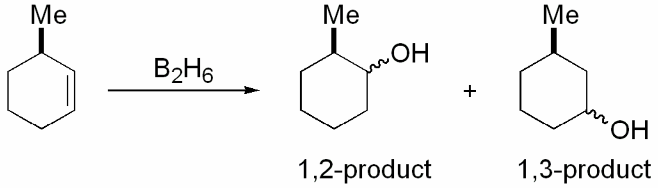
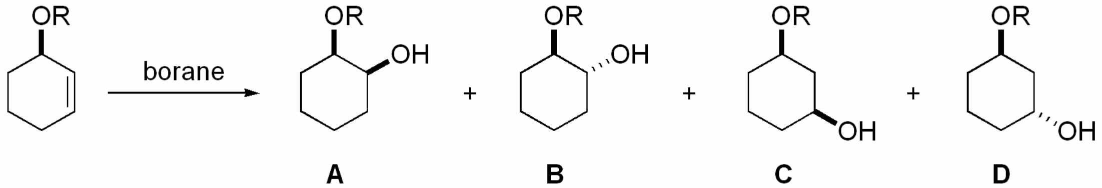
The Hydroboration Reaction

1. Regioselectivity



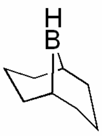
***trans* : *cis* = 2 : 1**

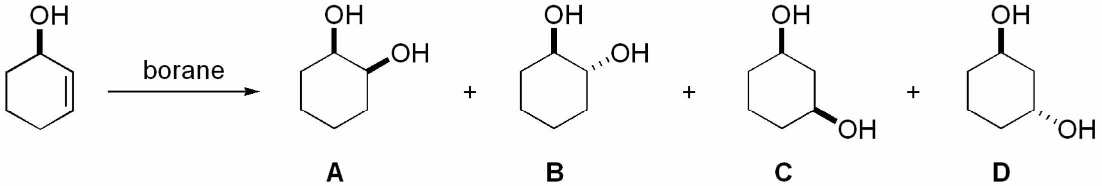


R	borane	ratio A	B	C	D
Me	B_2H_6	**10**	**81**	**9 (combined)**	
Bn	9-BBN	0	68	19	13
TBS	9-BBN	0	74	13	13

regioselectivity due to inductive effect

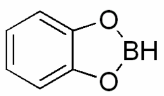
Both larger protecting groups and larger boranes give higher facial selectivity, but lead to reduced regioselectivity.

9-BBN (9-borabicyclononane) = 



borane	ratio A	B	C	D
B_2H_6	**6**	**86**	**8 (combined)**	
catechol borane, $(Ph_3P)_3RhCl$	1	18	9	72

inductive effect

catechol borane = 

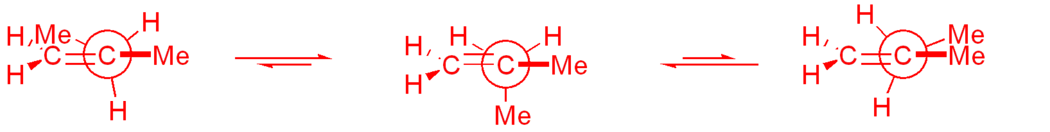
J. Am. Chem. Soc. **1988**, *110*, 6917.
J. Am. Chem. Soc. **1968**, *90*, 4445.
Tetrahedron **1972**, *28*, 1009.

Metal mediated and metal-free processes have complementary regioselectivities.

2. Substrate Stereocontrol

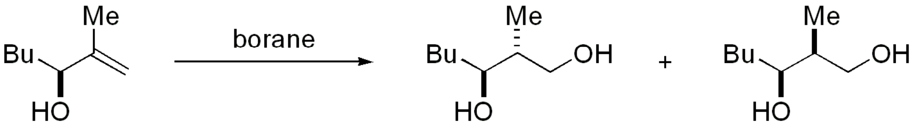
2.1. Allylic Stereocontrol

1,2-allylic stereocontrol:



allylic dihedral = 0°	allylic dihedral ~ 90°	allylic dihedral = 180°
E_s = ~ 0 kcal/mol	E_s = 0 kcal/mol	E_s = + 3.0 kcal/mol

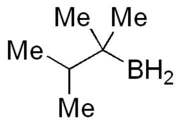
hydroboration: a classic in acyclic stereocontrol



anti ***syn***

borane	*anti* : *syn*
B_2H_6	1 : 1.4
$thxBH_2$	3.5 : 1
Cy_2BH	8.5 : 1
9-BBN	11 : 1

$thxBH_2$ (thexylborane) =

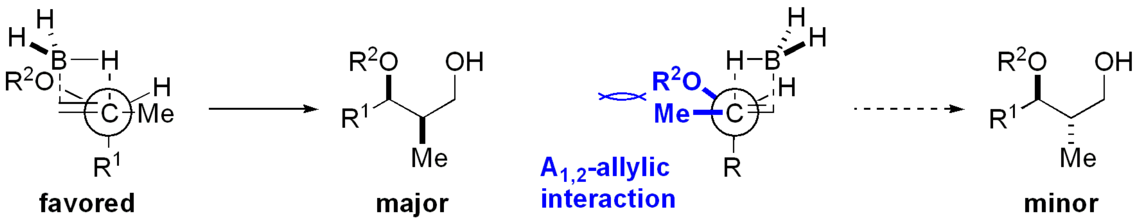


Cy_2BH = dicyclohexyl borane

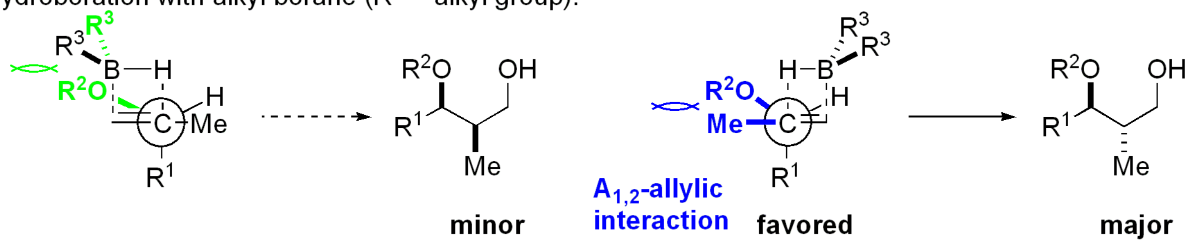
Still *J. Am. Chem. Soc.* **1983**, *105*, 2487.

explanation for difference between BH_3 and alkyl boranes:

for hydroboration with BH_3:



for hydroboration with alkyl borane (R^3 = alkyl group):

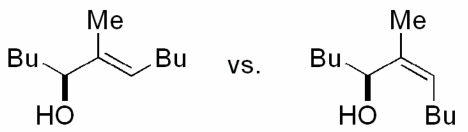


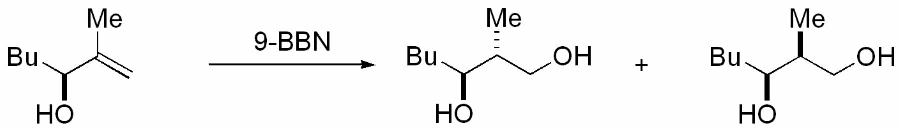
Interaction between R^3 and R^2O overrides $A_{1,2}$-allylic interaction between R^2O and Me. Consistent with this interpretation is the increase in selectivity with increasing size of R^3 on borane.

key point is interaction between substrate and reagent, see: Still *J. Am. Chem. Soc.* **1983**, *105*, 2487.

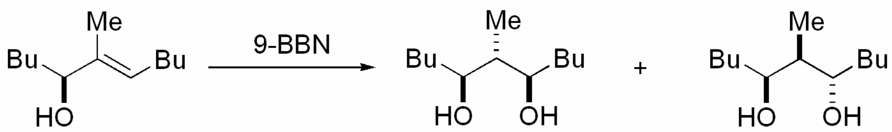
In addition to a careful conformational analysis of the substrates, interactions between reagent and substrate have to be taken into consideration.

1,3-allylic stereocontrol:



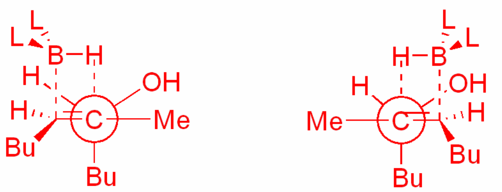


11 : 1

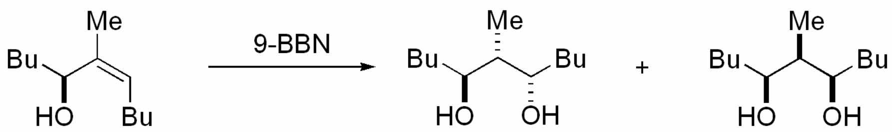


9 : 1

transition states:

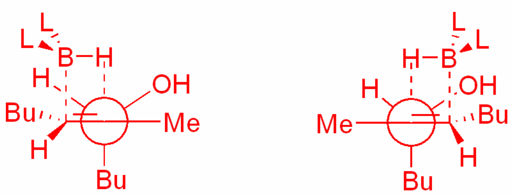


major **minor**



> 20 : 1

transition states:

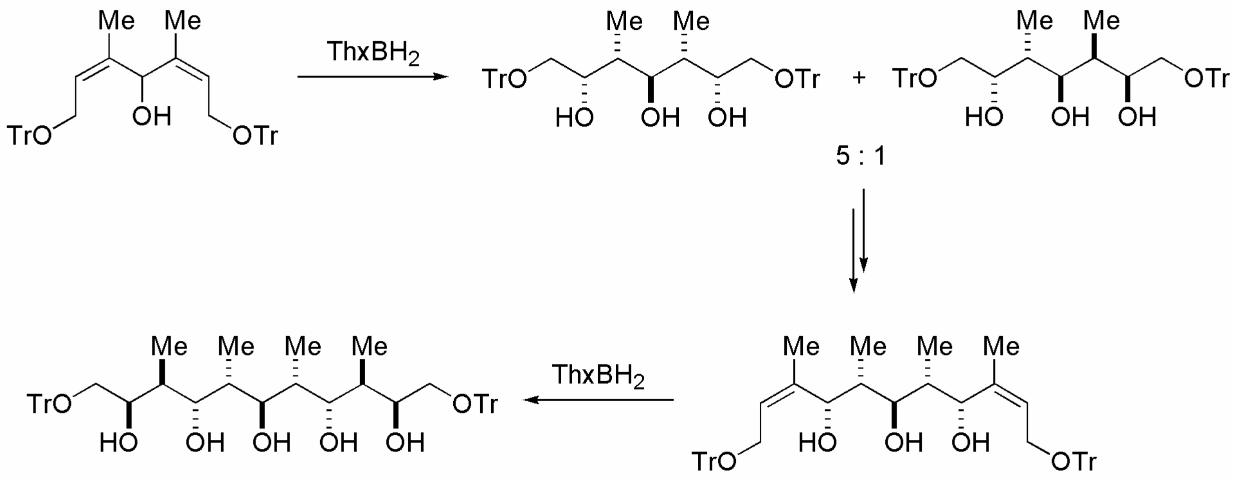


major **minor**

Still *J. Am. Chem. Soc.* **1983**, *105*, 2487.

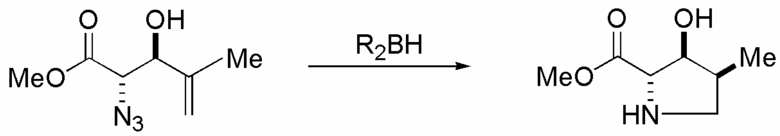
applications:

rifamycin synthesis:

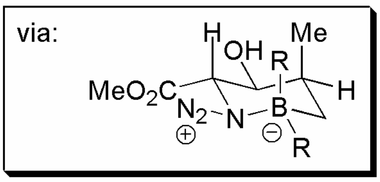


J. Am. Chem. Soc. **1983**, *105*, 2487.

echinocandin synthesis:

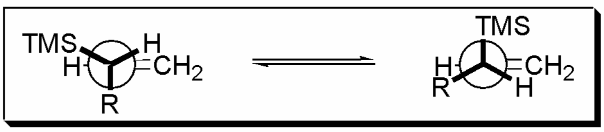


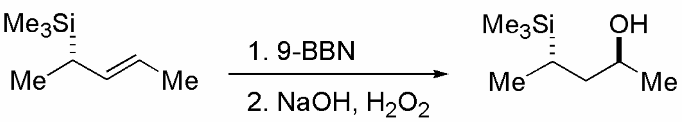
single isomer

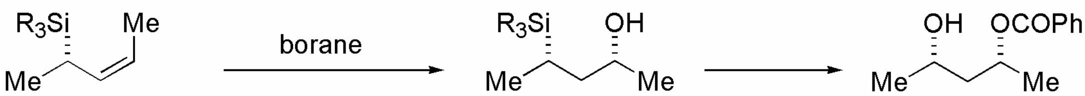


Evans *J. Am. Chem. Soc.* **1987**, *109*, 7151.

stereoelectronic effects:

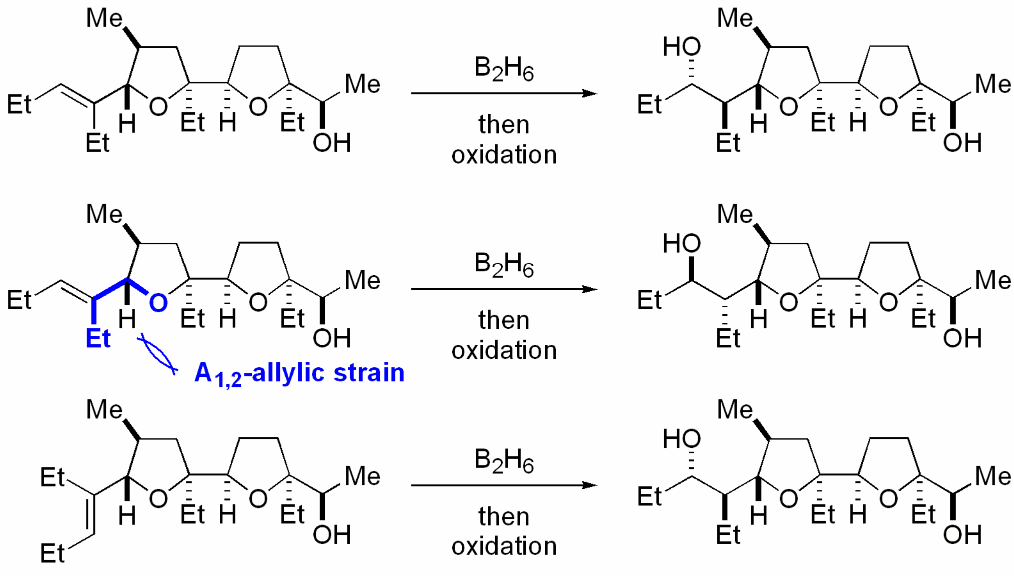




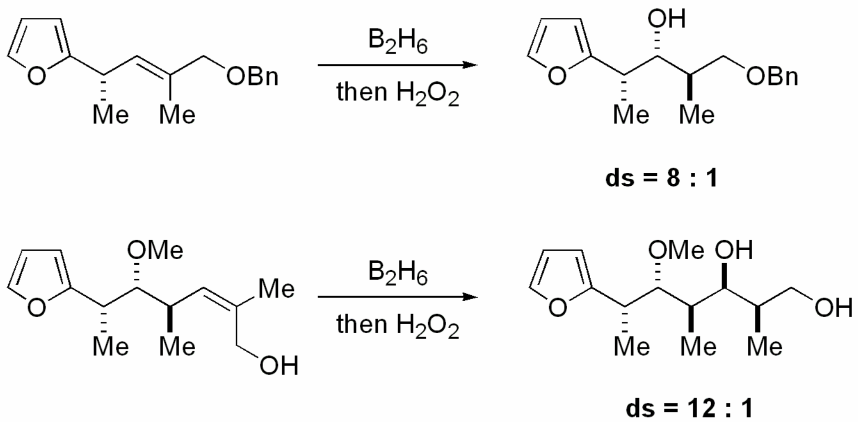


Fleming *Tetrahedron Lett.* **1988**, *29*, 2077.

monensin synthesis:

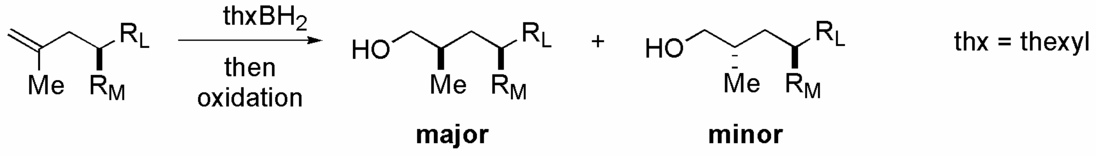


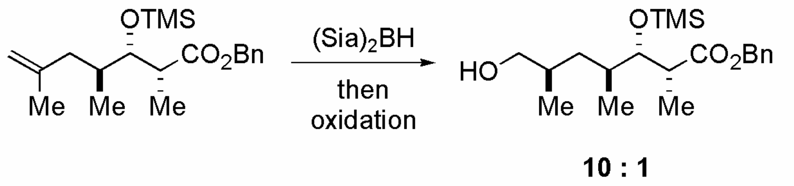
J. Am. Chem. Soc. **1978**, *100*, 2933.

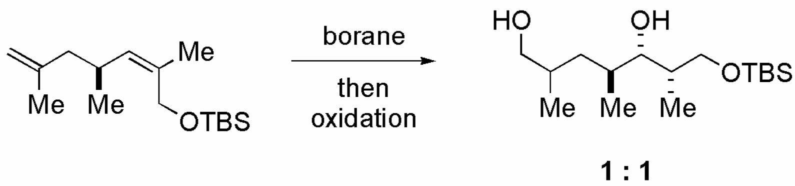


Kishi *J. Am. Chem. Soc.* **1979**, *101*, 259.

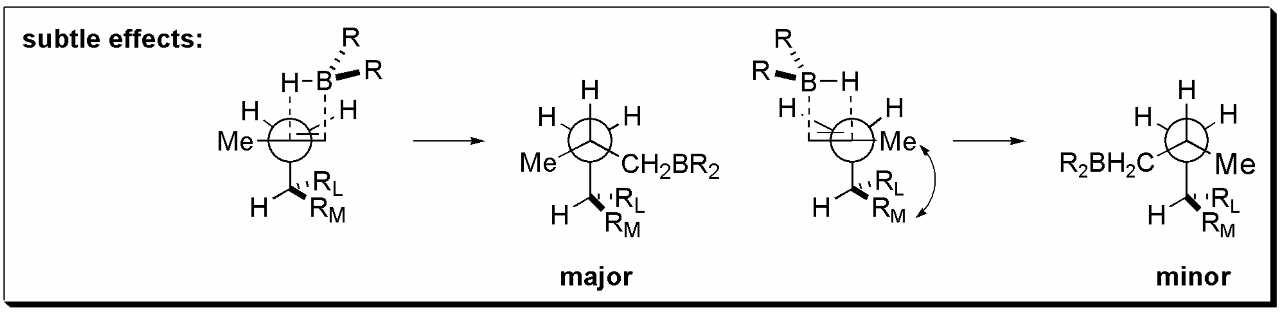
2.2. Homoallylic Stereocontrol

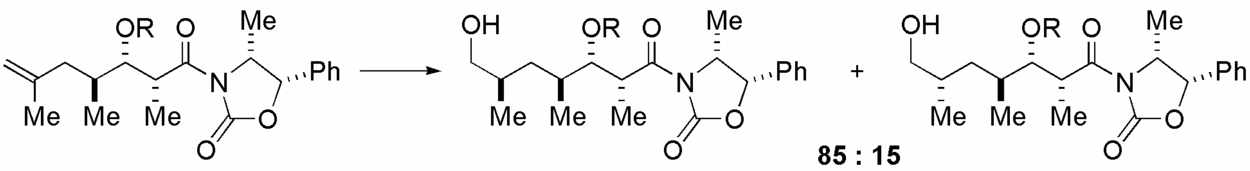


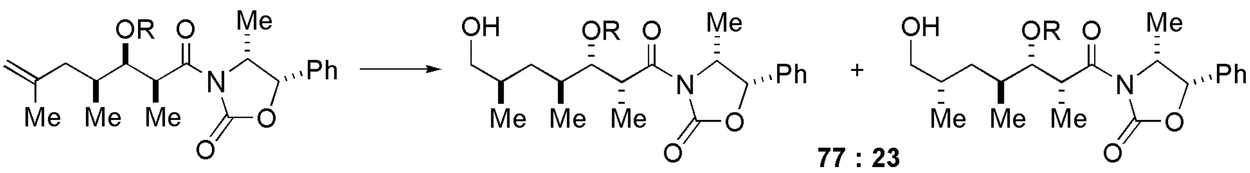




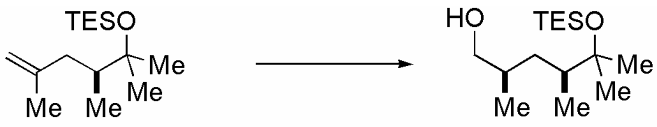
Evans *Tetrahedron Lett.* **1982**, *23*, 4577.



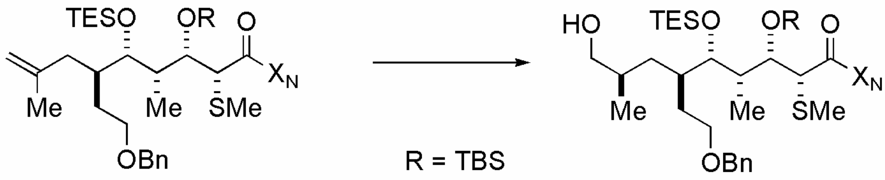




Same sense of induction observed, as reaction is directed by proximal chiral center.

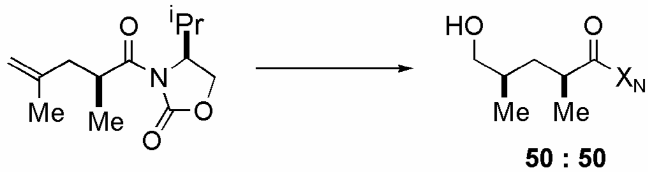


82 : 18



91 : 9

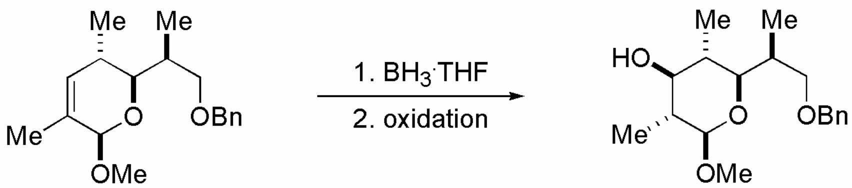
consider however:



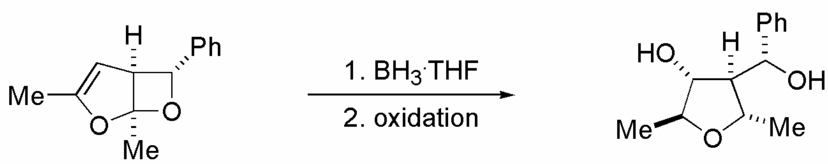
50 : 50

2.3. Cyclic Stereocontrol

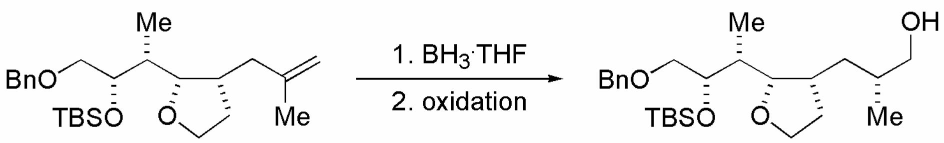
examples:



Danishefsky *J. Am. Chem. Soc.* **1987**, *109*, 862.

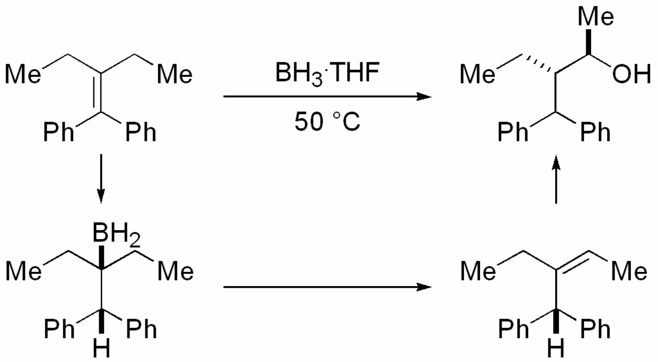


Schreiber *J. Am. Chem. Soc.* **1983** *105*, 660.



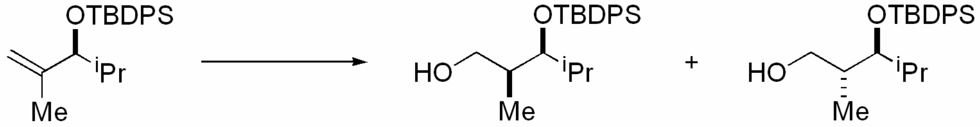
Nicolaou *J. Am. Chem. Soc.* **1982**, *104*, 2028.

2.4. Reversibility of the Hydroboration Reaction



J. Am. Chem. Soc. **2000**, *122*, 10218.

2.5. Rhodium-Catalyzed Hydroboration



syn ***anti***

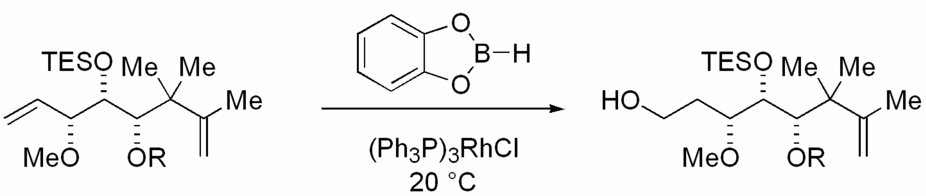
reagent	*syn* : *anti*
9-BBN	5 : 95
catechol borane, Wilkinson's catalyst	**97 : 3**

Evans *J. Am. Chem. Soc.* **1991**, *113*, 4042.
J. Am. Chem. Soc. **1992**, *114*, 6679.
J. Org. Chem. **1992**, *57*, 504.
Chem. Rev. **1991**, *91*, 1179.
Tetrahedron **1997**, *53*, 4957.

important features:

1. opposite sense of induction compared to uncatalyzed hydroboration
2. high selectivity for monosubstituted olefins

calyculin synthesis:

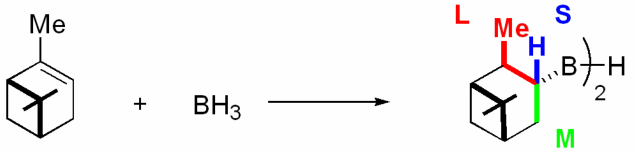


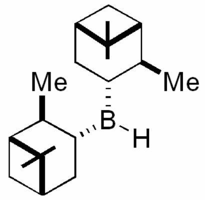
R = TBS

Evans *J. Am. Chem. Soc.* **1992**, *114*, 9434.
J. Org. Chem. **1992**, *57*, 1961.
J. Org. Chem. **1992**, *57*, 1964.

3. Enantioselective Hydroborations

Brown hydroboration:

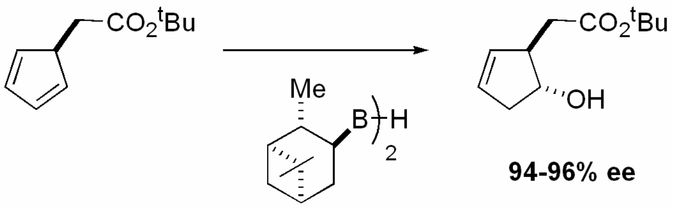




$(Ipc)_2BH$ = bis(isopinocampheyl) borane)

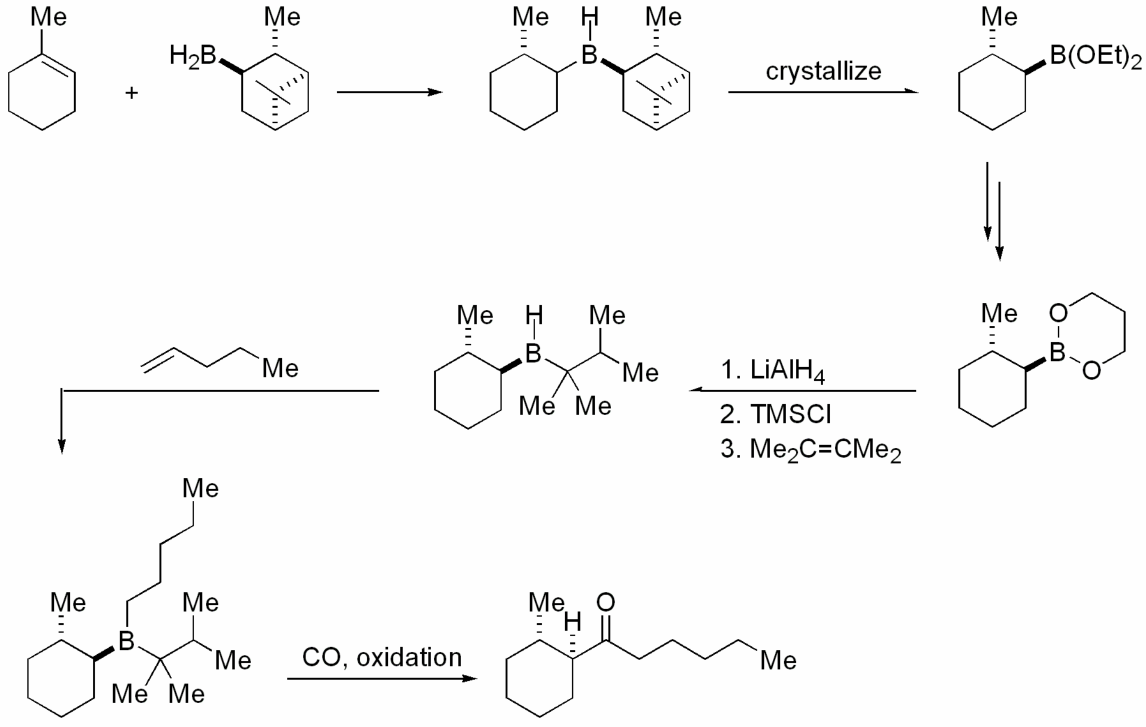
Tetrahedron **1981**, *37*, 2547.

(*Z*)-alkenes react with better selectivity (75-90% ee) than (*E*)-alkenes (5-30% ee).



94-96% ee

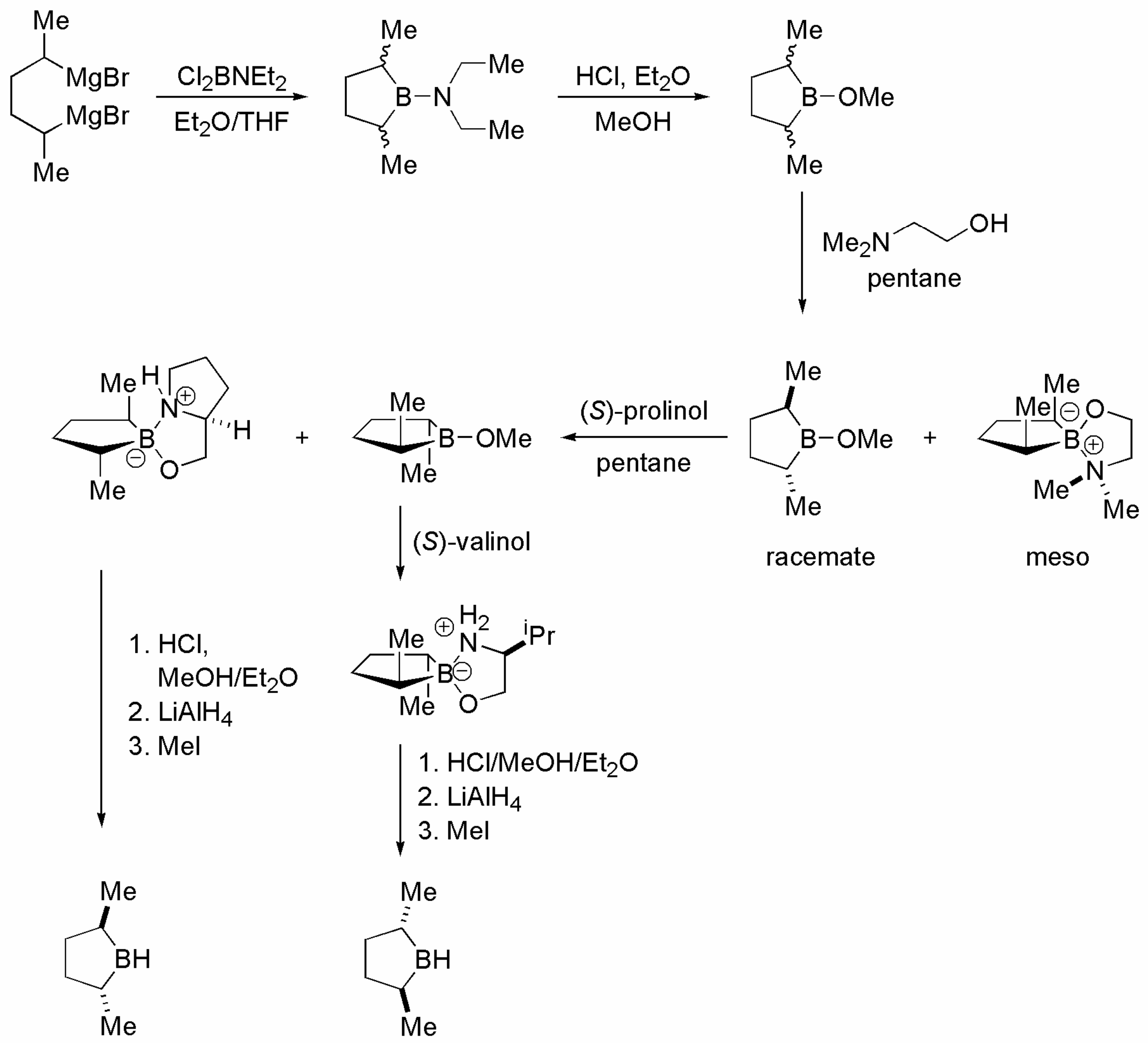
Org. Syn. **1985**, *63*, 44.
J. Am. Chem. Soc. **1985**, *107*, 4549.



> 99% ee
99% trans

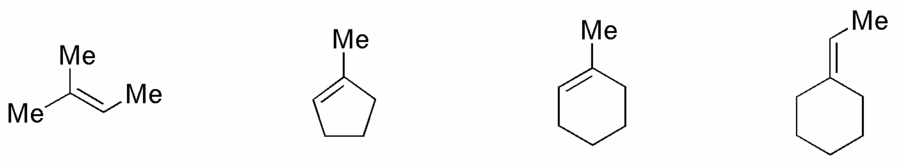
J. Am. Chem. Soc. **1988**, *110*, 1529.

Masamune hydroboration:



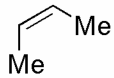
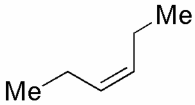
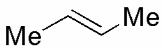
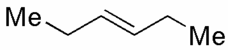
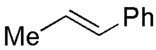
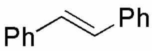
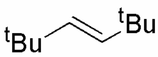
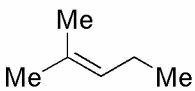
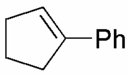
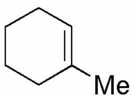
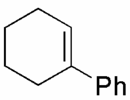
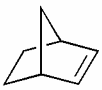
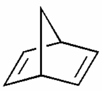
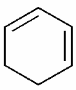
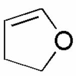
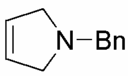
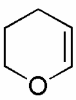
Masamune *J. Am. Chem. Soc.* **1985**, *107*, 4549.

selected substrates:



97.6% ee **100% ee** **95.6% ee** **99.3% ee**

substrate scope of the asymmetric hydroboration:

alkene	ee with 1 [%]	ee with Ipc_2BH [%]
	97.6	98
	99.9	93
	99.5	73
	99.5	75
		76
		65
		92
		58
		100
		72
		88
		83
		80
		93
		100
		100
		83

1 =