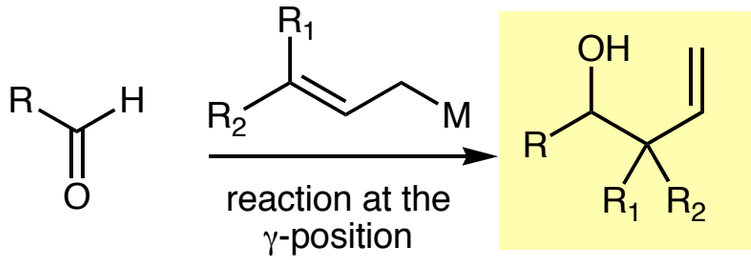
Allylmetals: Useful Reagents for Nucleophilic Addition Reactions

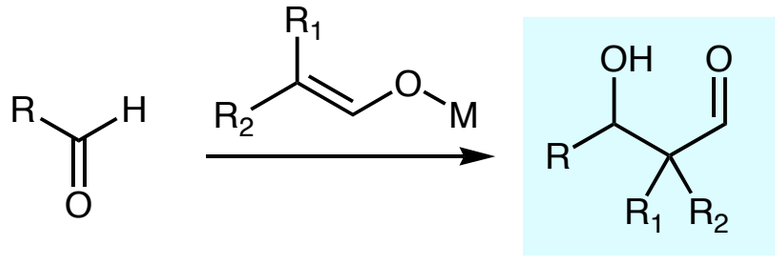
Why is this reaction so useful?

ALLYL METAL REACTION



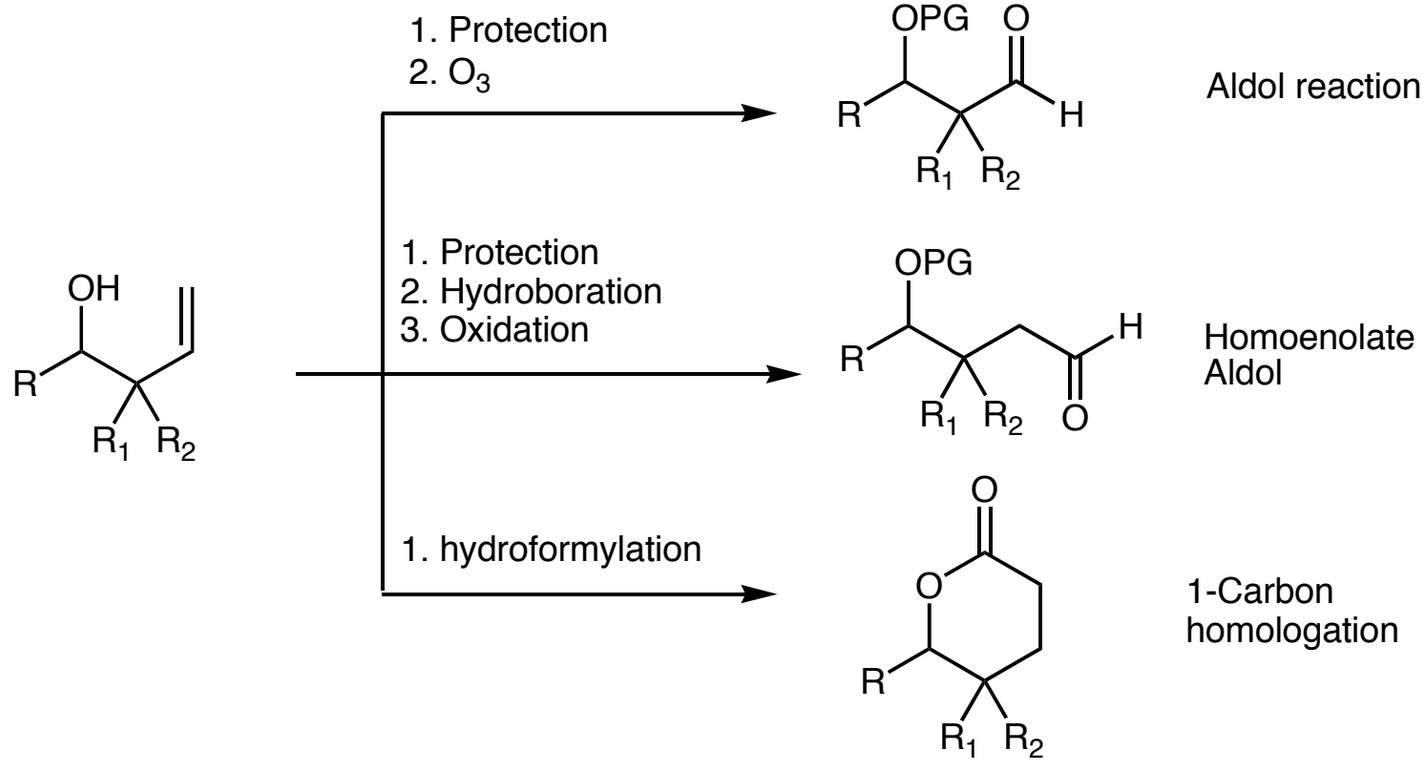
EQUIVALENT TO

ALDOL REACTION



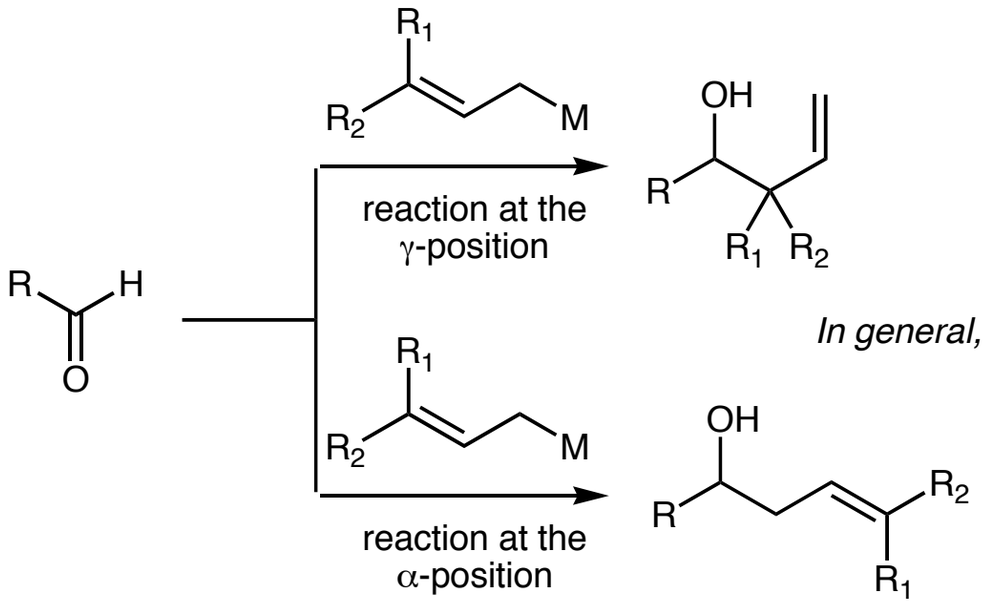
Up to 2 stereogenic center and a stereodefined olefin can be created.

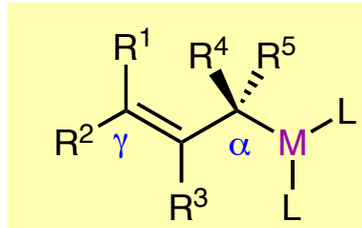
Advantage: Resulting olefin can easily be further functionalized



Allylmetal Chemistry: Background

A. Reaction can take place at the α- or at the γ-position.





In general, we will be interested in metal that are γ-selective.

B. Nature of the metal (M).

Many metals have been used. **The most widely used are in bold.**

Li, Na, **K,** **Mg,** Ba, **Zn,** Cd, **B,** Al, **In,** **Si,** Ge, **Sn,** Pb, As, Sb, Bi,

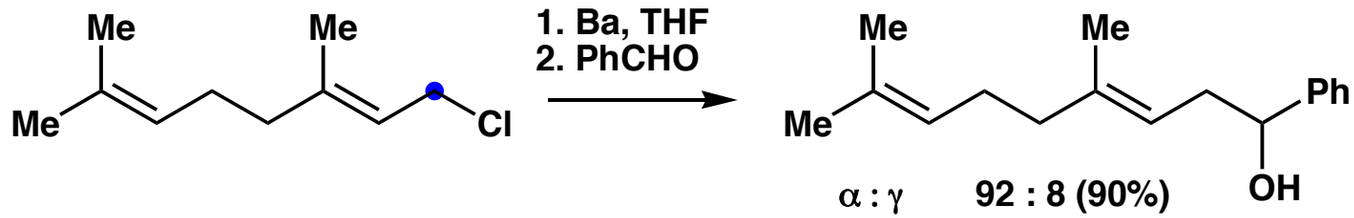
Te, Ce, La, Nb, Sm, Yb, **Ti,** Zr, **Cr,** Mo, Mn, Cu, Fe, Co, Ni.

C. Stereochemical Issues

1. **Stereochemistry of the olefin.**
2. **Presence of a stereogenic center at the α-position.**
3. **Presence of chiral ligands on the metal (M).**
4. **Reaction catalyzed by a chiral Lewis acid.**

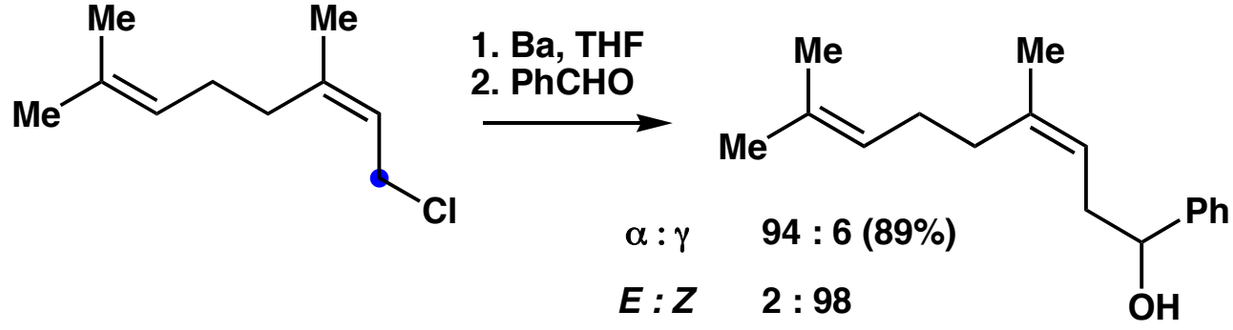
ALLYL BARIUM: α-selective reagents

H. Yamamoto *J. Am. Chem. Soc.* **1991**, *113*, 8955-8956 (allylation of carbonyl)
H. Yamamoto *J. Org. Chem.* **1992**, *57*, 6386-6387 (homocoupling of allyl halide)
H. Yamamoto *Synlett* **1992**, 593-594. (carboxylation of allyl barium)



α : γ 92 : 8 (90%)

E : Z 98 : 2



α : γ 94 : 6 (89%)

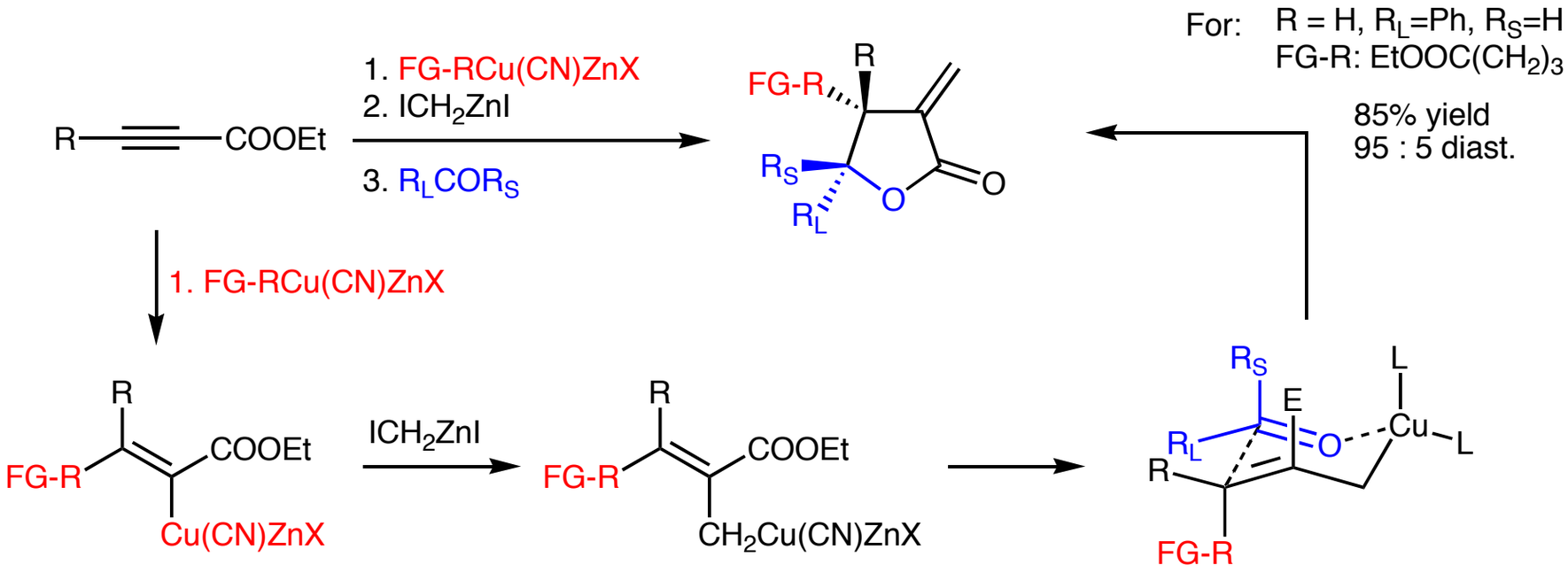
E : Z 2 : 98

ALLYL ZINC

Not use that much in stereoselective synthesis

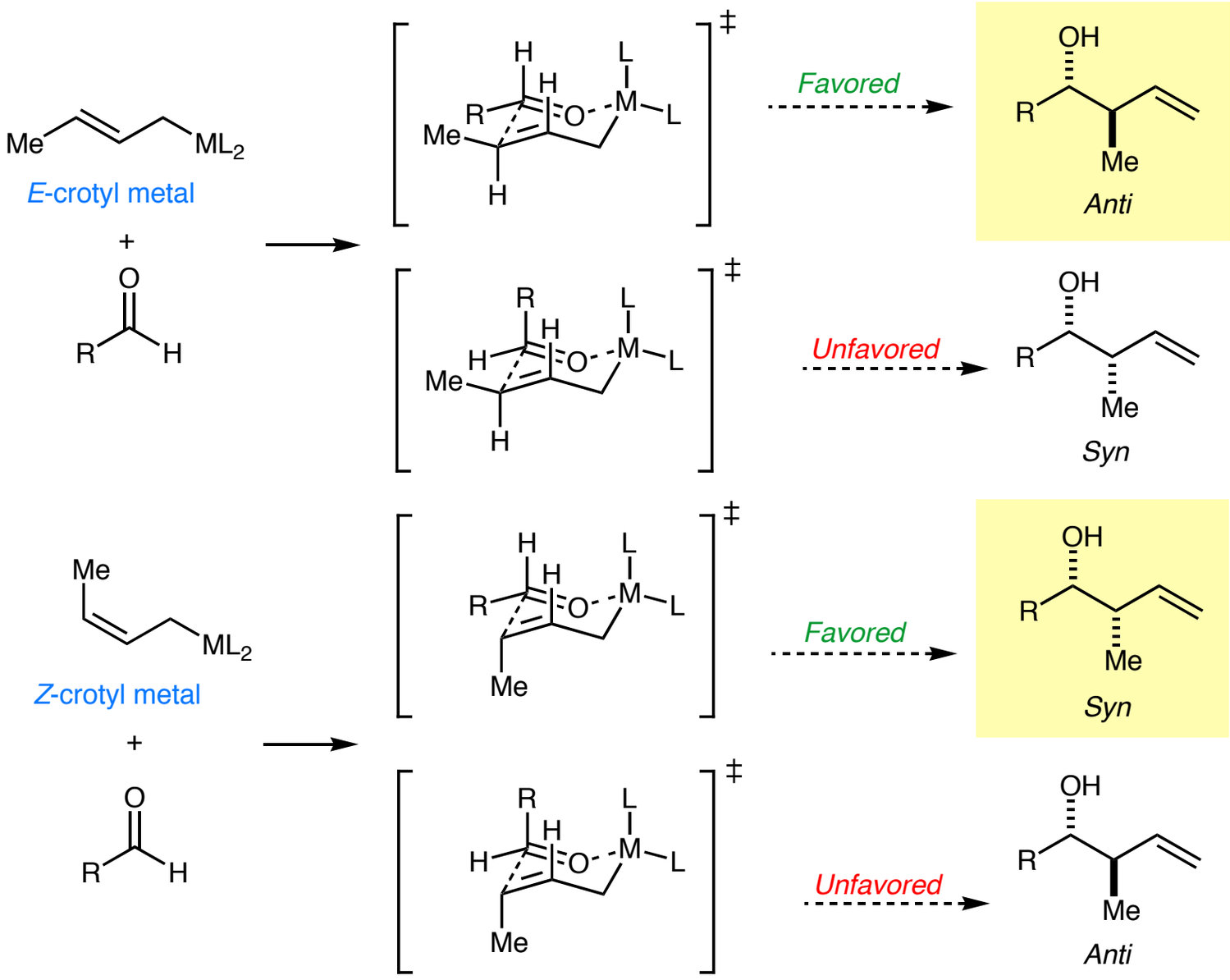
Interesting example:

Knochel, P. *J. Am. Chem. Soc.* **1992**, *114*, 7579-7581.



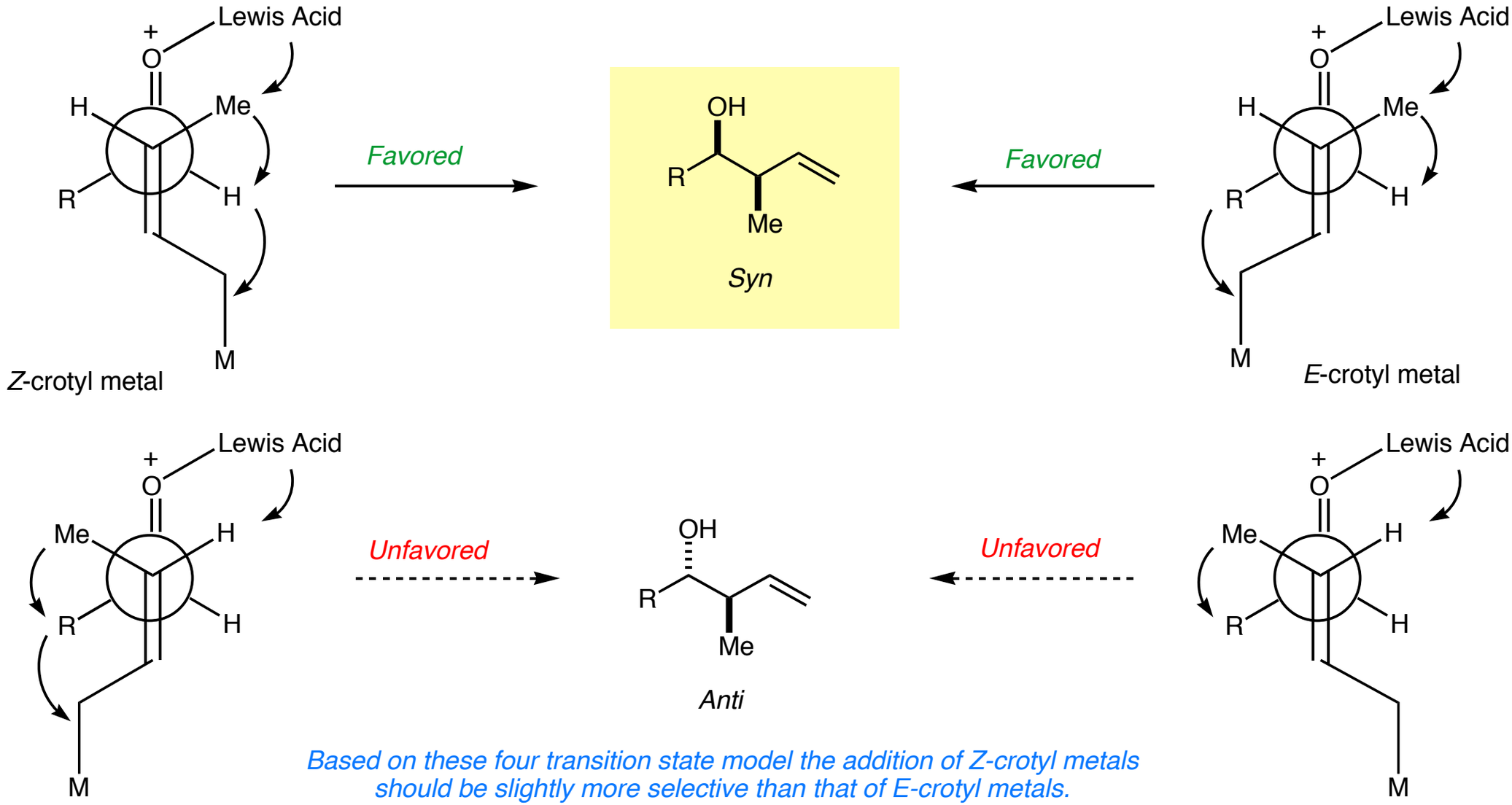
Other examples: See Table II (Yamamoto's review).

a. CYCLIC (CLOSED) TRANSITION STATE: The E/Z ratio of the reagent is important



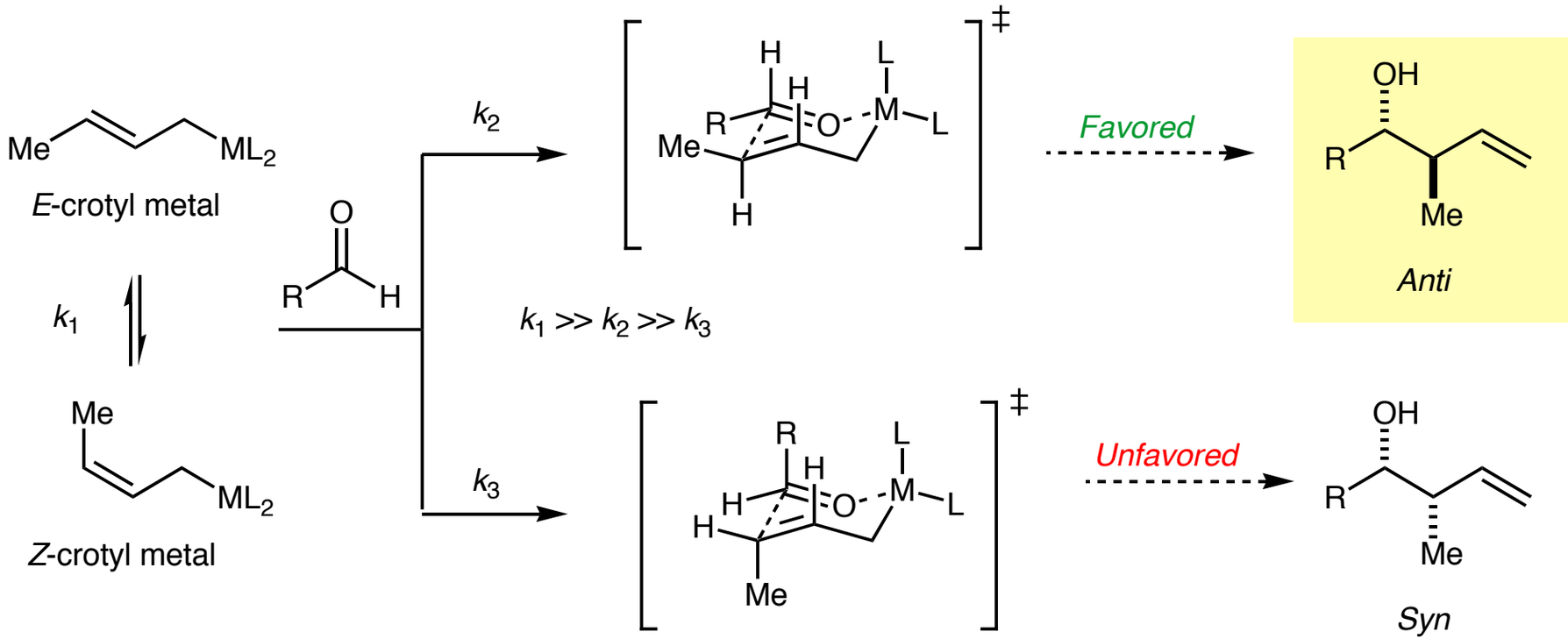
b. OPEN TRANSITION STATE

The E/Z ratio of the reagent has almost no effect on the diastereoselectivity.
Presence of a Lewis acid is required.



Based on these four transition state model the addition of Z-crotyl metals should be slightly more selective than that of E-crotyl metals.

c. CYCLIC TRANSITION STATE (Rapid equilibration between *E*- and *Z*-croylmetal)

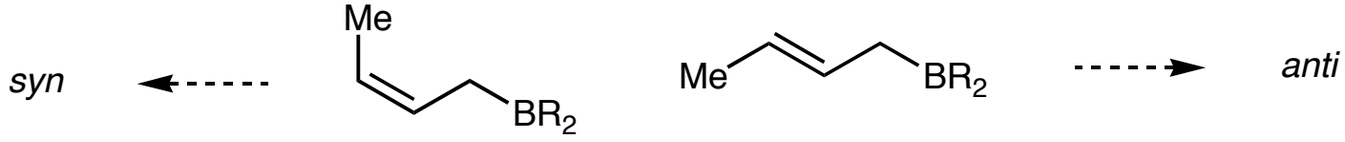


Allylboron Reagents

Four classes of reactions will be discussed:

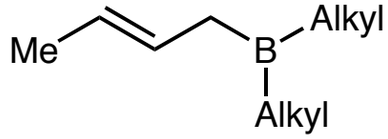
1. Achiral reagent + achiral aldehyde
2. Achiral reagent + chiral aldehyde
3. Chiral reagent + achiral aldehyde
4. Chiral reagent + chiral aldehyde (Double asymmetric induction)

Reagents of this type react through a cyclic transition state (type a):



R = Alkyl or OR'

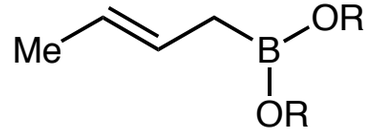
Z- and *E*-crotyldialkylboranes



More reactive
Less stable
(reactions must be
run at low temp. to avoid
E-*Z* interconversion)

vs

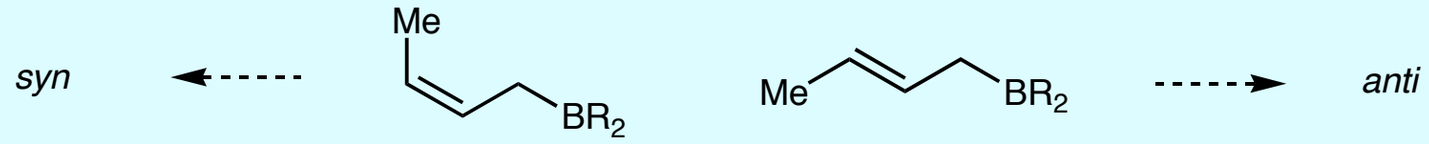
E-crotylboronates



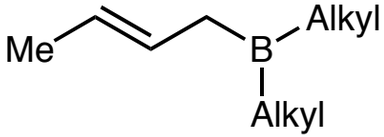
Less reactive
E- and *Z*-isomer are
more stable.

Allyl- and Crotylboron Chiral Reagents

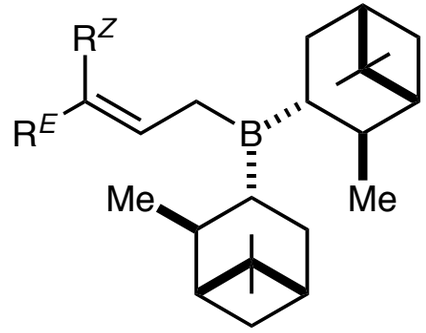
Reagents of this type react through a cyclic transition state (type a):

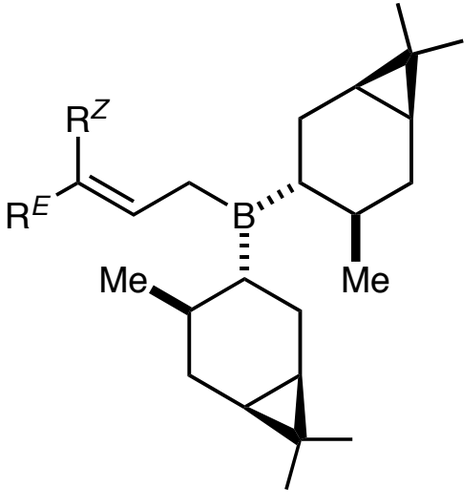


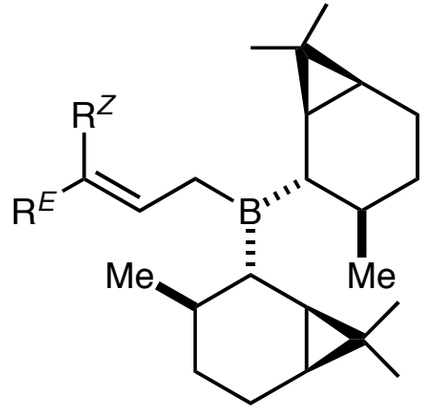
Z- and *E*-crotyldialkylboranes



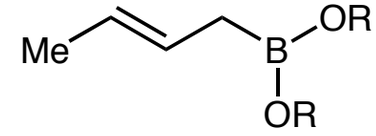
More reactive
Less stable
(reactions must be run at low temp. to avoid E-Z interconversion)



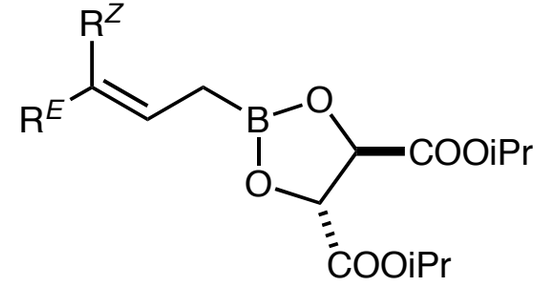


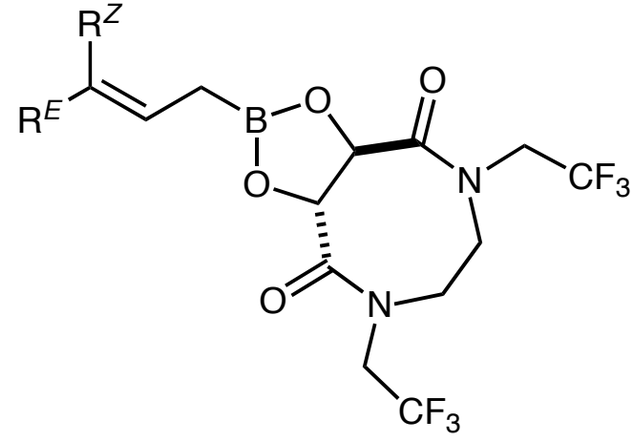


Z- and *E*-crotylboronates

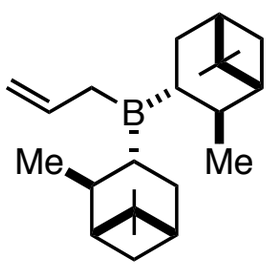


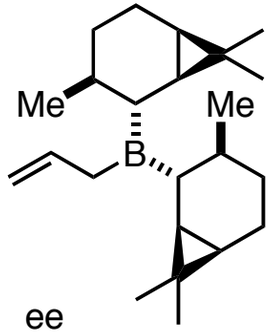
Less reactive
E- and Z-isomer are more stable.

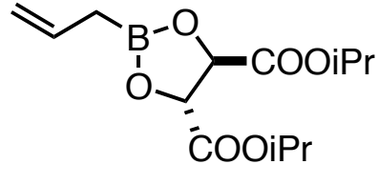




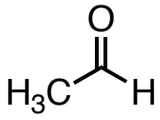
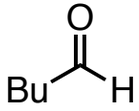
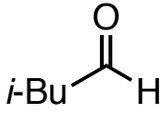
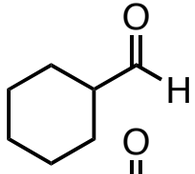
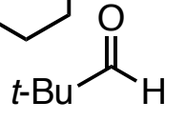
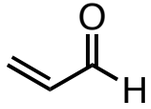
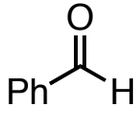
Allylation Reagents: Scope with Achiral Aldehydes





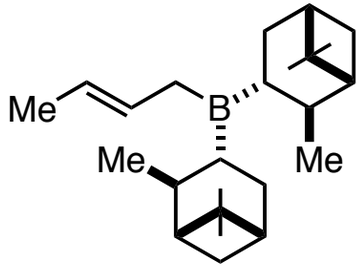


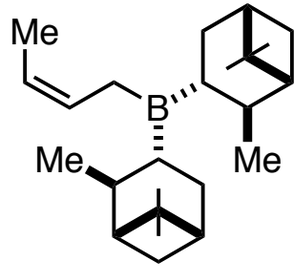
-100 ˚C

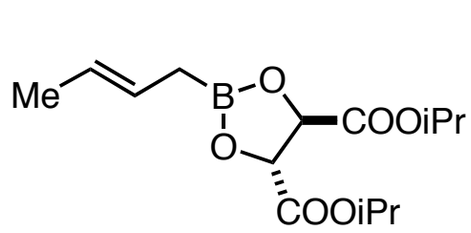
	ee	ee	ee
	92 (≥99)	≥99	---
	86 (96)	≥99	79 (94)
	88 (96)	≥99	---
	---	---	87 (97)
	83 (≥99)	≥99	82 (96)
	92 (96)	≥99	---
	94 (96)	≥99	71 (85)

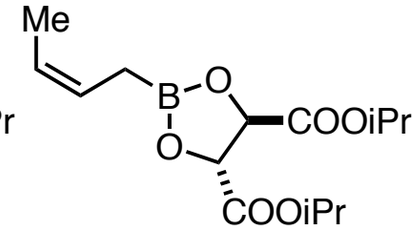
⇨ Catalytic methods are becoming more popular and more practical

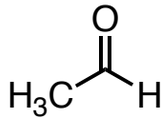
Allylation Reagents: Scope with Achiral Aldehydes





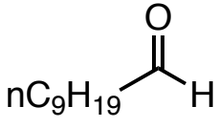






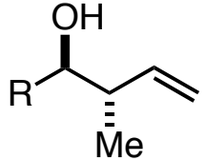
95% es, 99% ds

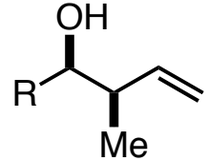
95% es, 99% ds

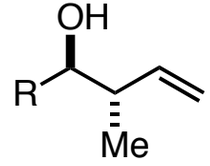


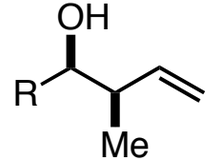
88% ee, 99% ds

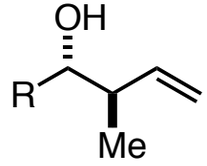
82% ee, 97% ds

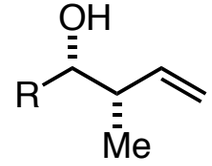


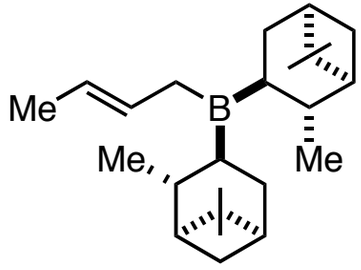


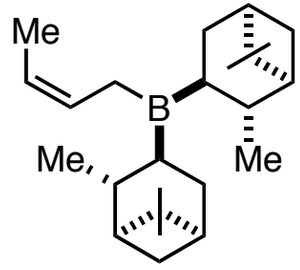




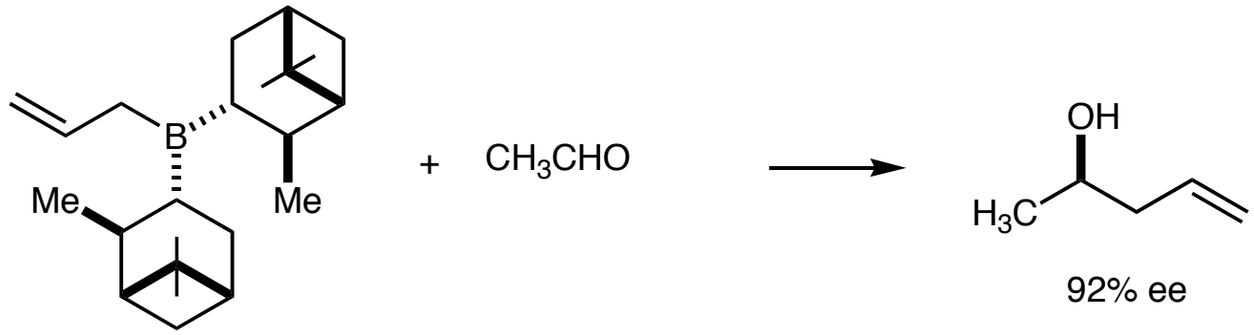








BROWN'S CHIRAL BORANE REAGENTS



Molecular mechanics model of Brown's reaction: Gennari, C.; Paterson, I. *J. Org. Chem.* 1993, *58*, 1711.

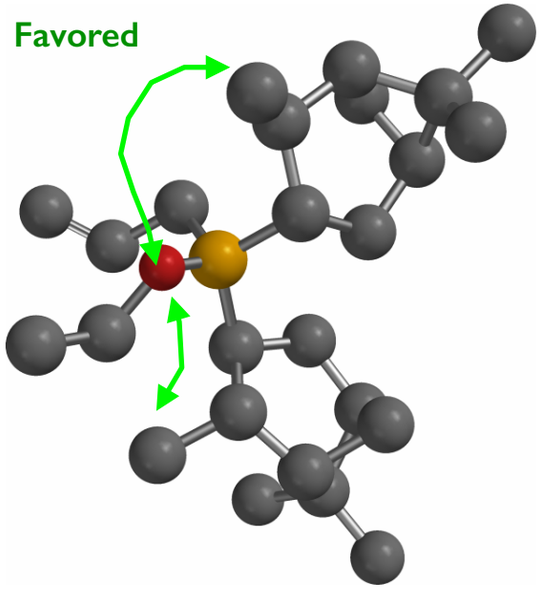
Key features:

- The relative conformation of the two isopinocampheyl groups is important. They have the same orientation in the two most stable models for si and re attack.

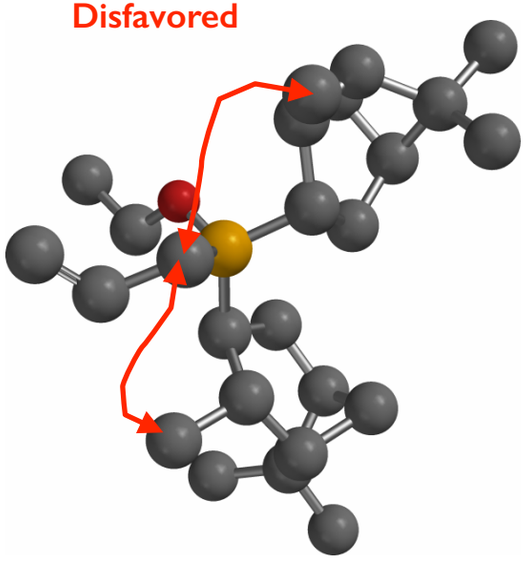
- In the most stable transition state model for si attack the methyl groups on the pinene ligands are directed toward the aldehyde proton whereas in the other model (re attack) these methyl groups are directed toward the CH allylic proton.

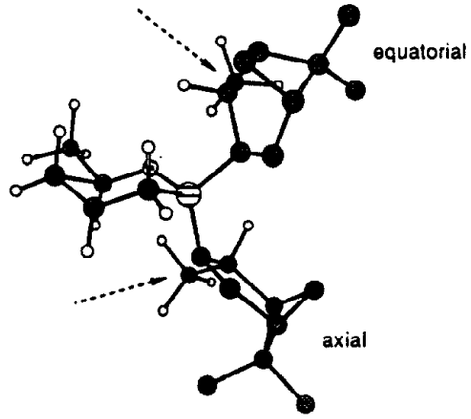
Transition State Models

Favored

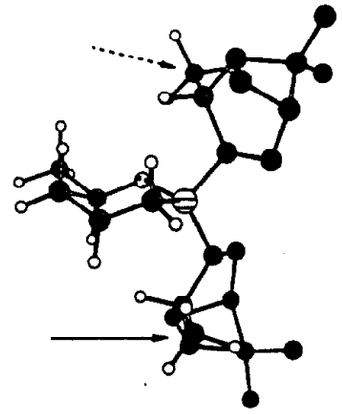


Disfavored



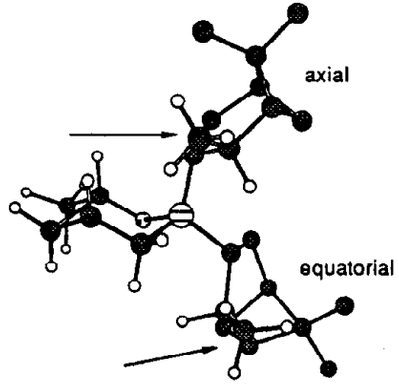


12 0.00 kcal mol^{-1}
C-B-C 118°

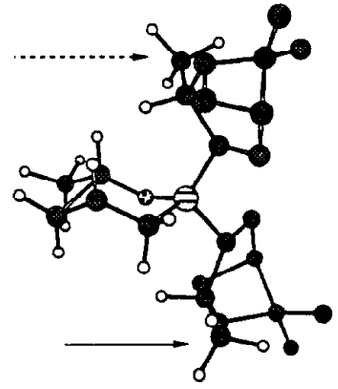


13 1.52 kcal mol^{-1}
C-B-C 111°

si-face attack

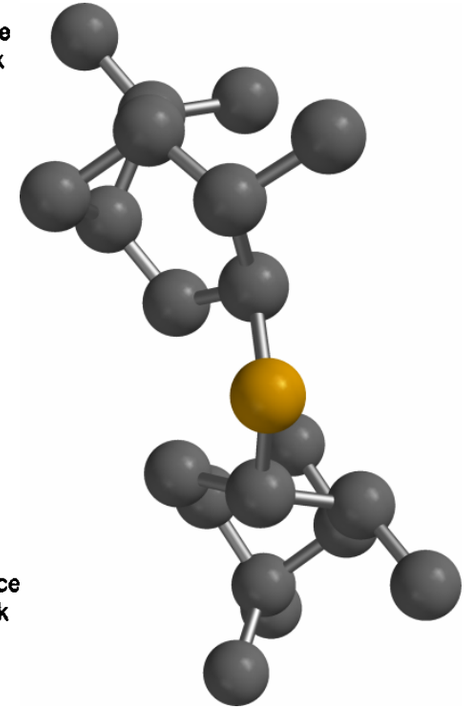


14 2.12 kcal mol^{-1}
C-B-C 118°



15 2.24 kcal mol^{-1}
C-B-C 109°

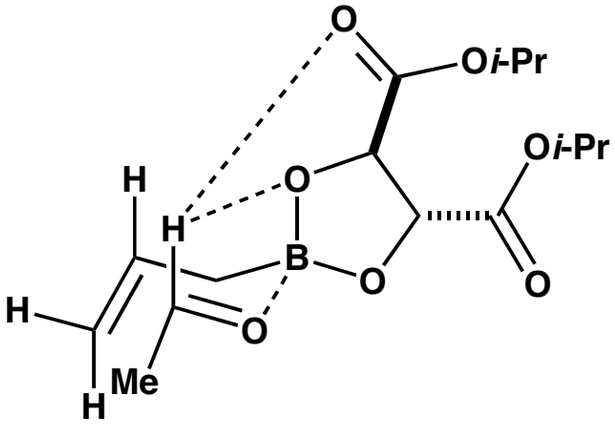
re-face attack

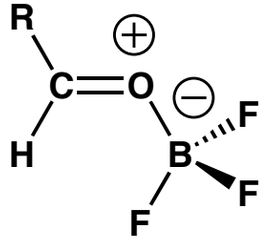


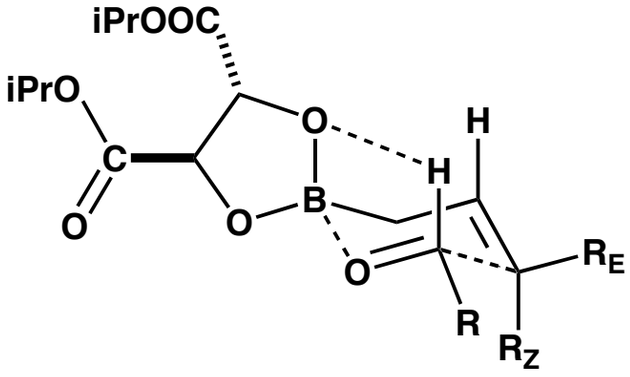
Roush's Allylation Reaction: Corey's and Roush's Proposals

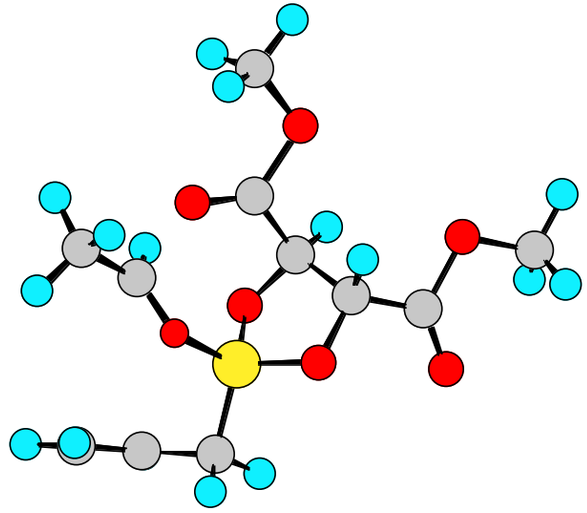
Corey, E. J.; Rohde, J. J. *Tetrahedron Lett.* **1997**, *38*, 37-40.

The following conformation appeared to be favored based upon a number of X-ray crystal structures:

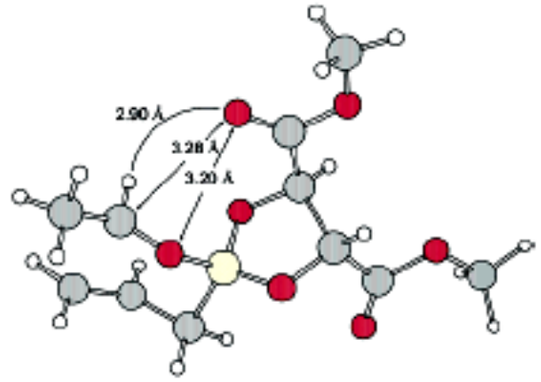




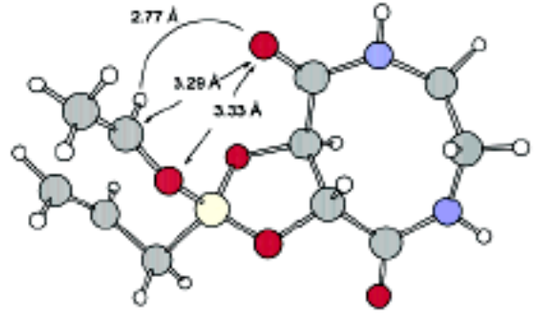




Gung, B. W.; Xue, X. W.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 10692-10697.



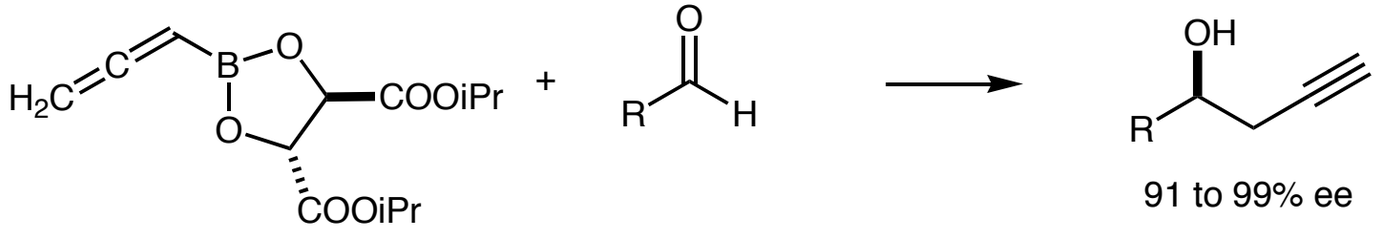
11a (0.0)



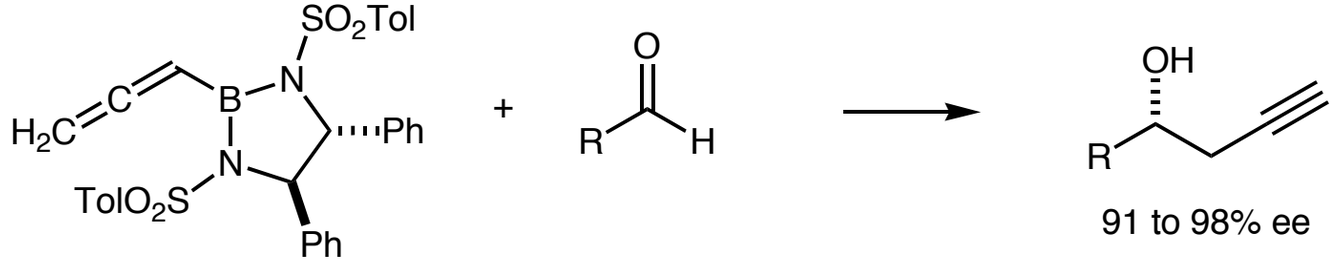
13 side view

ROUSH'S AUXILIARY:

Yamamoto, H. *J. Am. Chem. Soc.* **1986**, *108*, 483. *Tetrahedron Lett.* **1986**, 1175.

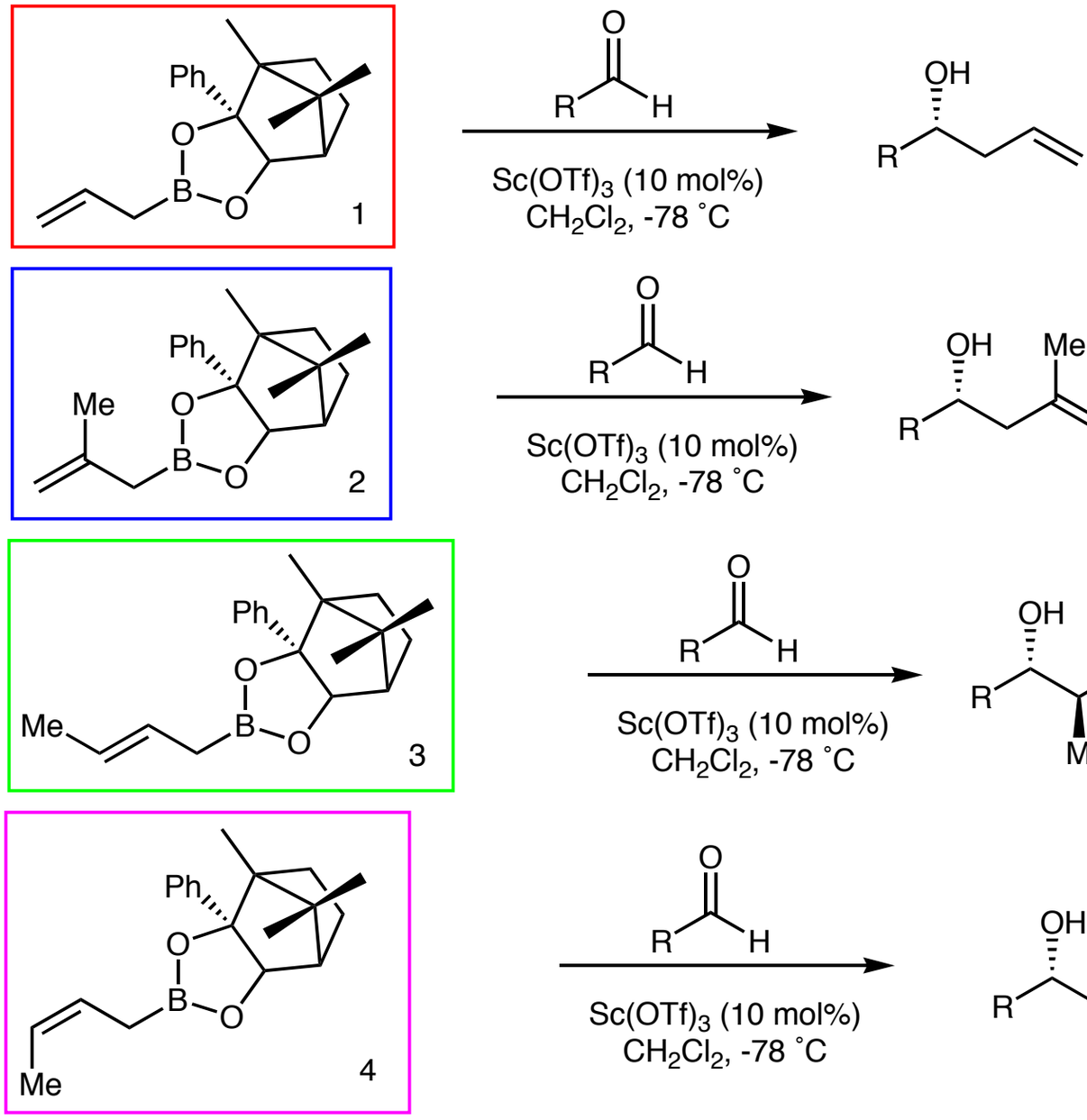


Corey, E. J. *J. Am. Chem. Soc.* **1990**, *112*, 878.



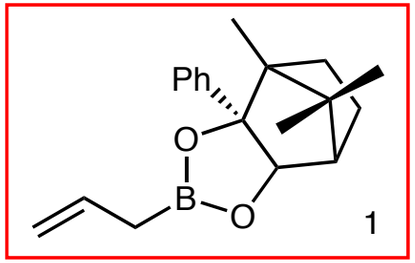
Allyl- and Crotylboronation of Aldehydes

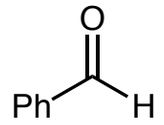
Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125,* 10160.



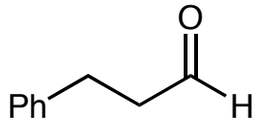
Allyl- and Crotylboronation of Aldehydes

Hall, D. G. *J. Am. Chem. Soc.* **2003,** *125,* 10160.

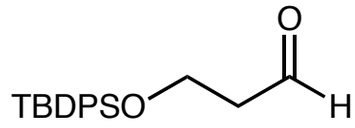




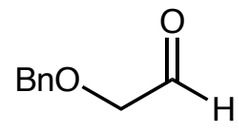
92% ee, 85%



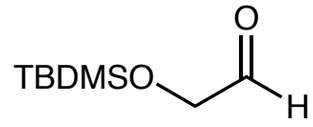
97% ee, 64%



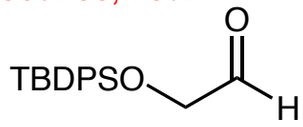
93% ee, 86%



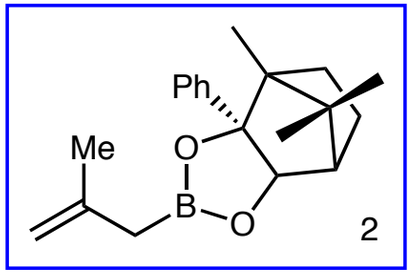
77% ee, 62%

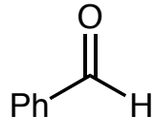


90% ee, 76%

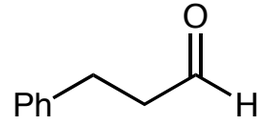


90% ee, 61%

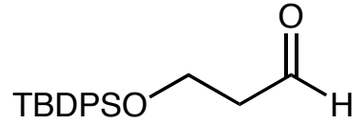




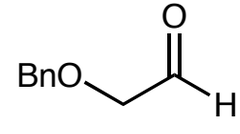
98% ee, 64%



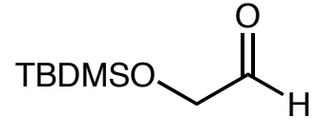
97% ee, 76%



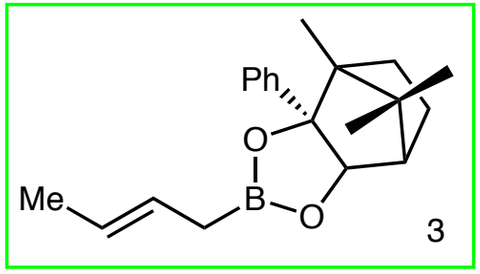
97% ee, 77%

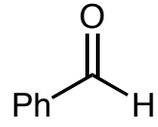


97% ee, 70%

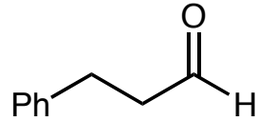


95% ee, 90%

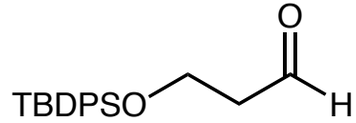




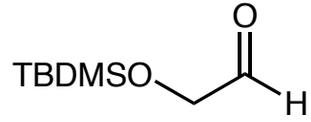
97% ee, 60%



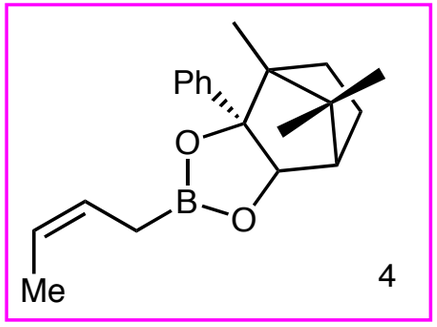
96% ee, 71%

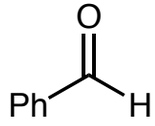


94% ee, 63%

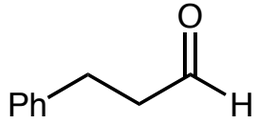


95% ee, 74%

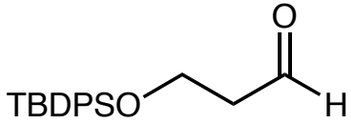




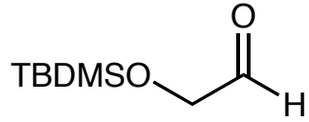
59% ee, 53%



96% ee, 52%

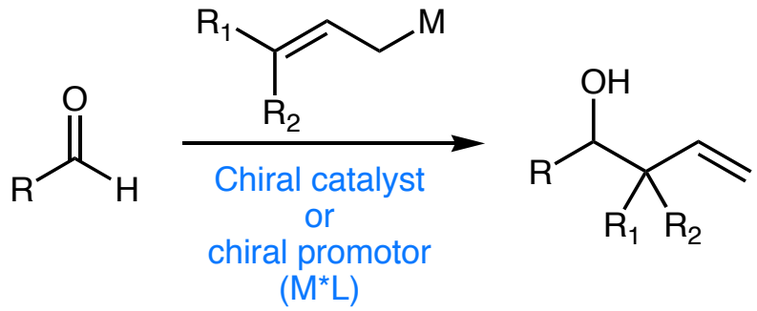


96% ee, 57%

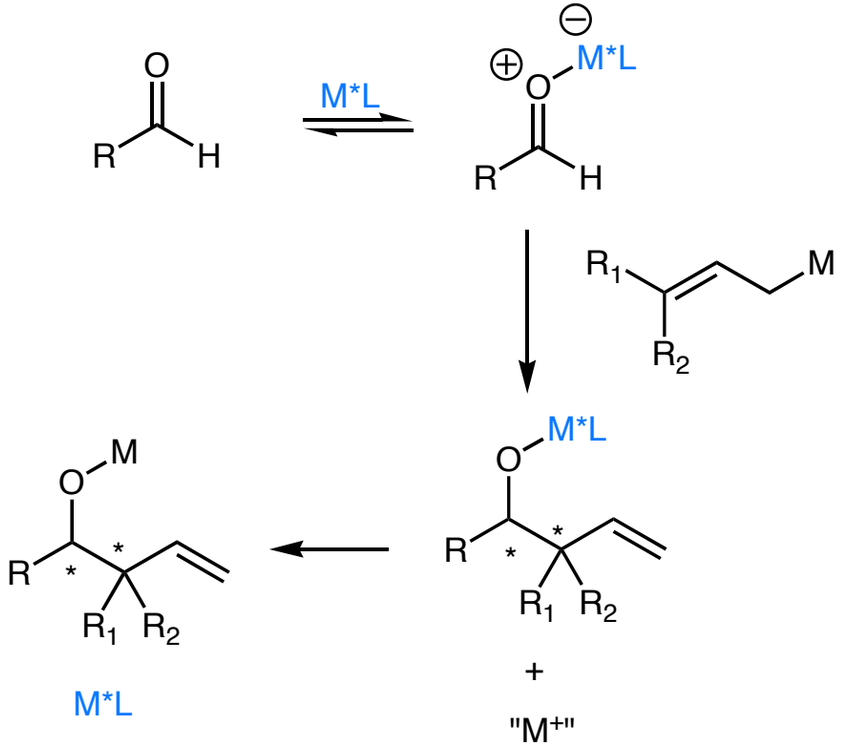


96% ee, 57%

General Mechanism for Asymmetric Catalysis

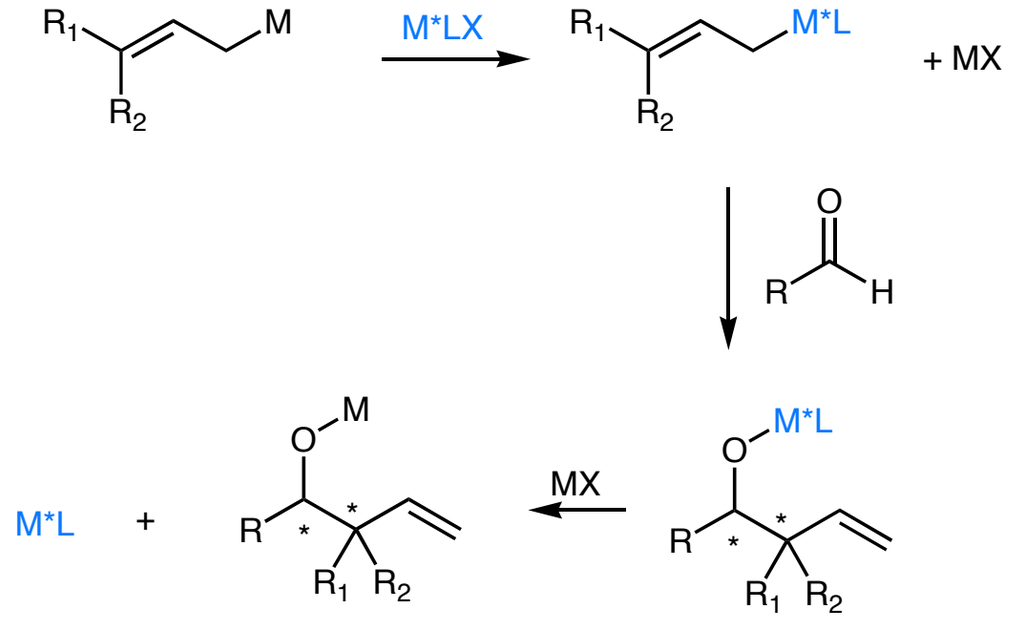


TYPE 1: Chiral catalyst acts as a Lewis Acid.



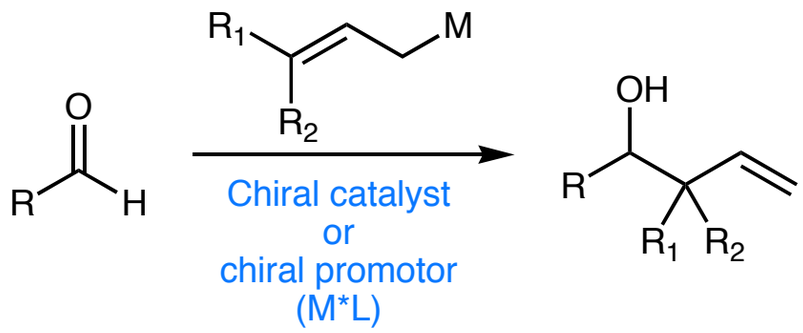
KEY STEP FOR CATALYSIS

TYPE 2: Transmetallation of the allyl reagent prior to the addition

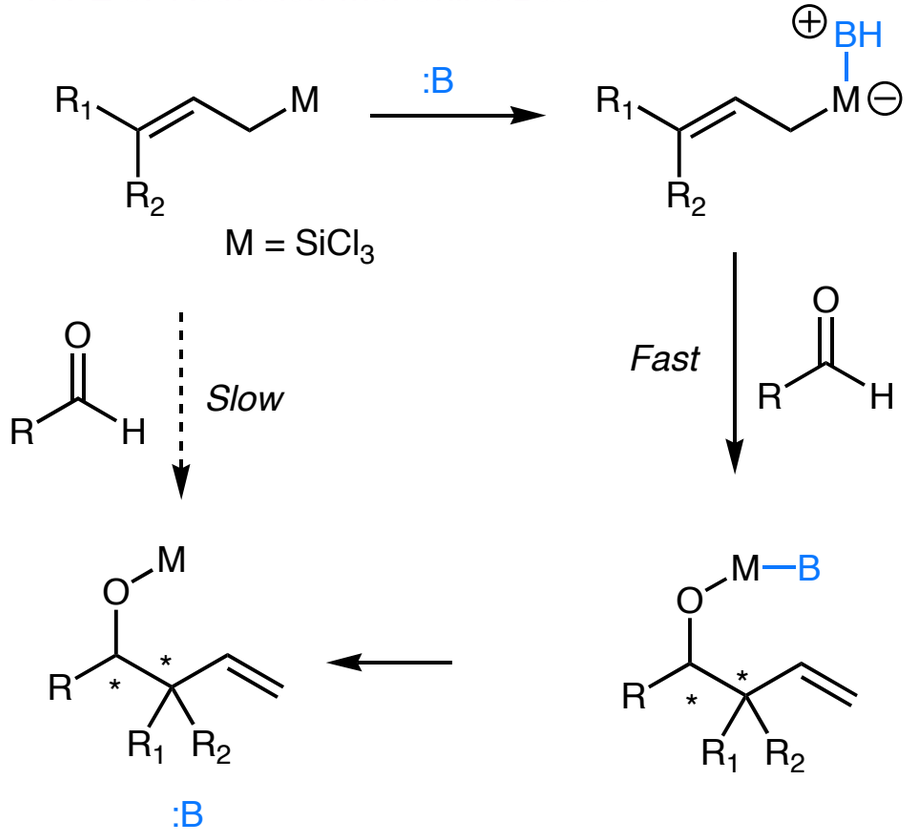


KEY STEP FOR CATALYSIS

General Mechanism for Asymmetric Catalysis

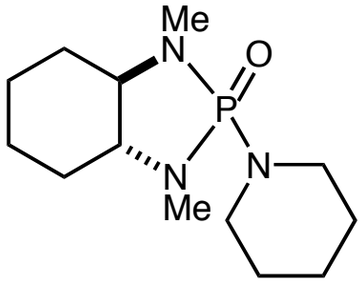


TYPE 3: Activation with Chiral Bases

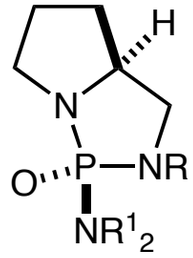


KEY STEP FOR CATALYSIS

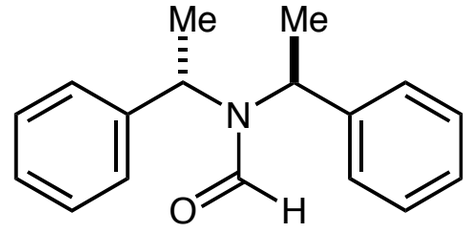
Chiral Lewis Bases for the Allylation of Aldehydes



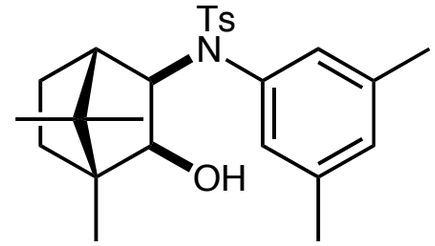
Denmark



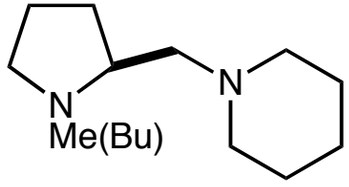
Iseki



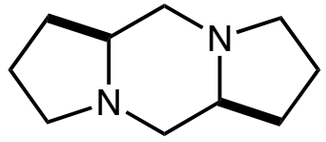
Iseki



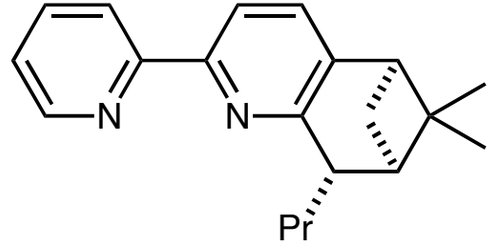
Hong



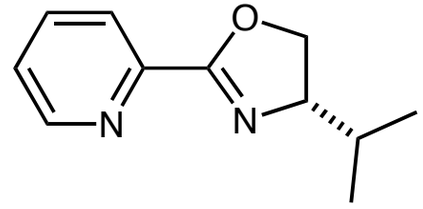
Mukaiyama, Kobayashi



Zadel



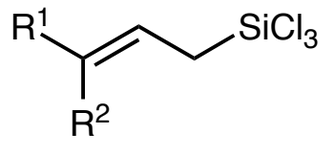
Kishi



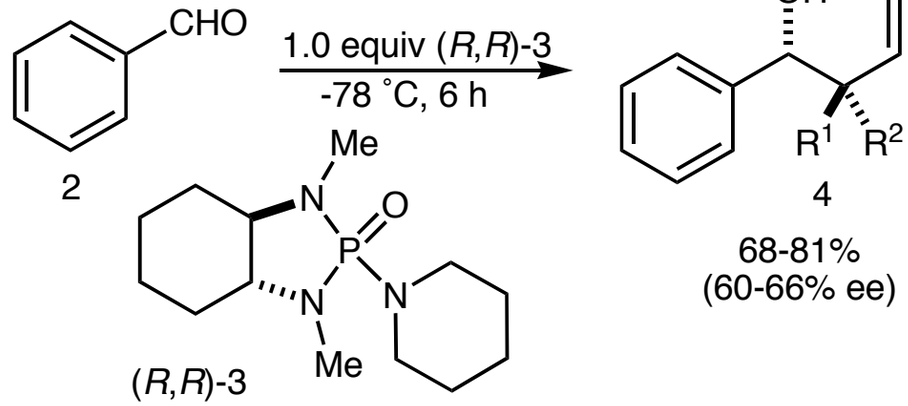
Barrett

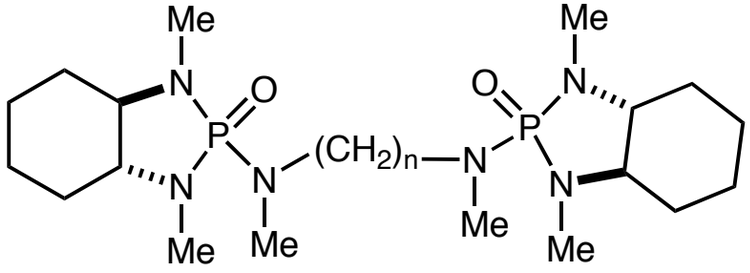
Allylmetal Chemistry: Acceleration by Chiral Lewis Bases

Denmark, Fu *JACS* **2000,** 12021

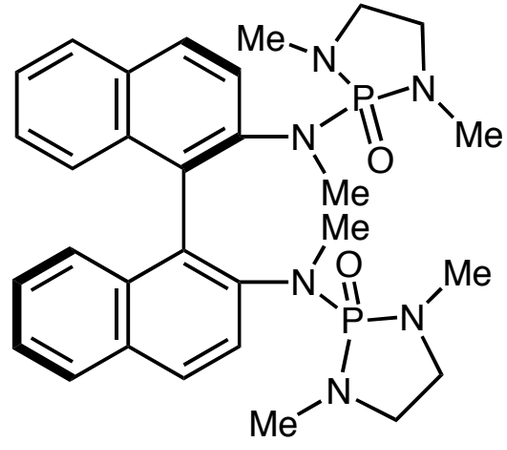


1a: $R^1 = R^2 = H$
1b: $R^1 = Me$, $R^2 = H$
1c: $R^1 = H$, $R^2 + Me$

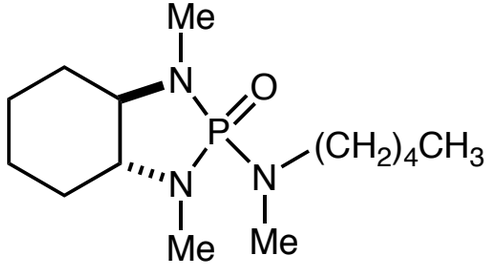




5a: n=2; 5b: n=3; 5c: n=4
5d: n=5; 5e: n=6



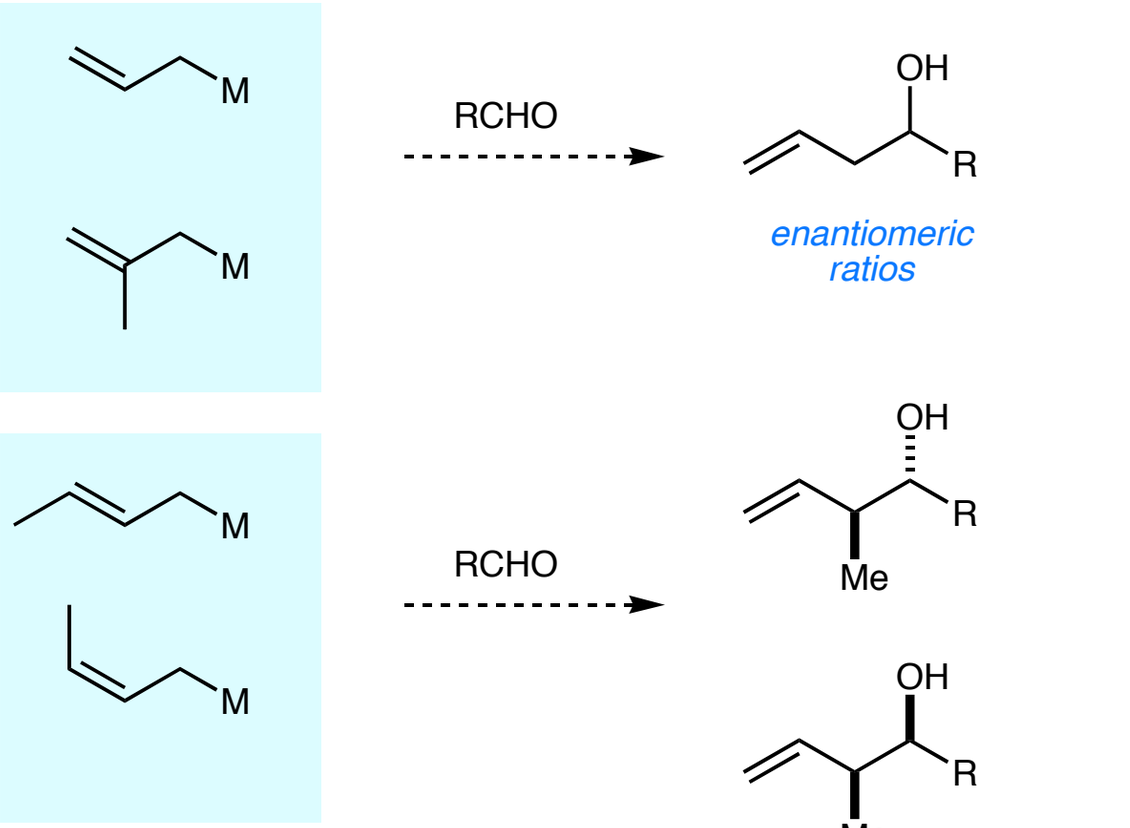
7



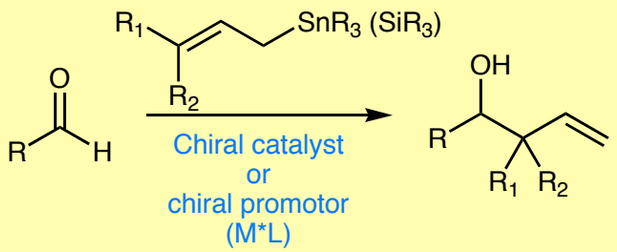
6

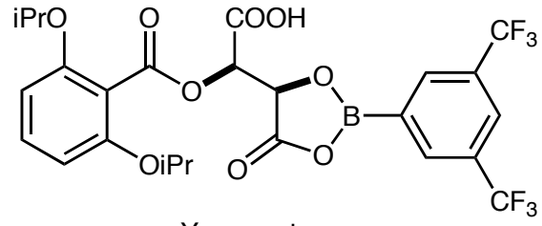
Lewis Acid-catalyzed Allylmetal Additions

M = SnR_3, SiR_3

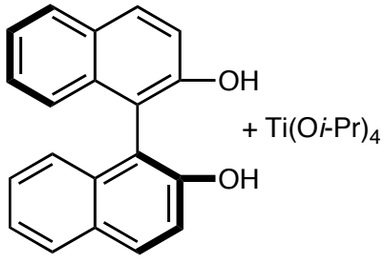


Chiral Lewis Acids Catalysts for Allylmetal Chemistry



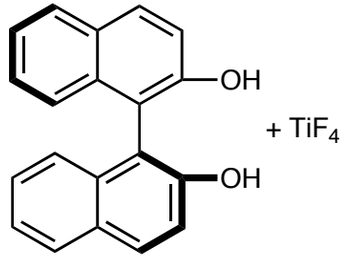


Yamamoto

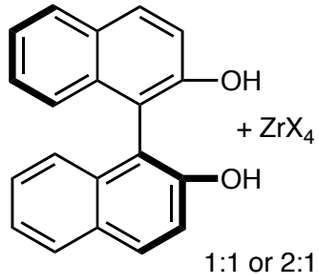


1:1 Keck (Faller, Wigand)

2:1 Keck, Brückner, Lipshutz

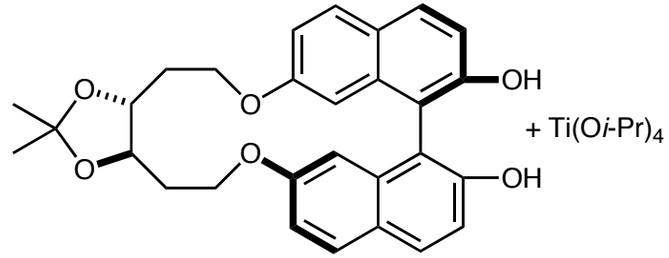


2:1 Carreira (Duthaler)

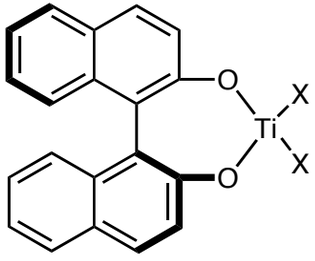


1:1 or 2:1

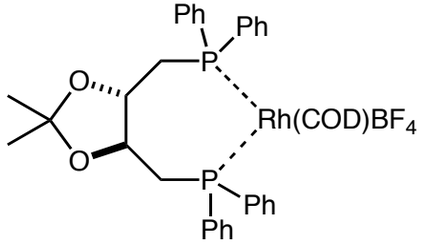
X = O*i*-Pr (Yu, Tagliavini)
X = Cl (Tagliavini)



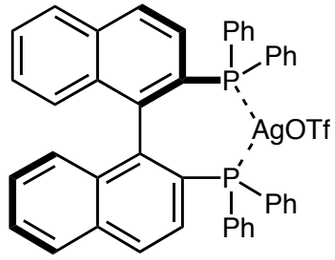
2:1 Lipshutz



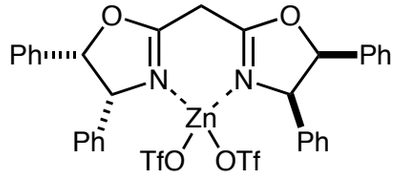
X = Cl, Tagliavini, Nakai
X = Br, Nakai



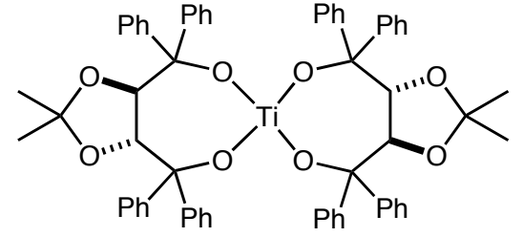
Nuss



Yamamoto

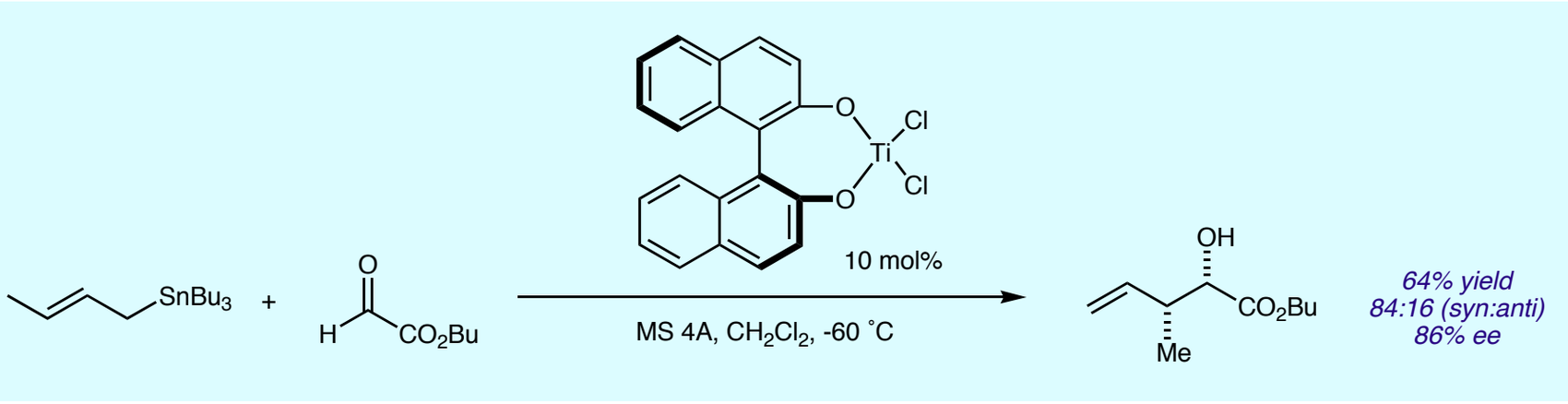


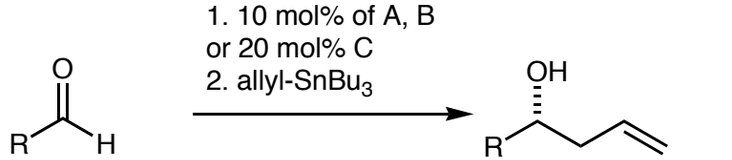
Tagliavini

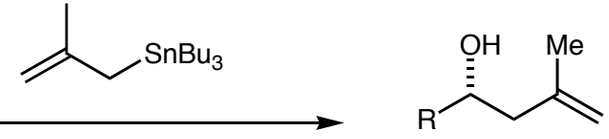


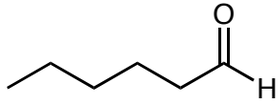
Seebach

Lewis Acid Catalyzed Tributylallyltin Addition: Major Breakthrough

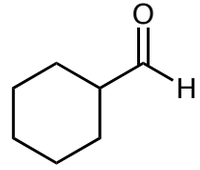




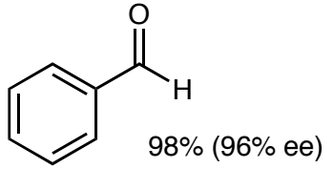




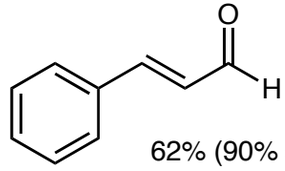
75% (98% ee)



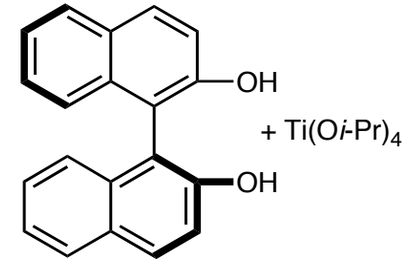
66% (94% ee)



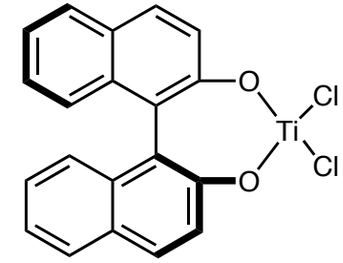
98% (96% ee)



62% (90% ee)



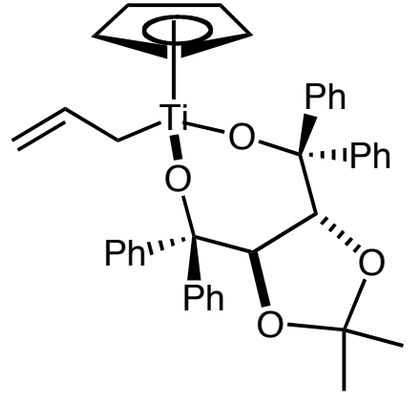
1:1 Keck (A)
2:1 Keck (B)

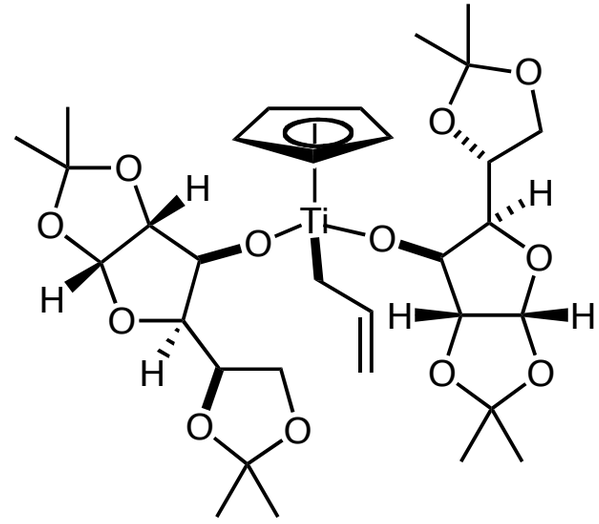


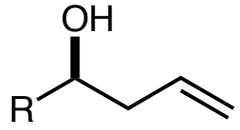
Tagliavini, Umani-Ronchi (C)

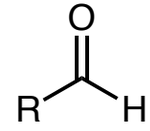
Allyl Metals: Chiral Titanium Reagents

References: Duthaler, R. O. *J. Am. Chem. Soc.* **1992**, *114*, 2321-2336.
Pure Appl. Chem. **1990**, *62*, 631.
Angew. Chem. Int. Ed. Engl. **1989**, *28*, 494.
Angew. Chem. Int. Ed. Engl. **1989**, *28*, 499.



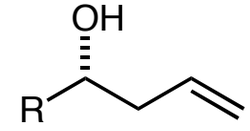






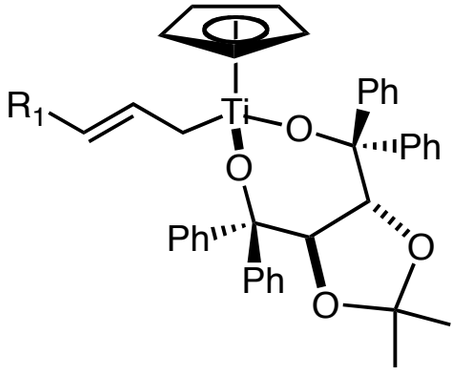
94-97% ee (63 - 94% yield)

Crotyl titanium: only *E*- isomer is available



85-94% ee

Allyl Metals: Chiral Titanium Reagents



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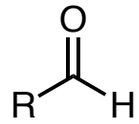
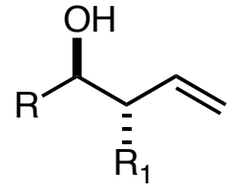
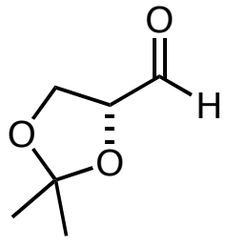
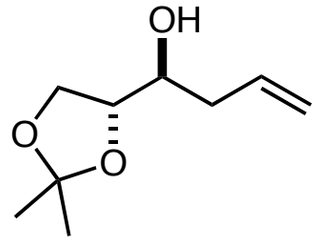




R_1 = Me, Ph, OEt, OPMB, TMS

ee: 86 to >99% de: >9 : 1





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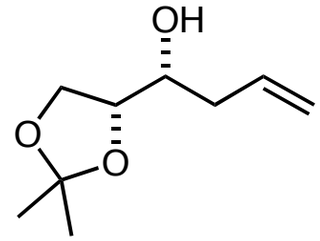
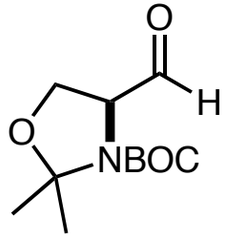
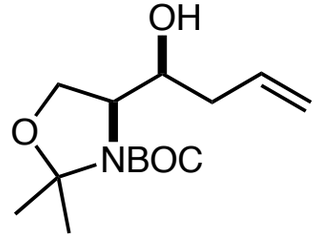


R,R	98 : 2
S,S	2 : 98





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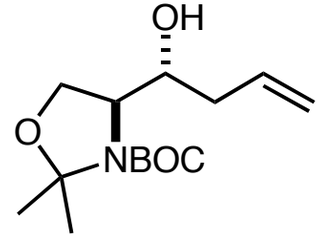
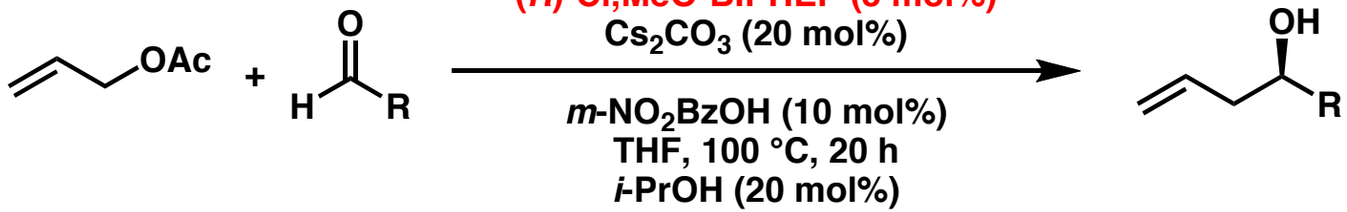


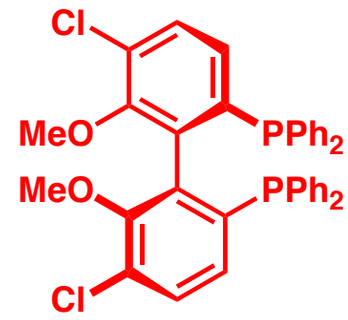
R,R	98 : 2
S,S	0.5 : 99.5

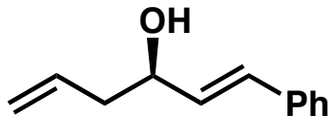
Diacetone glucose: 37 : 63
Allyl MgCl 55 : 45

Krische's Allylation Chemistry

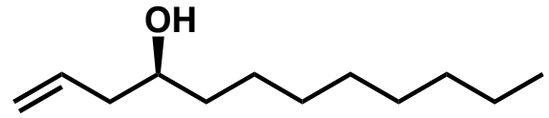
JACS 2008, 14891.



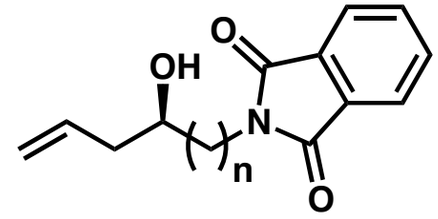




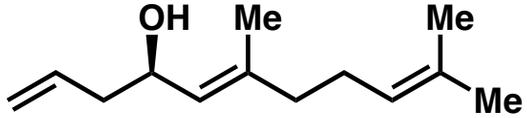
73% (94% ee)



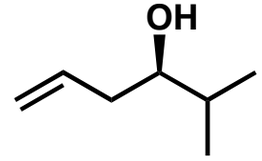
77% (97% ee)



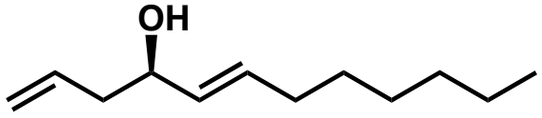
n = 1: 51% (97% ee)
n = 2: 61% (98% ee)



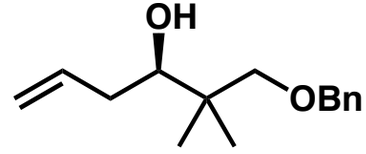
77% (96% ee)



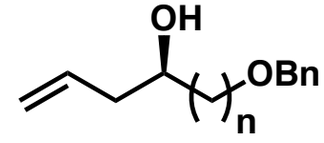
74% (95% ee)



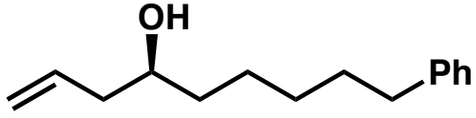
71% (93% ee)



81% (94% ee)



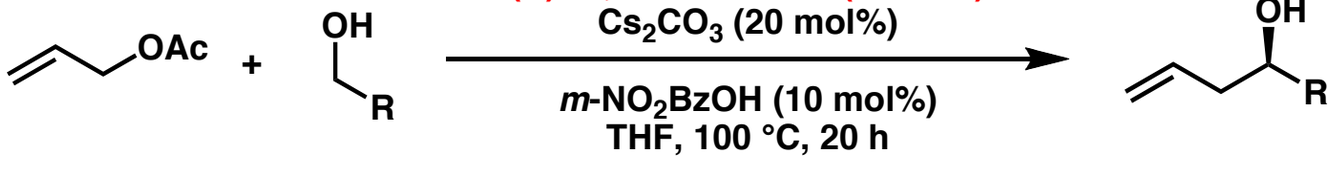
n = 1: 41% (92% ee)
n = 2: 45% (96% ee)
n = 3: 88% (97% ee)

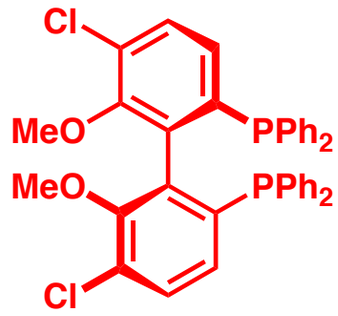


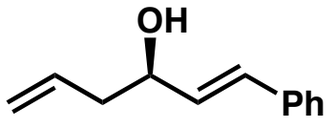
83% (96% ee)

Krische's Allylation Chemistry

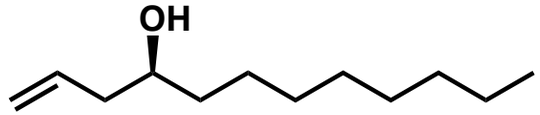
JACS 2008, 14891.



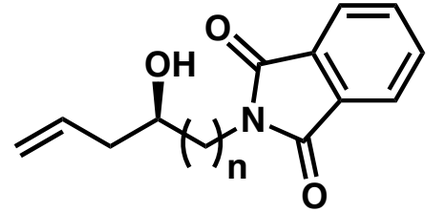




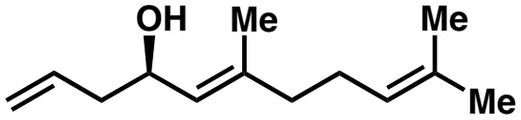
72% (91% ee)



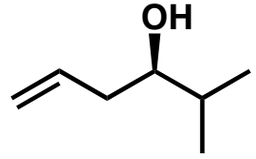
78% (95% ee)



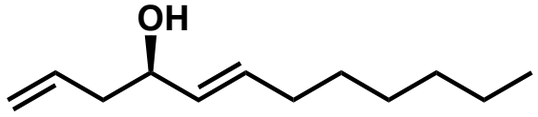
n = 1: 51% (88% ee)
n = 2: 83% (93% ee)



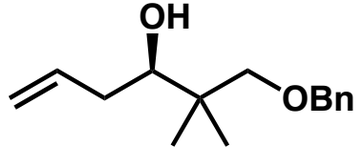
76% (86% ee)



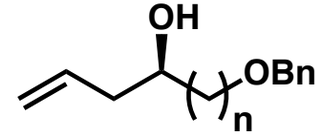
83% (94% ee)



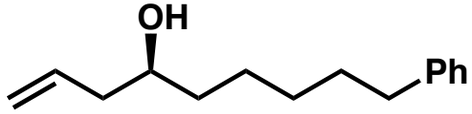
72% (91% ee)



63% (93% ee)

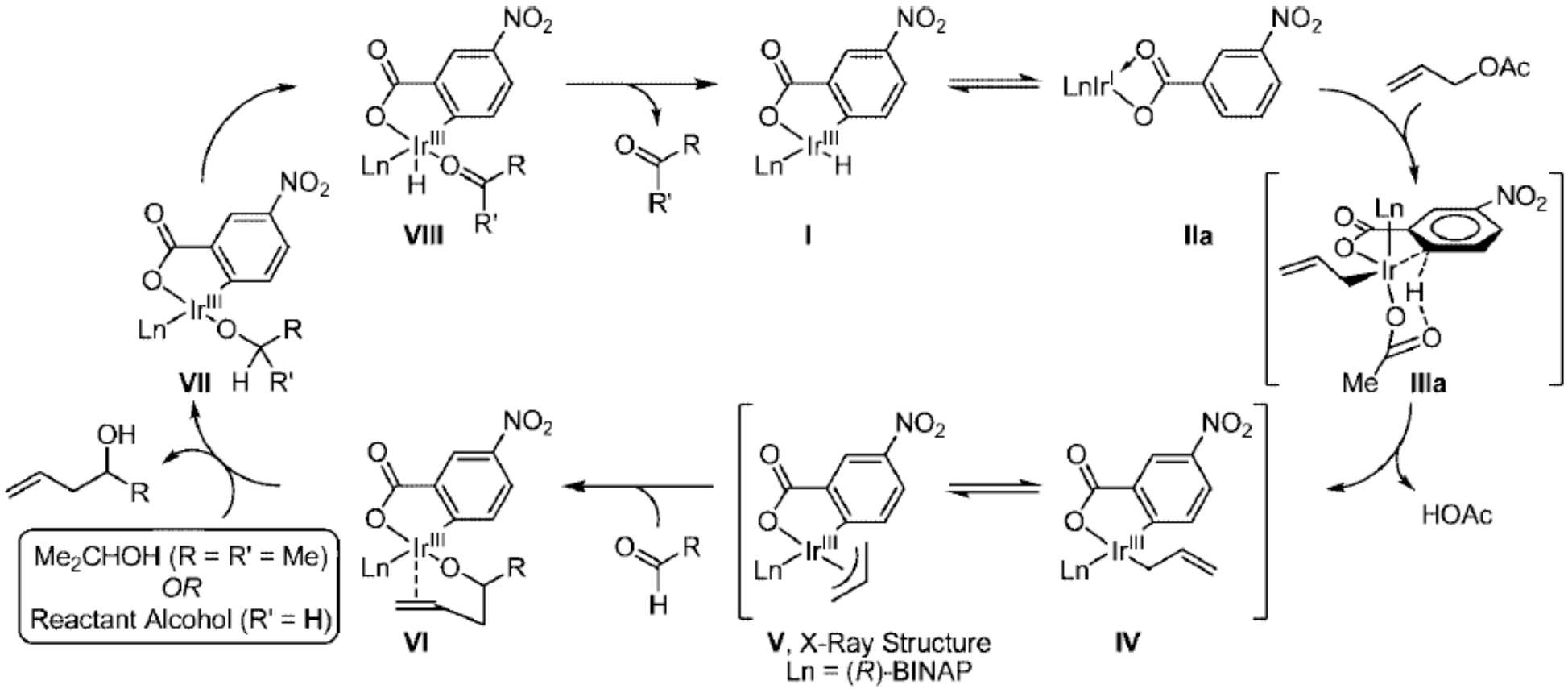


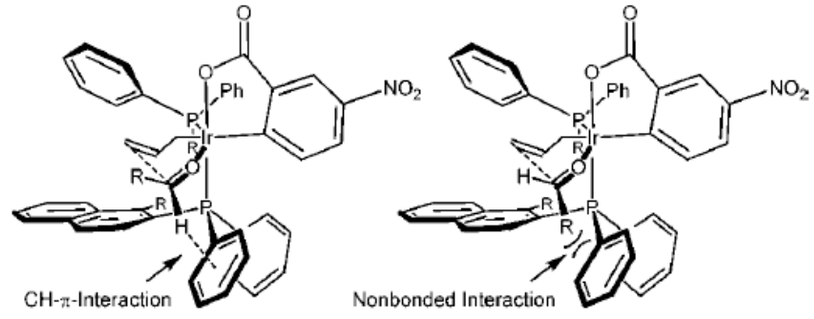
n = 1: 68% (88% ee)
n = 2: 63% (94% ee)
n = 3: 78% (95% ee)



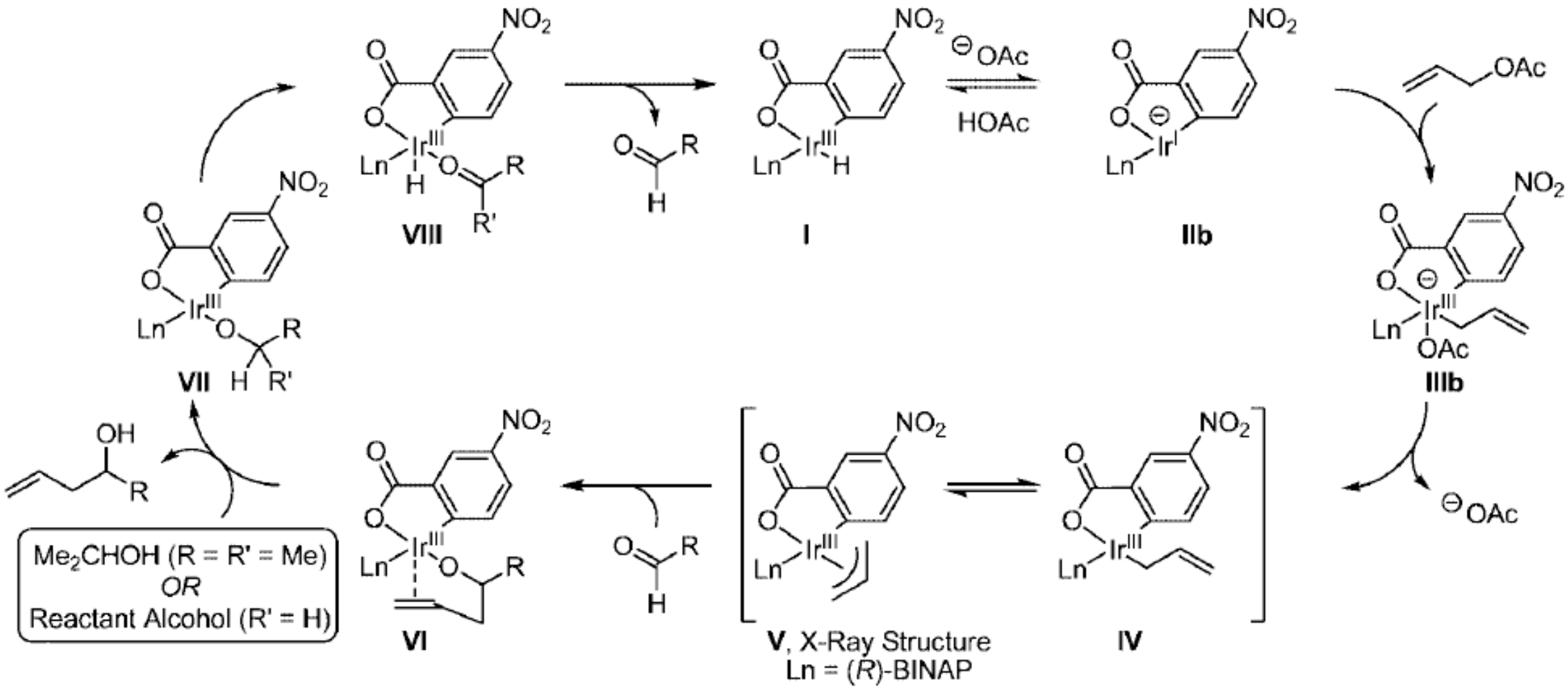
81% (95% ee)

Krische's Allylation Chemistry





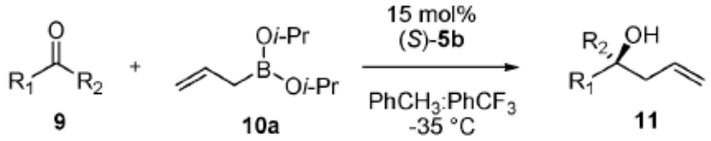
Krische's Allylation Chemistry



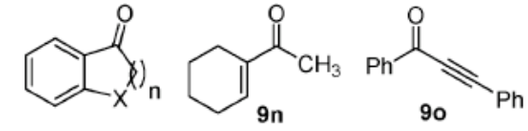
Schaus' Allylation of Ketones

JACS 2006, 12660

Table 2. Asymmetric Allylboration of Ketones[a]



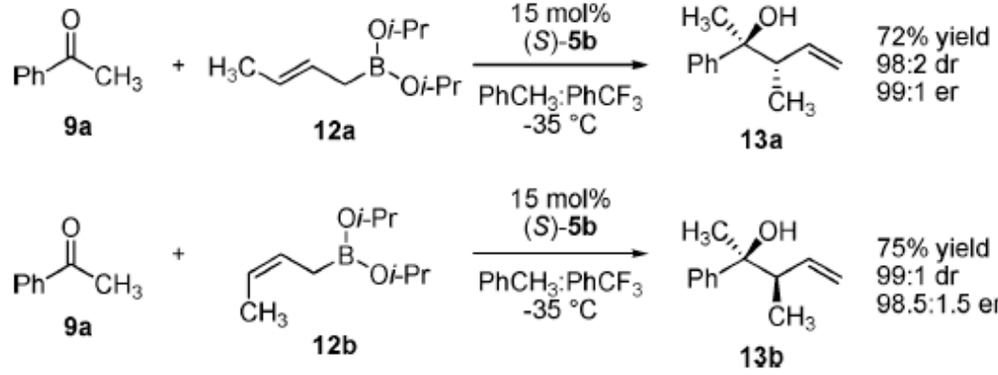
9b R_1 = 3-BrC_6H_4, R_2 = CH_3
9c R_1 = 4-BrC_6H_4, R_2 = CH_3
9d R_1 = 3-$CF_3C_6H_4$, R_2 = CH_3
9e R_1 = 4-$MeOC_6H_4$, R_2 = CH_3
9f R_1 = 2-Naphthyl, R_2 = CH_3
9g R_1 = 2-C_4H_3S, R_2 = CH_3
9h R_1 = 3-C_4H_3S, R_2 = CH_3
9i R_1 = C_6H_5, R_2 = CH_2CH_3
9j R_1 = C_6H_5, R_2 = CH_2Cl

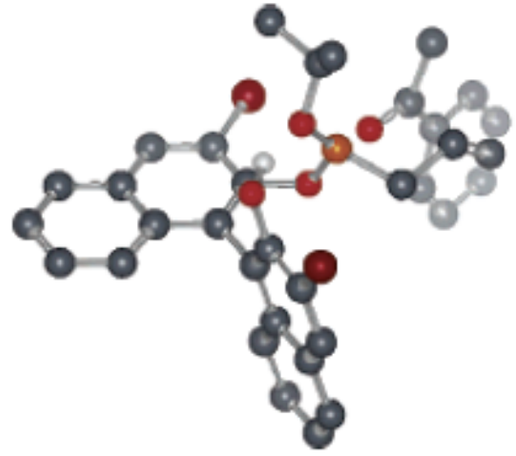


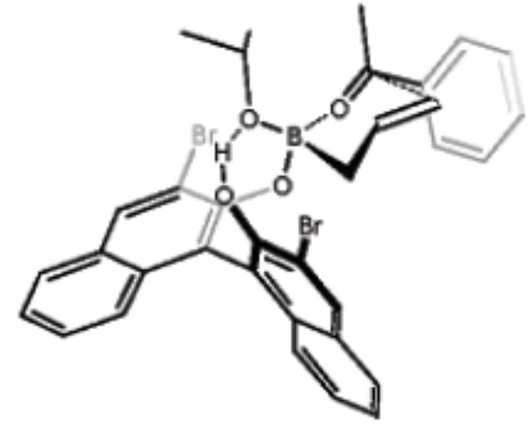
9k n = 1, X = CH_2
9l n = 2, X = CH_2
9m n = 2, X = O

entry	ketone	product	% yield[b]	er[c]
1[d]	**9a**	**11a**	83	97:3
2[d]	**9b**	**11b**	81	95.5:4.5
3	**9c**	**11c**	86	99.5:0.5
4	**9d**	**11d**	89	95.5:4.5
5	**9e**	**11e**	83	99.5:0.5
6	**9f**	**11f**	81	96.5:3.5
7	**9g**	**11g**	87	97:3
8	**9h**	**11h**	88	97:3
9[d]	**9i**	**11i**	83	97.5:2.5
10	**9j**	**11j**	76	98:2
11	**9k**	**11k**	88	96.5:3.5
12	**9l**	**11l**	87	97.5:2.5
13	**9m**	**11m**	83	96:4
14	**9n**	**11n**	91	96.5:3.5
15[d]	**9o**	**11o**	93	95:5

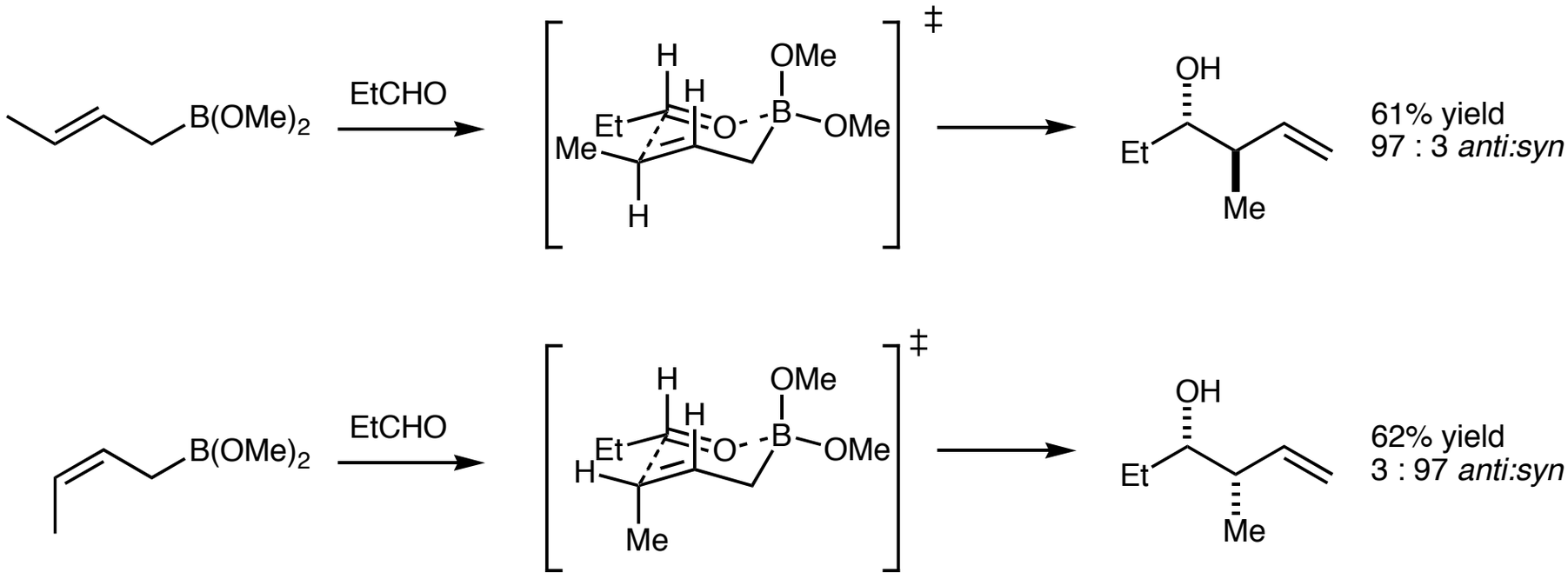
[a] Reactions were run with 0.125 mmol **10a**, 0.19 mmol ketone, and 15 mol % of catalyst in a $PhCF_3$:$PhCH_3$ (3:1) mixture (0.1 M) for 15 h under Ar, followed by flash chromatography on silica gel. [b] Isolated yield. [c] Determined by chiral HPLC and chiral GC analysis. [d] Reactions were run with 0.5 mmol **10a** and 0.75 mmol acetophenone.







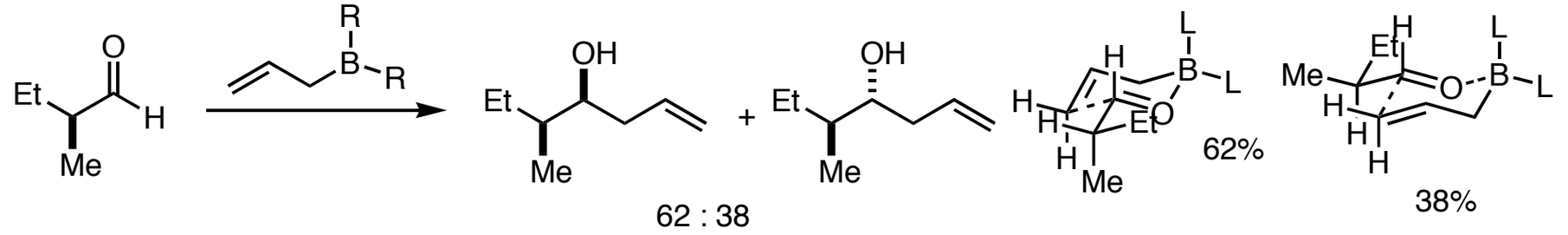
1. ACHIRAL REAGENT + ACHIRAL ALDEHYDE

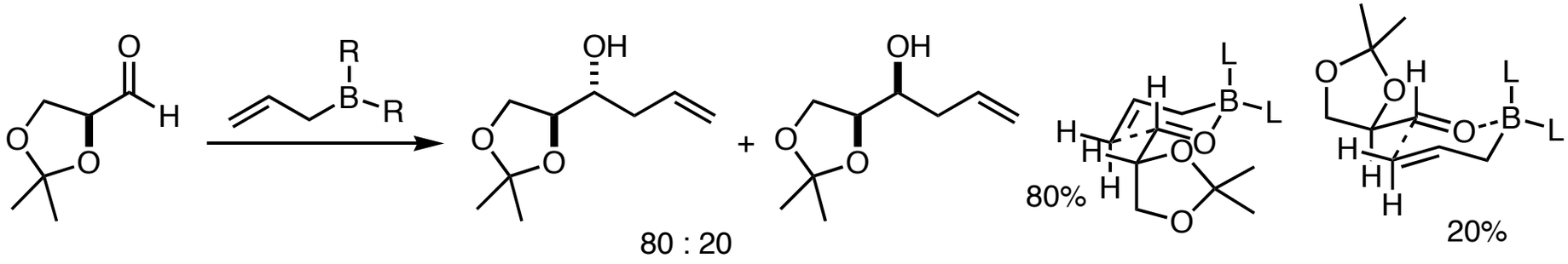


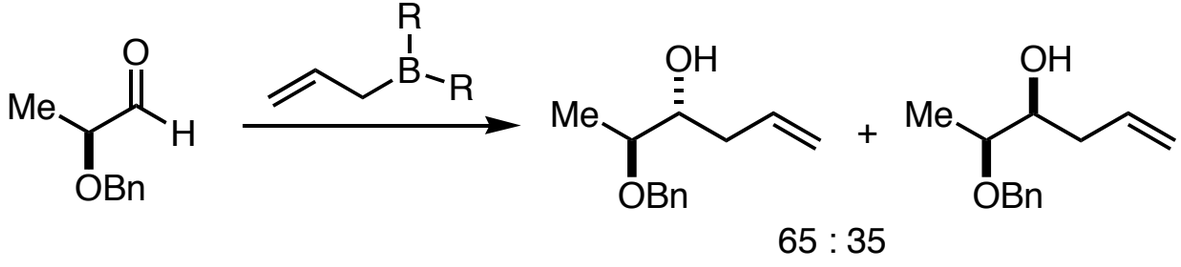
See other examples in Table IV (Yamamoto's review)

2. ACHIRAL REAGENT + CHIRAL ALDEHYDE

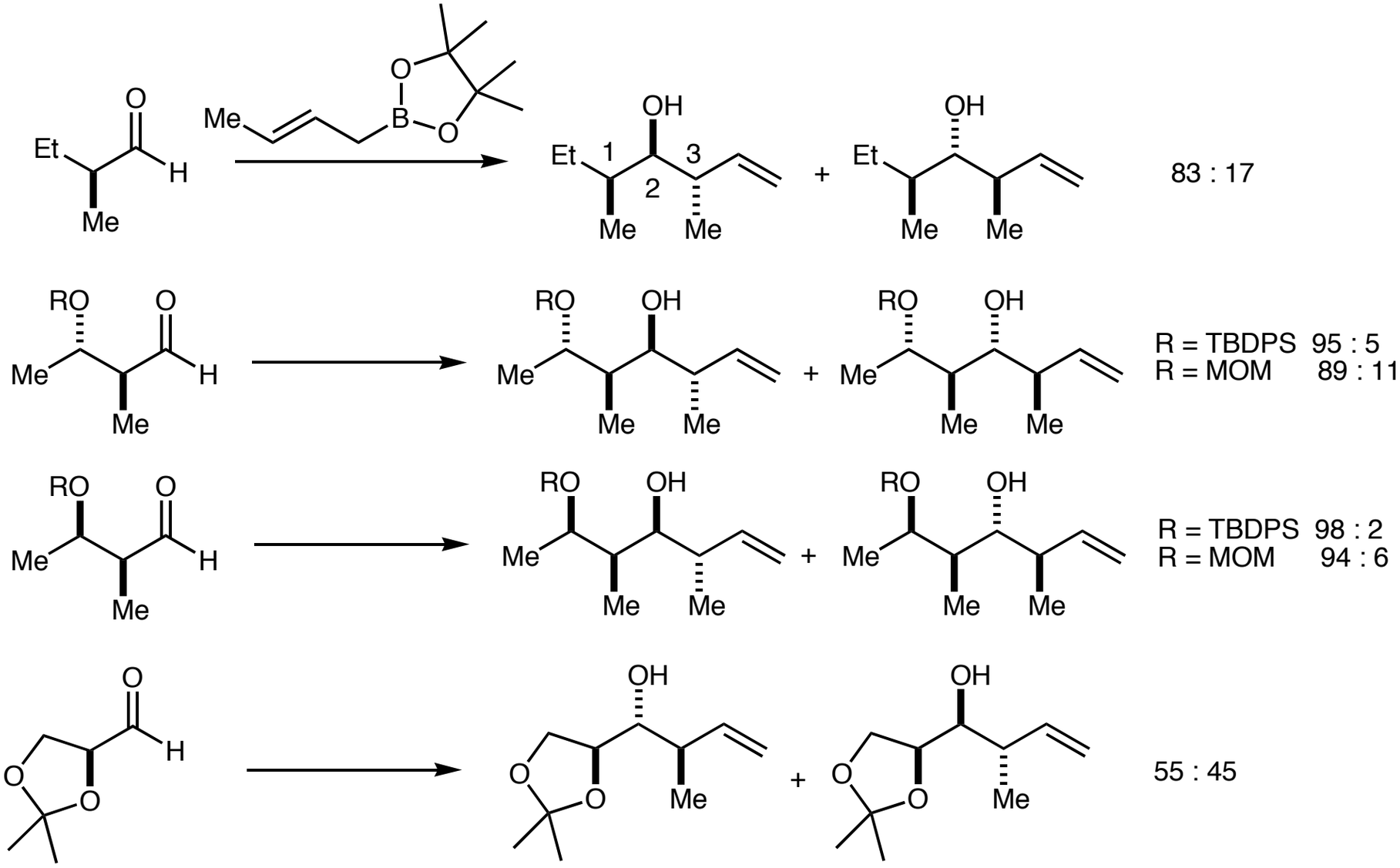
a. Allyl boron reagent: Cram products



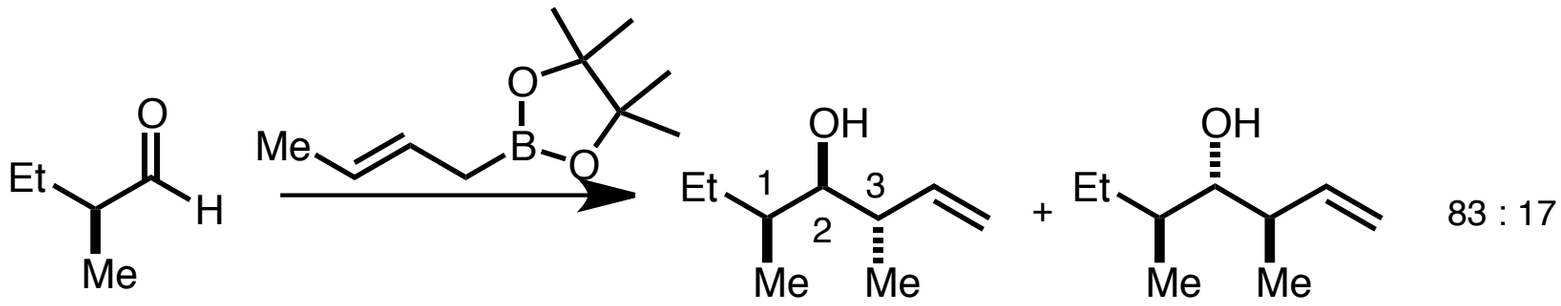


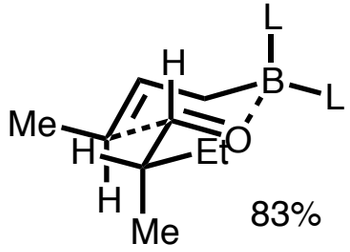


b. *E*-Crotyl boron (1,2-Cram/Felkin-Anh model; 2,3-Cyclic transition state)

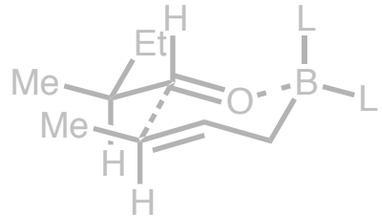


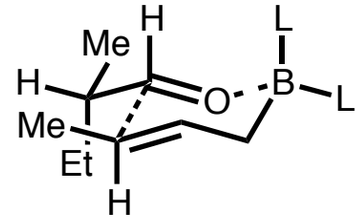
E-Crotylboronates: Felkin-Anh Selectivity





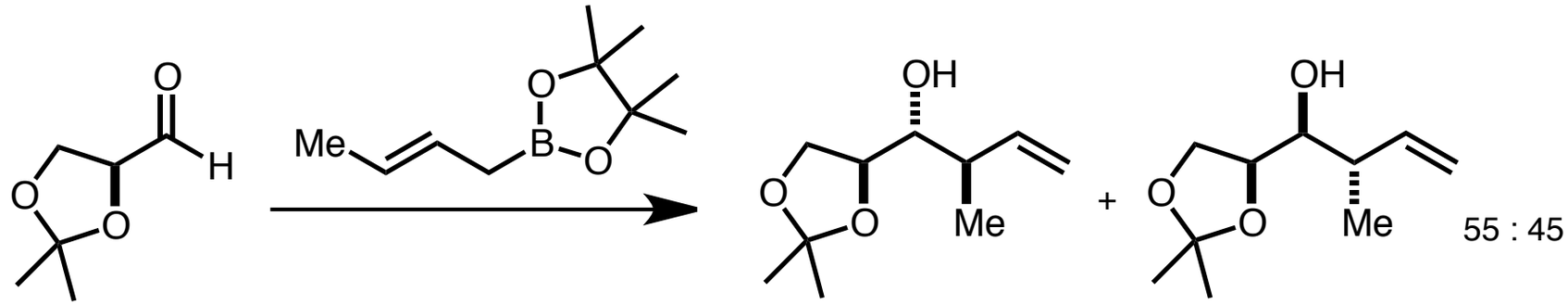
83%





17%

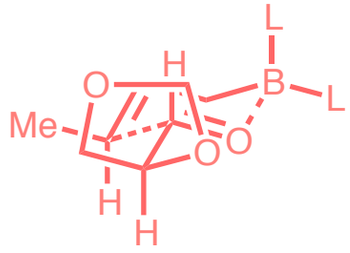
Allyl- and Crotylboron Chemistry

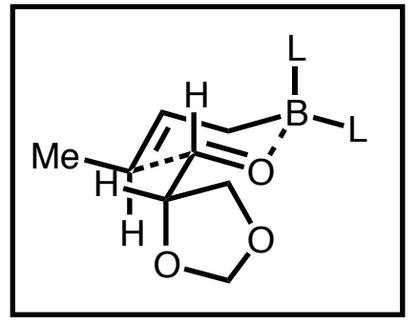


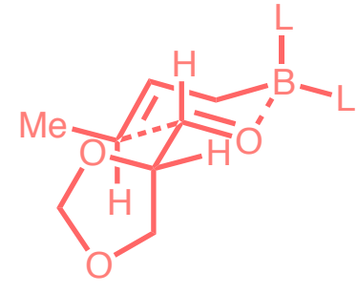
Why is the diastereoselection so low?

Anti-Felkin

45%

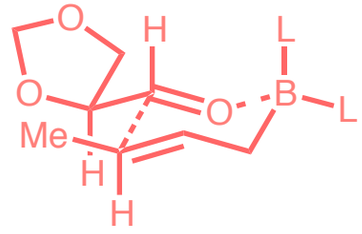




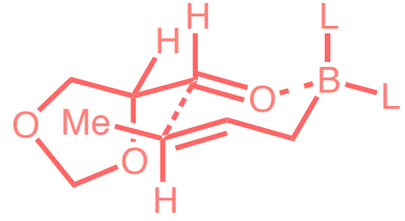


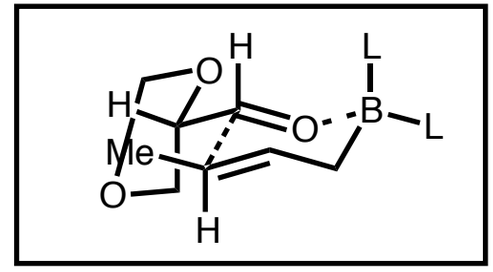
Felkin Product

55%



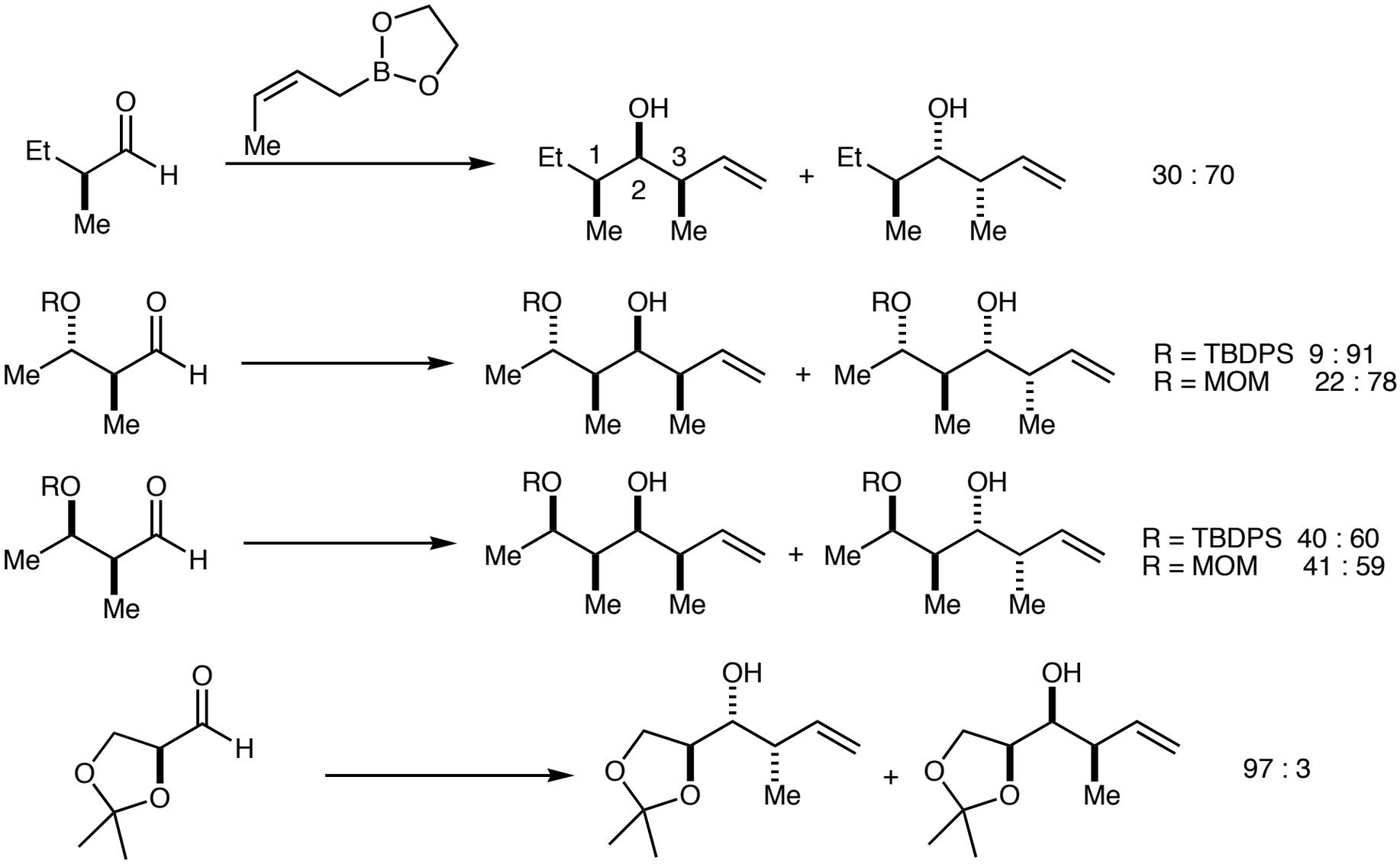
Cornforth Model





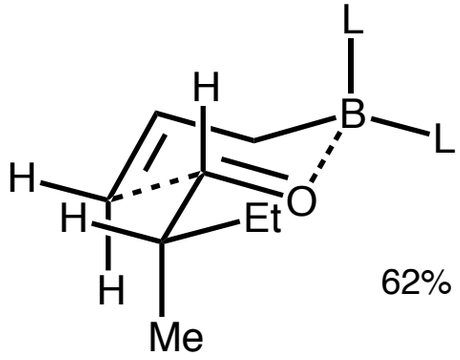
Felkin-Anh Model

c. *Z*-Crotyl boron (Make model and see which one is the most stable)

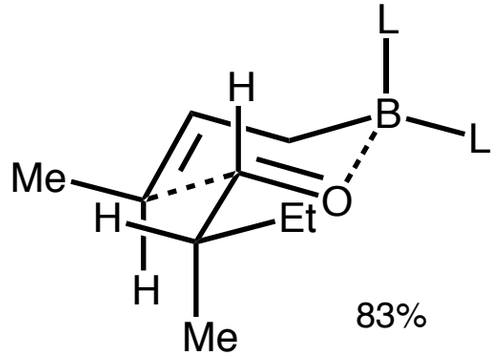


Transition Structures of Allyl-/Crotylboronation

Felkin



62%



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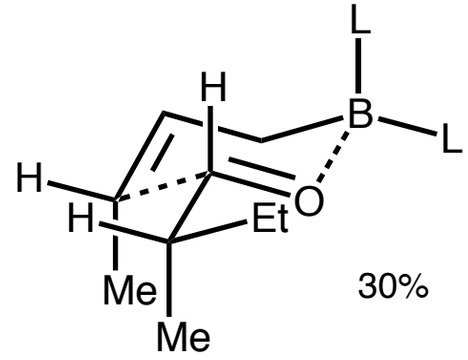
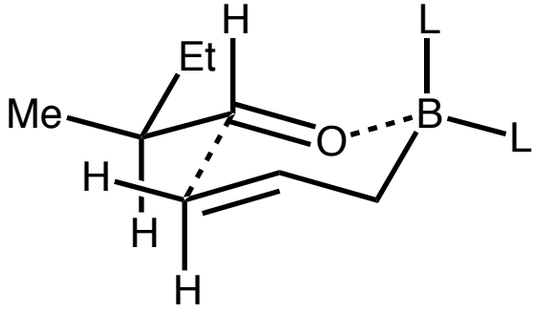


30%

Anti-Felkin



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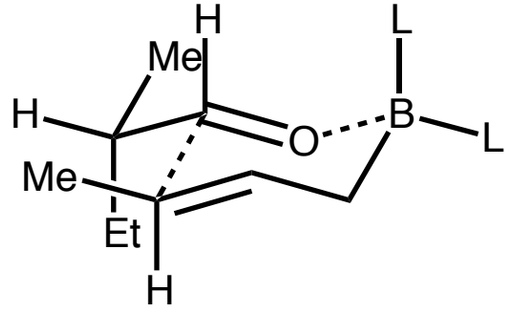

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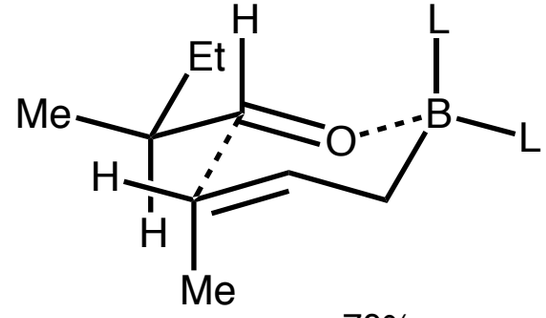
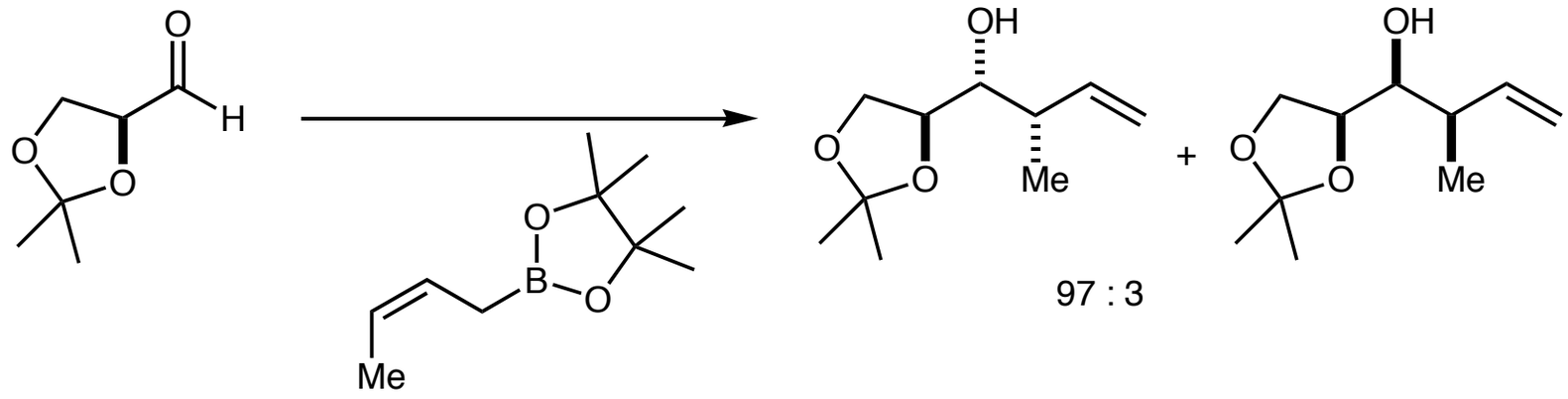


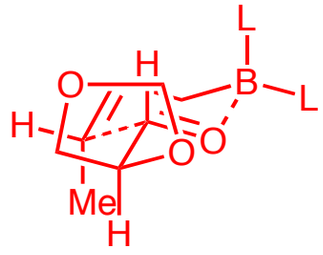
70%

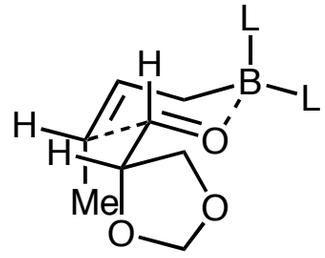
Allyl-/Crotyl Boronation: Transition Structures

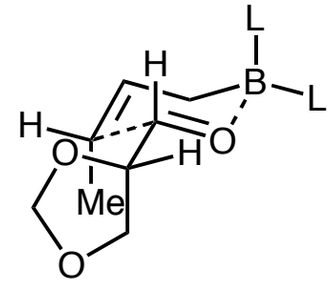
c. *Z*-Crotyl boron



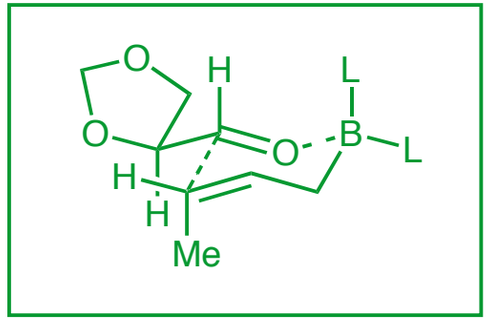
Anti-Felkin



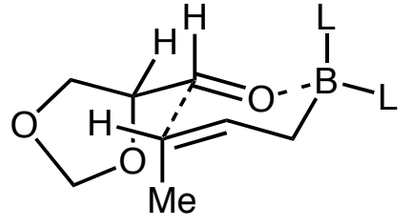


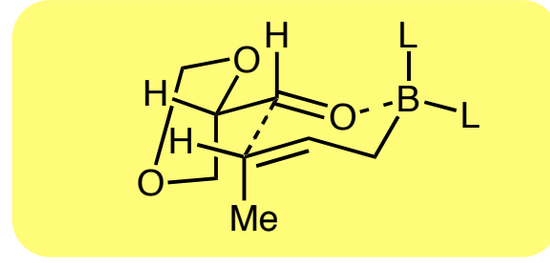


Felkin



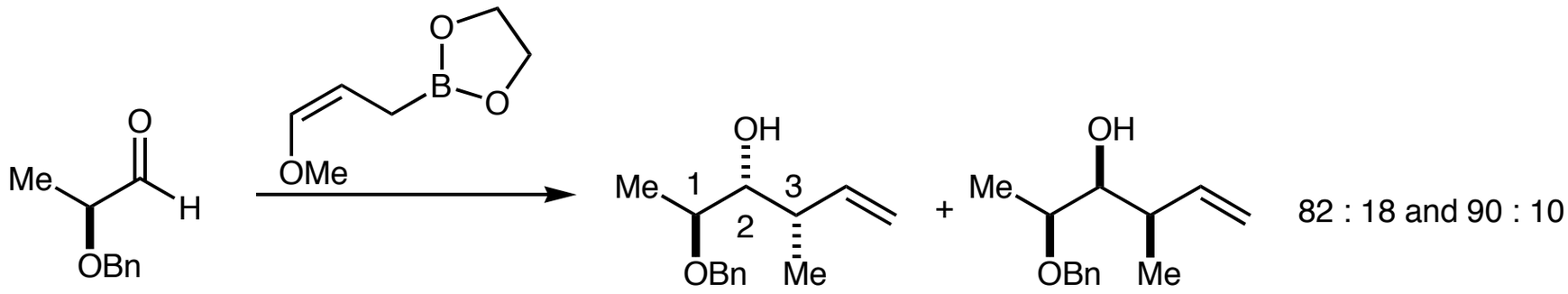
Cornforth Model

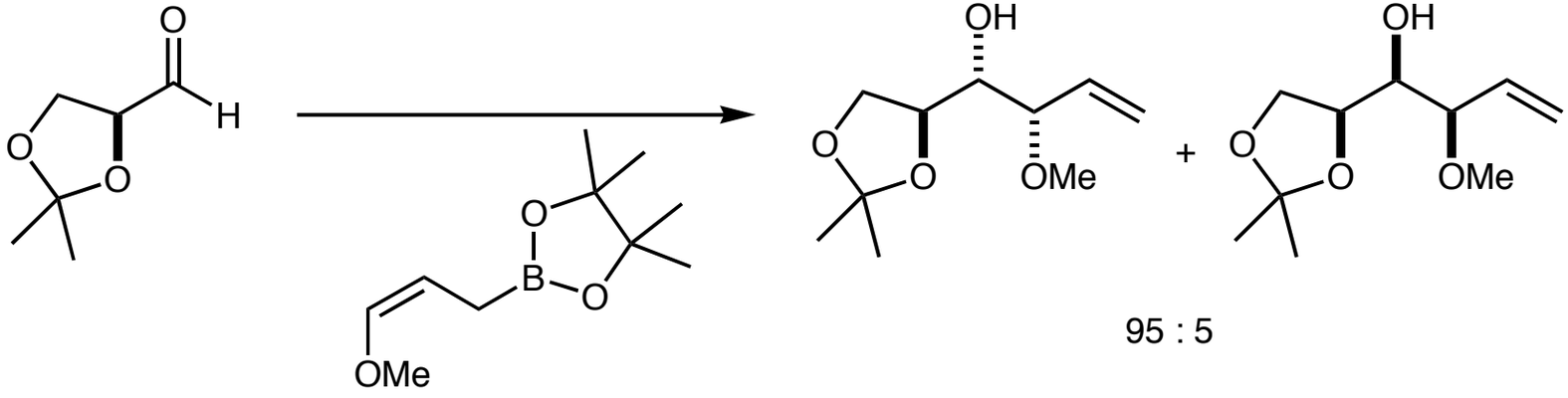




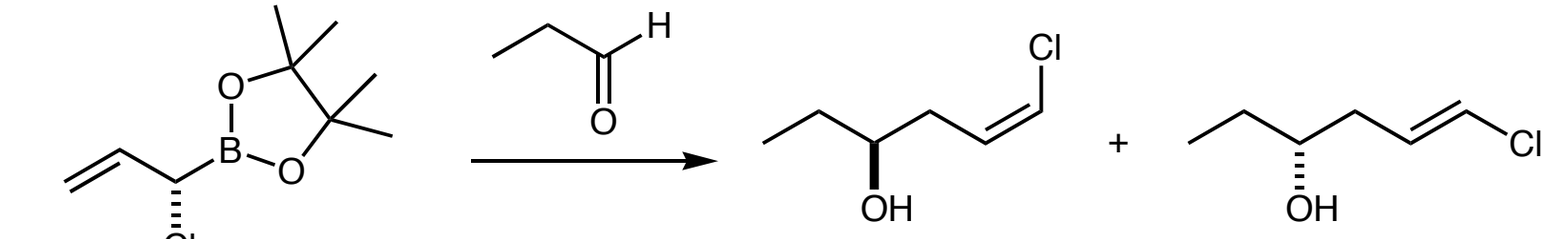
Felkin-Anh Model

Allyl-/Crotyl Boronation: γ-Substituted Alkoxy Reagents

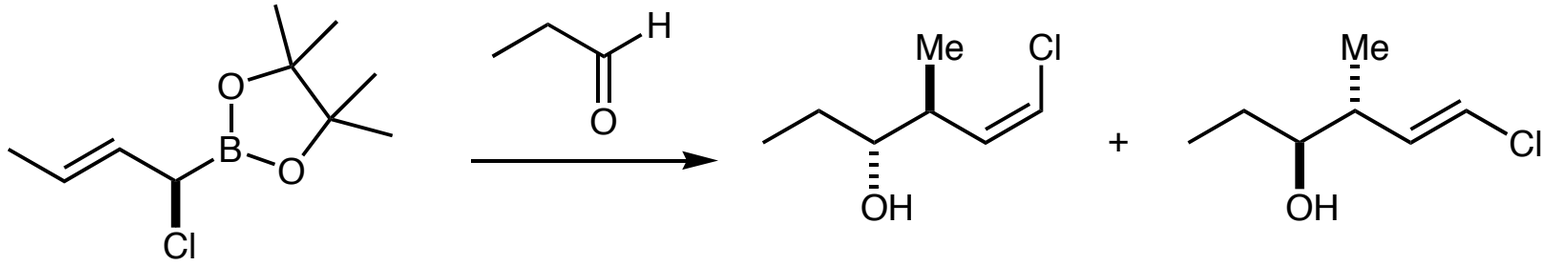




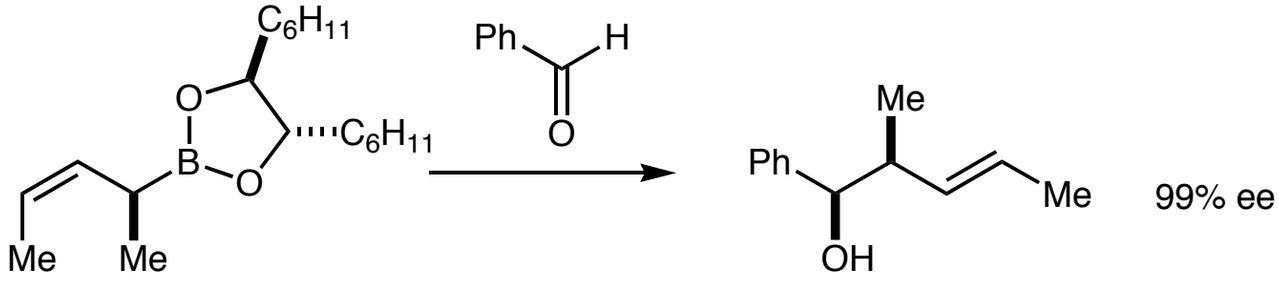
b. Stereogenic center on the allyl boron reagent



96 : 4 (89% ee)

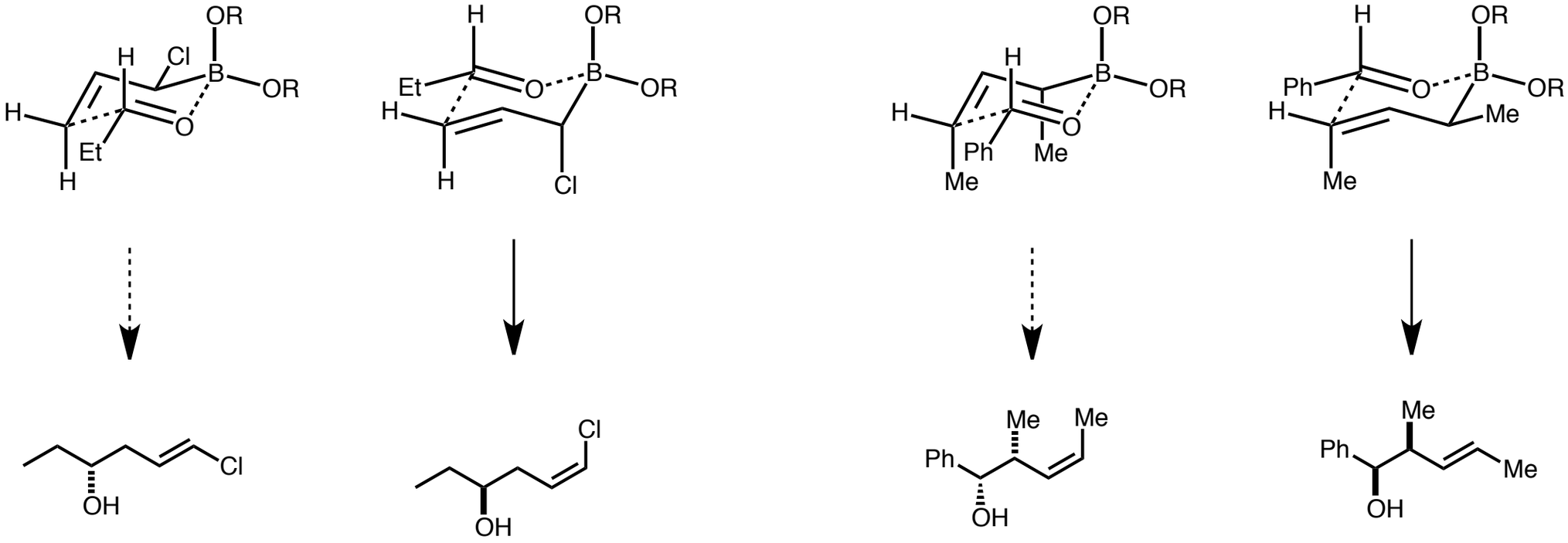


95 : 5 (96% ee)



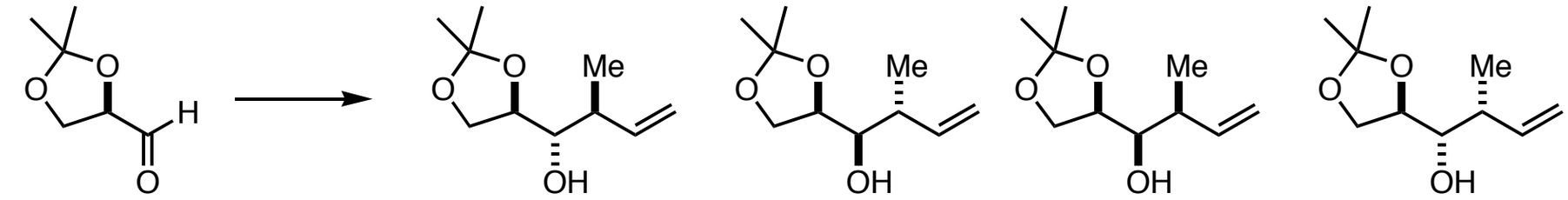
99% ee

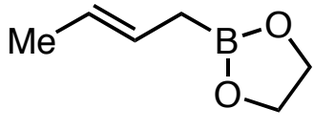
Allyl- and Substituted-allyl Metal Chemistry



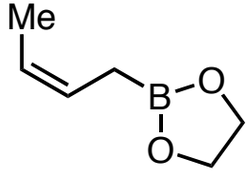
Double Stereodifferentiation

4. CHIRAL REAGENT + CHIRAL ALDEHYDE: DOUBLE ASYMMETRIC INDUCTION





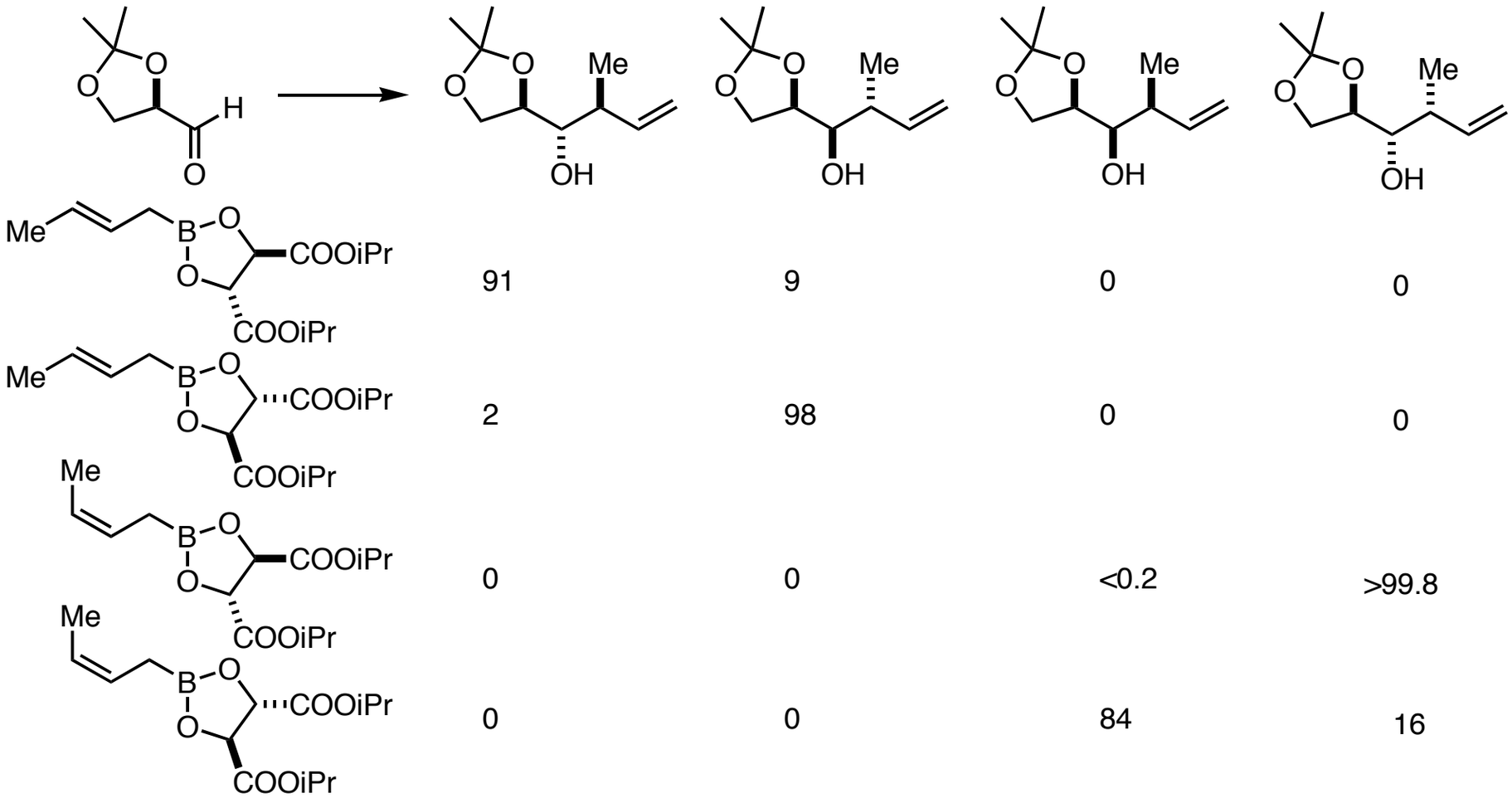
	55	45	0	0



	0	0	3	97

Roush Reagent: Double Stereodifferentiation

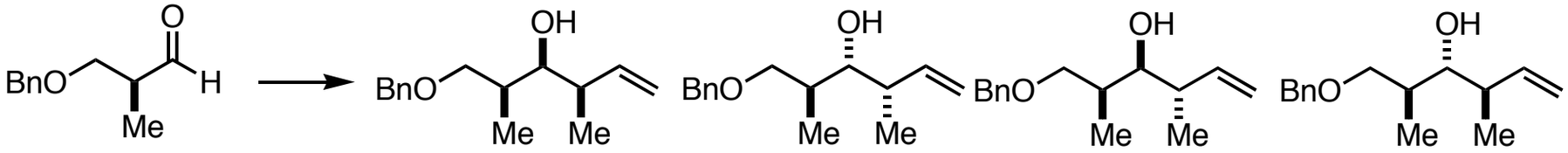
Roush's reagent (*J. Org. Chem.* **1990**, *55*, 4117-4126).

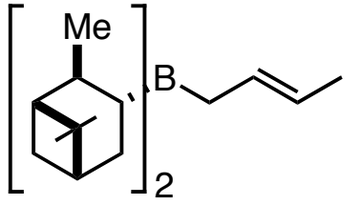
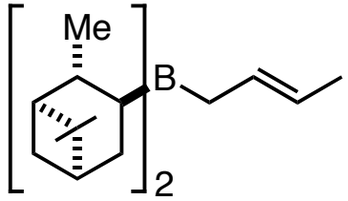
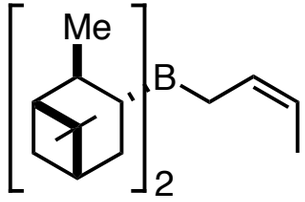
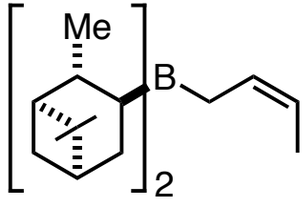


91	9	0	0
2	98	0	0
0	0	<0.2	>99.8
0	0	84	16

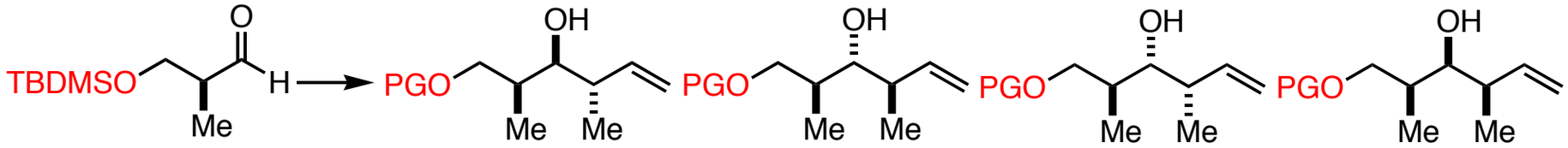
4. CHIRAL REAGENT + CHIRAL ALDEHYDE: DOUBLE ASYMMETRIC INDUCTION

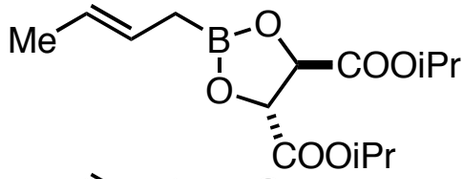
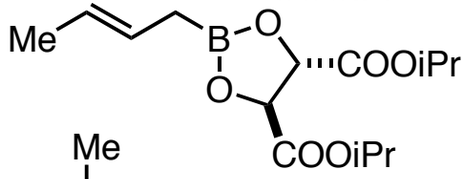
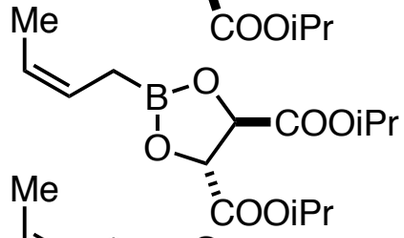
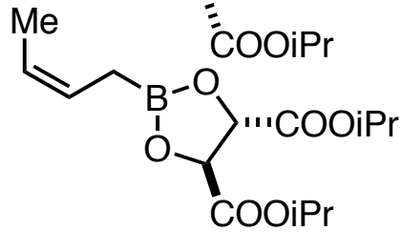
Brown's reagent (*J. Org. Chem.* **1989**, *54*, 1570).



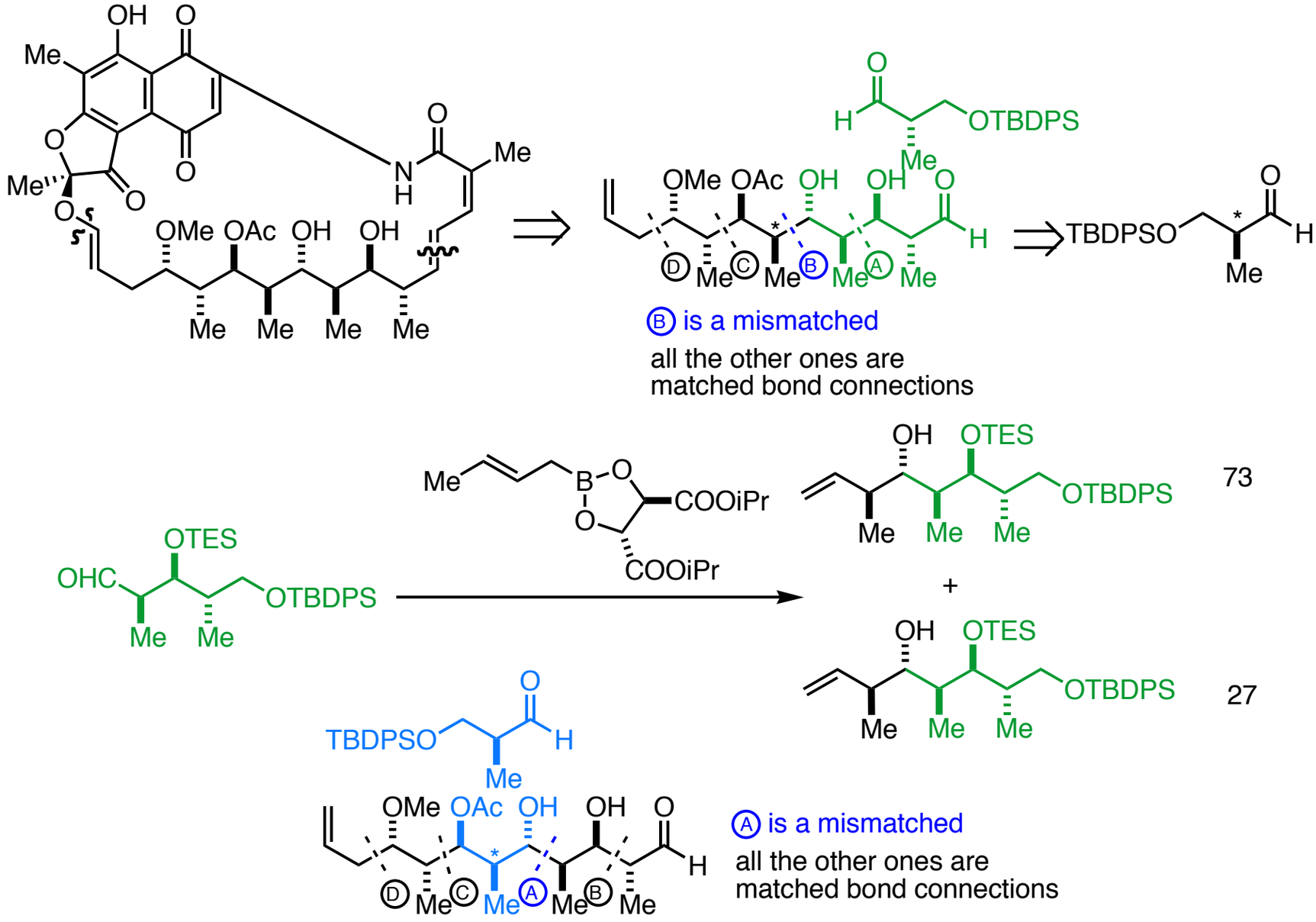
	0	0	98	2
	0	0	5	95
	92	8	0	0
	5	95	0	0

Chiral Allyl and Crotyl Metal: the Rifamycin S Problem



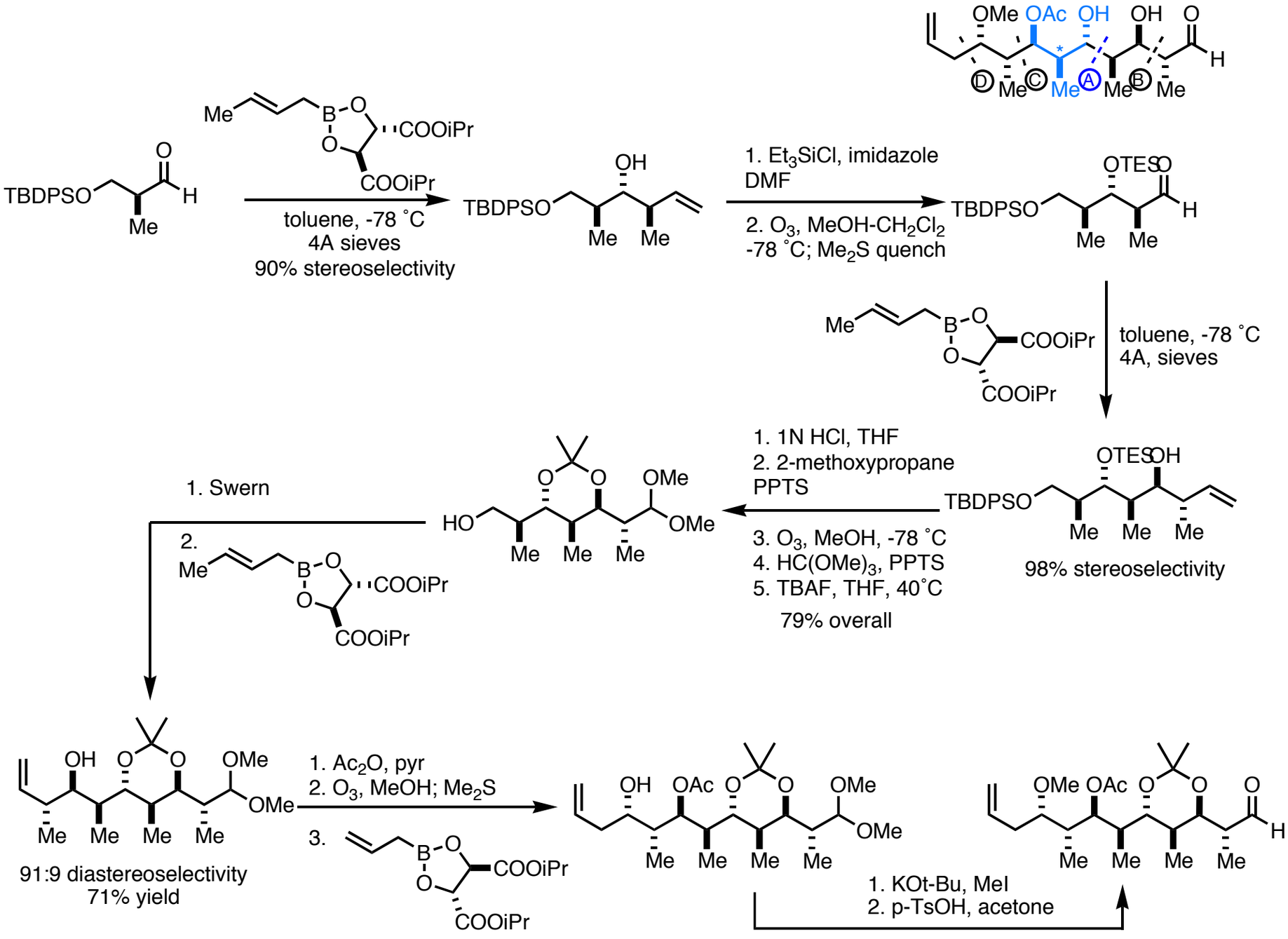
	97	3	-	-
	10	90 (TBDPS)	-	-
	9	3	24	64
	-	4	95	1

Roush's Rifamycin Synthesis



JACS **1990**, *112*, 6348

Roush's Synthesis of Rifamycin Segment

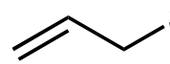
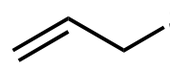
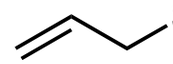
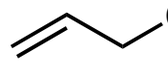
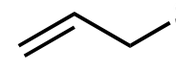
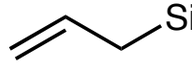
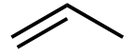


Allylsilanes and Allylstannanes

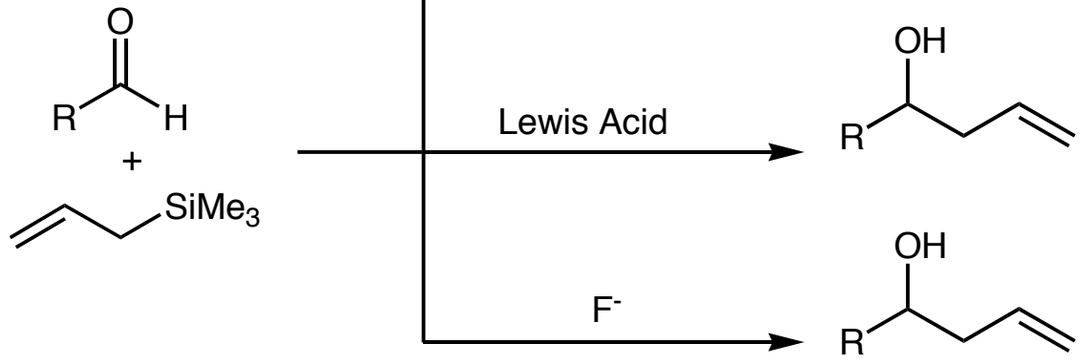
General nucleophilicity of allyl silane and stannanes

More reactive

Less reactive

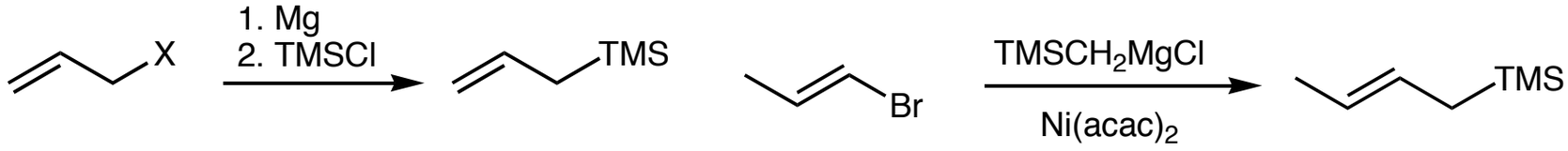
Allyl metal	k_{rel}
	2.70×10^9
	5.52×10^6
	1.99×10^5
	1.91×10^4
	3.42×10^3
	2.94×10^2
	1.0

Allyl silanes

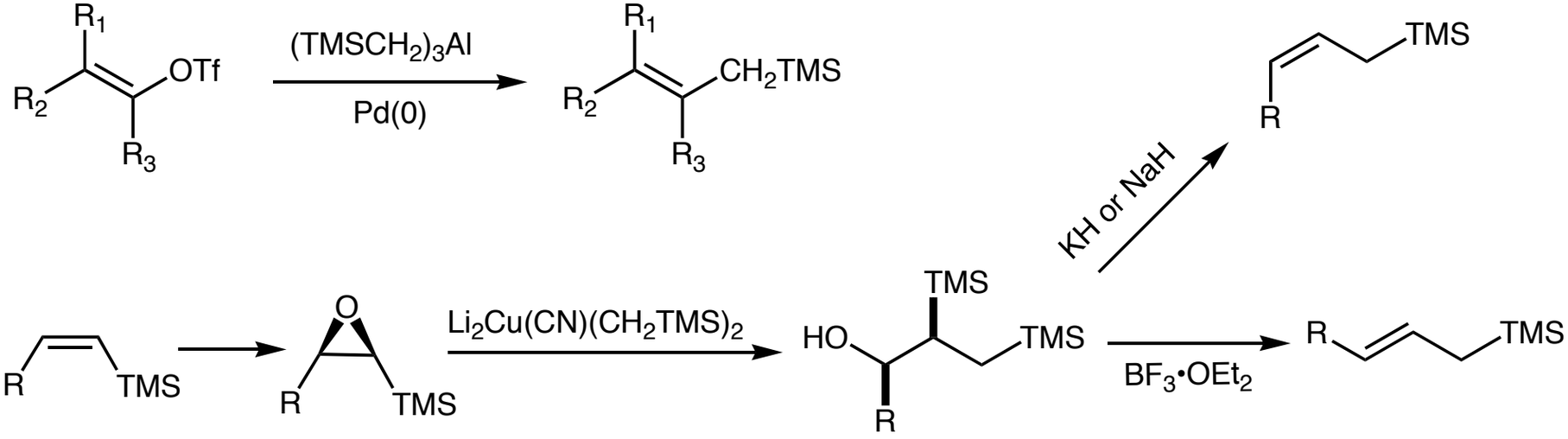


Preparation of Allylsilanes

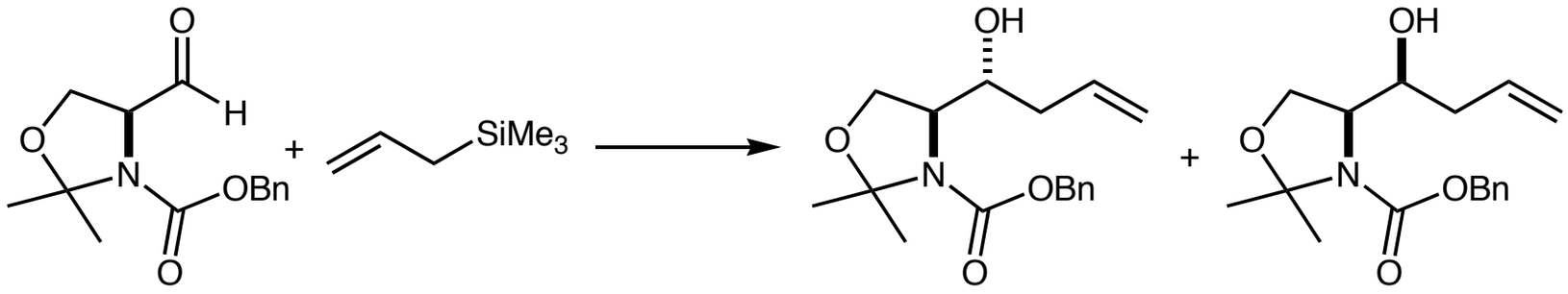
a. simple silanes



b. complex silanes



Fujiyama, R. *J. Org. Chem.* **1989**, *54*, 5409.

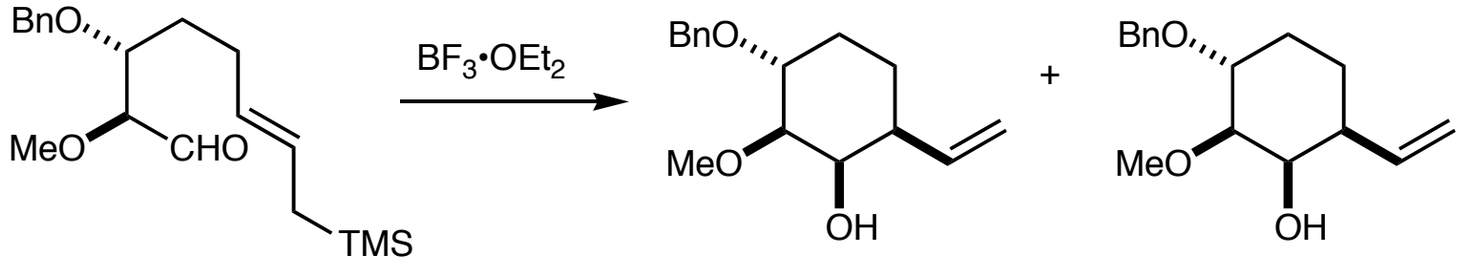


$TiCl_4$, 1 eq — 20 : 1 — (β-chelation)

$TiCl_4$, 0.5 eq — 1 : 8 — (no β-chelation, 2:1 complex)

Intramolecular cyclization:

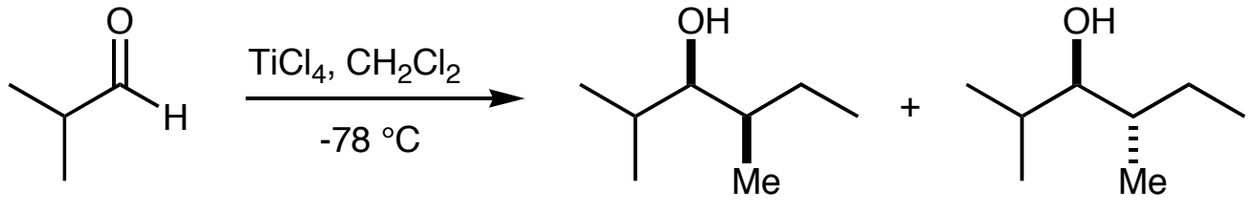
Maier *Tetrahedron Lett.* **1990**, 3007.



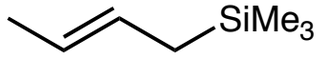
47 53

Substituted silanes: *E*- is much more selective than the *Z*-crotyl silane

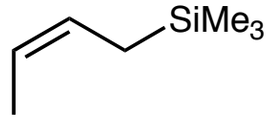
Hayashi, T. *Tetrahedron Lett.* **1983**, *24*, 2865.



+



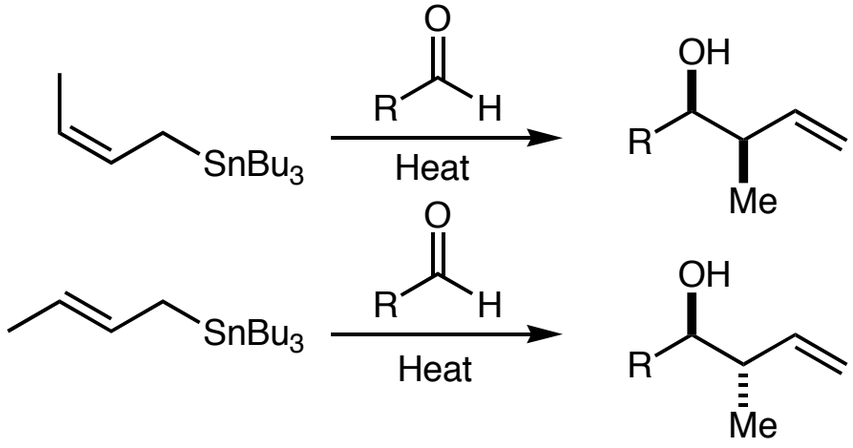
97 : 3



64 : 36

Reactivity of Allylstannanes: Thermal Reaction

TYPE 1: In the absence of a Lewis acid (Cyclic Transition State)



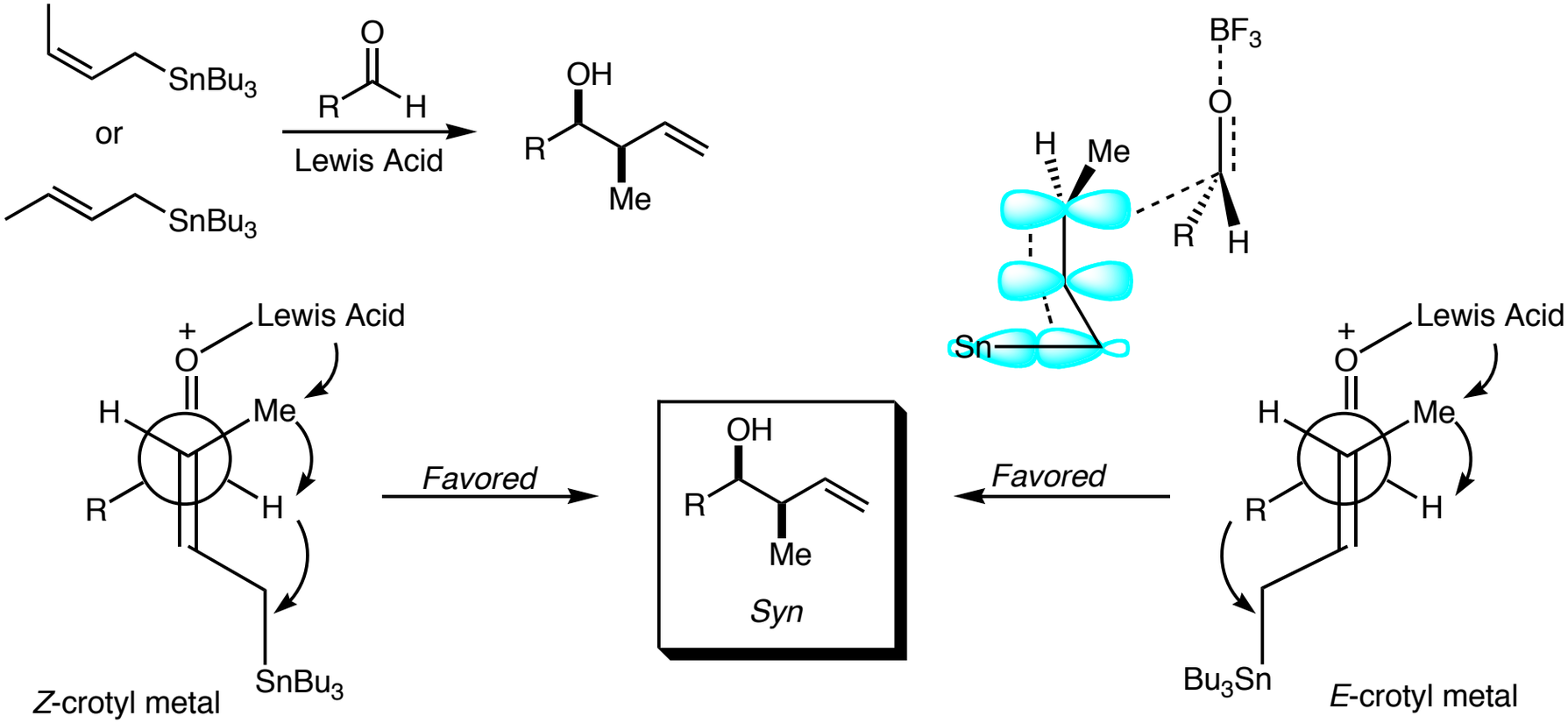
References:

Thomas, E. J. *Tetrahedron Lett.* **1990**, *31*, 6239.
Thomas, E. J. *Tetrahedron* **1989**, *45*, 1007.
Thomas, E. J. *J. C. S. Chem. Comm.* **1982**, 1115.
Thomas, E. J. *J. C. S. Chem. Comm.* **1984**, 800.

Not that much used in synthesis

TYPE 2: In the presence of a Lewis acid (Acyclic or open Transition State)

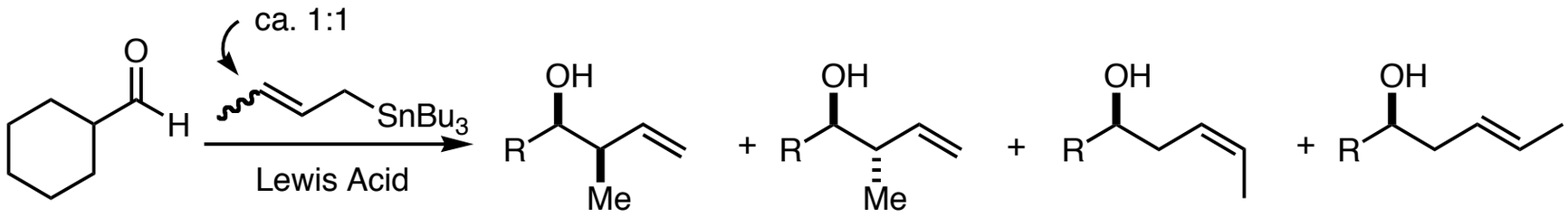
Yamamoto, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7107.



N.B. The C-$SnBu_3$ bond is in the same plane as the π-bond:

Allylstannanes: Diastereoselectivity Issues

Keck, G. E. *Tetrahedron Lett.* **1984**, *25*, 3927. (Mode of addition)

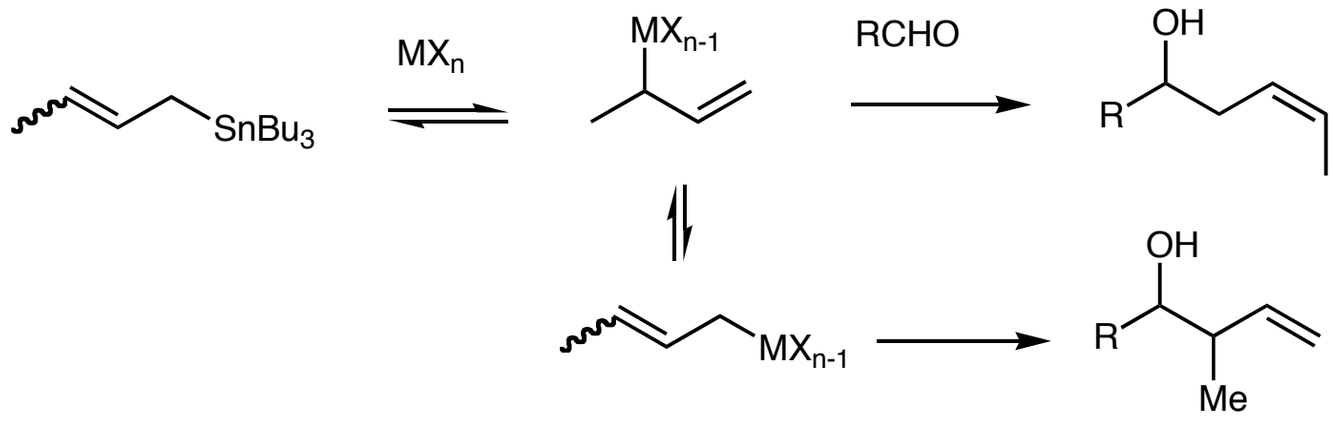


$BF_3 \cdot OEt_2$	96.1	3.9	0	0
$BF_3 \cdot OEt_2$ (reverse adn)	96.1	3.9	0	0
$MgBr_2 \cdot OEt_2$	52.2	36.3	11.6	0
ZnI_2	33.7	29.8	29.3	7.2
$SnCl_4$	22.8	26.0	36.4	14.8
$SnCl_4$ Reverse addition	21.8	74.9	1.2	2.2
$TiCl_4$	90.5	7.0	2.1	0.5
$TiCl_4$ Reverse addition	4.4	90.8	0	4.9

Reverse addition: Lewis acid is mixed with the allyl tin reagent prior to the addition of RCHO

Allylstannanes: Diastereoselectivity Issues

Evidence for these transmetallation reactions:



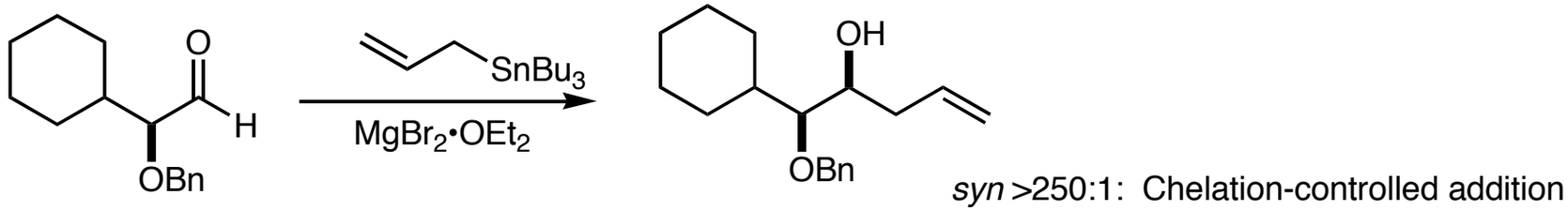
Usually ML_{n-1} reacts via cyclic transition state

For NMR studies:

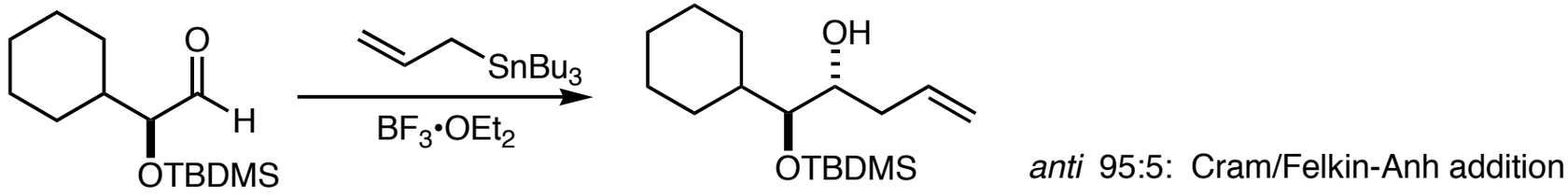
Keck, G. E. *J. Am. Chem. Soc.* **1989**, *111*, 8136.
Denmark, S. E. *J. Am. Chem. Soc.* **1988**, *110*, 984.

Reactions of Allylstannanes with α-Alkoxyaldehydes

Keck, G. E. *Tetrahedron Lett.* **1984**, *25*, 265. (α-alkoxy aldehydes)



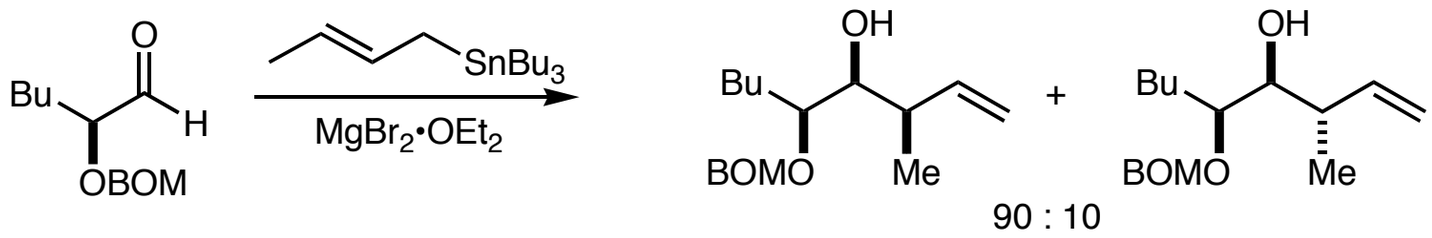
syn >250:1: Chelation-controlled addition



anti 95:5: Cram/Felkin-Anh addition

Reactions of Crotylstannanes with α-Alkoxyaldehydes

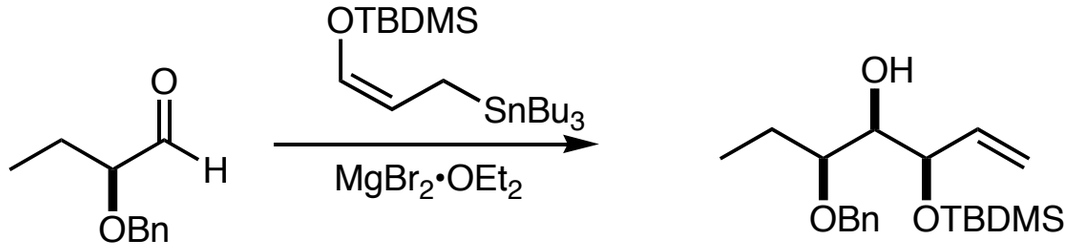
Keck, G. E. *Tetrahedron Lett.* **1984**, *25*, 1879. (α-alkoxy aldehydes)



90 : 10

Keck, G. E. *Tetrahedron Lett.* **1987**, *28*, 139.

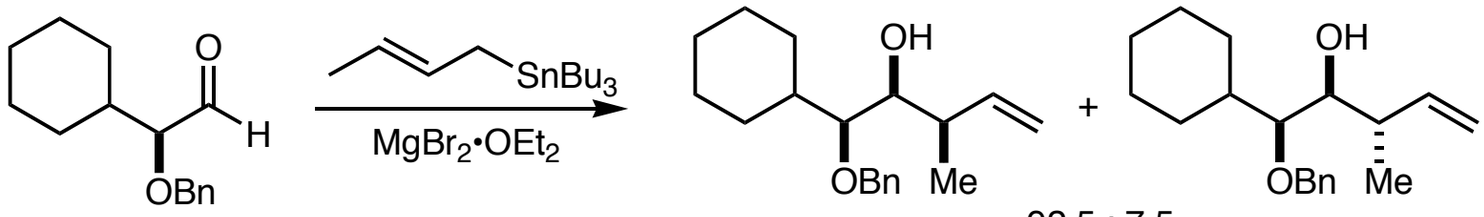
(Chelation-controlled addition + acyclic T.S.)



single diastereomer

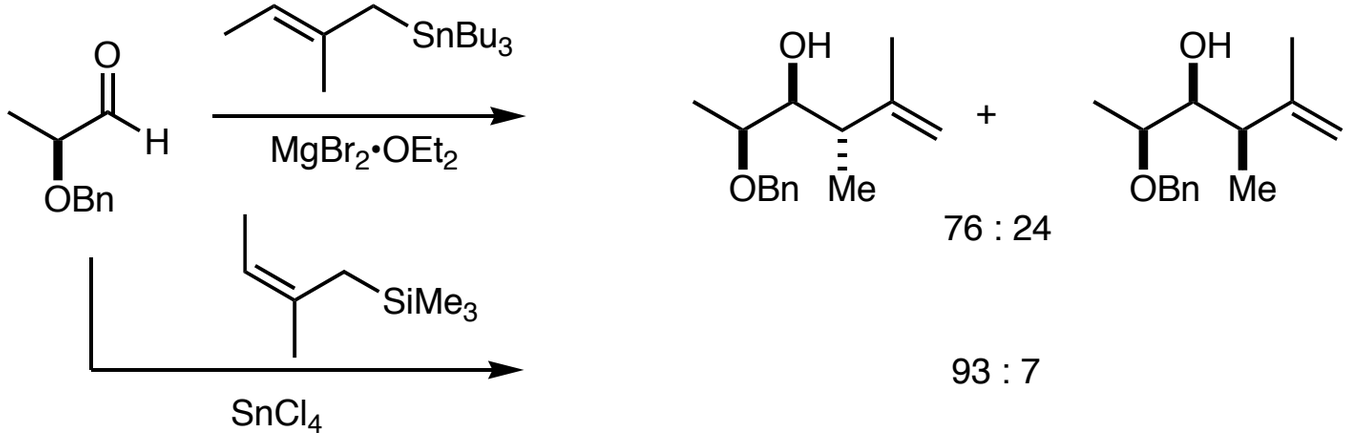
Reactions of Crotylstannanes with α-Alkoxyaldehydes

Mikami, *J. C. S. Chem. Comm.* **1990**, 1161.



92.5 : 7.5

(Chelation-controlled addition + acyclic T.S.)

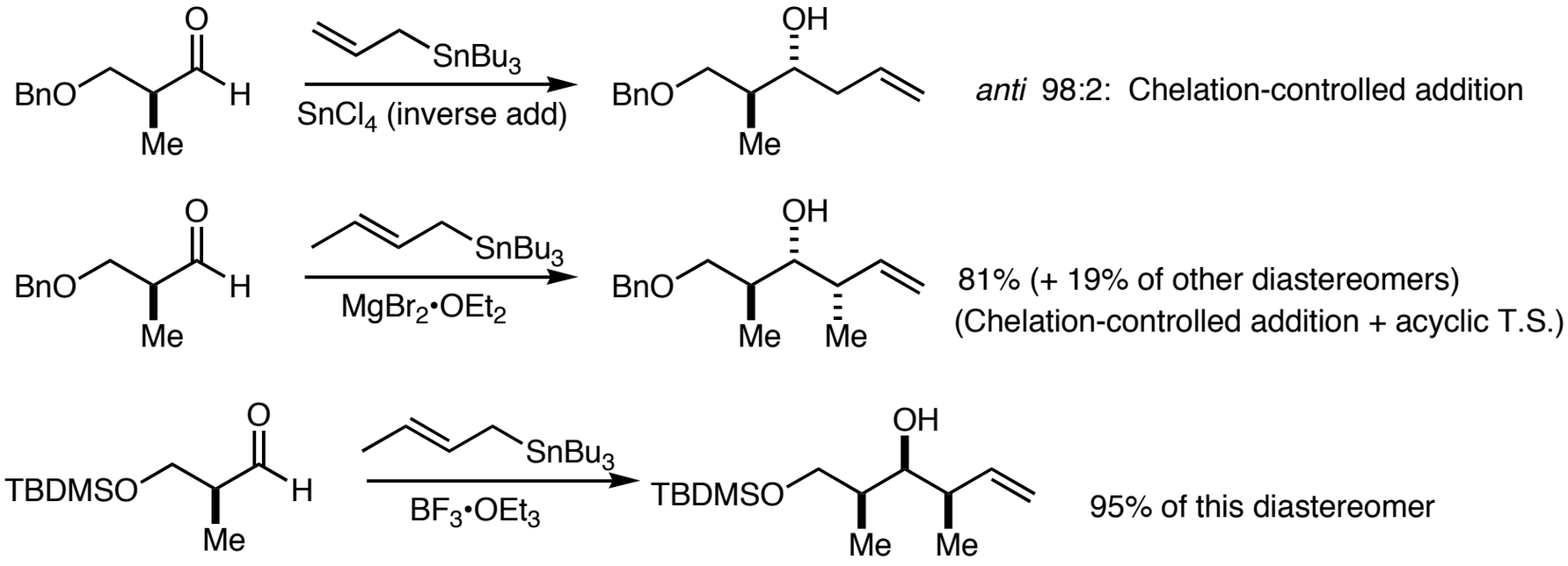


76 : 24

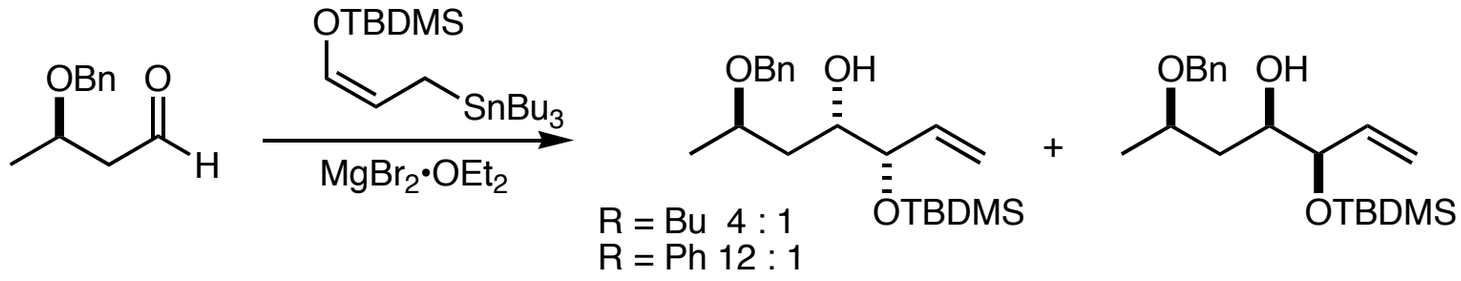
93 : 7

Reactions of Allylstannanes with β-Alkoxyaldehydes

Keck, G. E. *Tetrahedron Lett.* **1984**, *25*, 1883. (β-alkoxy aldehydes)

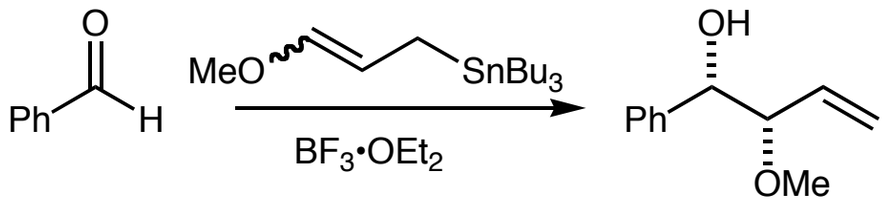


Reetz, *Ang. Chem. Int. Ed. Engl.* **1984**, 556.



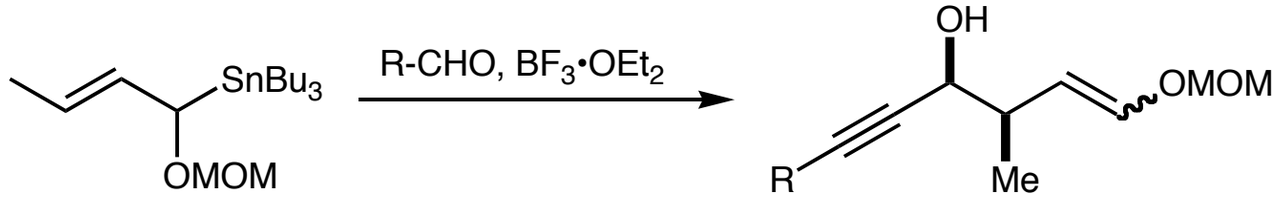
Reactions of Functionalized Allylstannanes

Koreeda, M. *Tetrahedron Lett.* **1987**, *28*, 143.



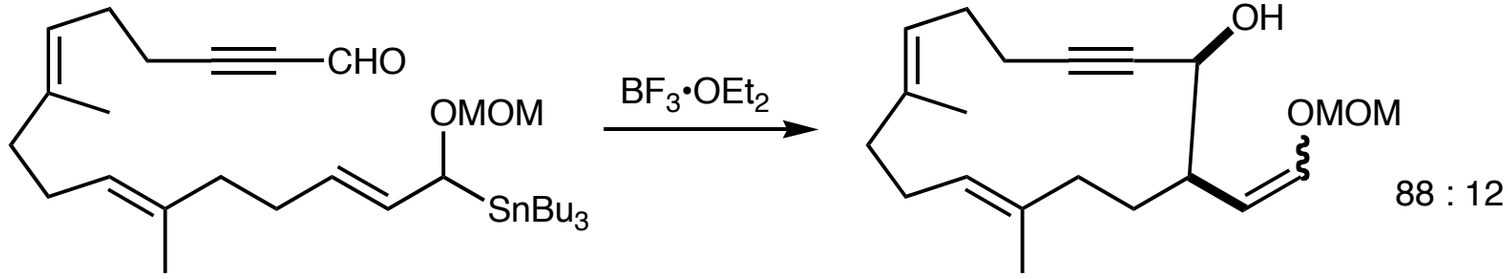
14 : 1 (from the *E*-isomer)
10 : 1 (from the *Z*-isomer)

Marshall, J. A. *Tetrahedron Lett.* **1987**, *28*, 527. *J. Org. Chem.* **1988**, *53*, 1616.



70 : 30

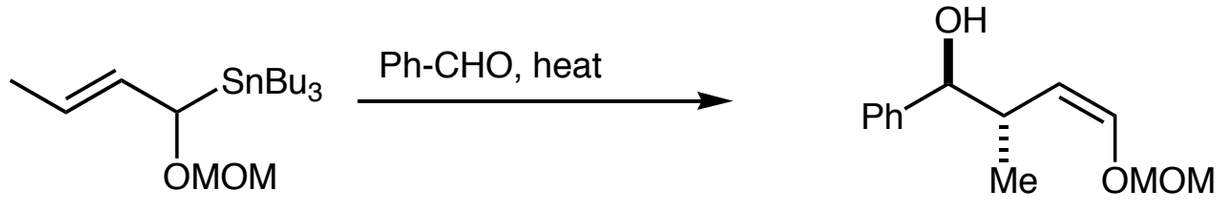
Application to:



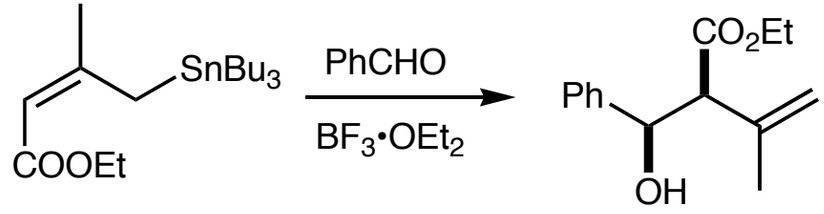
88 : 12

Reactions of Functionalized Allylstannanes

Thomas, E. J. *Perkin I* **1989**, 1521.

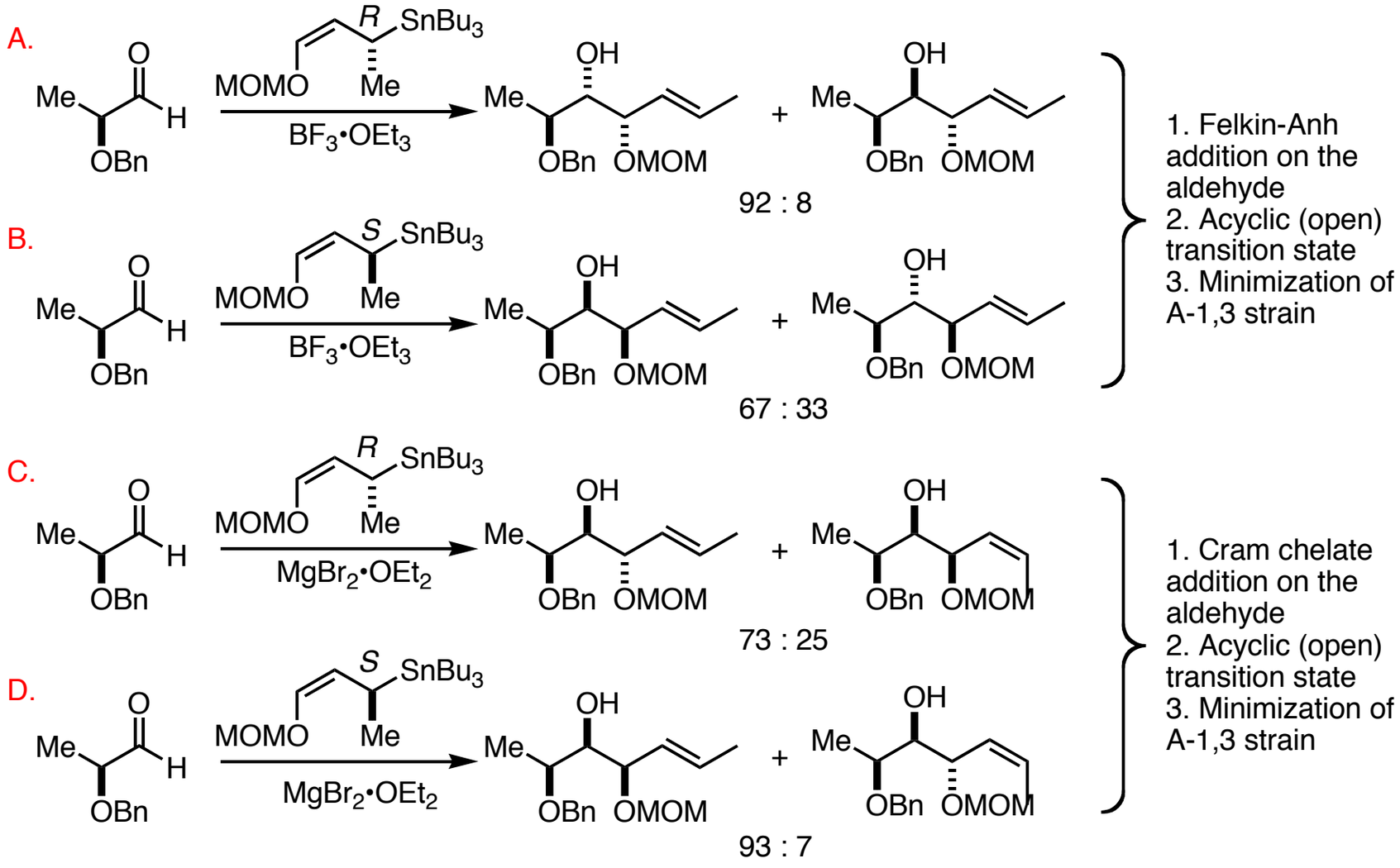


Yamamoto, Y. *J. C. S. Chem. Comm.* **1987**, 561.

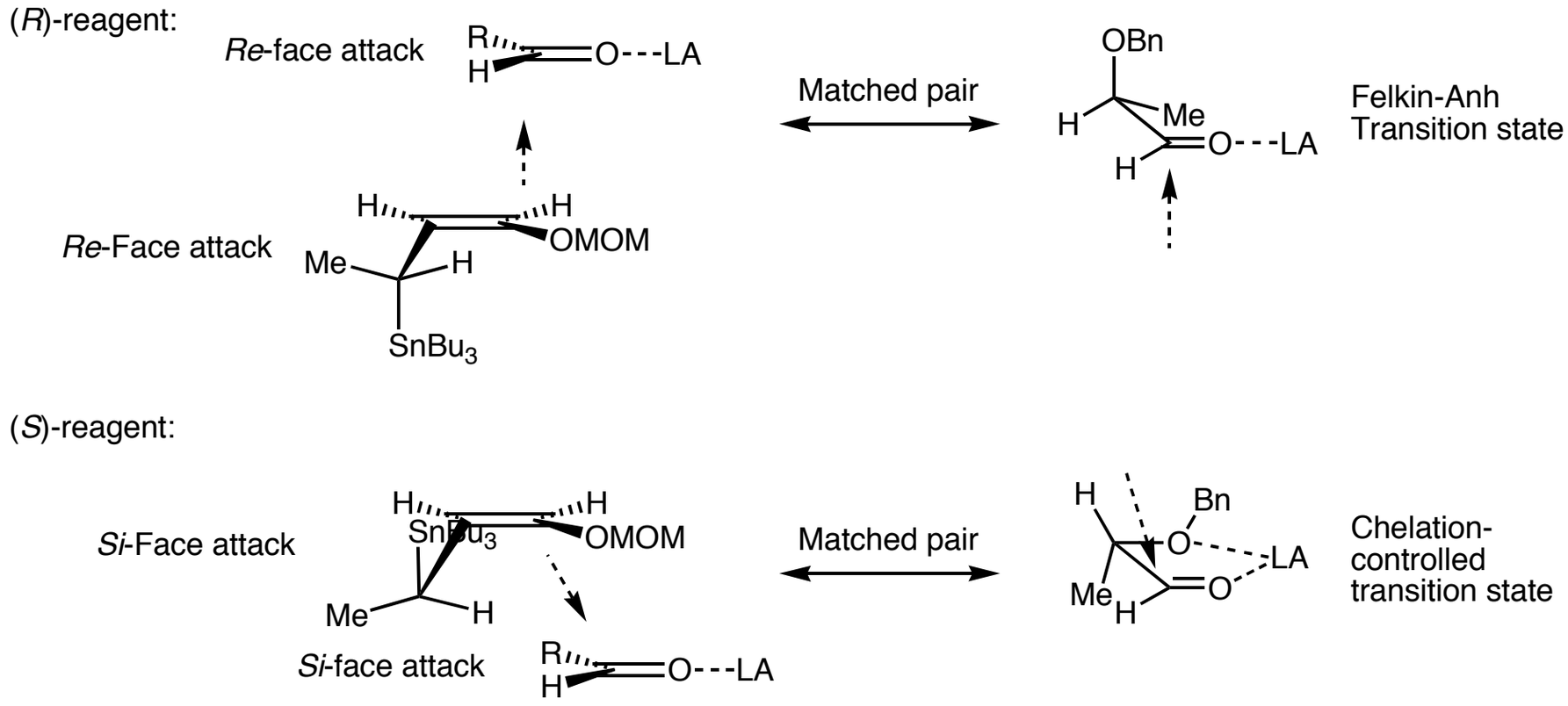


Reactions of Functionalized Allylstannanes

Marshall, J. A. *J. Org. Chem.* **1991**, *56*, 483.

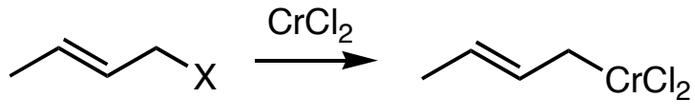


Reactions of Functionalized Allylstannanes

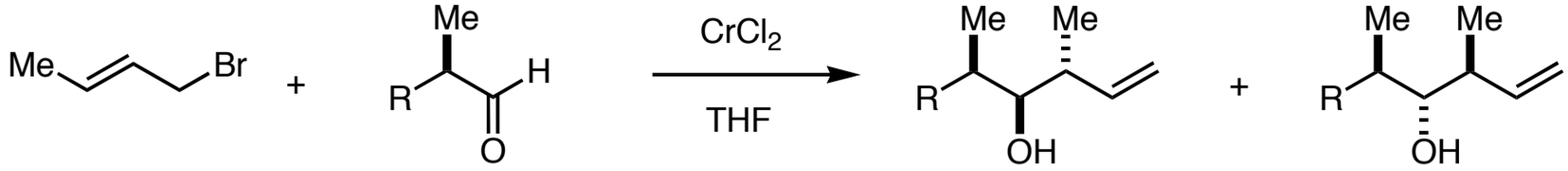


Crotyl Chromium Reagents: Anti-addition

Crotyl chromium: Preparation



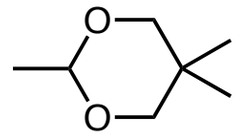
Cyclic transition state; No chelation control addition (Felkin-Anh control)

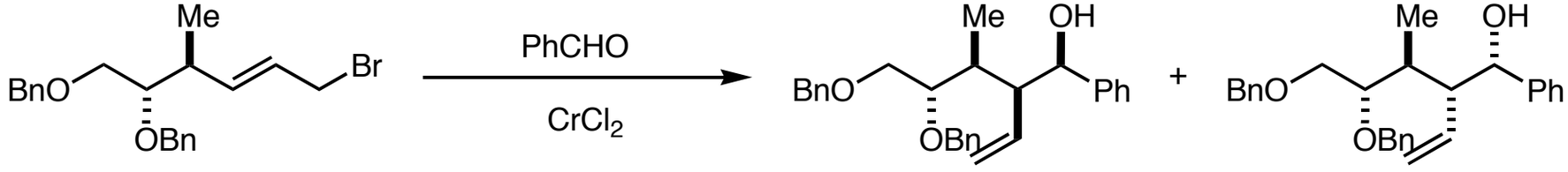


Tetrahedron Lett. **1982**, 2343.

R = -Ph 2.6 : 1

R = -CH_2OTHP 1 : 1

R =  11 : 1



96 : 4

J. Am. Chem. Soc. **1991**, 4218.

How would you prove the relative configuration?

Two-directional Chain Synthesis: Other Examples

Wang, Z.; Deschênes, D. *J. Am. Chem. Soc.* **1992**, *114*, 1090-1091.