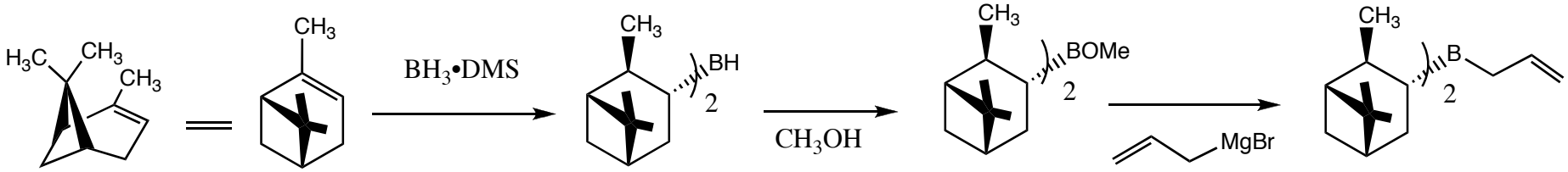
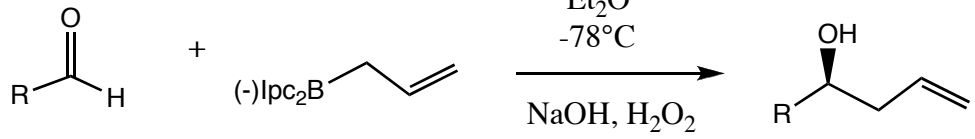
Brown Allylation and Crotylation Reactions

1. Reagent Synthesis



α-pinene (-)-Ipc_2BH 99%ee

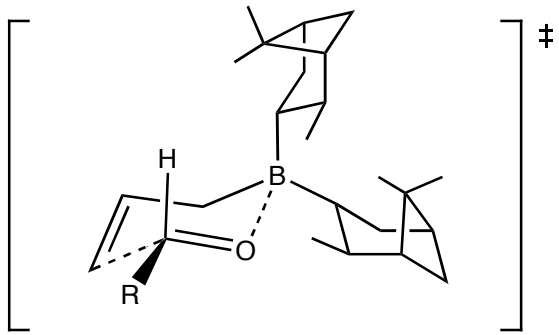
•both enantiomers commercially aailable and inexpensive



R	ee%
CH_3	>99
Bu	96
Ph	96
t-Bu	99

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

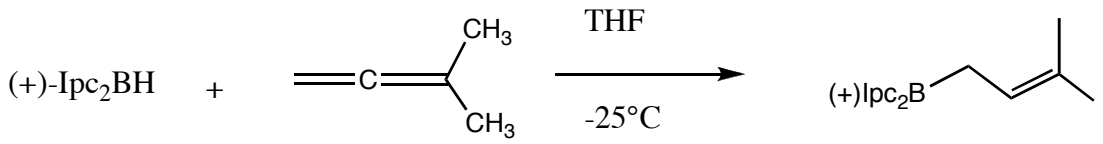
Stereochemical Rationale:



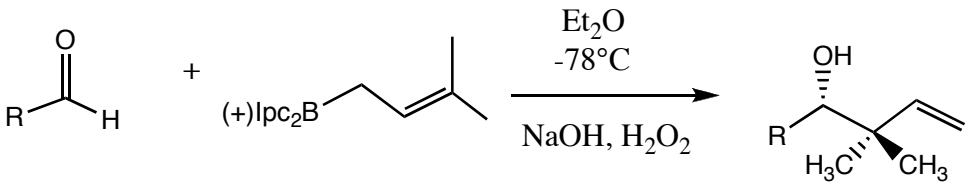
allylation proceeds through a chair-like transition state where R occupies an equatorial position, and the aldehyde facial selectivity derices from minimization of steric interactions between the Ipc ligands and the allyl group

Brown Asymmetric Methallylation and Isoprenylation of Aldehydes

Asymmetric Isoprenylation of aldehydes:



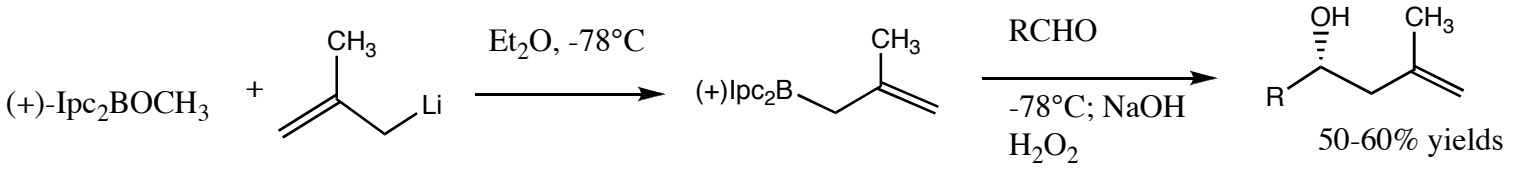
•both enantiomers commercially aailable and inexpensive



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



50-60% yields

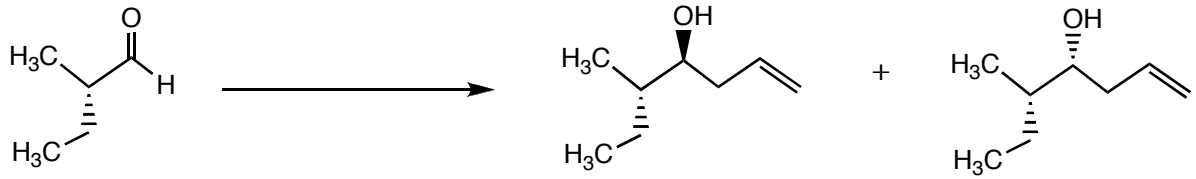
The yields of methallylation are lower than in simple allylation reactions.

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

R	ee%
CH_3	90
Bu	91
CH_2=CH	92
t-Bu	92

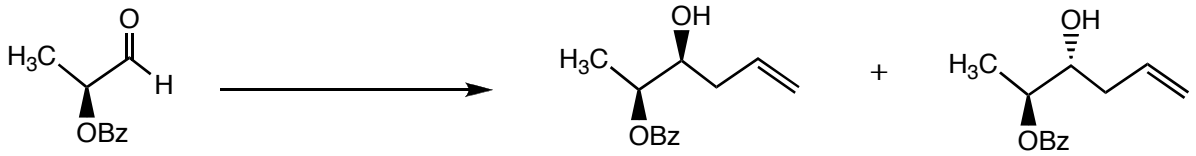
Diastereoselective Allylboration of Chiral, α–substituted aldehydes

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



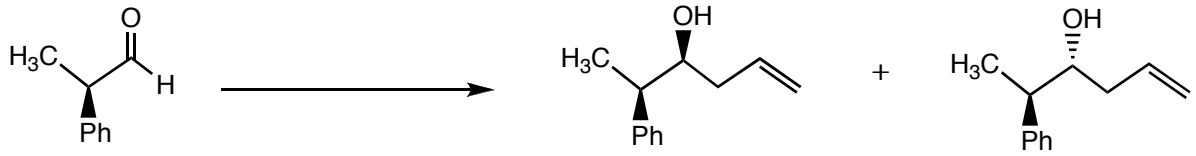
Reagent Controlled facial addition

Matched: (-)-$Ipc_2BCH_2CH{=}CH_2$	96	:	4
Mismatched: (+)-$Ipc_2BCH_2CH{=}CH_2$	5	:	95



Mismatched: (-)-$Ipc_2BCH_2CH{=}CH_2$	94	:	6
Matched: (+)-$Ipc_2BCH_2CH{=}CH_2$	4	:	96

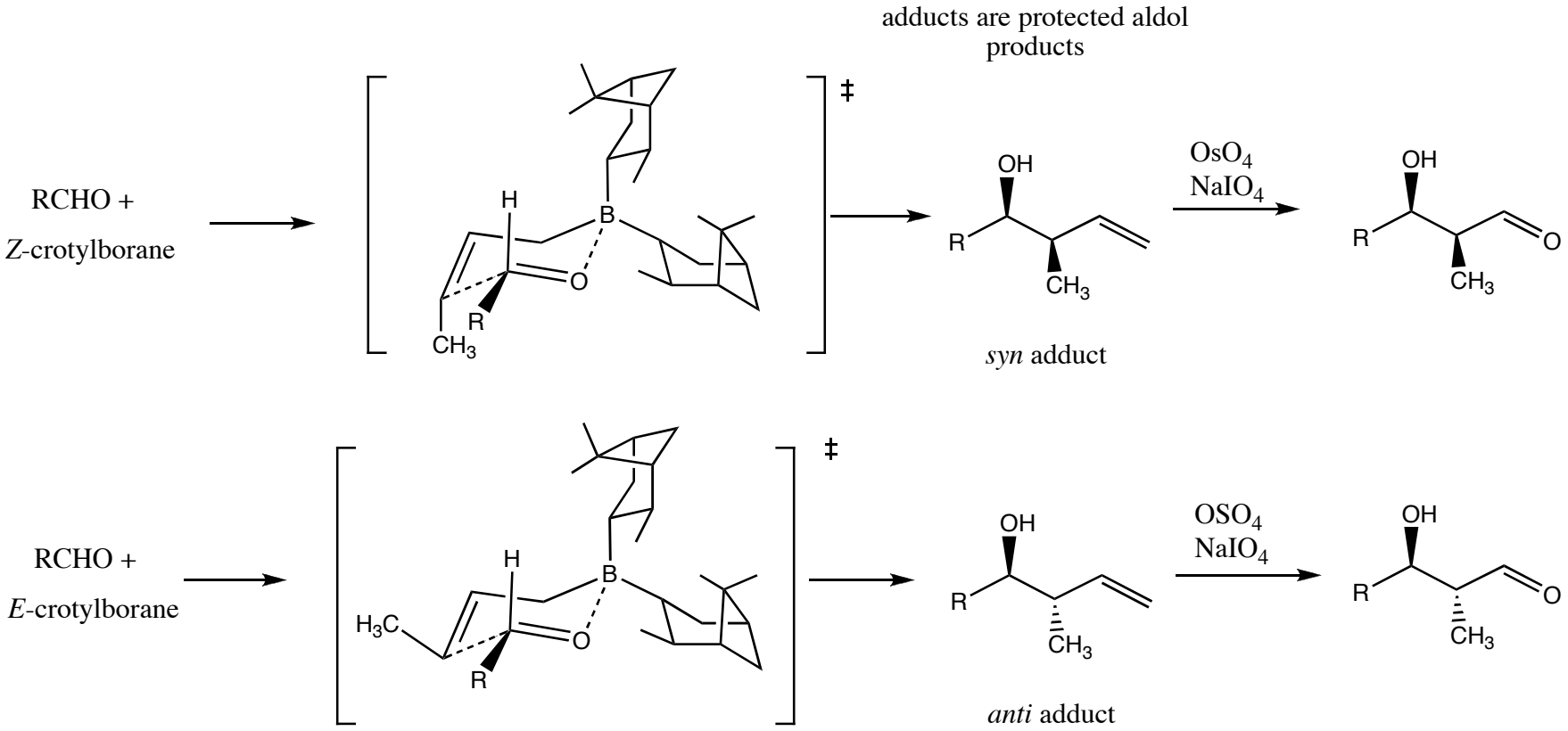
Challenge:



Mismatched: (-)-$Ipc_2BCH_2CH{=}CH_2$	67	:	33
Matched: (+)-$Ipc_2BCH_2CH{=}CH_2$	2	:	98

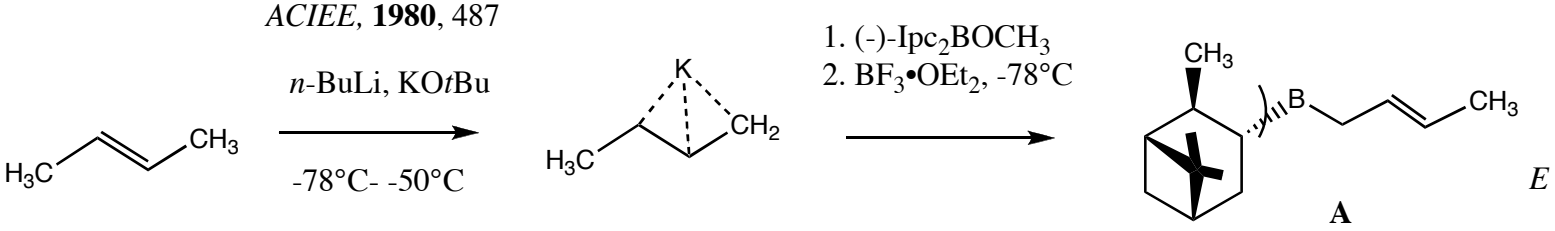
JOC, **1987**, 319
JOC, **1989**, 1570

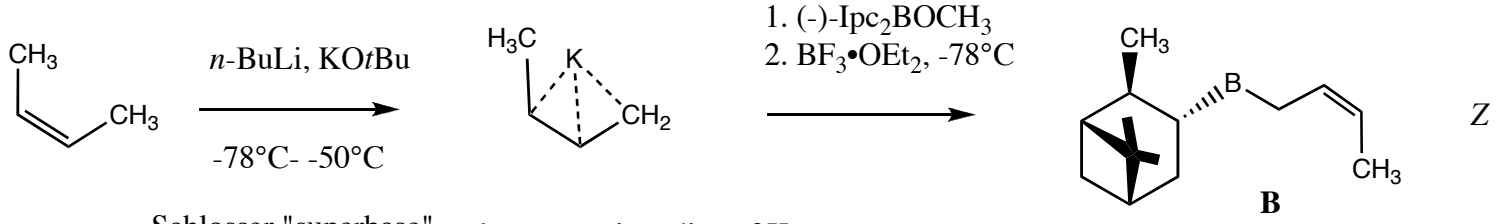
E and *Z*-Crotylboranes



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

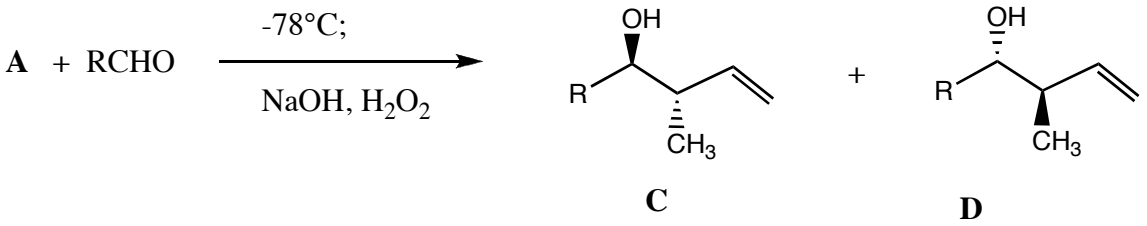
ACIEE, **1980**, 487



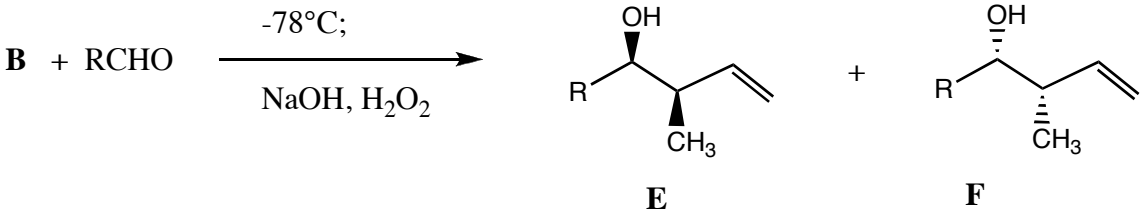


Schlosser "superbase" conditions for allylic deprotonation

large atomic radius of K favors η^3-bonding



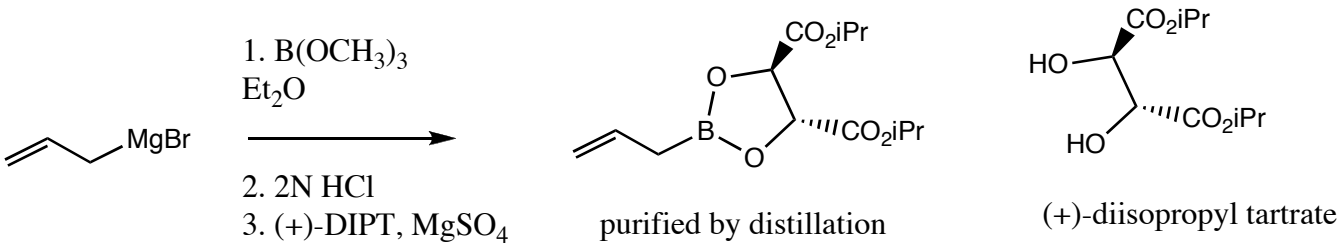
pinene	R	C:D	ee%
+	CH_3	95:5	90
-	CH_3	4:96	92
+	Ph	94:6	88
+	CH_2=CH	95:5	90

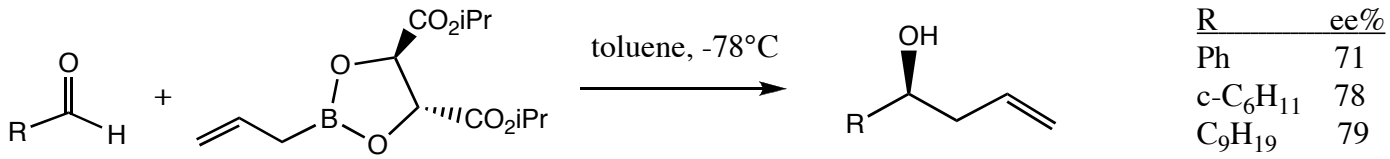


pinene	R	E:F	ee%
+	CH_3	95:5	90
-	CH_3	4:96	92
+	Ph	94:6	88
+	CH_2=CH	95:5	90

JACS, **1986**, 293
JACS, **1986**, 5919

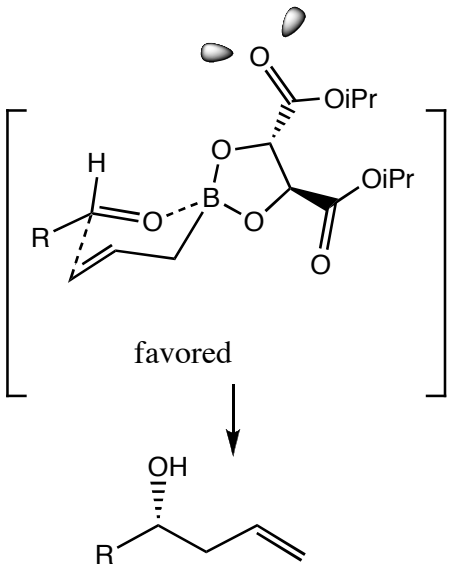
Roush Allylation and Crotylation Reactions

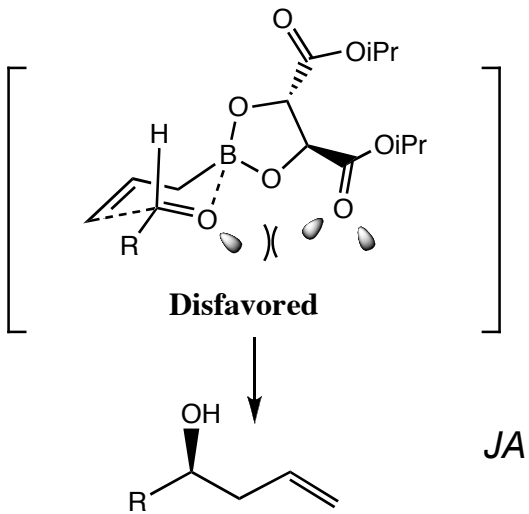




R	ee%
Ph	71
c-C_6H_{11}	78
C_9H_{19}	79

Enantioslectivities are moderate

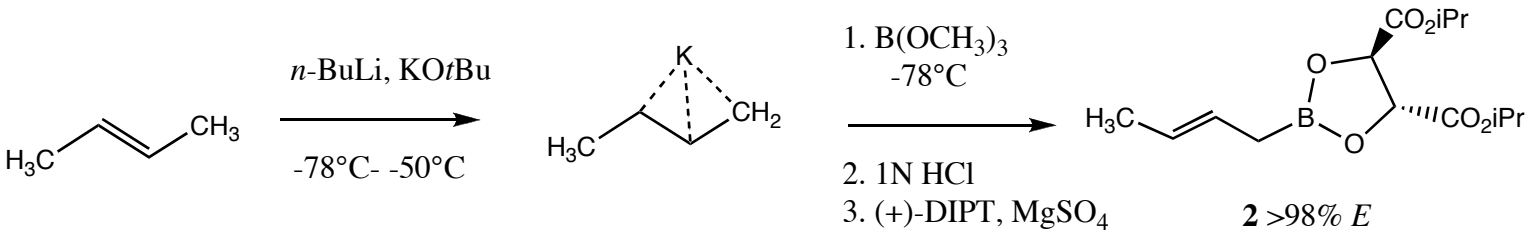


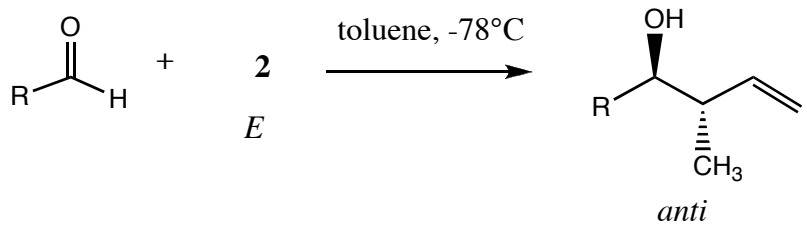


The favored TS is believed to minimize unfavorable lone-pair lone-pair interctions

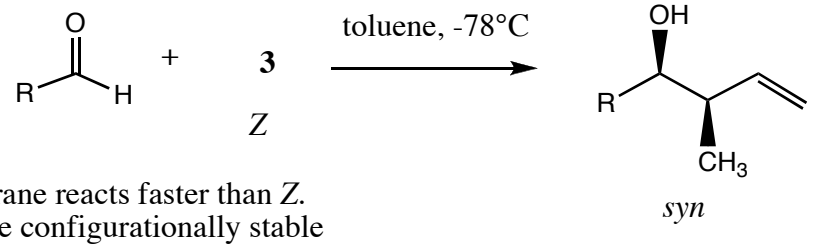
JACS, **1985,** 8186.

Roush Crotylboronates: Synthesis and Utility





R	ee%	anti:syn
C_9H_{19}	86	95:5
c-C_6H_{11}	86	>99:1
$POCH_2CH_2$_	85	>98:2



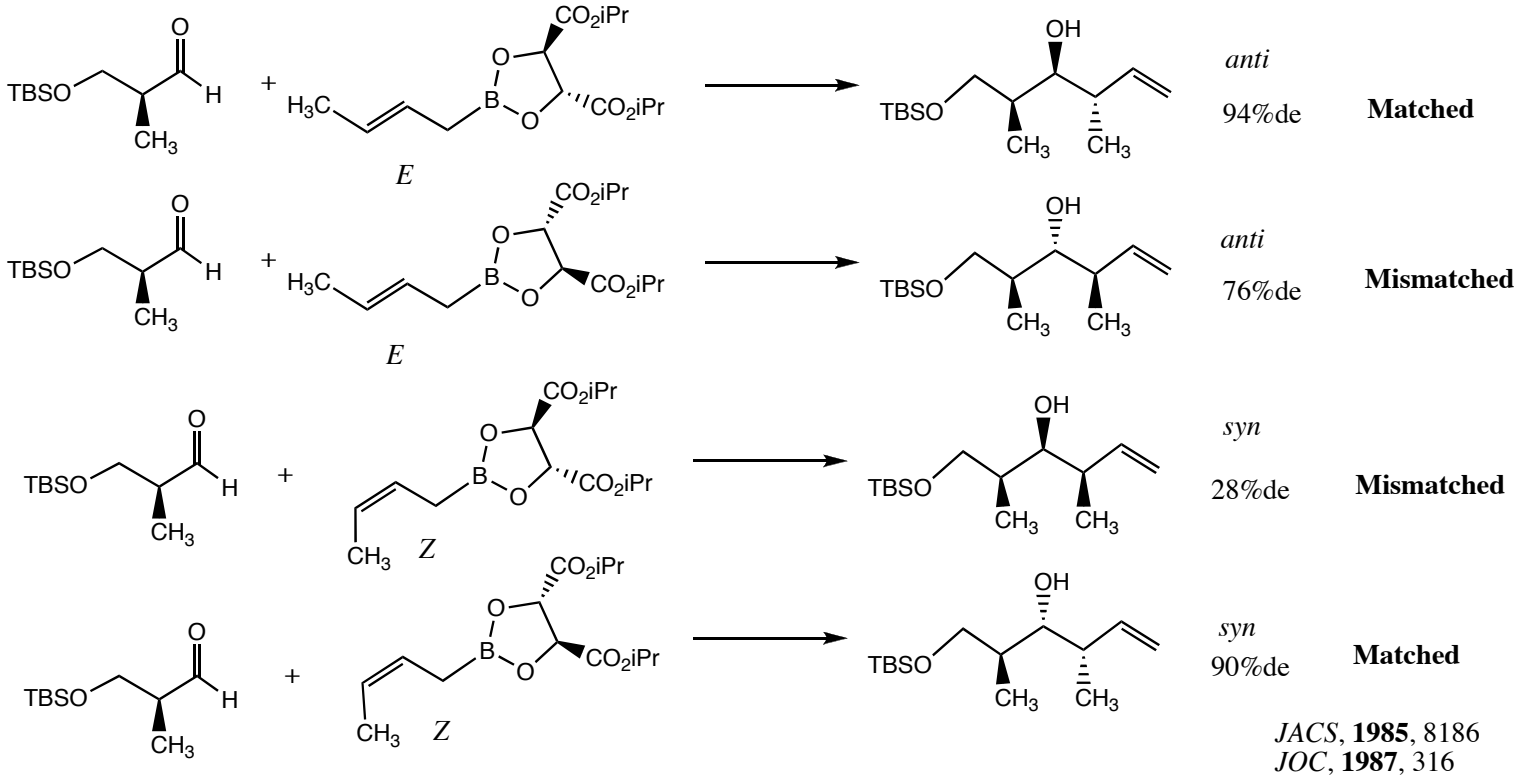
R	ee%	anti:syn
C_9H_{19}	77	1:99
c-C_6H_{11}	83	2:98
$POCH_2CH_2$_	72	2:98

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

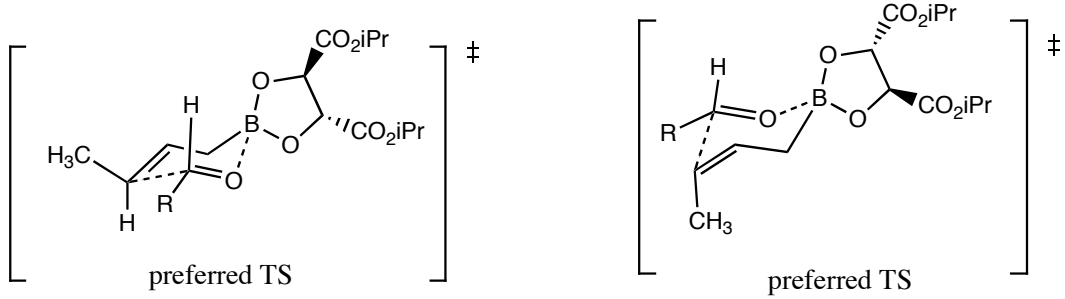
JACS, **1990**, 6339
JOC, **1987**, 316.

Roush Allyl and Crotylboration - Examples

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

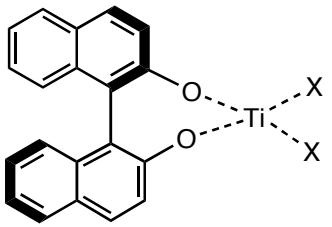


JACS, **1985**, 8186
JOC, **1987**, 316

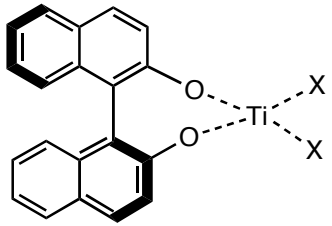


See also the total synthesis of Bafilomycin: *ACIEE*, **1999**, 1652.

Catalytic, Enantioselective Allylation of Aldehydes

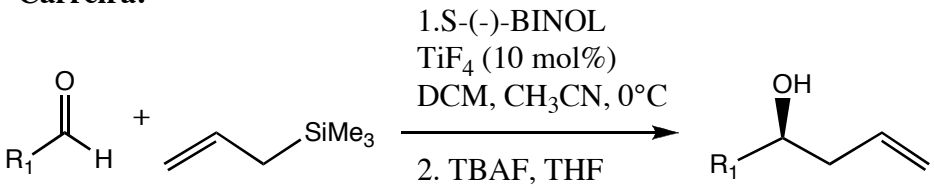


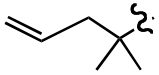
R-(+)-BINOL - titanium complex



S-(-)-BINOL - titanium complex

Carreira:



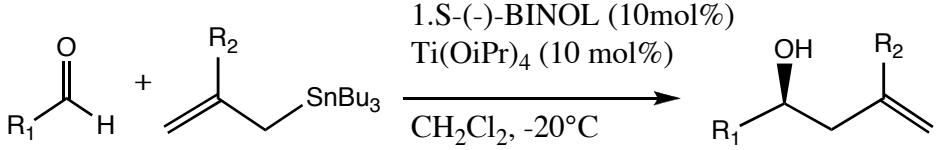
R_1	ee%
Ph	80
$(CH_3)_3C$	94
	94
$PhCH_2CH_2$	61

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.

ACIEE, **1996**, 2363

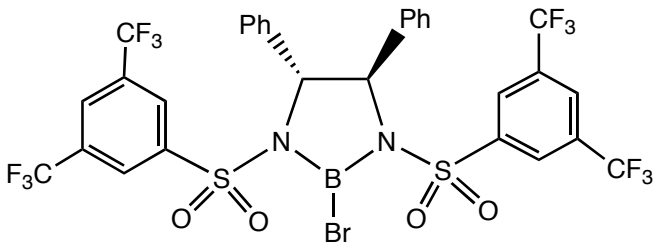
Keck Allylation:



R_1	R_2	ee(%)
C_6H_5	H	95%
C_6H_5	CH_3	91%
c-C_6H_{11}	H	94%
c-C_6H_{11}	CH_3	84%

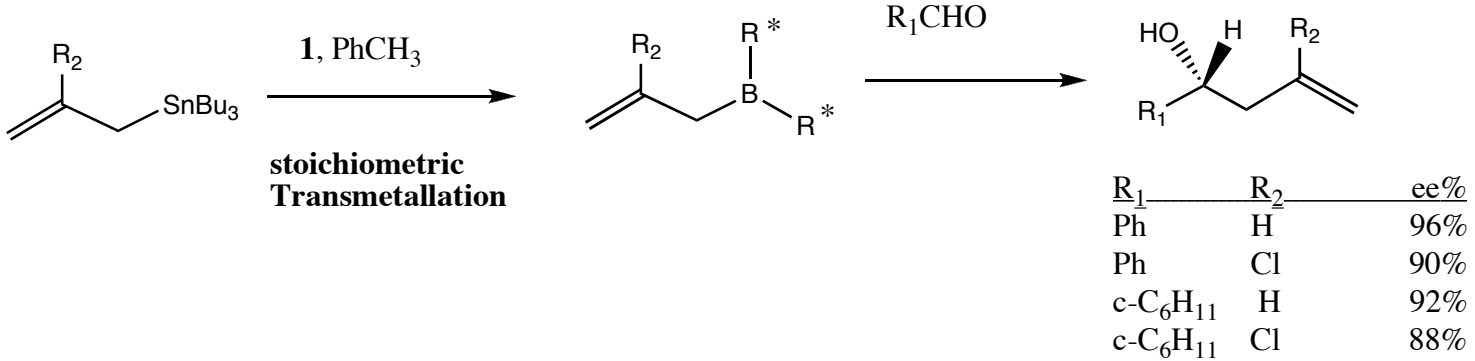
JACS, **1993**, 8467

Corey Enantioselective Allylation using a Chiral Controller

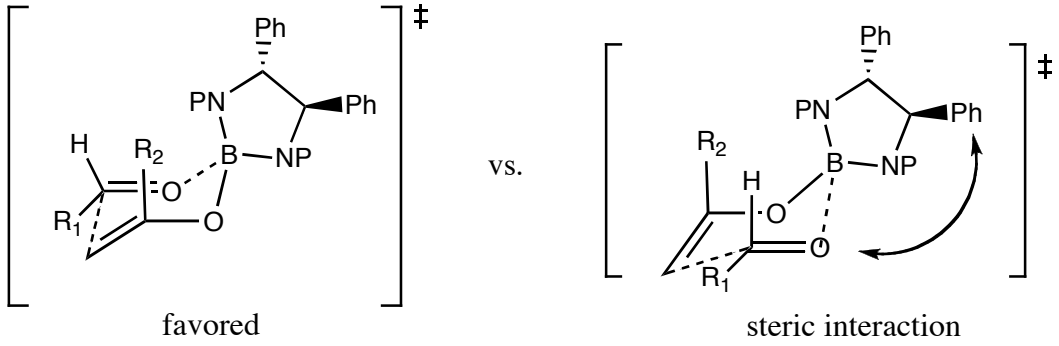


TL, **1990**, 3715

1



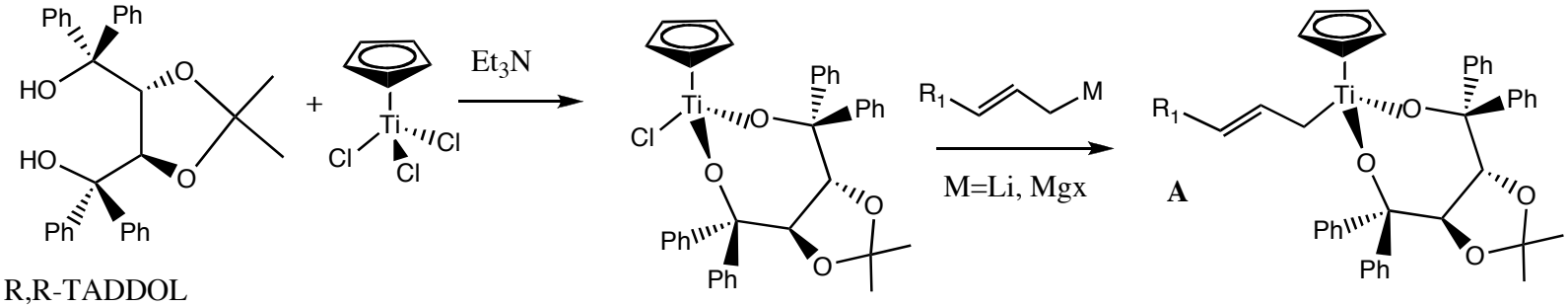
R_1	R_2	ee%
Ph	H	96%
Ph	Cl	90%
c-C_6H_{11}	H	92%
c-C_6H_{11}	Cl	88%



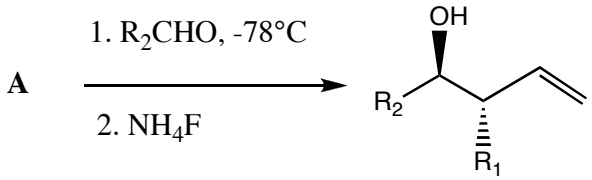
favored steric interaction

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

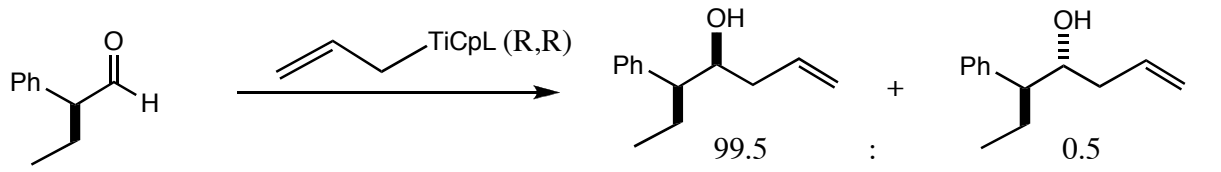


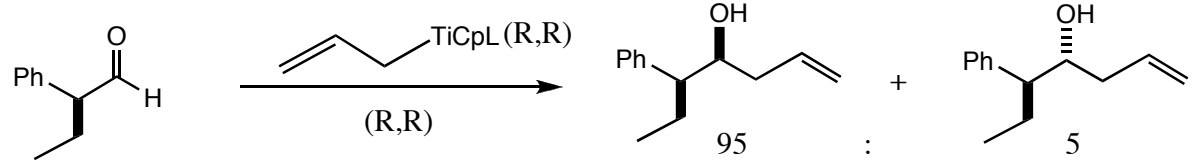
anti

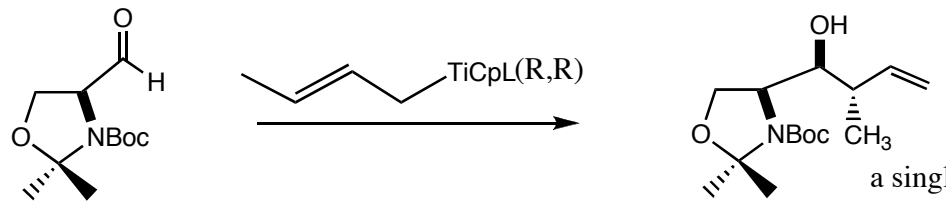
R_1	R_2	ee%	de%
H	Ph	95	
CH_3	Ph	98	97
$(CH_3)_3Si$	Ph	98	98
CH_3	$CH_3(CH_2)_8$	98	98

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

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







JACS, **1992**, 2321.

a single diastereomer