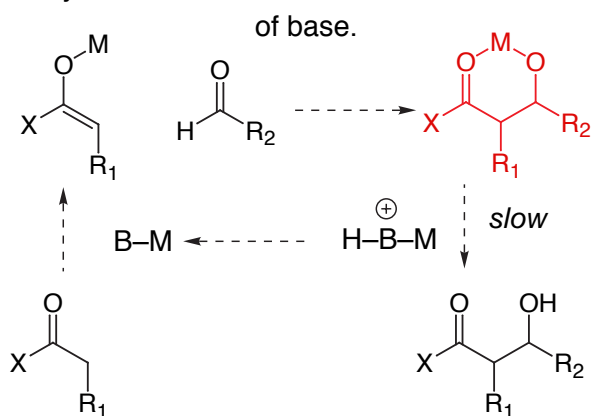
2:1 mixture of diastereomers

**Model Studies****Background****The Aldol Fragment Coupling**

**Bafilomycin A<sub>1</sub> Synthesis: An example of polypropionate assemblage**Evans, Calter, *Tetrahedron Lett.* **1993**, 34, 6871Bafilomycin A<sub>1</sub>**Critical Aldol Disconnection****Required:** Syn aldol addition**Aldehyde Fragment:** Target contains syn aldol retron with anti-Felkin relationship at 1 & 2**Enolate Fragment:** Can the needed enolate facial bias be built into the reaction??**Aldol Model Studies** Enolization Conditions: PhBCl<sub>2</sub>, *i*-Pr<sub>2</sub>NEt, CH<sub>2</sub>Cl<sub>2</sub>, -78°C.**The Critical Observation**Enolization Conditions: PhBCl<sub>2</sub>, *i*-Pr<sub>2</sub>NEt, CH<sub>2</sub>Cl<sub>2</sub>, -78°C.**Critical Aldol Disconnection**

**Type I Aldol Reaction: Metal Aldol Process**

This reaction may be run with either a stoichiometric or catalytic amount

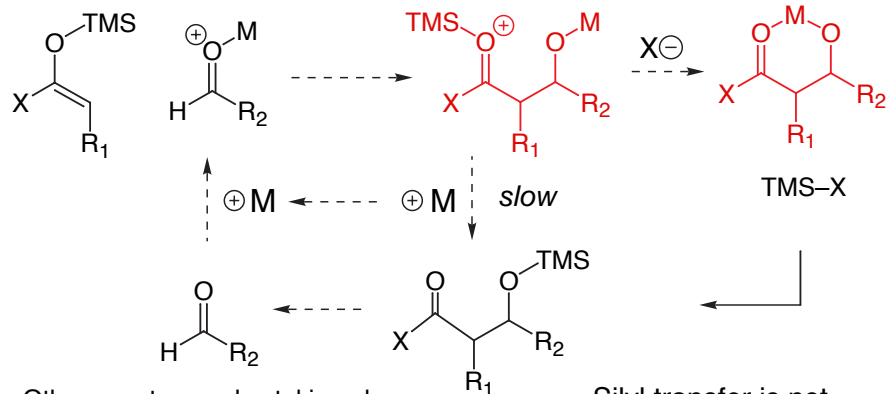


**Catalytic Version:** Slow step in the catalytic variant is protonation of the intermediate metal aldolate

**Type II Aldol Reaction: Mukaiyama Aldol Process**

This reaction may be run with either a stoichiometric or catalytic amount of Lewis acid.

The minimalist mechanism:  $MX = \text{Lewis acid}$



Other events are also taking place:  
Carreira *Tet. Lett* **1994**, 35, 4323

Silyl transfer is not necessarily intramolecular

**Recent Reviews**

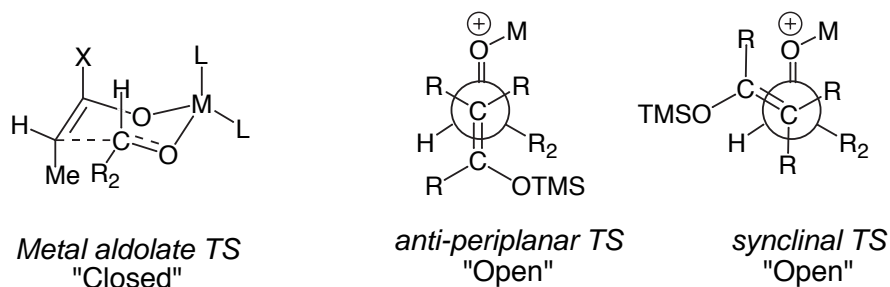
R. Mahrwald, *Diatereoselection in Lewis Acid Mediated Aldol Additions*, *Chem. Rev.* **1999**, 99, 1095-1120

S. G. Nelson, *Catalyzed enantioselective aldol additions of latent enolate equivalents* *Tetrahedron: Asymmetry* **1998**, 9, 357-389.

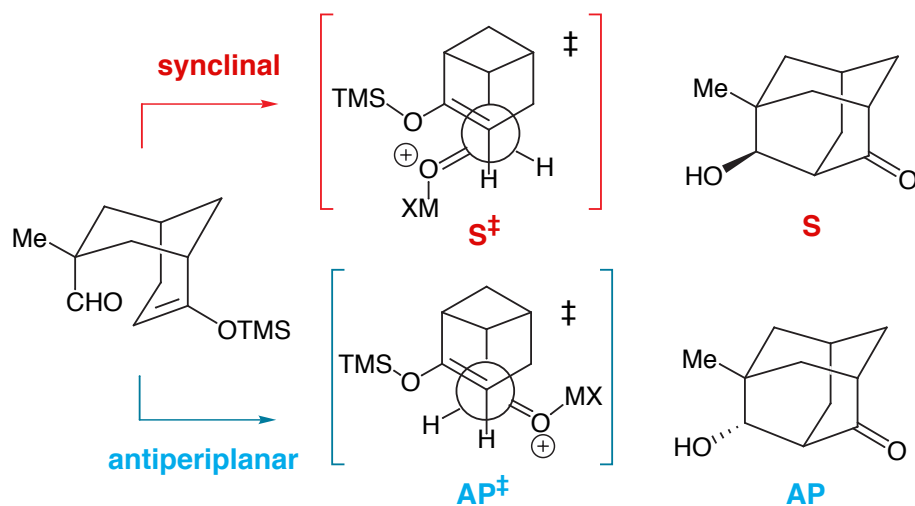
*Mukaiyama Aldol Reaction*, E. Carreira In *Comprehensive Asymmetric Catalysis*, Jacobsen, E. N.; Pfaltz, A.; and Yamamoto, H. Editors; Springer Verlag: Heidelberg, **1999**; Vol III, 998-1059.

**Reaction Mechanism: "Closed" versus "Open" Transition States**

The Mukaiyama aldol reaction proceeds through an "open" transition state. The two illustrated competing TS orientations do not differ significantly in energy. For most reactions in this family there is not a good understanding of reactants-pair orientation. There is a prevalent view that the anti-periplanar TS is favored on the basis of electrostatic effects.



Denmark has designed a nice substrate to distinguish between synclinal and antiperiplanar transition states:  
Denmark, *J. Org. Chem.* **1994**, *59*, 707-709

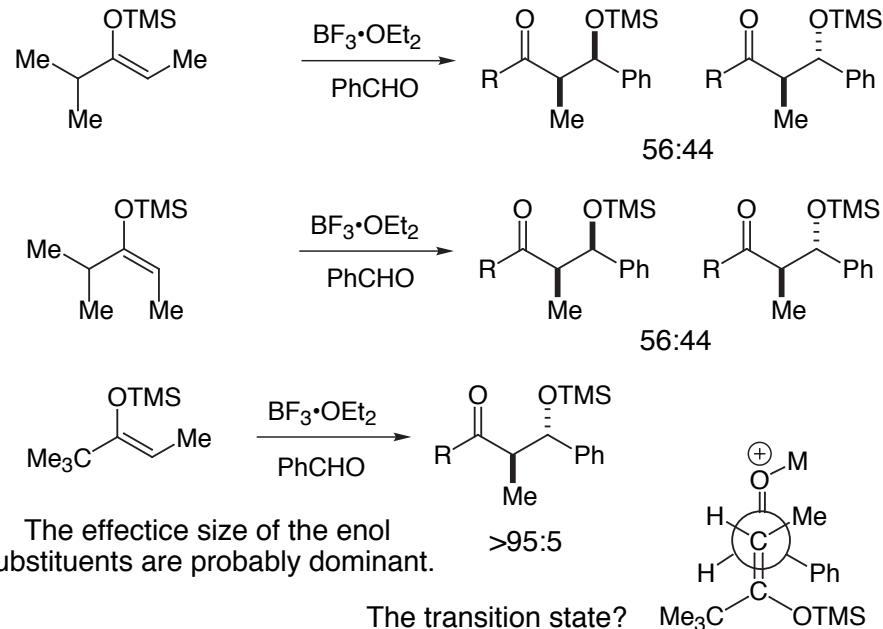


Lewis Acid	syn:anti
TiCl <sub>4</sub>	21:79
SnCl <sub>4</sub>	18:82
BF <sub>3</sub> ·OEt <sub>2</sub>	29:71
TrClO <sub>4</sub>	27:73
SnCl <sub>2</sub>	78:22

conclusion: there is a modest preference for the antiperiplanar TS

### Syn-Anti Aldol Diastereoselection

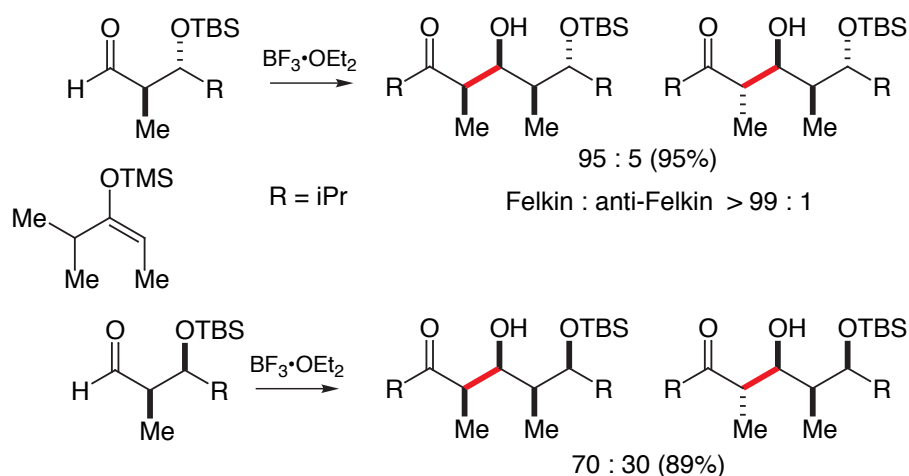
Heathcock: *J. Org. Chem.* **1986**, *51*, 3027



These reactions "exhibit little simple diastereoselection except in special cases."....Heathcock

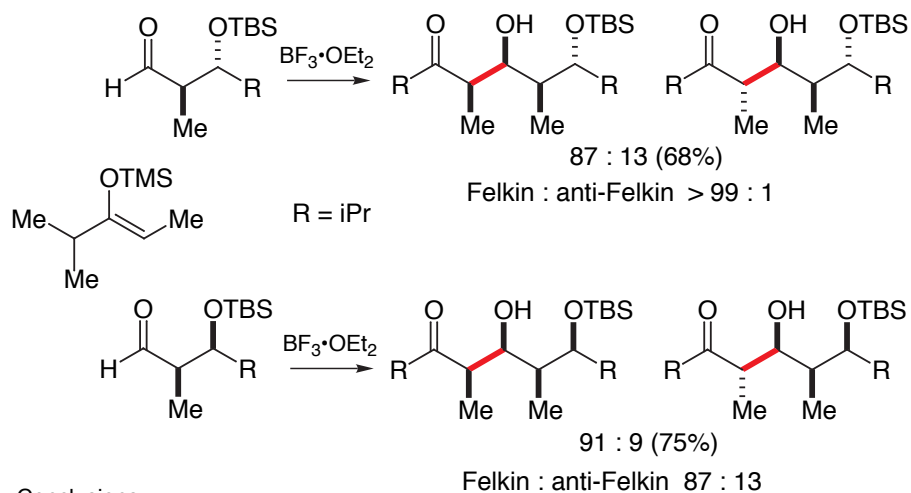
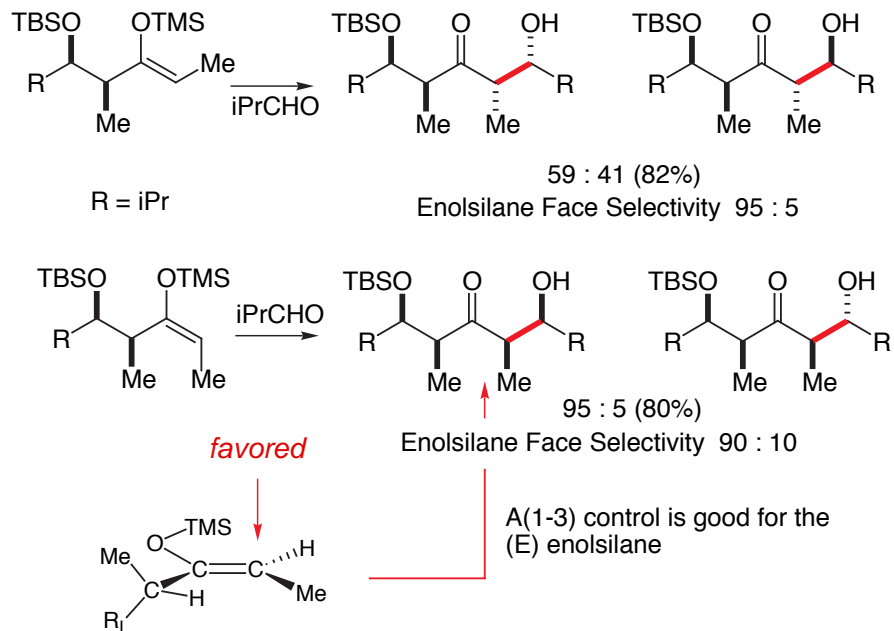
## Merged Syn-Anti &amp; Felkin Diastereoselection

Evans: JACS 1995, 117, 9598



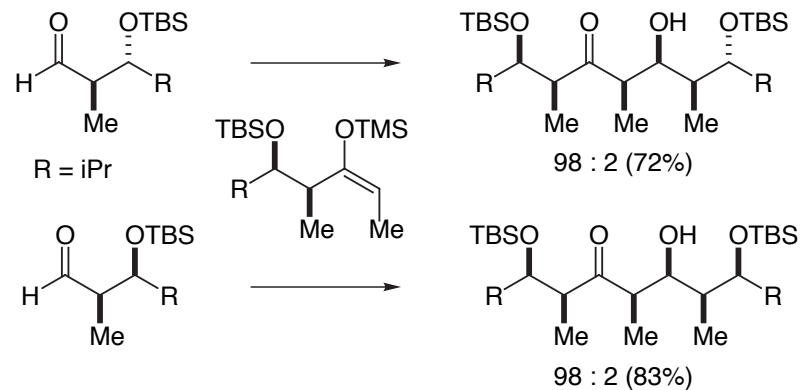
Conclusions:  
 Moderate to Good syn diastereoselection  
 Excellent Felkin diastereoselection

## Enolsilane Face Selection



Conclusions:  
 Moderate to Good syn diastereoselection  
 Excellent Felkin diastereoselection

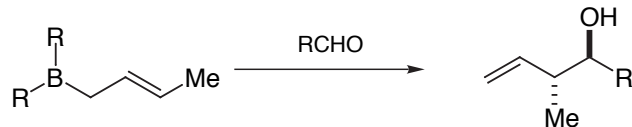
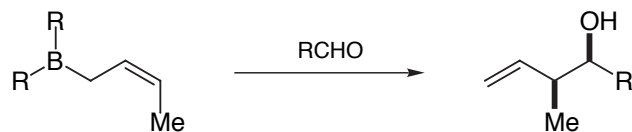
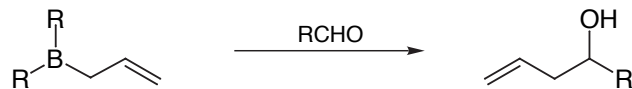
## Double Stereodifferentiating Syn Aldol Rxns with Enolsilanes



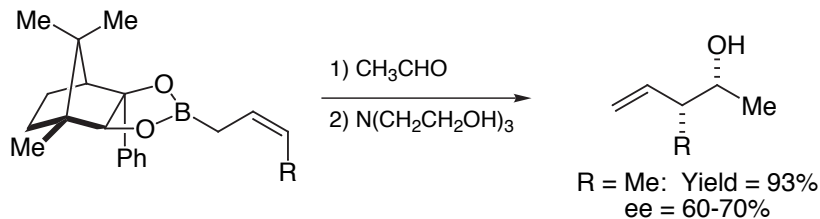


■ General Reviews of Allyl Metal Reagents:  
Comprehensive Organic Synthesis, **1991**; Vol. 2.

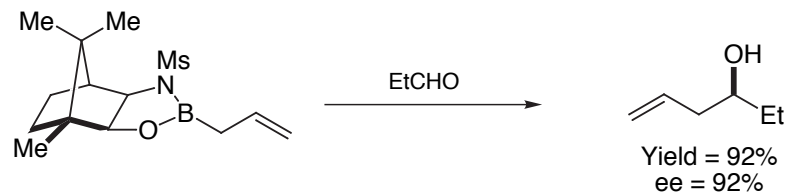
■ The General Reactions



■ The Hoffman Chiral Allylboronic Esters

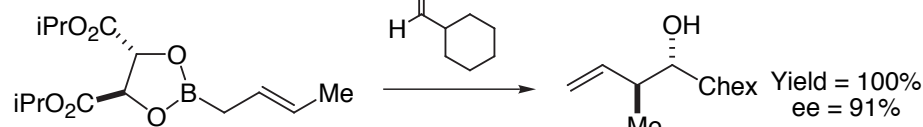


R. Hoffman *Tetrahedron Lett.* **1979**, 4653-4656.  
*ACIEE*, **1978**, 17, 768-769.

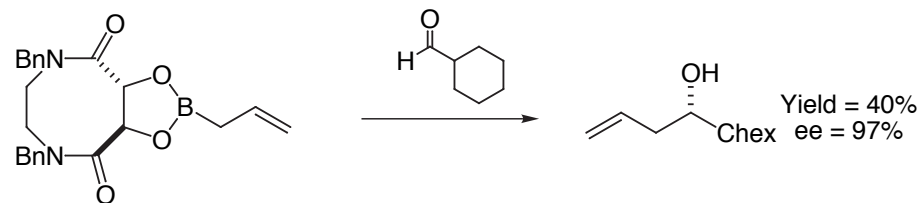


M. Reetz *Chem. Ind. (London)* **1988**, 663-664.

■ The Tartrate-derived Allylboronic Esters

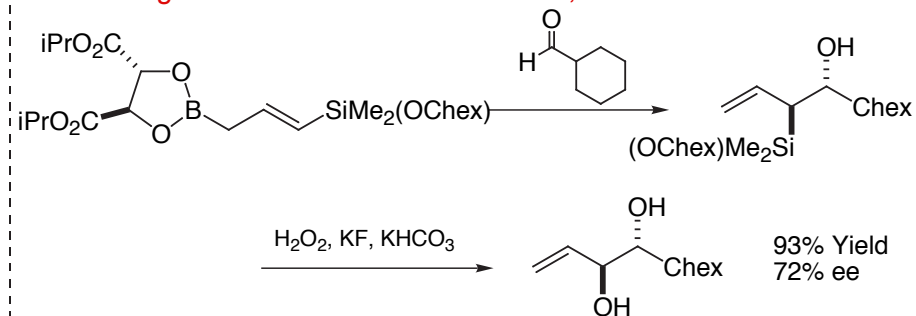


W. Roush, *J. Am. Chem. Soc.* **1985**, 107, 8186-8190.  
*Tetrahedron Lett.* **1988**, 29, 5579-5582.



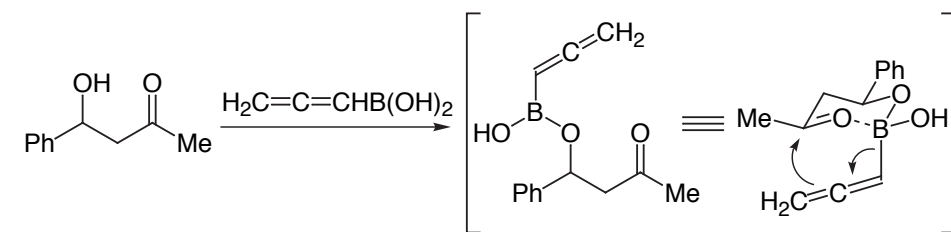
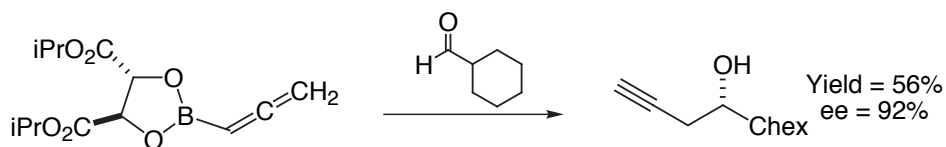
W. Roush, *J. Am. Chem. Soc.* **1988**, 110, 3979-3982.

■ A Reagent for the Generation of Anti-1,2-Diols



W. Roush, *Tetrahedron Lett.* **1990**, 31, 7563-7566.

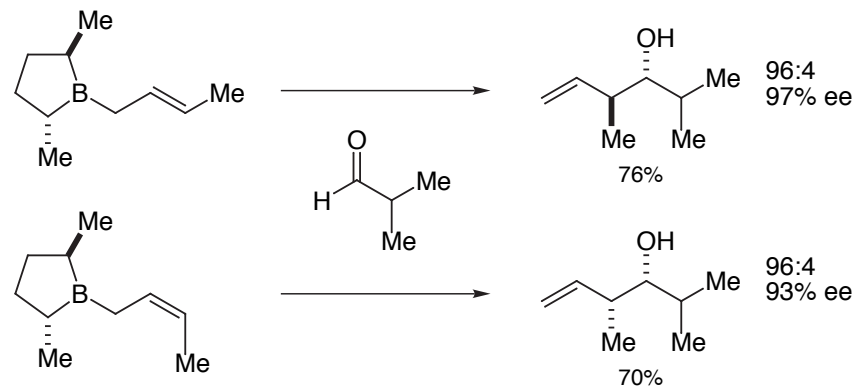
### ■ Allenylboronic Esters: Tartrate-derived Controllers and Internal Delivery



H. Yamamoto, *J. Am. Chem. Soc.* **1982**, *104*, 7667-7669  
*Tetrahedron Lett.* **1986**, *27*, 1175-1178.

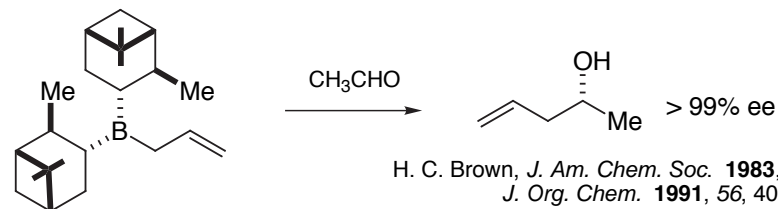
95% Yield  
 >99:1

### ■ The Masamune Borolane

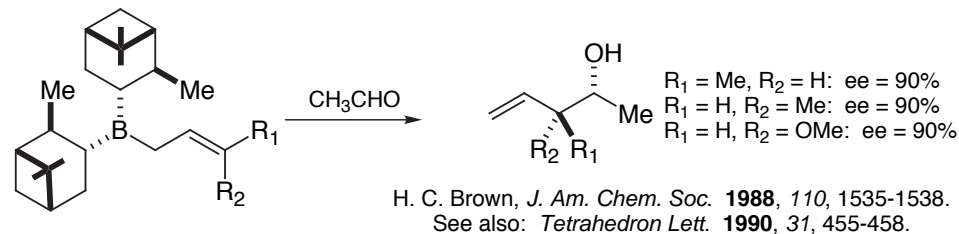


S. Masamune, *J. Org. Chem.* **1987**, *52*, 4831-4832.

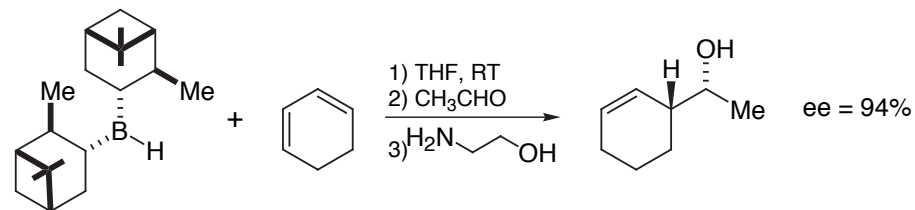
### ■ The Brown IPC Controller



H. C. Brown, *J. Am. Chem. Soc.* **1983**, *105*, 2092-2093.  
*J. Org. Chem.* **1991**, *56*, 401-404.  
*J. Org. Chem.* **1992**, *57*, 6614.

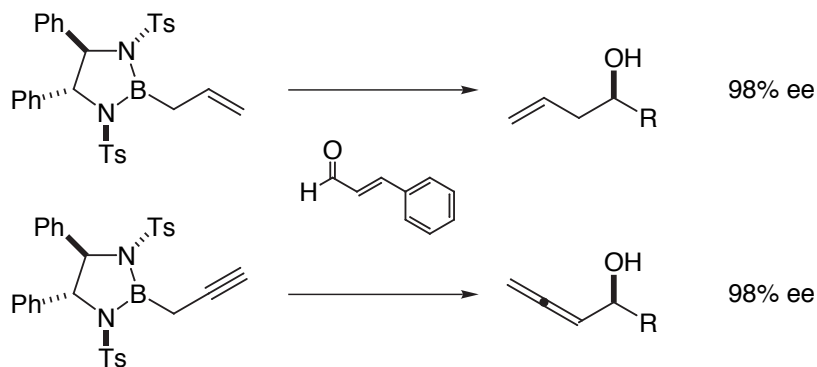


H. C. Brown, *J. Am. Chem. Soc.* **1988**, *110*, 1535-1538.  
 See also: *Tetrahedron Lett.* **1990**, *31*, 455-458.



H. C. Brown, *J. Chem. Soc., Perkin Trans. 1*, **1991**, 2633.

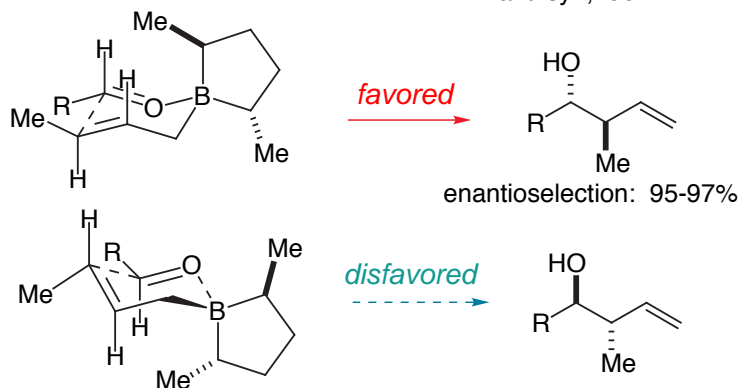
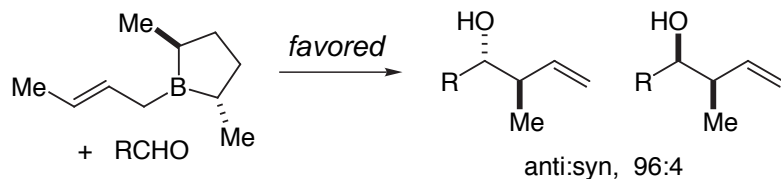
### ■ The Corey Stein Controller



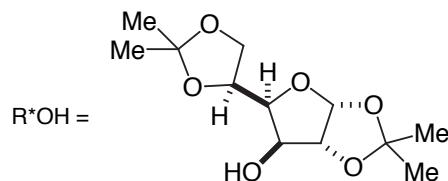
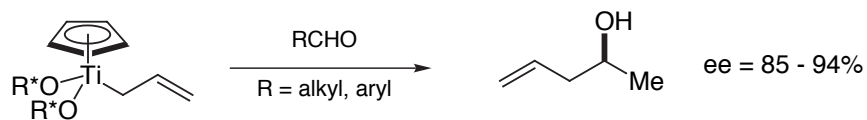
E. J. Corey, *J. Am. Chem. Soc.* **1989**, *111*, 5495-5496.  
*J. Am. Chem. Soc.* **1990**, *112*, 878-879.

### The Allylboron Reagents Add to Carbonyl Compounds via a Zimmerman-Traxler Transition State

Masamune, Sato, Kim, Wollmann *J. Org. Chem.* **1987**, 52, 4831

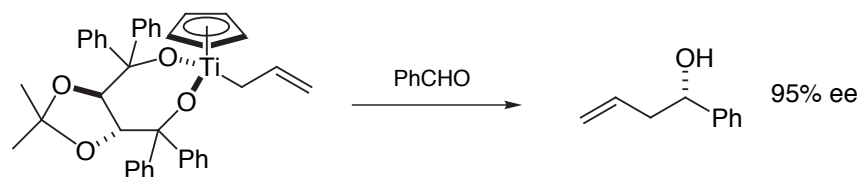


### An Enantioselective Allyltitanium Reagent



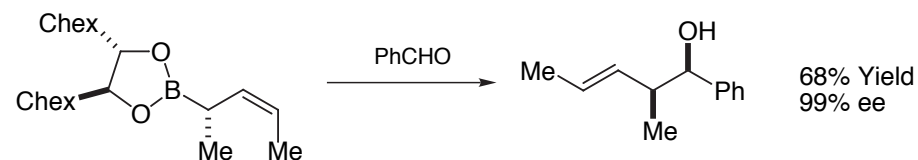
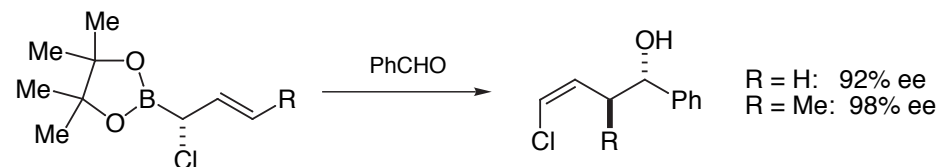
M. Riediker, R. Duthaler, *ACIEE*, **1989**, 28, 494-495.  
In *Organic Synthesis via Organometallics*, **1991**, 285-309.  
*J. Am. Chem. Soc.* **1992**, 114, 2321-2336.  
Duthaler *Chem. Rev.* **1992**, 92, 807

### Another Enantioselective Allyltitanium Reagent

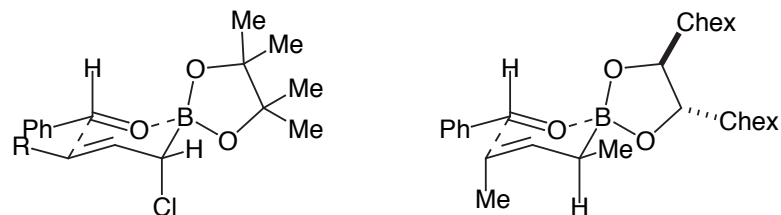


R. Duthaler, *J. Am. Chem. Soc.* **1992**, 114, 2321-2336.

### Chiral $\alpha$ -Substituted Allyl Metal Reagents: Boron

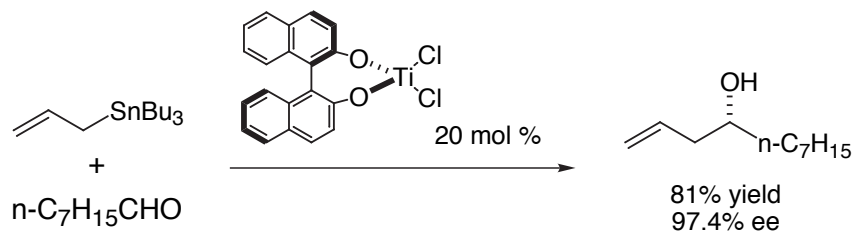
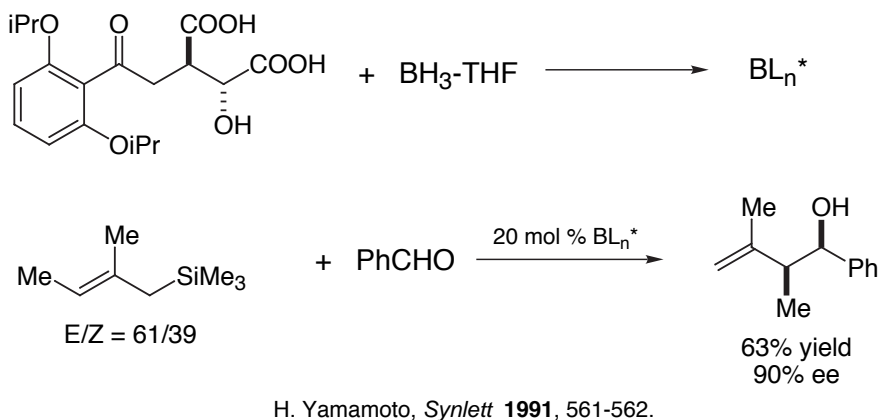


R. Hoffman, *Chem. Ber.* **1986**, 119, 2013-2024.  
*Chem. Ber.* **1988**, 121, 1501-1507.  
*ACIEE*, **1986**, 25, 1028-1030.

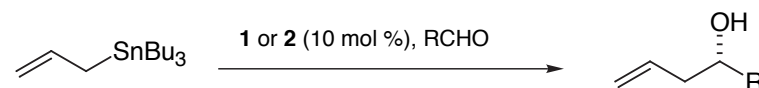
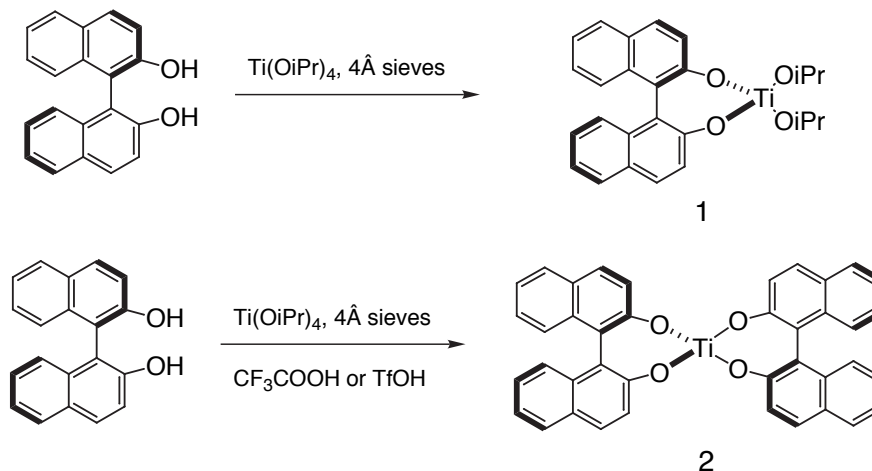


The favored transition states

■ Three Catalytic Asymmetric Allylations of Aldehydes are Known



E. Tagliavini, A. Umani-Ronchi *J. Am. Chem. Soc.* **1993**, 115, 7001-7002.



R	Catalyst	Yield (%)	ee (%)
Ph	1	88	95
Ph	2	98	92
Chex	1	66	94
Chex	2	95	92
	1	42	89
	2	78	77

G. Keck *J. Am. Chem. Soc.* **1993**, 115, 8467-8468.

■ Many Other Metals Have Been Employed in the Allylation Reaction ...

- Pb: S. Torii, *Chem. Lett.* **1986**, 1461-1462.
- Mo: J. Faller, *Tetrahedron Lett.* **1991**, 32, 1271-1274.
- Cr: Y. Kishi, *Tetrahedron Lett.* **1982**, 23, 2343-2346.
- P. Knochel, *J. Org. Chem.* **1992**, 57, 6384-6386.
- Sb: Y. Butsugan, *Tetrahedron Lett.* **1987**, 28, 3707-3708.
- Mn: T. Hiyama, *Organometallics*, **1982**, 1, 1249-1251.
- Zn: T. Shono, *Chem. Lett.* **1990**, 449-452.
- Ba: H. Yamamoto, *J. Am. Chem. Soc.* **1991**, 113, 8955-8956.