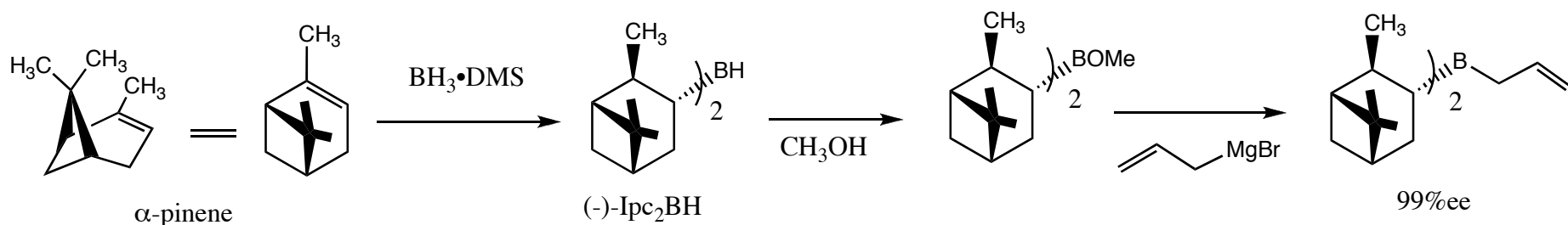
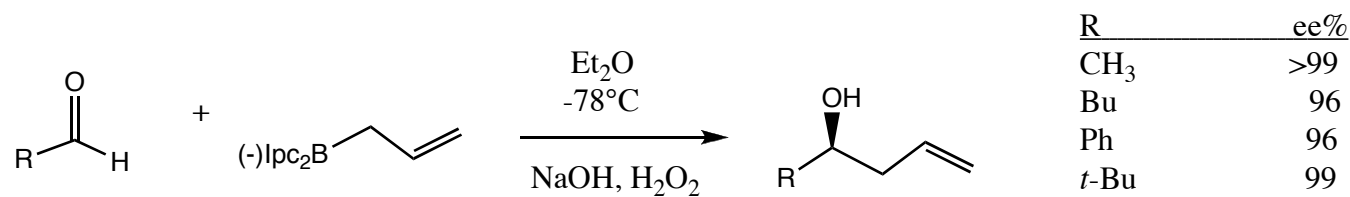


Brown Allylation and Crotylation Reactions

1. Reagent Synthesis

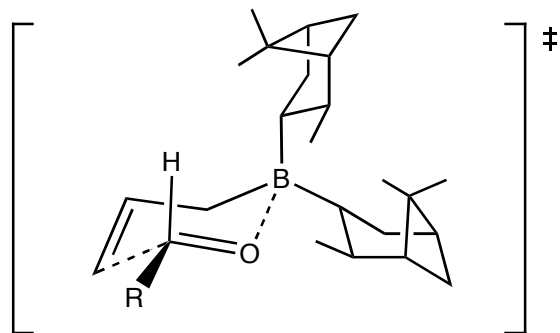


- both enantiomers commercially available and inexpensive



- low temperatures lead to increased enantioselectivity
- Allylboration of aldehydes is instantaneous at -78°C

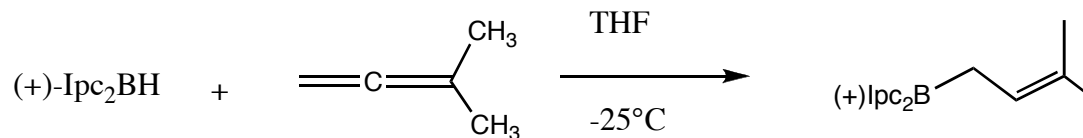
Stereochemical Rationale:



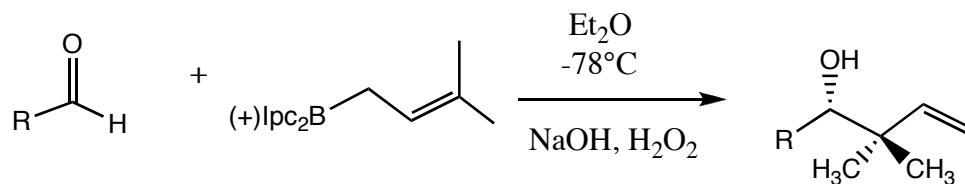
allylation proceeds through a chair-like transition state where R occupies an equatorial position, and the aldehyde facial selectivity derives from minimization of steric interactions between the Ipc ligands and the allyl group

Brown Asymmetric Methallylation and Isoprenylation of Aldehydes

Asymmetric Isoprenylation of aldehydes:



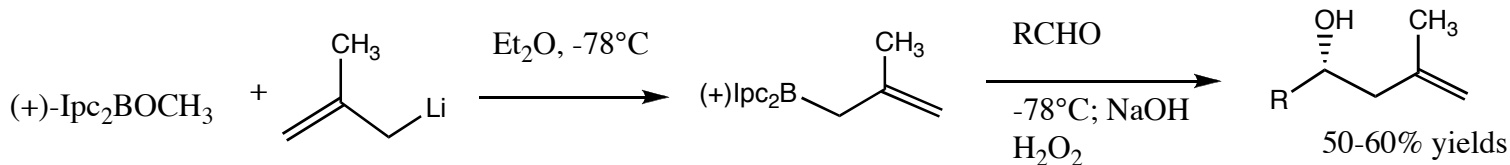
•both enantiomers commercially available and inexpensive



R	ee%
CH ₃	91
Bu	92
CH ₂ =CH	95
(CH ₃) ₂ C=CH	96

TL, **1984**, 1215
JOC, **1986**, 432

Methallylation of Aldehydes



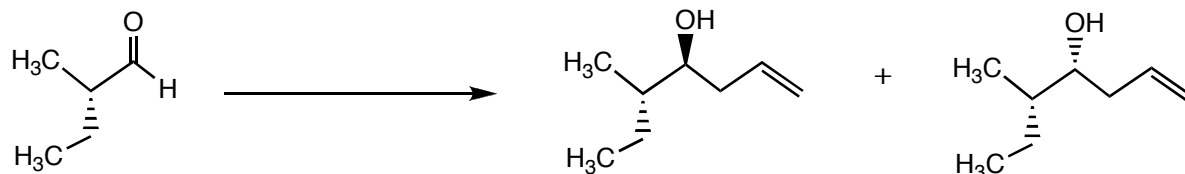
The yields of methallylation are lower than in simple allylation reactions.

TL, **1984**, 5111
JOC, **1986**, 432

R	ee%
CH ₃	90
Bu	91
CH ₂ =CH	92
<i>t</i> -Bu	92

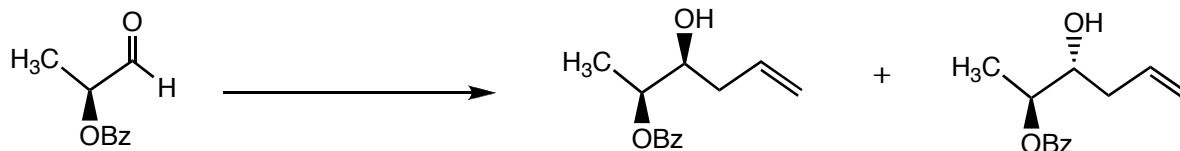
Diastereoselective Allylboration of Chiral, α -substituted aldehydes

The diastereofacial selectivity of the *B*-allyldiisopinocampheylborane reagent typically overrides any facial preference of the aldehyde for nucleophilic attack



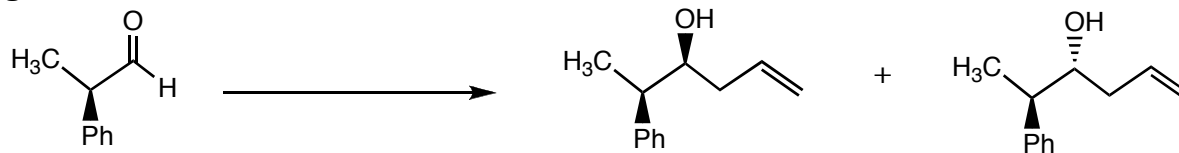
Reagent Controlled facial addition

Matched: (-)-Ipc ₂ BCH ₂ CH=CH ₂	96	:	4
Mismatched: (+)-Ipc ₂ BCH ₂ CH=CH ₂	5	:	95



Mismatched: (-)-Ipc ₂ BCH ₂ CH=CH ₂	94	:	6
Matched: (+)-Ipc ₂ BCH ₂ CH=CH ₂	4	:	96

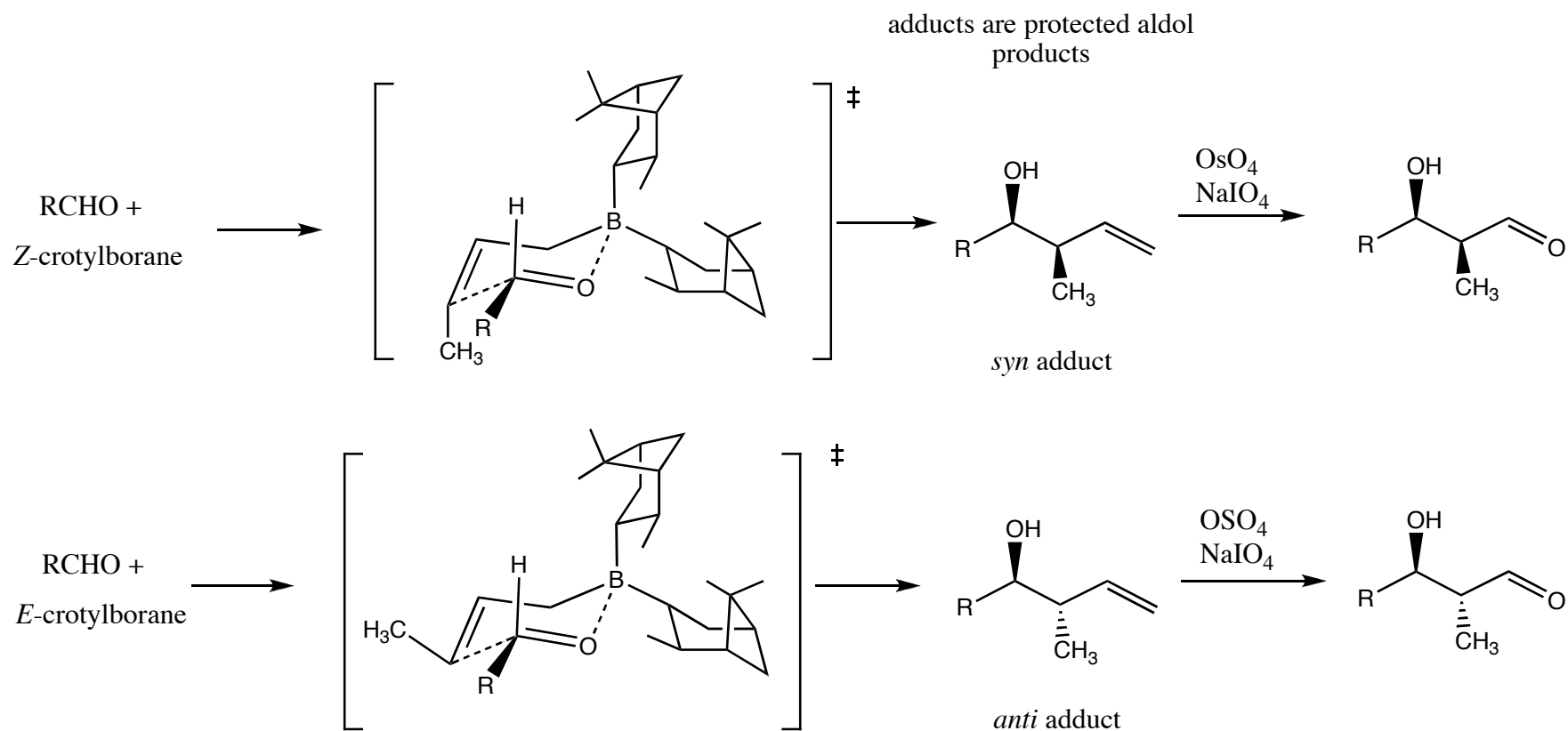
Challenge:



Mismatched: (-)-Ipc ₂ BCH ₂ CH=CH ₂	67	:	33
Matched: (+)-Ipc ₂ BCH ₂ CH=CH ₂	2	:	98

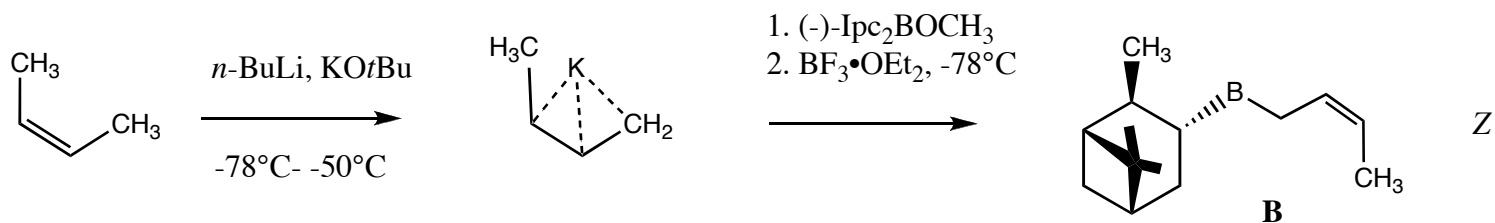
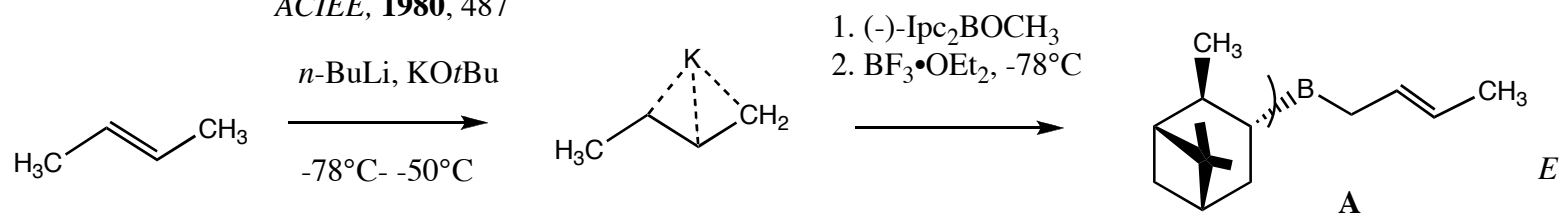
JOC, **1987**, 319
JOC, **1989**, 1570

E and *Z*-Crotylboranes



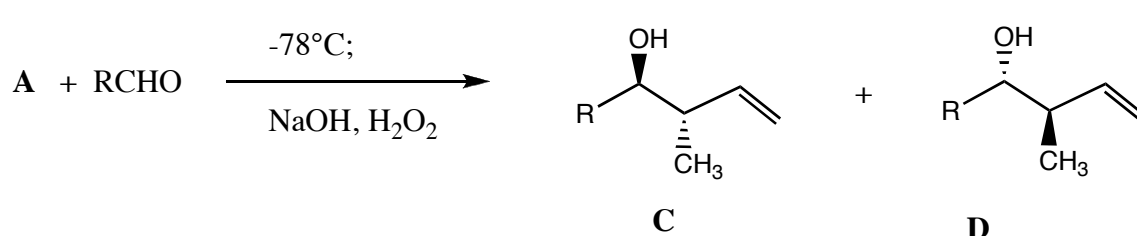
Synthesis and Utility of Chiral *E* and *Z* Crotylboranes

ACIEE, 1980, 487

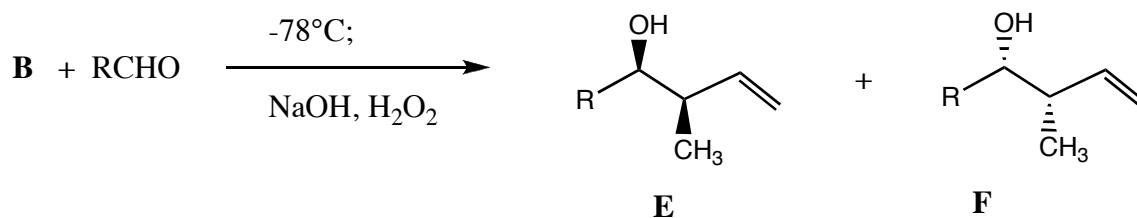


Schlosser "superbase" conditions for allylic deprotonation

large atomic radius of K favors η^3 -bonding



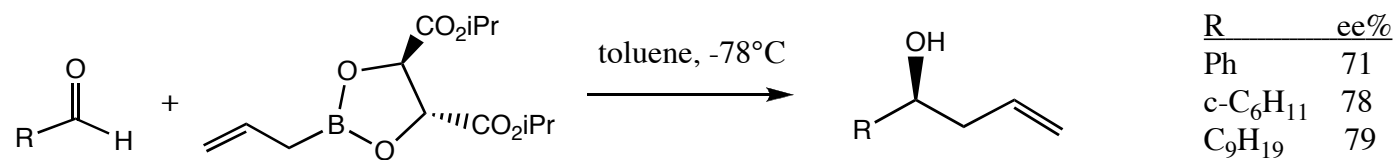
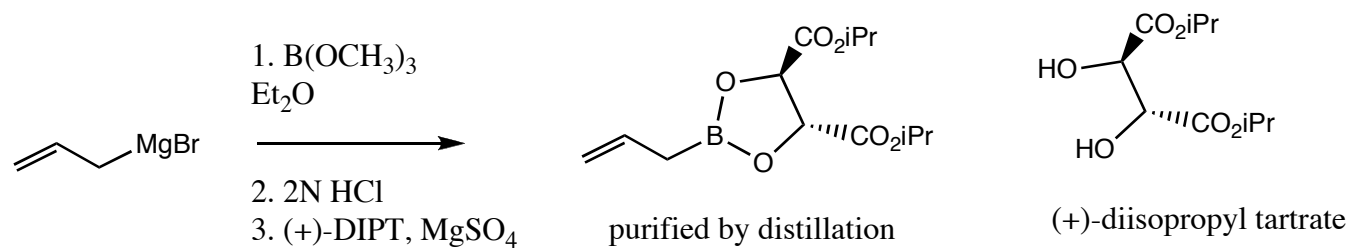
pinene	R	C:D	ee%
+	CH ₃	95:5	90
-	CH ₃	4:96	92
+	Ph	94:6	88
+	CH ₂ =CH	95:5	90



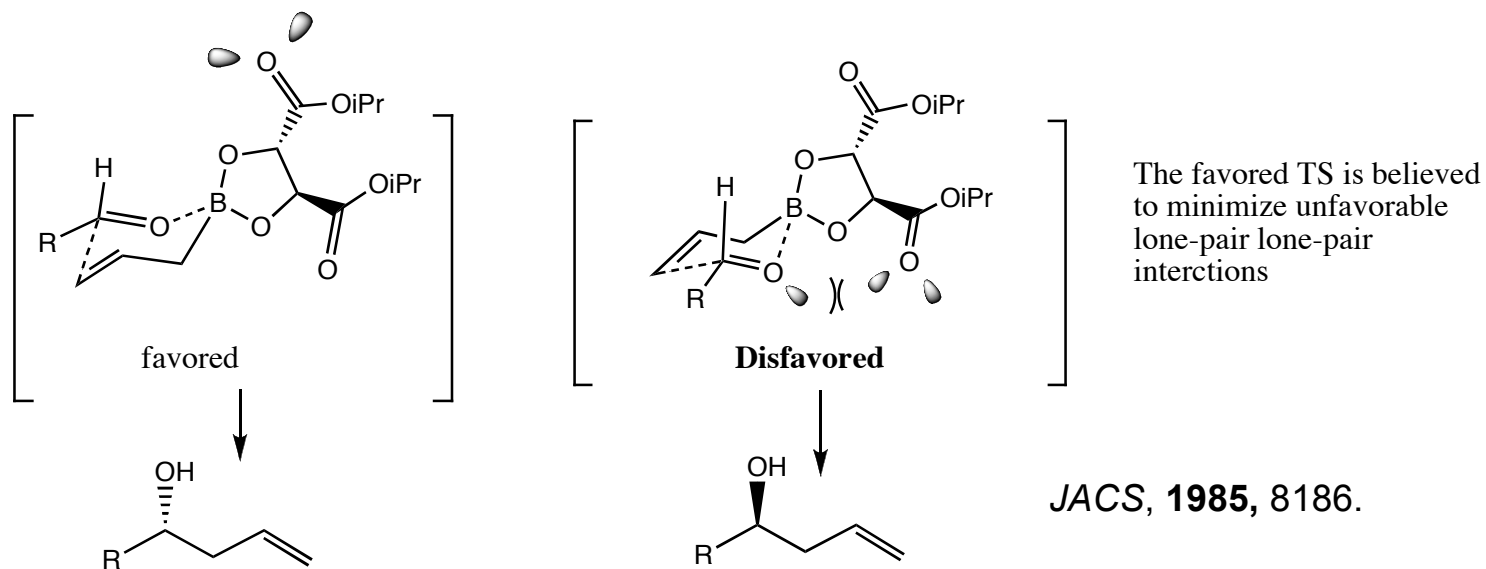
pinene	R	E:F	ee%
+	CH ₃	95:5	90
-	CH ₃	4:96	92
+	Ph	94:6	88
+	CH ₂ =CH	95:5	90

JACS, 1986, 293
JACS, 1986, 5919

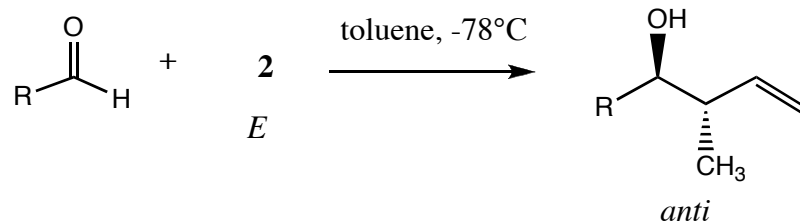
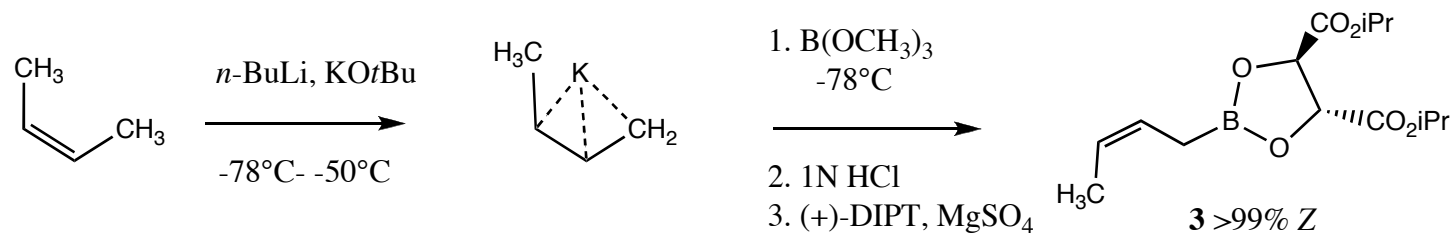
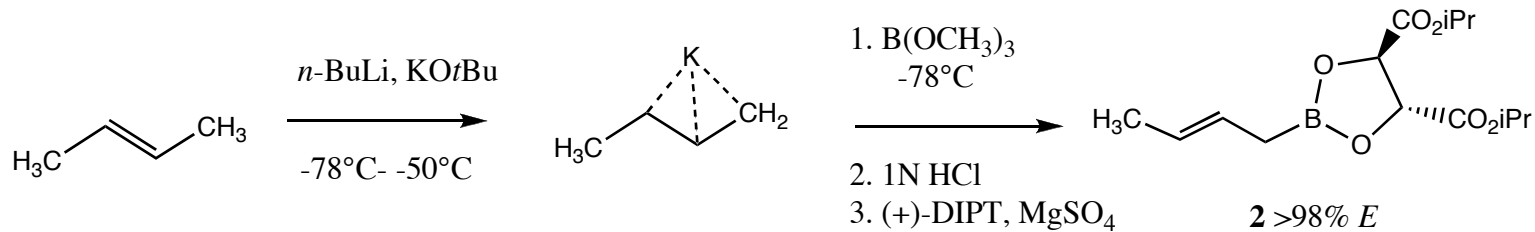
Roush Allylation and Crotylation Reactions



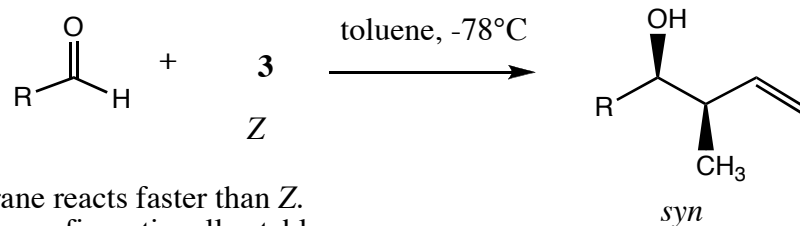
Enantioselectivities are moderate



Roush Crotylboronates: Synthesis and Utility



R	ee%	anti:syn
C ₉ H ₁₉	86	95:5
c-C ₆ H ₁₁	86	>99:1
POCH ₂ CH ₂ -	85	>98:2



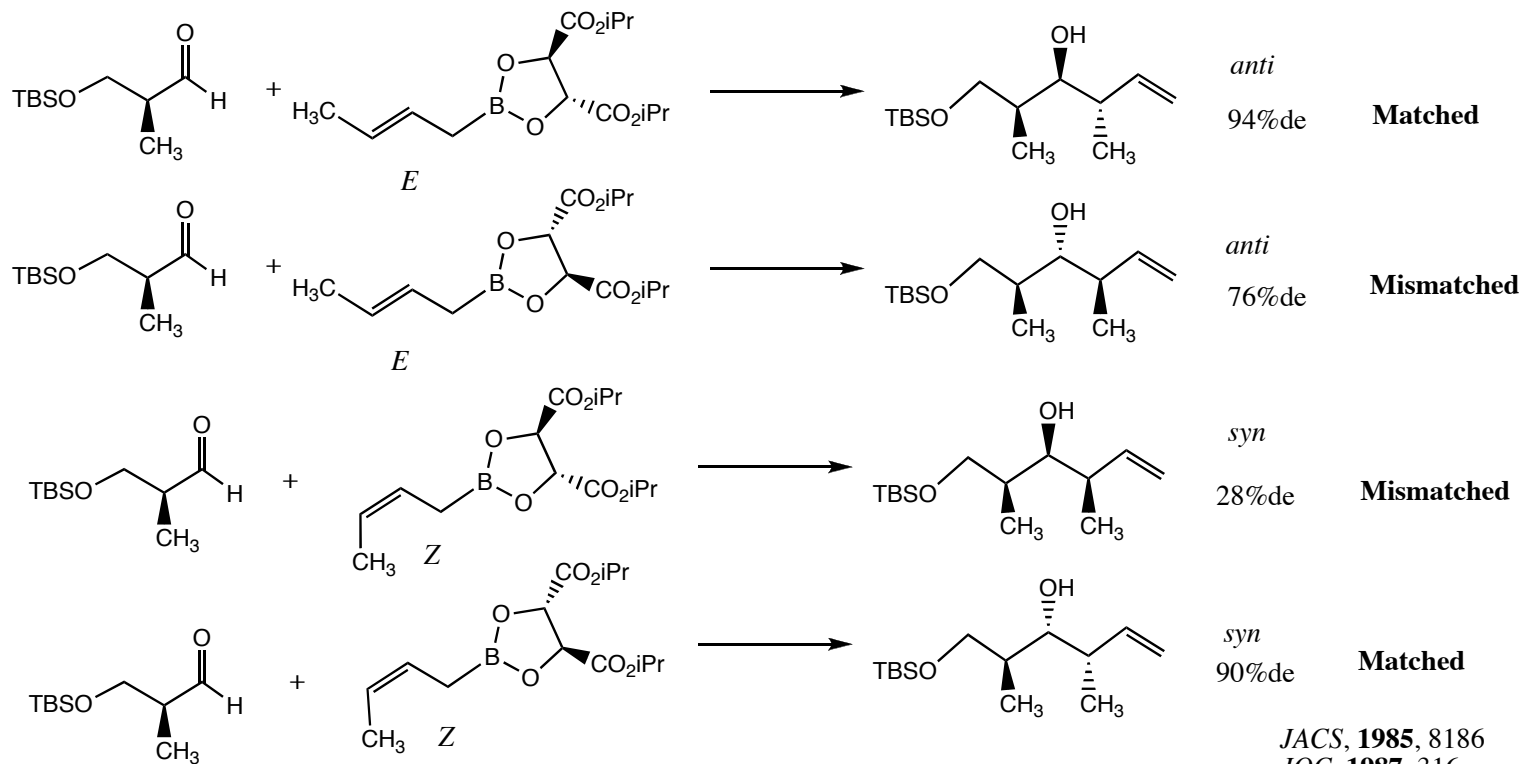
R	ee%	anti:syn
C ₉ H ₁₉	77	1:99
c-C ₆ H ₁₁	83	2:98
POCH ₂ CH ₂ -	72	2:98

- *E* crotylborane reacts faster than *Z*.
- boranes are configurationally stable
- *E* reagent gives the *anti* product; *Z* reagent gives *syn*.

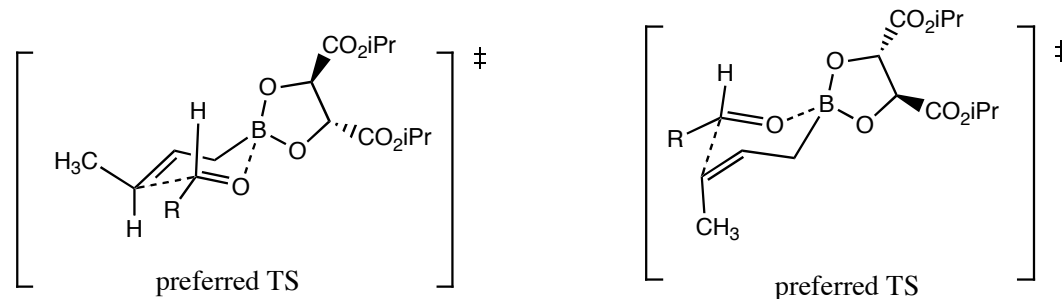
JACS, **1990**, 6339
JOC, **1987**, 316.

Roush Allyl and Crotylboration - Examples

Although stereochemical outcome is dictated by the boron ligand, α -stereochemistry in aldehyde may decrease selectivity due to inherent substrate pi-facial bias

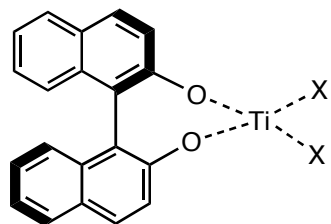


JACS, **1985**, 8186
JOC, **1987**, 316

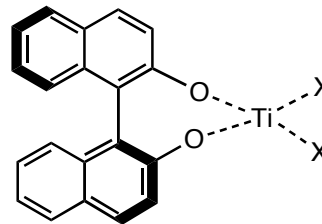


See also the total synthesis of Bafilomycin: *ACIEE*, **1999**, 1652.

Catalytic, Enantioselective Allylation of Aldehydes

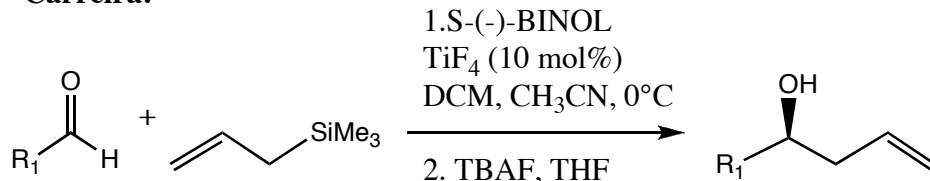


R-(+)-BINOL - titanium complex



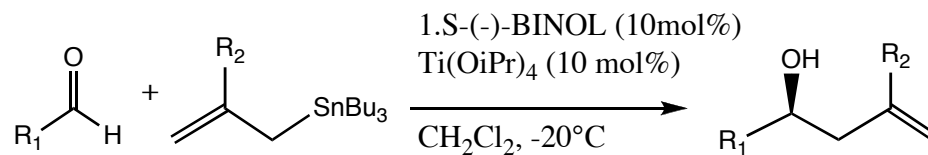
S-(-)-BINOL - titanium complex

Carreira:



R ₁	ee%
Ph	80
(CH ₃) ₃ C	94
	94
PhCH ₂ CH ₂	61

Keck Allylation:

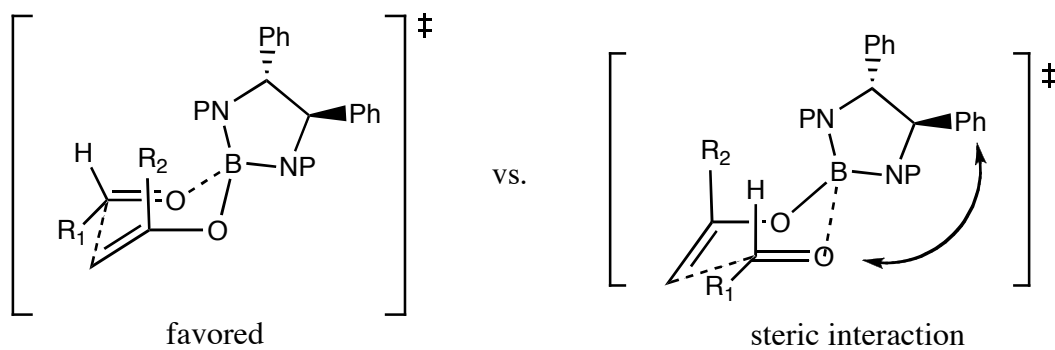
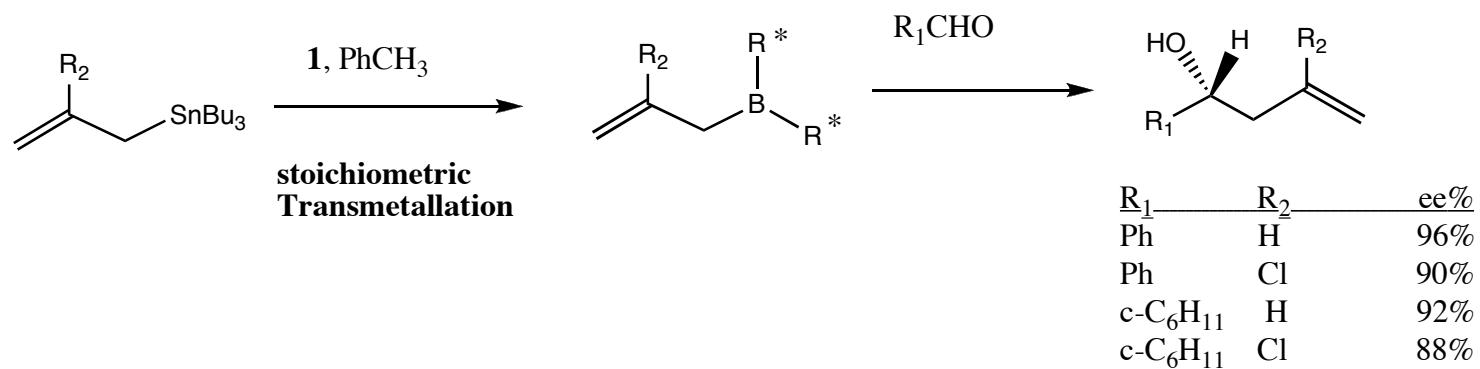
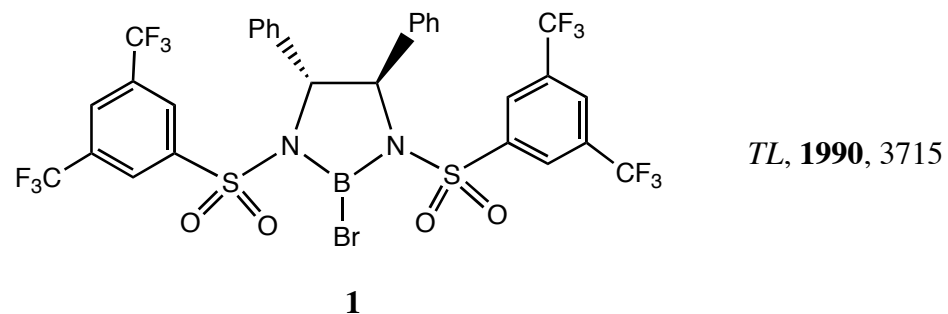


R ₁	R ₂	ee(%)
C ₆ H ₅	H	95%
C ₆ H ₅	CH ₃	91%
c-C ₆ H ₁₁	H	94%
c-C ₆ H ₁₁	CH ₃	84%

α,α -disubstituted aldehydes afford the highest enantioselectivities

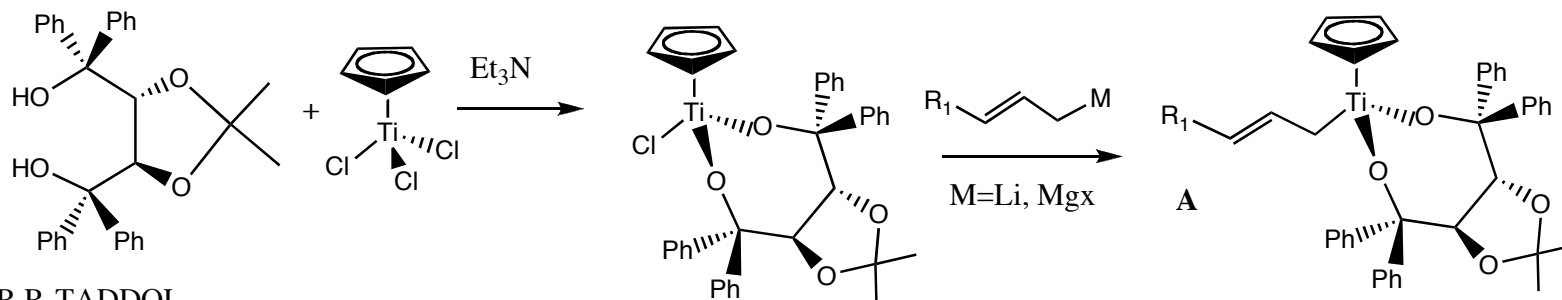
Catalyst coordinates aldehyde oxygen and blocks one face (*Re*, or *Si*) from nucleophilic attack. The transition state is open, not closed, chair-like.

Corey Enantioselective Allylation using a Chiral Controller

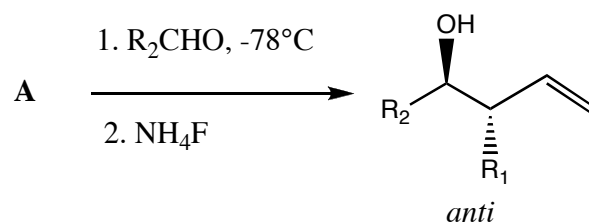


pi-facial selectivity dictated by the controller's Ph group.

Stoichiometric, Enantioselective Allyltitanation of Aldehydes



(R,R)-TADDOL
chiral diol available
in both enantiomeric
forms



R_1	R_2	ee%	de%
H	Ph	95	
CH ₃	Ph	98	97
(CH ₃) ₃ Si	Ph	98	98
CH ₃	CH ₃ (CH ₂) ₈	98	98

presumed chair-like T.S. leads to *anti* products

Chiral Controller determines product stereochemistry, not preexisting stereocenters in substrate:

