Massachusetts Institute of Technology

Organic Chemistry 5.512

April 20, 2007
Prof. Rick L. Danheiser

Unit 5

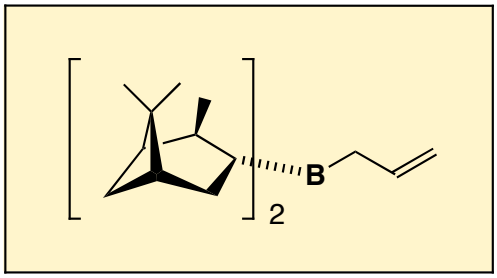
Stereocontrolled 1,2–Addition of Allylmetal Compounds to Carbonyl Groups

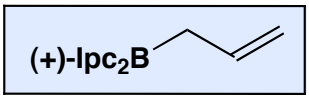
- ★ Substrate Control: Addition of Achiral Allylmetals to α–Chiral Aldehydes
- ★ Reagent Control: Addition of Chiral Allylmetals to Achiral Aldehydes
- ★ Reagent Control: Addition of Allylmetals to Achiral Aldehydes (w/ Chiral Lewis Acids)
- ★ Addition of Chiral Allylmetals to α–Chiral Aldehydes
- ★ Crotylmetal Additions: 3,4-Stereochemistry (Intrinsic Diastereoselection)
- ★ Crotymetal Additions to α–Chiral Aldehydes

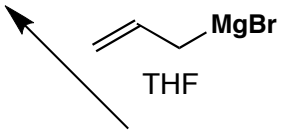
★ Reagent Control: Addition of Chiral Allylmetals to Achiral Aldehydes

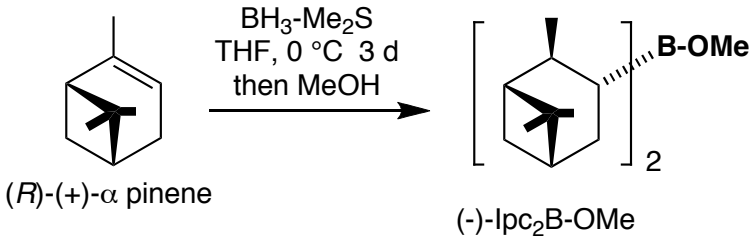
Allylboron Compounds

H. C. Brown
1912-2004









(*R*)-(+)-α pinene

(-)-Ipc$_2$B-OMe

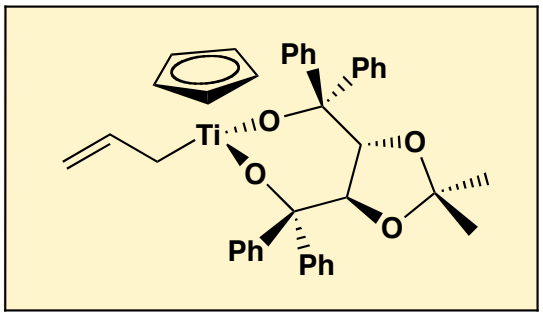
Allyltitanium Compounds

Reviews:

"Synthesis and Reactivity of Allyltitanium Derivatives" Szymoniak and Moise, C. In *Titanium and Zirconium in Organic Synthesis*, Marek, I., Ed.; Wiley-VCH, 2002, pp 451-474

"Chiral Titanium Complexes for Enantioselective Addition of Nucleophiles to Carbonyl Groups" Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807

"In the Arena of Enantioselective Synthesis, Titanium Complexes Wear the Laurel Wreath" Ramon, D. J.; Yus, M. *Chem. Rev.* **2006**, *106*, 2126

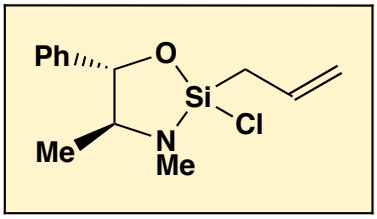


(R,R)-(TADDOL)CpTi

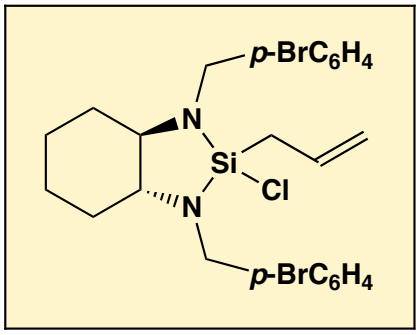
Dieter Seebach

TADDOL Ligands

Allylsilicon Compounds



J. L. Leighton

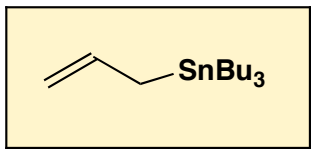


See "Highly Diastereo- and Enantioselective Reagents for Aldehyde Crotylation" Hackman, B. M.; Lombardi, P. J.; Leighton, J. L. *Org. Lett.* **2004**, *6*, 4375 and references cited therein

"Origins of Stereoselectivity in Strain-Release Allylations" Zhang, X.; Houk, K. N.; Leighton, J. L. *Angew. Chem. Int. Ed.* **2005,** *44,* 938

★ Reagent Control: Addition of Allylmetals to Achiral Aldehydes (w/ Chiral Lewis Acids)

Allylstannanes



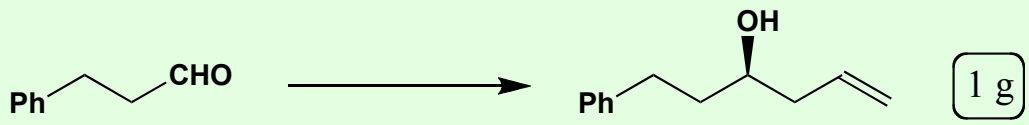
Keck, G. E.; Krishnamurthy *Org. Synth.* **1998,** *75*, 12

Review: J. A. Marshall *Chem. Rev.* **1991**, *91*, 31

Useful recent **review:** "BINOL: A Versatile Chiral Reagent" Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857

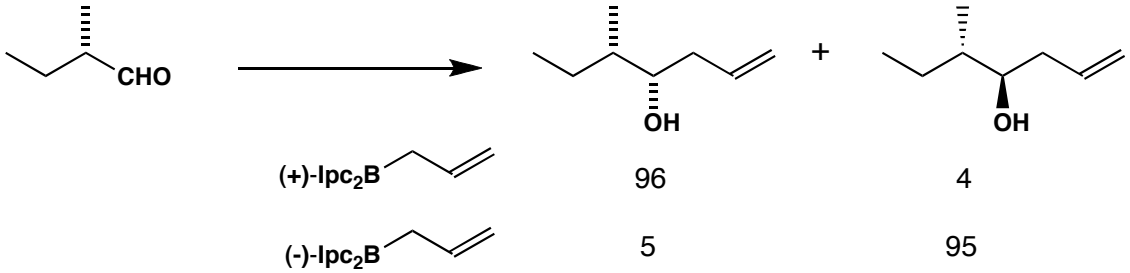
Gary E. Keck

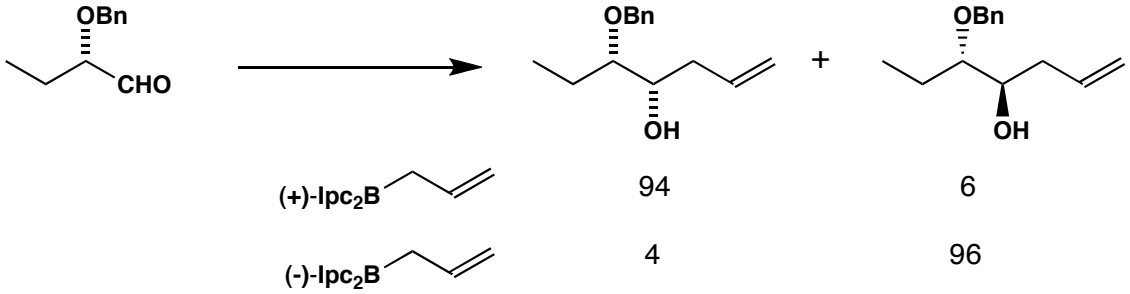
Allylmetal Showdown



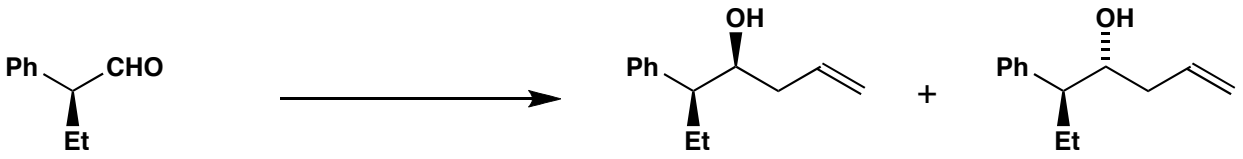
Method	Cost	Selectivity	Preparation (steps)
Roush	$5	80:20	2 (Storable)
Carriera (only non-enolizable)	$14	80:20	0
Brown	$14	98:2	1 (*in situ*)
Leighton (pseudoephedrine)	$20	94:6	1 (Storable)
Keck	$19	98:2	0
Duthaler	$414	97:3	2 (Storable)

★ **Addition of Chiral Allylmetals to α–Chiral Aldehydes**
(Double Asymmetric Synthesis)

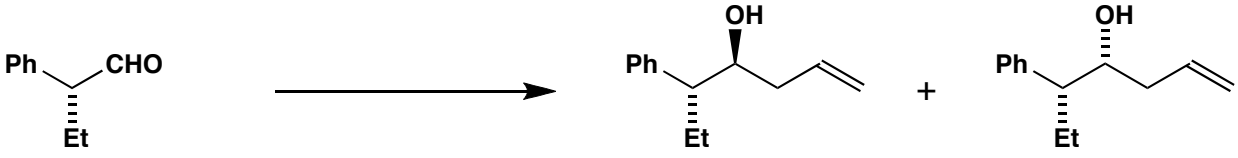




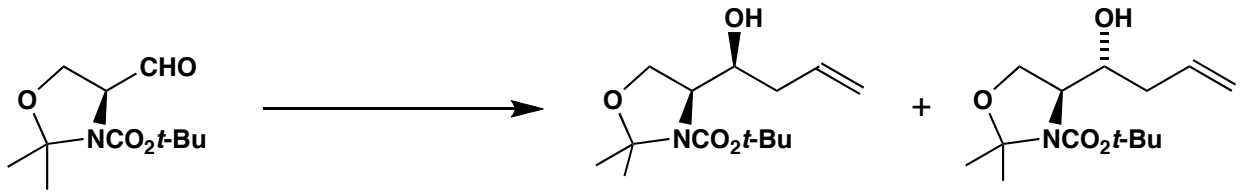
★ Addition of Chiral Allylmetals to α–Chiral Aldehydes
(Double Asymmetric Synthesis)



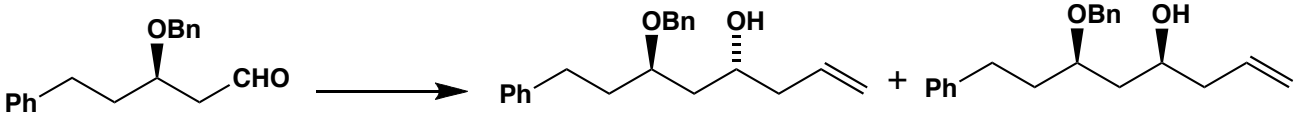
(R,R)-(TADDOL)CpTi	99.5	0.5
(+)-Ipc$_2$B	97	3

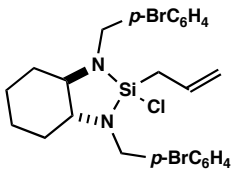


(R,R)-(TADDOL)CpTi	95	5
(+)-Ipc$_2$B	67	33



(*i*-PrO)$_2$CpTi		37	63
(R,R)-(TADDOL)CpTi	93%	98	2
(S,S)-(TADDOL)CpTi	95%	0.5	99.5





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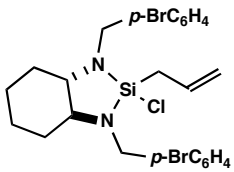

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