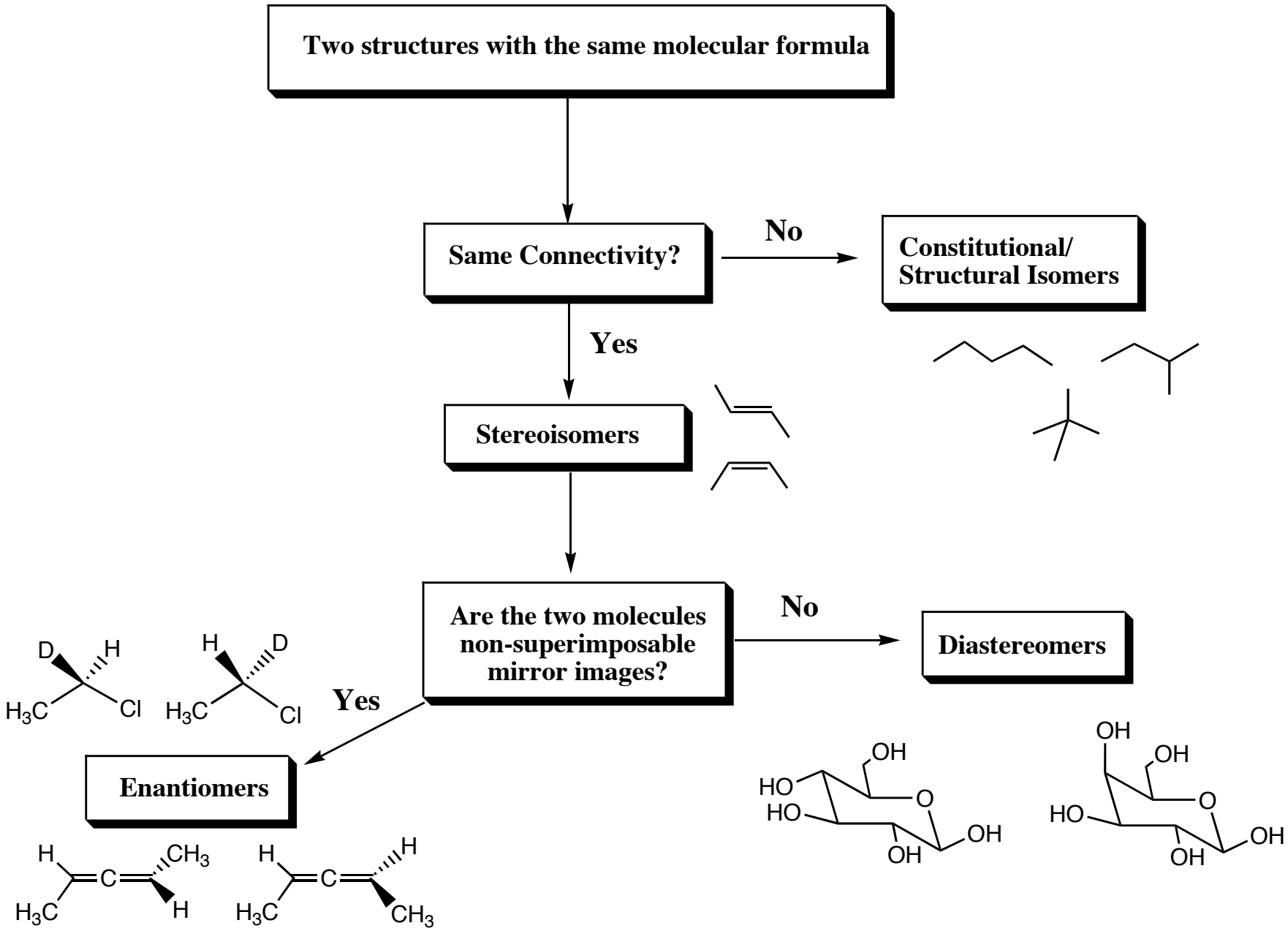
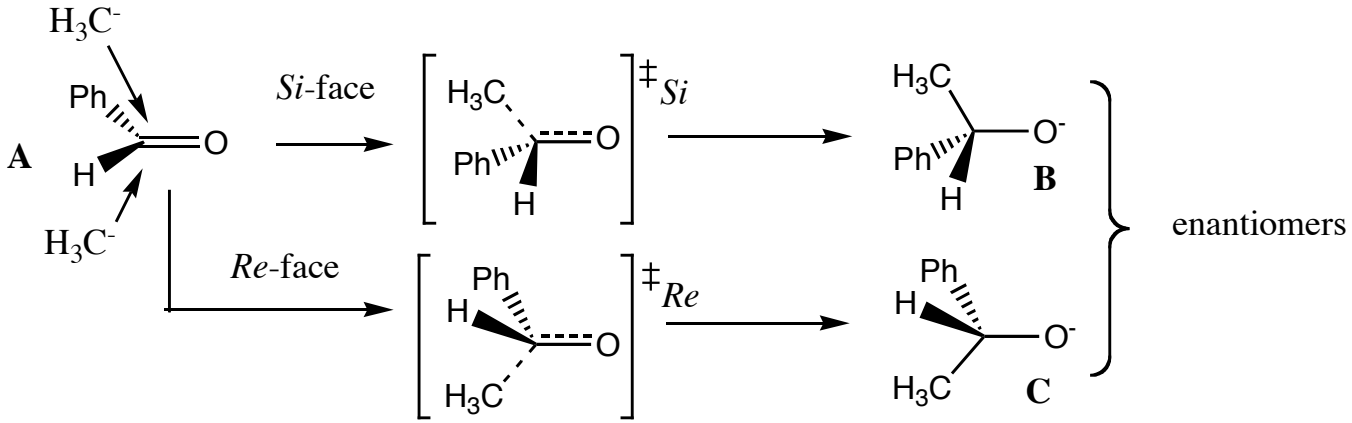
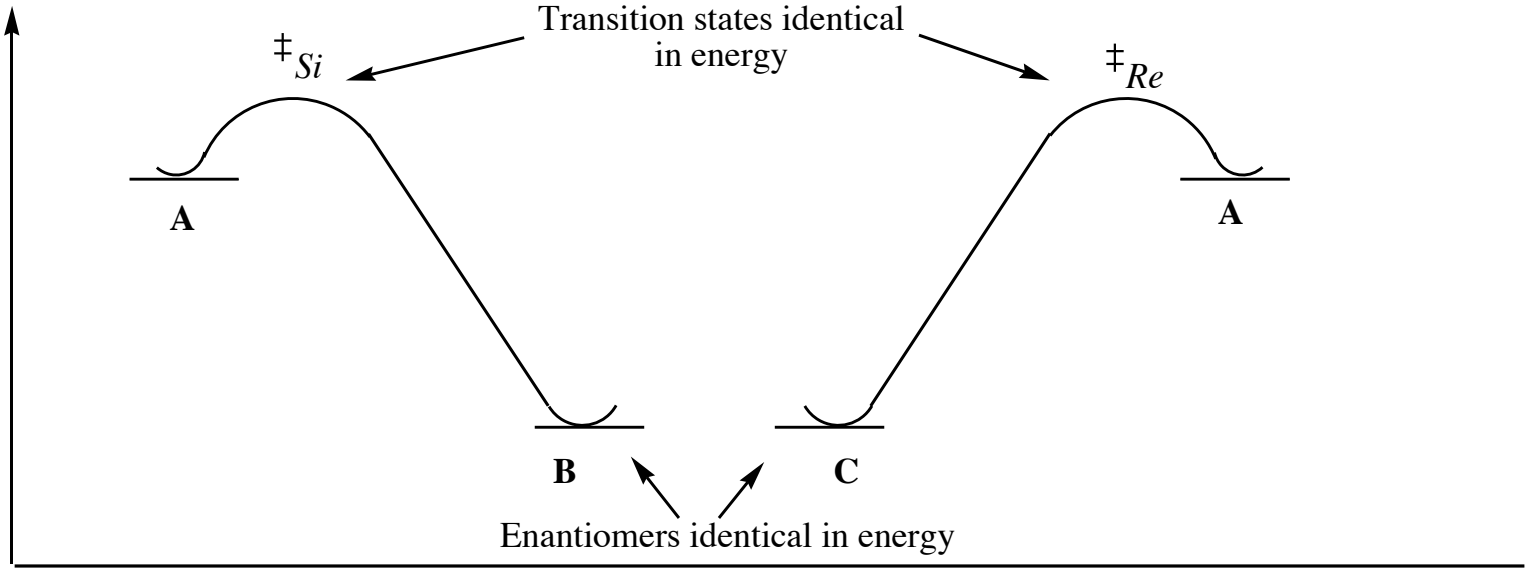
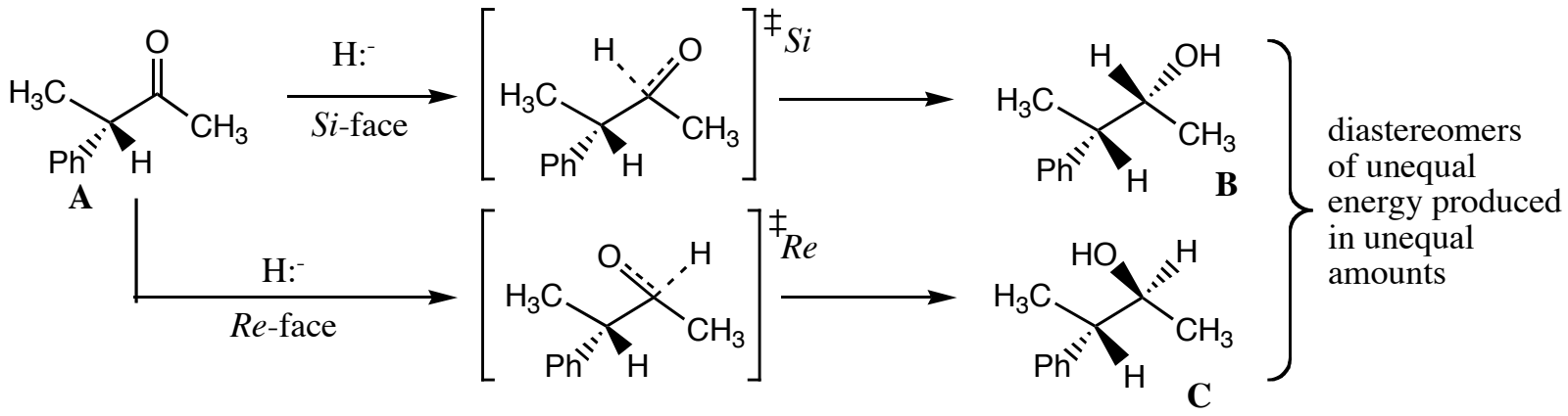

Two structures with the same molecular formula
Same Connectivity?
No
Constitutional/
Structural Isomers
Yes
Stereoisomers
Are the two molecules
non-superimposable
mirror images?
No
Diastereomers
Yes
Enantiomers

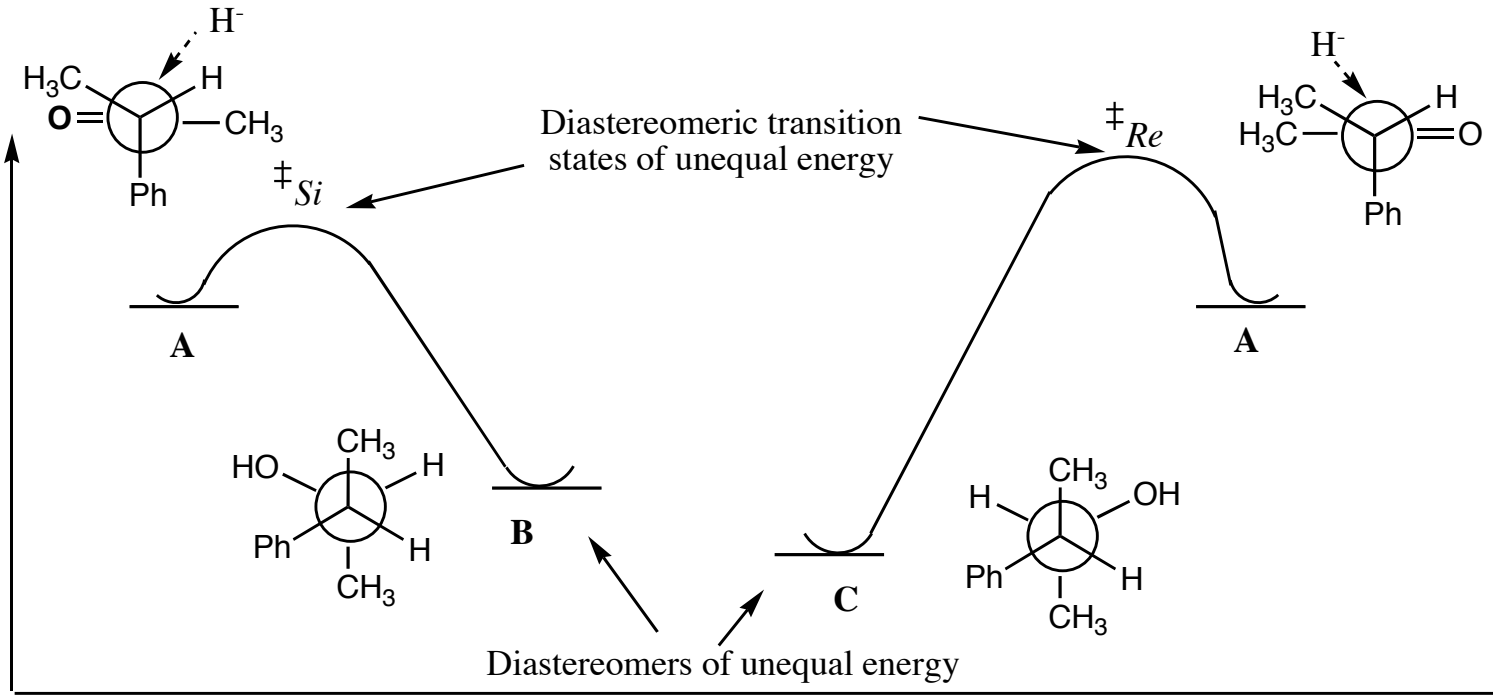
Addition to a carbonyl with enantiotopic faces produces equal amounts of enantiomers





Addition to a carbonyl with diastereotopic faces produces unequal amounts of diastereomers





Reaction Stereochemical Outcomes

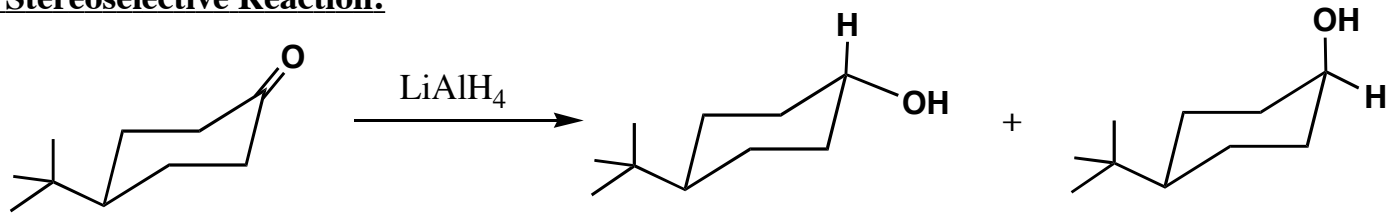
Reagent Control of the stereochemical outcome of a reaction: The selection of reagent/catalyst dictates the ultimate absolute stereochemistry of reaction products irrespective of the stereofacial bias of the substrate. Often chiral catalysts or reagents will act on racemic or achiral starting materials to generate products with enantiomeric excess.

Substrate Control of the stereochemical outcome of a reaction: The stereochemistry of reaction products is dictated by the inherent stereofacial bias of the substrate.This typically means there is an existing stereochemical element within the starting material/ substrate which directs the interaction of a reagent or reagents with the substrate

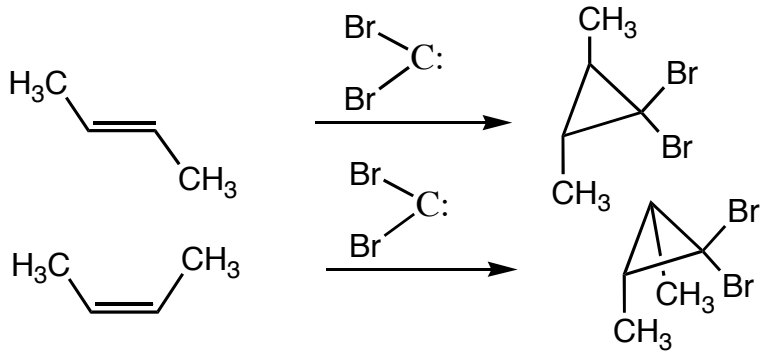
Substrate Control

Stereochemical Terminology

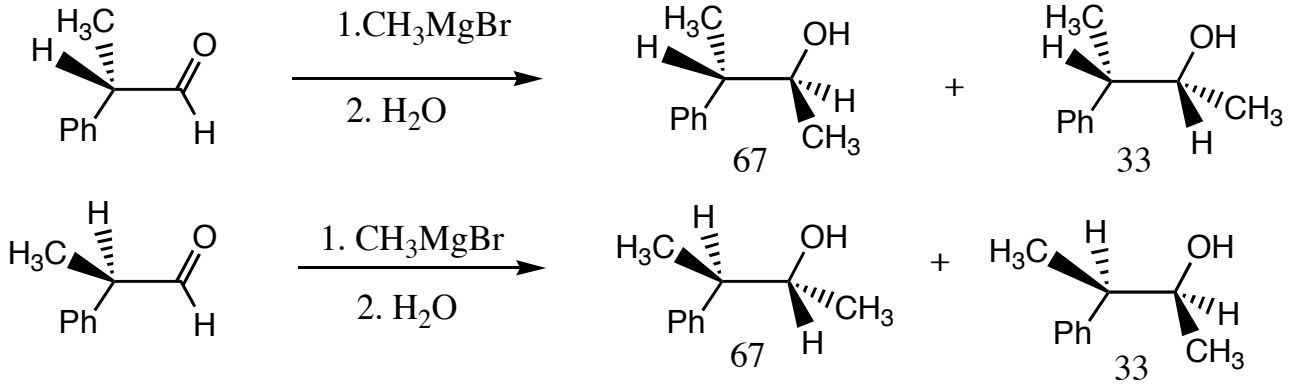
A Stereoselective Reaction:



A Stereospecific Reaction



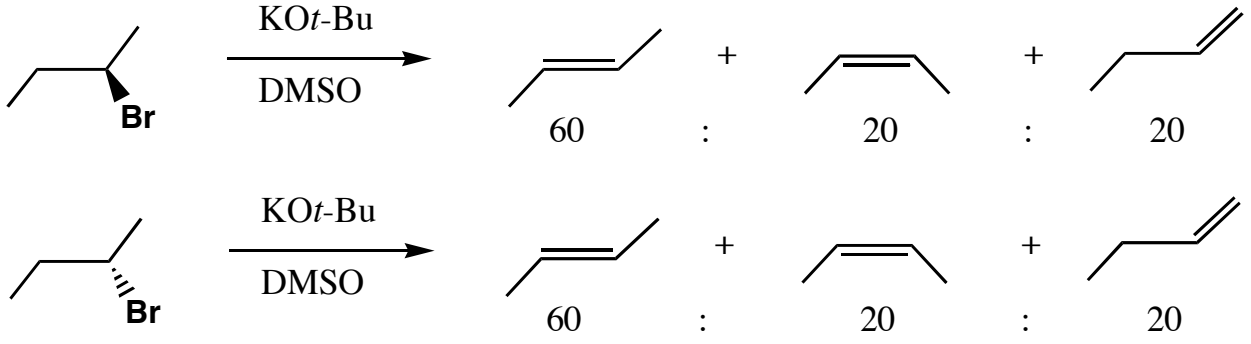
A Stereospecific Reaction



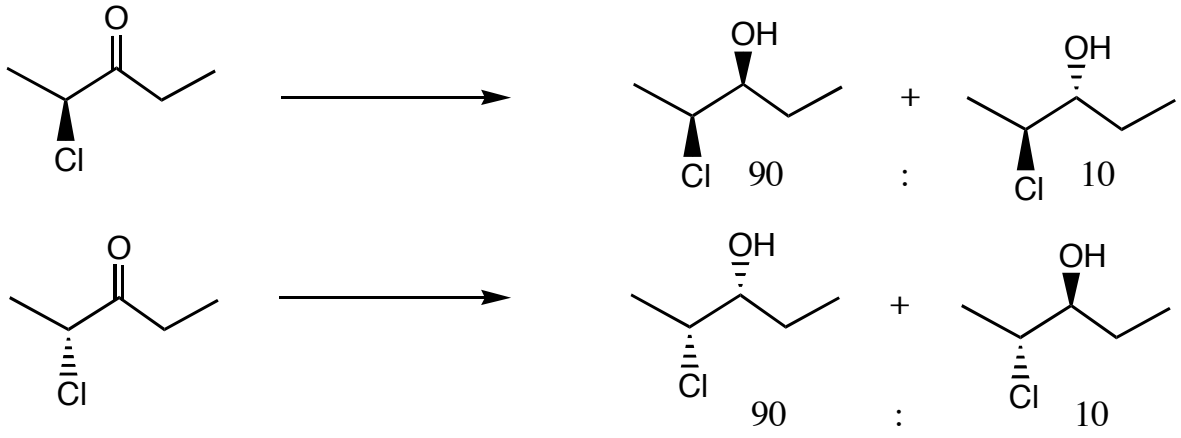
Substrate Control

Stereochemical Terminology

Stereoselective, not Stereospecific:

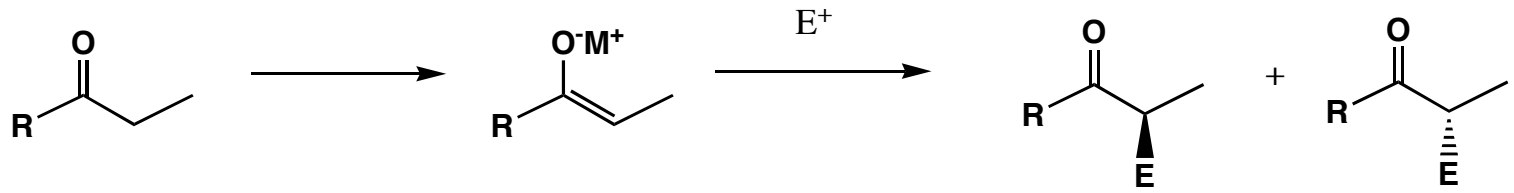


Diastereoselective and Stereospecific:



Substrate Control of the Stereochemical Course of a Reaction

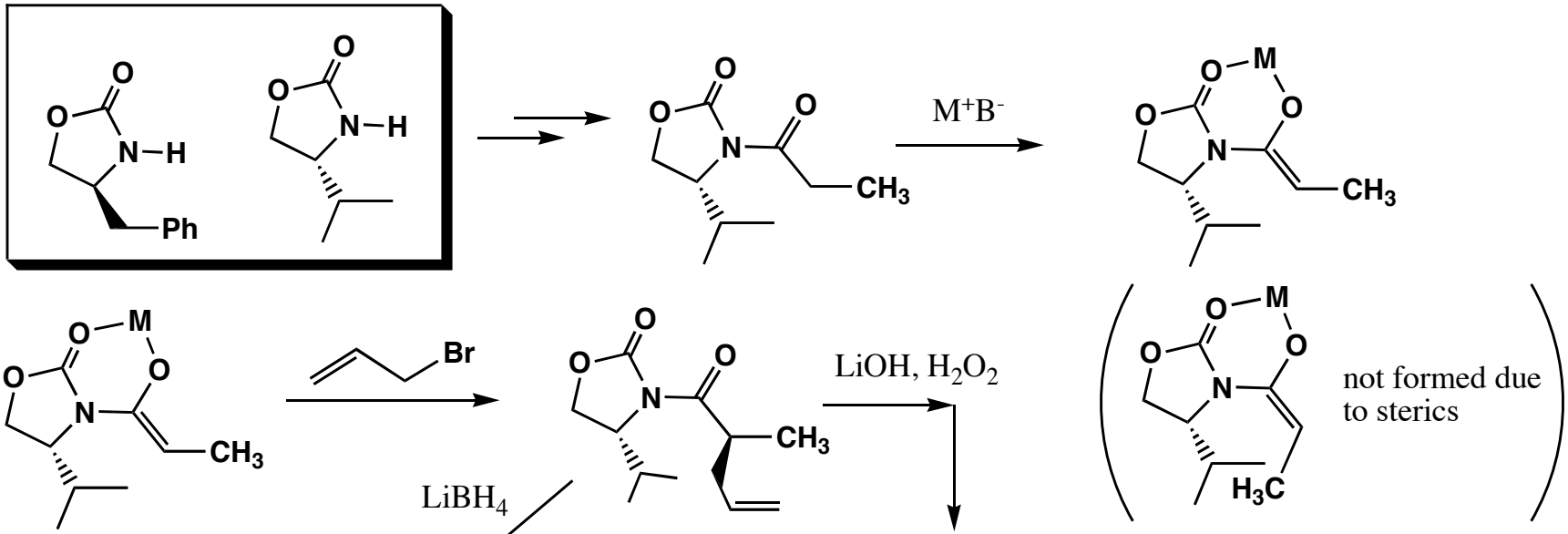
Removable Chiral Auxiliaries for Enolate Alkylation



Solution: use a chiral R group which is removable.

enantiomeric excess?

Evan's Chiral Oxazolidinones, X_C:



not formed due to sterics

isopropyl directs addition of E^+ to *Si* face.

Products in high enantiomeric excess!

JACS, **1982**, *104*, 1737

Effective for aldol reactions also, where E^+ = RCHO.

•Homotopic Groups or Faces *Cannot* be distinguished by Chiral Reagents

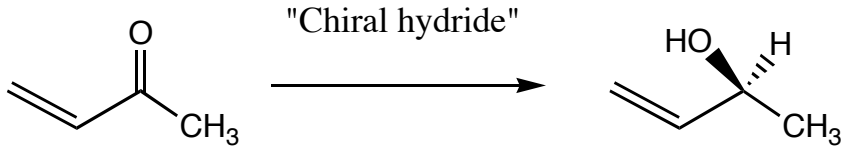
•Enantiotopic Groups or Faces *Can* be distinguished by Chiral Reagents

•Diastereotopic Groups or Faces *Can* be distinguished by *both* Chiral and Achiral Reagents

Reagent Control

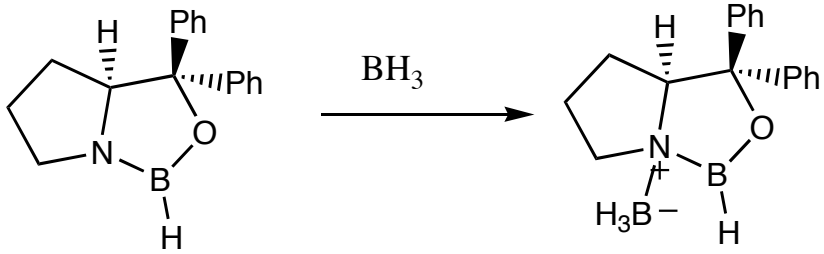
Distinguishing Enantiotopic Reactant Faces, I

Catalytic Asymmetric Carbonyl Reduction

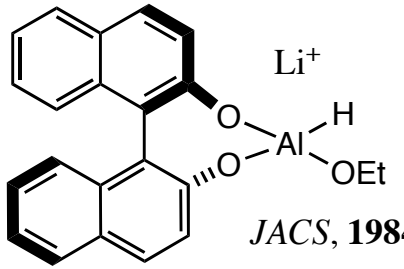


enantiomeric excess = the percentage excess of one enantiomer over another= ***R***-***S***/***R*** +***S*** x 100

Corey Oxazaborolidine *ACIEE,* **1998**, *37,* 1985.

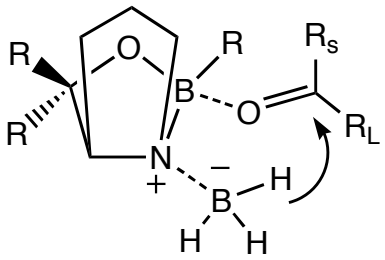


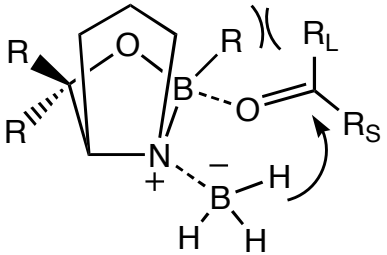
Noyori BINAL-H



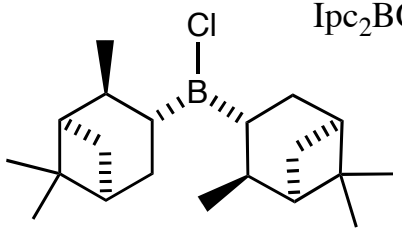
JACS, **1984**, *106*, 6709

Diastereomeric complexes lead to diastereomeric transition states, thusgiving rise to enantiomeric excess in the product mixture.





Ipc_2BCl



Brown and Midland, *JOC*, **1989**, *54*, 159, 4504.

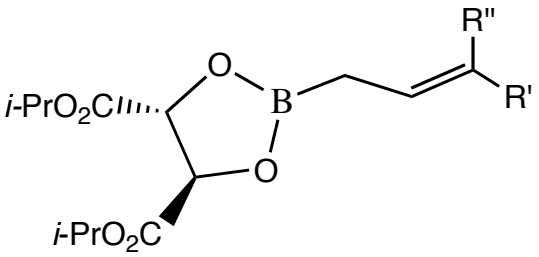
Reagent Control

Distinguishing Enantiotopic Reactant Faces, II

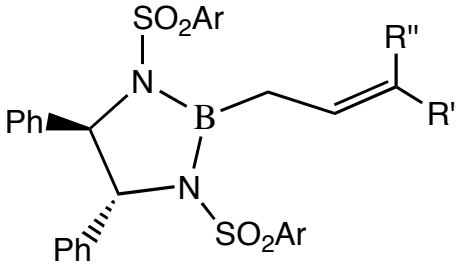
Chiral Boron Reagents and Asymmetric Allylation

Asymmetric Synthesis: a synthesis proceeding from enantiomerically enriched starting materials, or a synthesis in which one (or more) of the steps generates enantioenriched material.

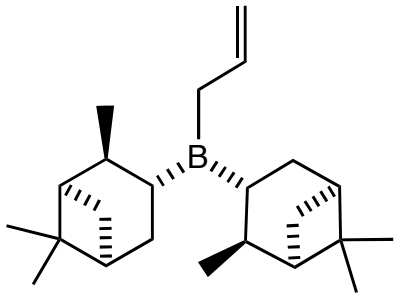
Chiral, C2-symmetric allyl boronates:



Brown, Roush
JOC, **1990**, *55*, 4109, 4117.

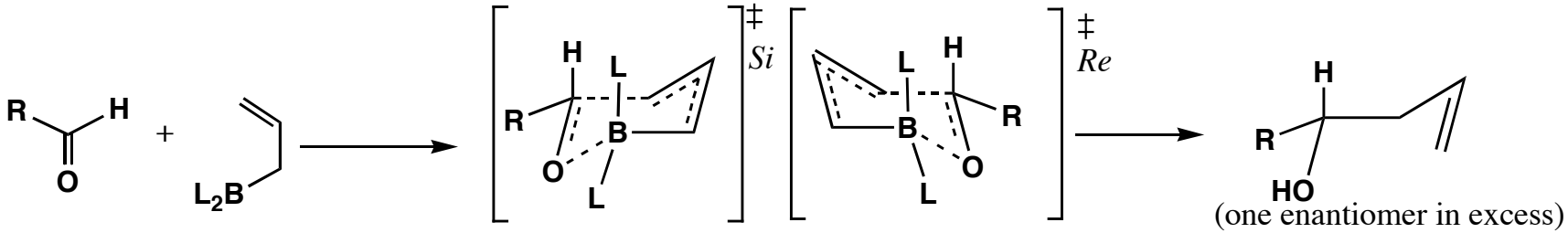


Corey
JACS, **1990**, *112*, 878



Brown
JOC, **1991**, *56*, 401.

A Chair Transition State is common for such reactions:



prochiral aldehyde

coordination of *Si*-face of prochiral aldehyde preferred because of spatial orientation of chiral ligand on boron

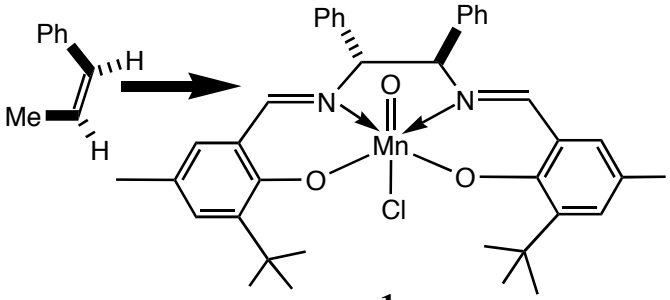
(one enantiomer in excess)

Note: the opposite enantiomer of allylboronate gives the enantiomeric homoallylic alcohol product

Reagent Control

Alkenes have prochiral faces, also!

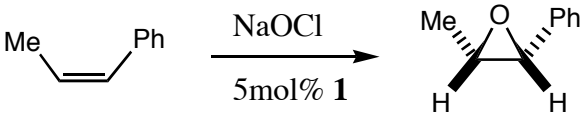
Catalytic Asymmetric Epoxidation



1

side-on perpendicular approach of alkene to metal-oxo species

chiral manganese-salen complex

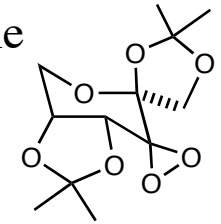


84%ee, 88% yield

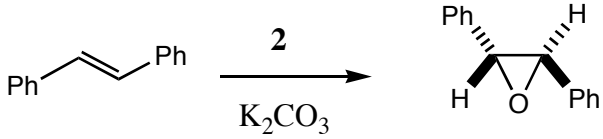
JACS, **1991**, *113*, 7063.

Shi Chiral Dioxirane Reagent

JOC, **1997**, *62*, 2328.

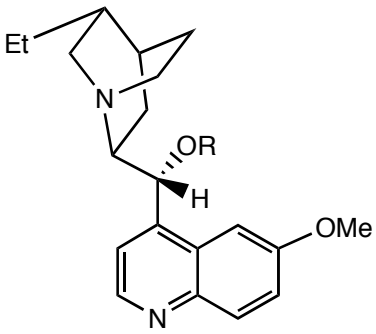


2

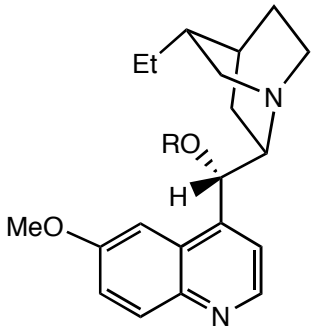


Sharpless Catalytic Asymmetric Dihydroxylation (AD): ligand accelerated catalysis

*Chem.Rev.***1994**, *94*, 2483.

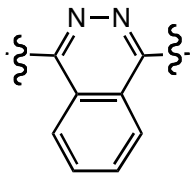


DHQ (dihydroquinine)

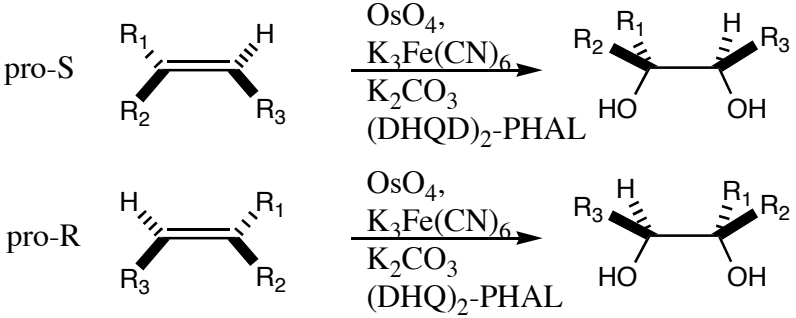


DHQD (dihydroquinidine)

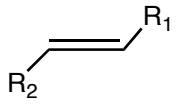
R=PHAL



linker



84-93% ee

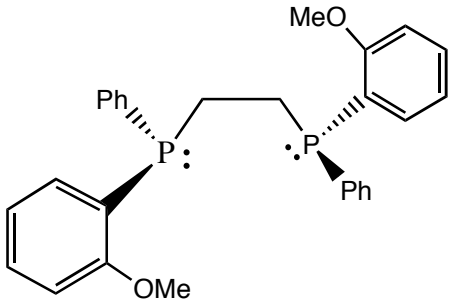


94-99% ee

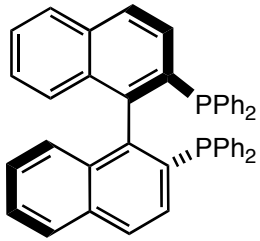
Reagent Control

Alkenes have prochiral faces, also!

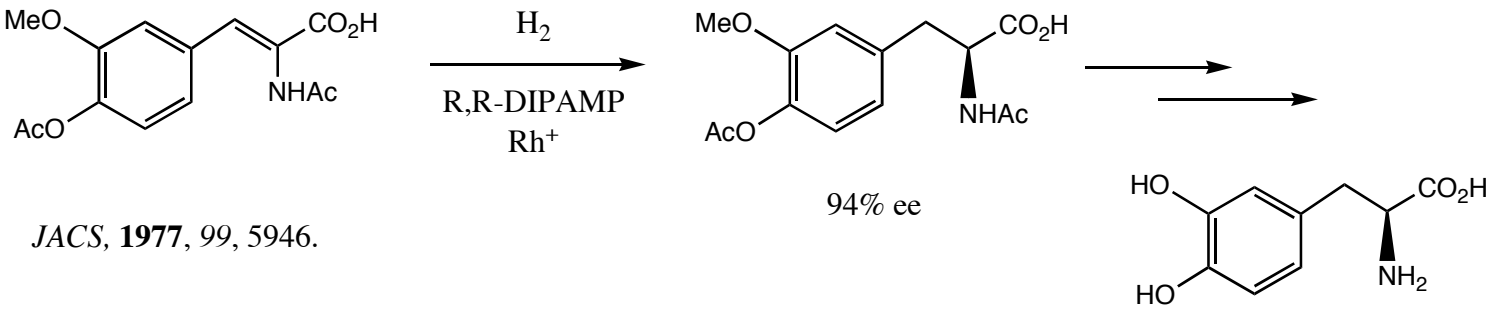
Enantioselective Hydrogenation of Alkenes



(R,R)-DIPAMP (Chiral at phosporous)



(S) - BINAP



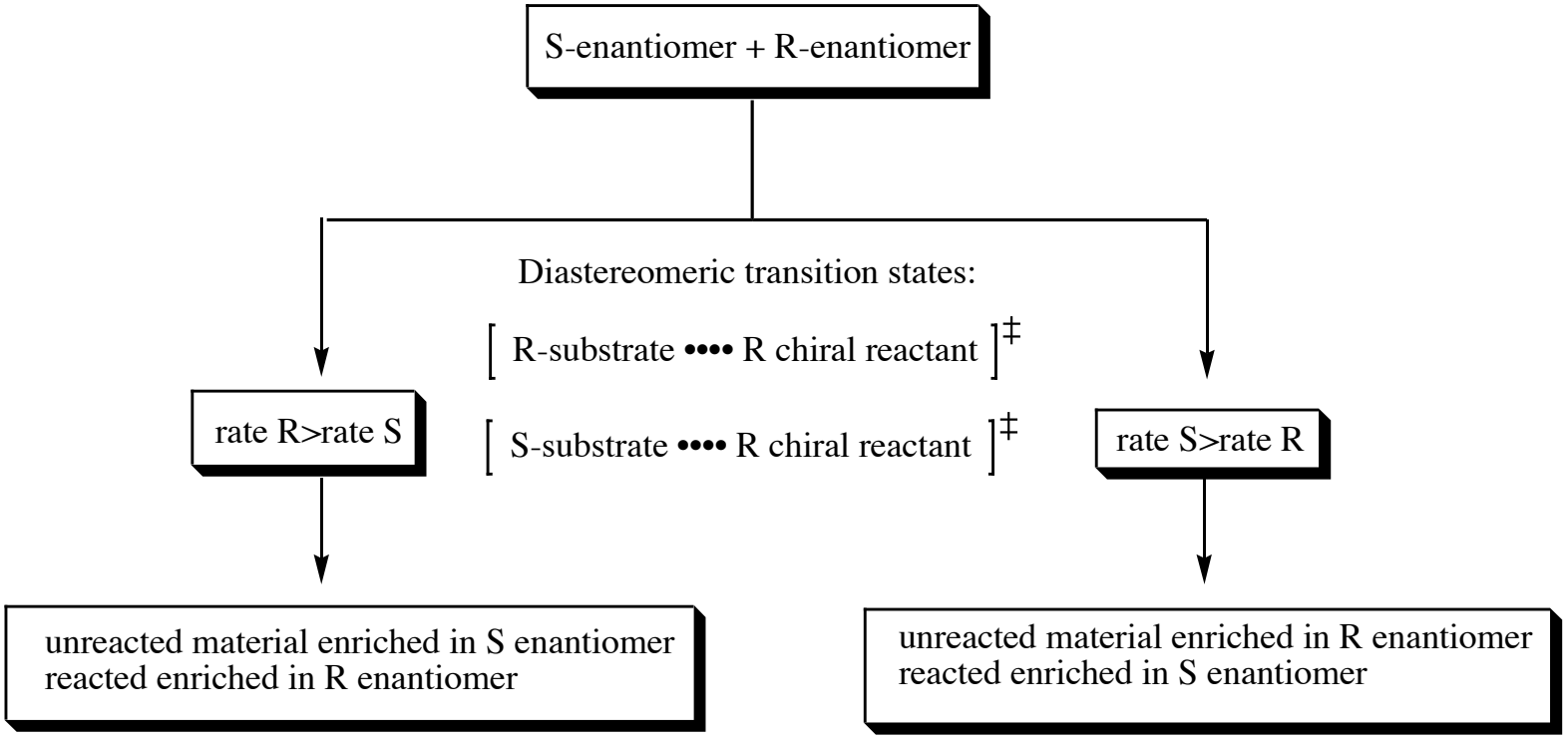
94% ee

L-DOPA

JACS, **1977**, *99*, 5946.

Kinetic Resolution

The separation of enantiomers based the different reaction rates of each enantiomer with enantiomerically pure reagents. The greater the difference in the two rates (k_S/k_R), the higher the ee of both the reacted and unreacted enantiomers.



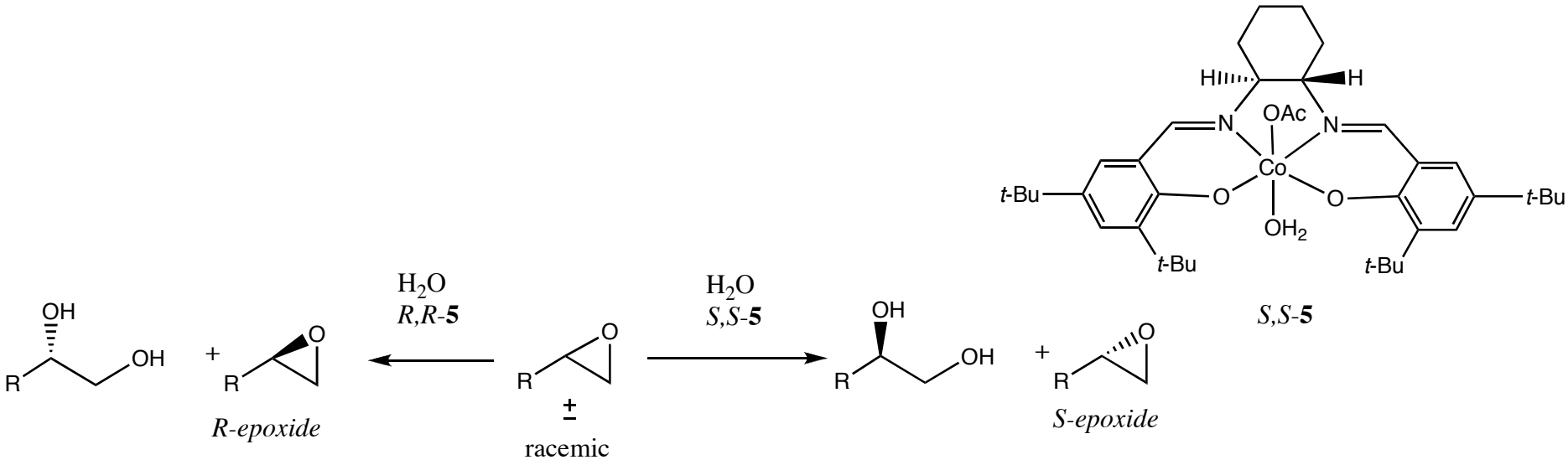
The ratio of the rate constants k_S/k_R determines e.e. of the reacted material. As the degree of conversion increases, the ee of the unreacted enantiomer becomes very high, but the yield decreases.

consider a reaction in which $k_S/k_R=15$

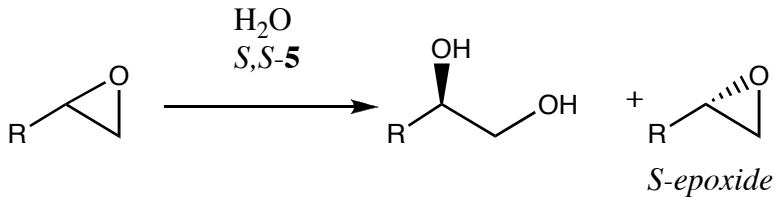
time:	0	1	2	3	4	5
	R:S	R:S	R:S	R:S	R:S	R:S
unreacted	100:100	99:85	98:70	97:55	96:40	95:25
reacted	0:0	1:15	2:30	3:45	4:60	5:75

notice that the unreacted ee increases, but the reacted ee remains the same

As the purity of the unreacted increases, the yield decreases!



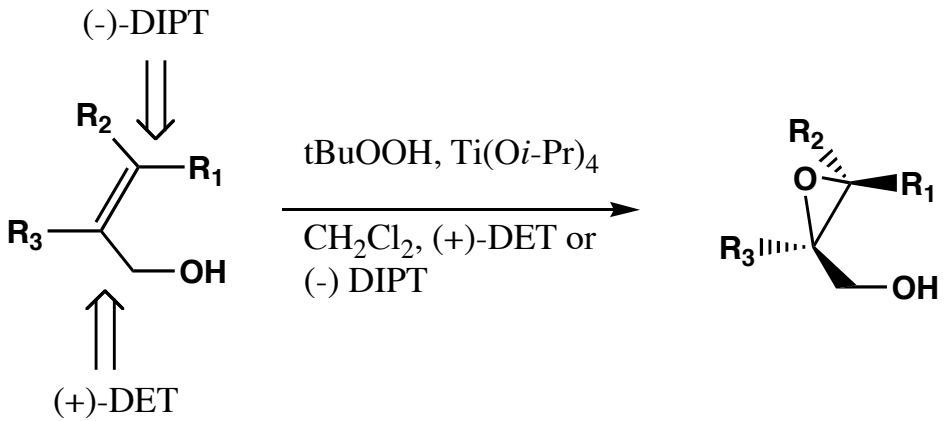
Selective complexation of chiral cobalt to the epoxide oxygen atom of one enantiomer of the racemic pair



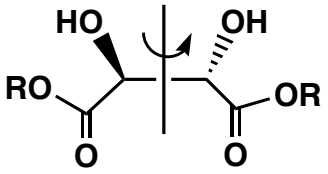
R	**Epoxide ee, yield**	**diol ee, yield**
CH_3	>98, 44	98, 50
$(CH_2)_3CH_3$	98, 46	98, 48
Ph	98, 38	98, 39
H_2C=CH	84, 44	94, 49

Science, **1997**, 936.

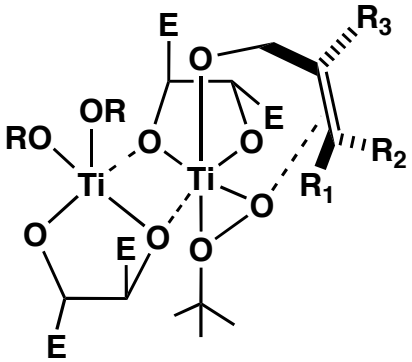
Sharpless Asymmetric Epoxidation



Ligand: Tartrates are C-2 symmetric. Such symmetry is useful in ligand design, furnishing predictable and repetitive structural units which reduce the number of diastereomeric transition states



The active catalyst is dimeric, providing a chiral environment for the substrate, allowing distinction of the enantiotopic faces of the alkene



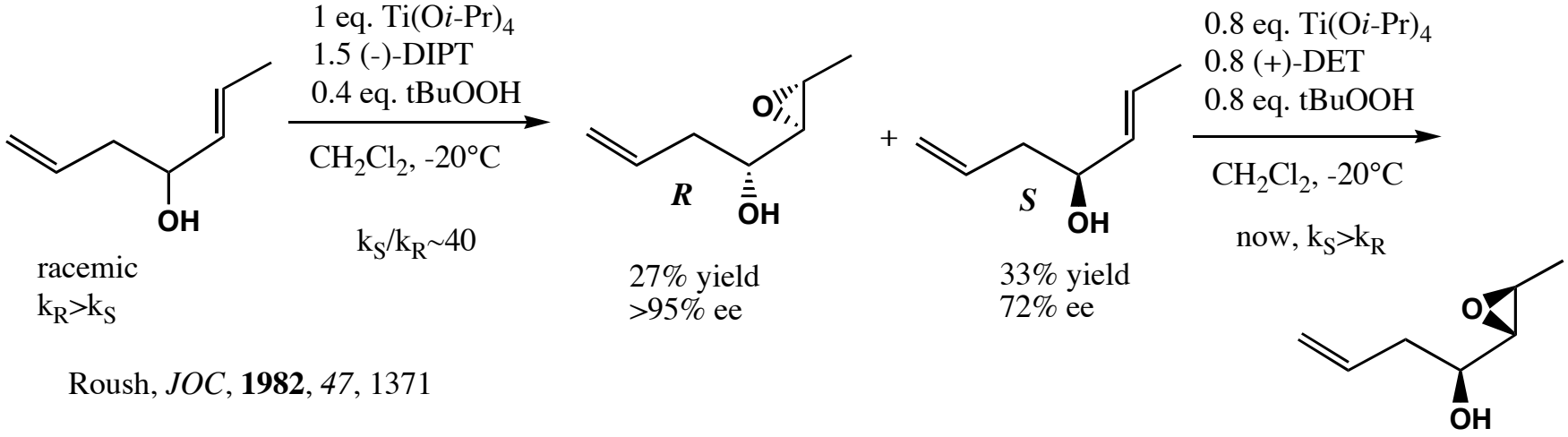
only one face of the alkene is presented to the coordinated peroxide ligand.
The alkene pi bond attacks along the O-O bond axis

The peroxide is activated by bidentate coordination to the titanium

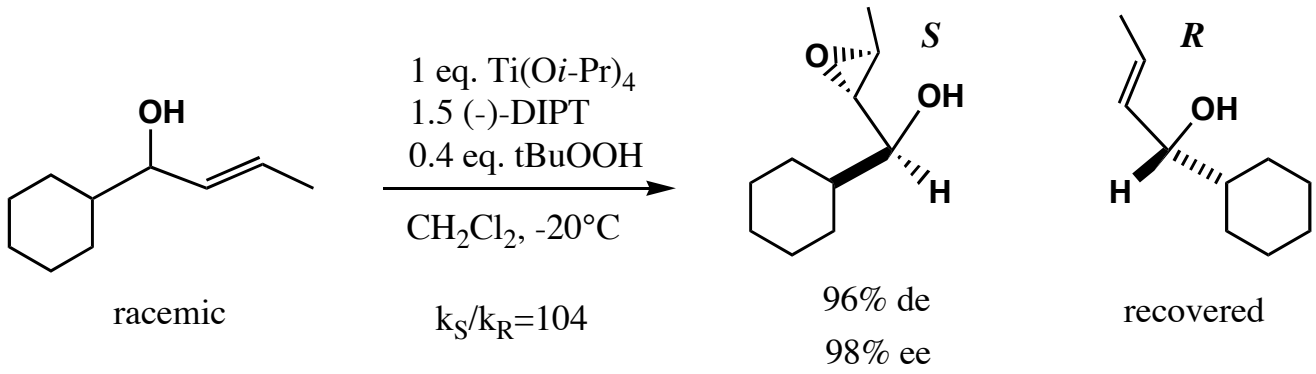
This is an example of **Ligand-Accelerated Catalysis**: The reaction in the absence of the chiral ligand is much slower than in its presence, thus ensuring the enantioselective pathway is the predominant one.

Sharpless, *JACS*, **1980**, *102*, 5974.
JACS, **1987**, *109*, 1279.

Kinetic Resolution via the Shapless Epoxidation



Roush, *JOC*, **1982**, *47*, 1371



Sharpless, *JACS*, **1981**, *103*, 6237.