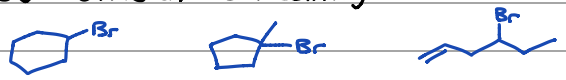
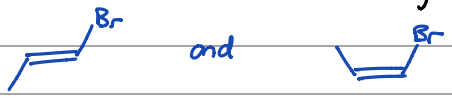
Isomers - Different compounds with the same molecular formula

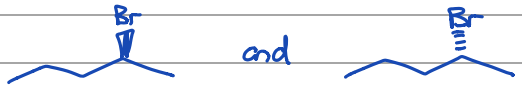
- Constitutional Isomers - different connectivity

$C_6H_{11}Br$ 

- Stereoisomers - identical connectivity, but different spatial arrangements

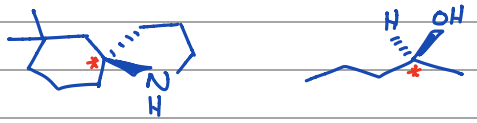


- Enantiomers - Chiral stereoisomers that are non-superimposable mirror images
  - ↳ a molecule that is not superimposable on its mirror image
  - ↳ recognized by a lack of an internal plane of symmetry

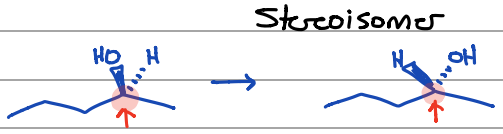


- Diastereomers - Stereoisomers that are not enantiomers

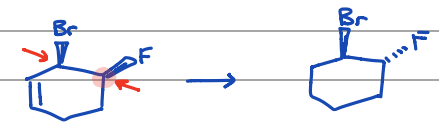
Chiral Center - atom with four different groups attached. (older term)



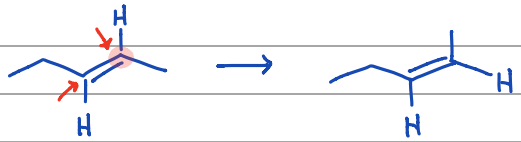
Stereogenic Center - an atom at which the interchange of two groups produces a Stereoisomer



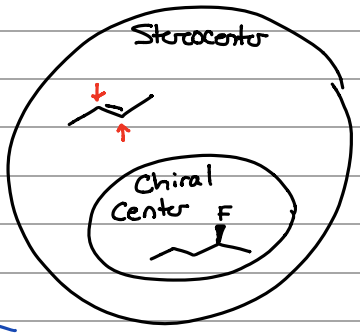
enantiomers



diastereomers



diastereomers



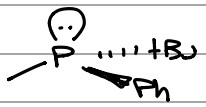
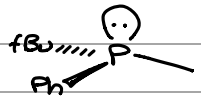
Stereogenic unit - an atom or grouping of atoms at which interchange of any two groups produces a Stereoisomer

Non-Carbon Stereocenters


and


neither enantiomer is isolable

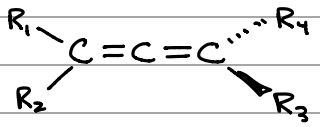
Low inversion barrier

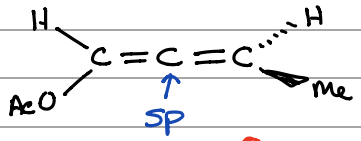
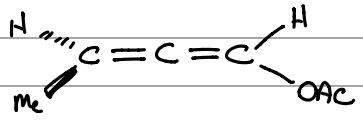
Stable & isolable

* Chiral phosphine ligands can be used for asymmetric synthesis.

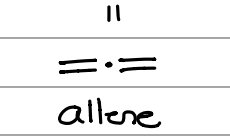
Chiral Molecules Without Chiral Centers

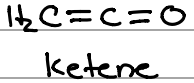


Chiral if $R_1 \neq R_2$ and $R_3 \neq R_4$

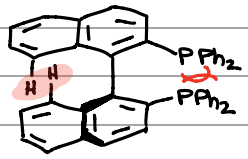
enantiomers


allene


ketene

Atropisomers - Stereoisomers resulting from restricted bond rotation

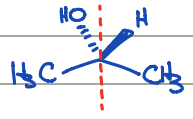
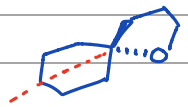
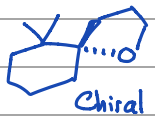
BINAP



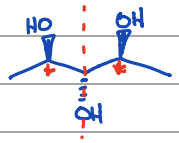
Can't occupy the same plane as the two H's would bump

Hindered rotation

Achiral Molecules Possess a plane of Symmetry

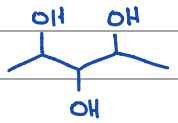
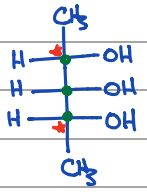




Chiral



achiral

meso Compound = Compound with one or more chiral Centers that is achiral due to a plane of symmetry


=


3 Stereocenters

* Draw all Stereoisomers & identify relationships

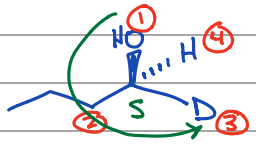
Stereochemical Descriptors

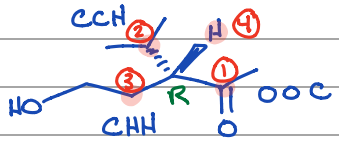
1. R + S for Chiral Centers

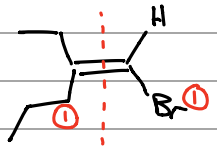
Lone Pair < H < D < T

- Prioritize the four groups around the Chiral Center
- Highest AN = 1, Lowest AN = 4 (usually H)
- Tie → examine connected groups → tie → move out one atom + compare
- Point #4 to back
- 1 → 2 → 3 (R) (S)

Can also use for E/Z

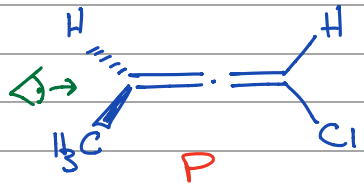






2. Axial Chirality

- Sight down the axis
- Prioritize Groups
- (P) (M)



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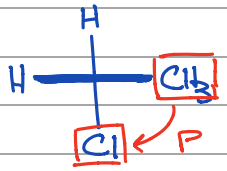
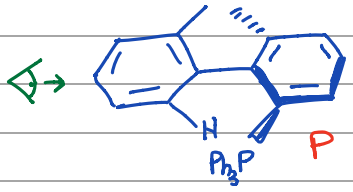


Highest priority near group to highest priority far group



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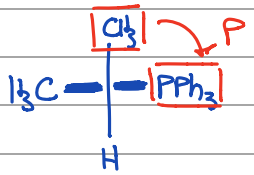
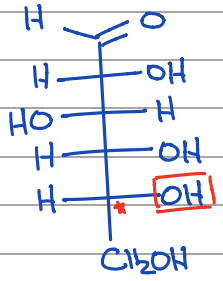


3. D + L

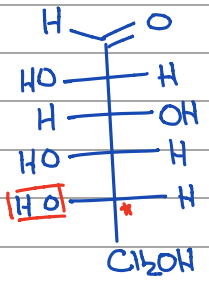
- Used in Fisher Projections
- Typically Carbohydrates + amino acids



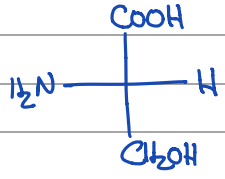
Naturally occurring

OH on Right = D

D-Glucose

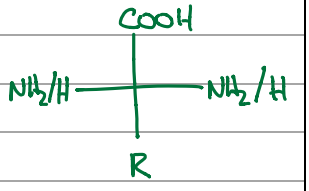


L-Glucose



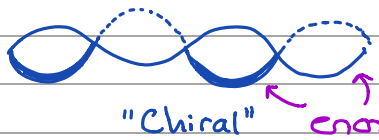
L-serine
↳ naturally occurring

Convertion



Optical Activity and Chirality

Plane Polarized Light



→ Chiral Soln → one enantiomer of light is slowed more than the other

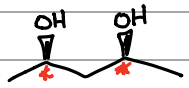
↓

different indices of refraction

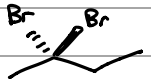
↓

detected to give optical rotation

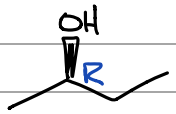
all electric fields oscillating in the same plane



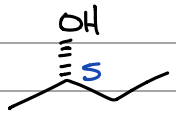
achiral
optically inactive



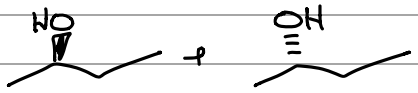
achiral
optically inactive



$[\alpha]_D^{20} = -15°$
optically active



$[\alpha]_D^{20} = +15°$
optically active

50:50 

racemic mixture (±)

optically inactive

Specific rotation $[\alpha]_D^{20} = \dfrac{\text{observed rotation}}{\text{path length (dm)} \cdot \text{concentration (g/cm}^3\text{)}}$

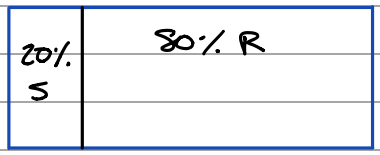
Ex: A 1.20g sample of cocaine dissolved in 7.5 mL of $CHCl_3$ in a 5.0 cm sample tube had an $\alpha = -1.3°$. What is $[\alpha]_D$?

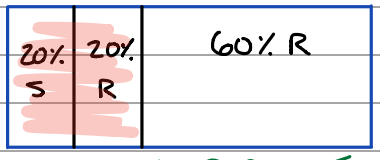
$$[\alpha]_D = \frac{-1.3°}{(0.50\,dm)(1.20\,g/7.5\,cm^3)} = -16°$$

Chiral, non-racemic = mixture of enantiomers that is not 1:1

When a rxn produces a non 50:50 mixture of enantiomers, you have an excess of one enantiomer

$$\text{enantiomeric excess (ee)} = \frac{\alpha_{mix}}{\alpha_{pure}} \times 100 = \frac{E_1 - E_2}{E_1 + E_2} \times 100$$

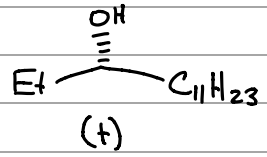




Racemic — excess of R

$ee = \frac{80-20}{80+20} \times 100 = 60\%$

$er = 80:20 = 4:1$ ← enantiomeric ratio

Ex: 

$[\alpha]_D^{20} = +6.7°$ pure en

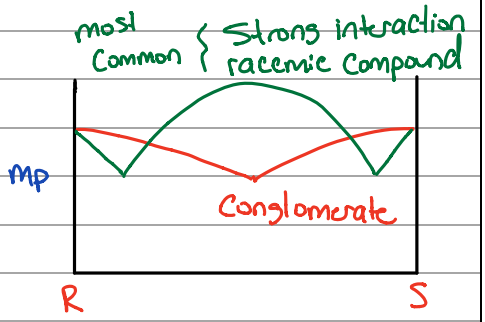
You prepare the molecule + record $[\alpha]_D^{20} = +5.1°$. What is ee?

$ee = \frac{5.1}{6.7} \times 100 = 76\%\ ee$

Enantiomers

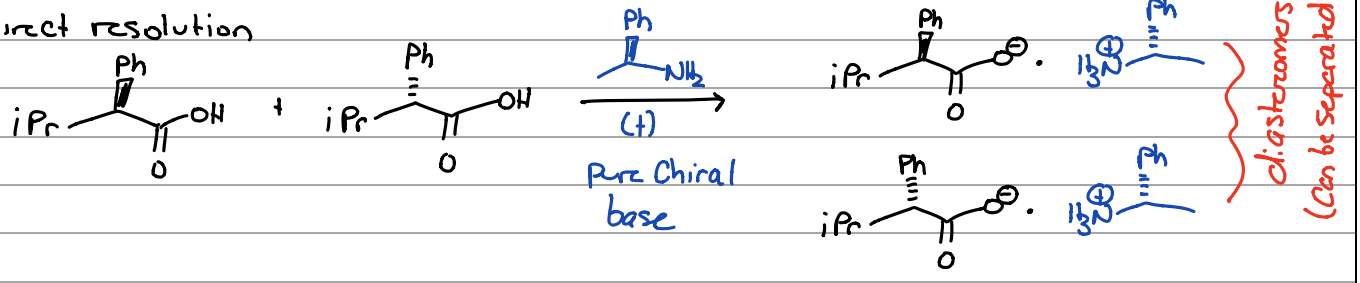
Interact with achiral entities in an identical manner:

- heat → same mp, same bp
- light → same refractive index
- silica gel → can't be separated
- Enantiomers smell differently (our body is chiral)



Separation

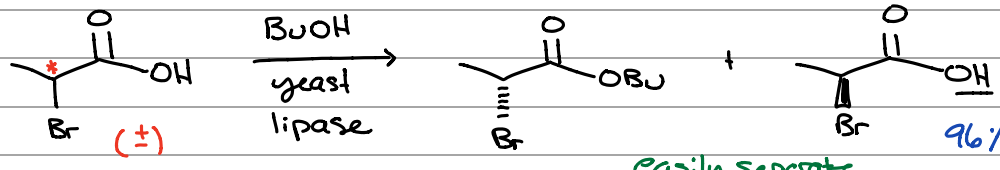
1. Direct resolution



2. Kinetic Resolution

Taking advantage of the fact that enantiomers will react w/ Chiral reagents through diastereomeric transition states

↳ unequal energy → rate difference



easily seperate

96% ee

45% Conversion

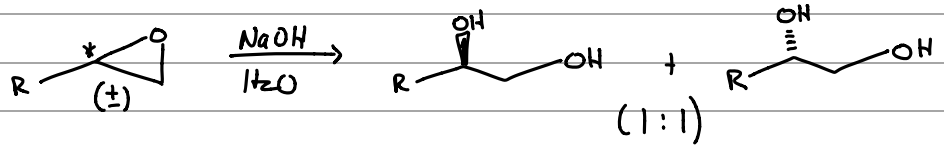
Jacobsen Hydrolytic Kinetic Resolution

JACS 2002, 124, 1307

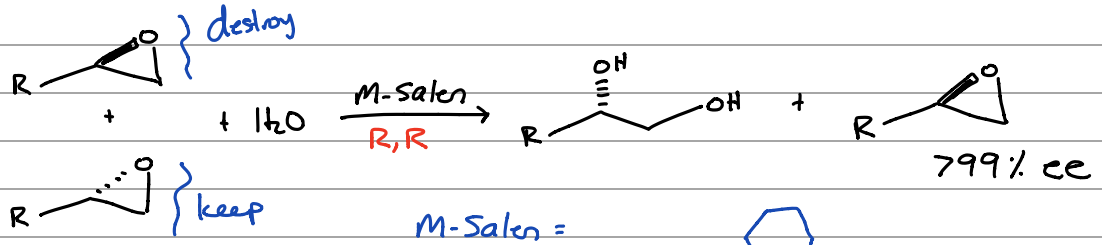
↳ Post Doc w/ Sharpless

↳ ½ of 2001 Nobel Prize for asymmetic epoxidation

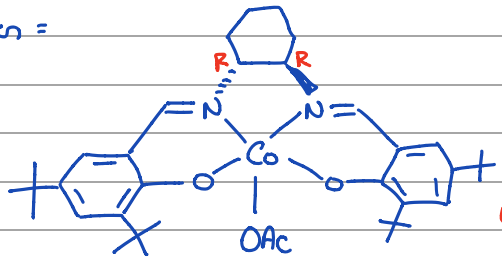
Nu epoxide opening



Jacobsen



M-Salen =

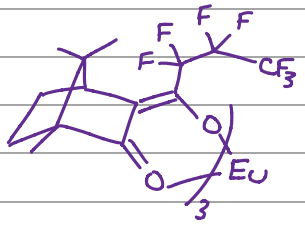


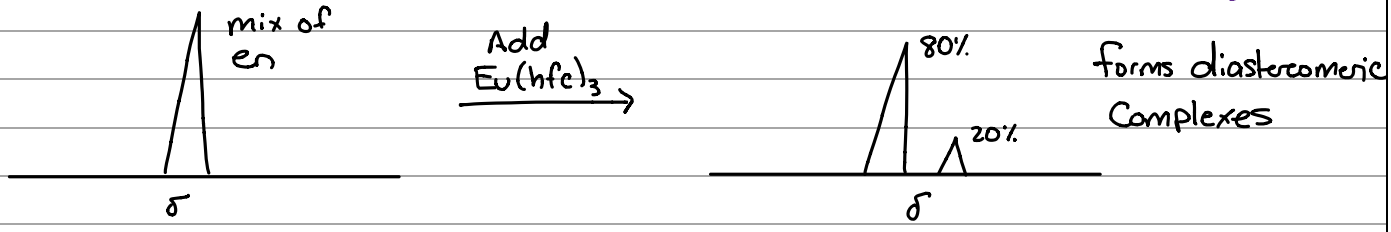
* (S,S) Will give the other epoxide enantiomer

3. Chiral Shift Reagent

Lanthanide metal w/ Chiral ligand

$Eu(hfc)_3$ =





4. Chromatography

HPLC, GC, TLC, etc.

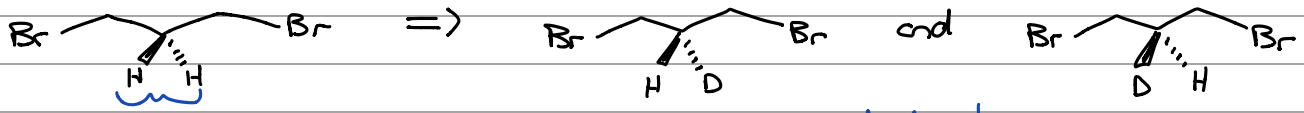
R + S → Chiral St Phase → R + S

mix

different retention times

- minimally destructive
- High selectivity
- Low detection limit
- Limit: no universal Chiral stationary plase
- Limit: Chiral Column $$

Topicity Relationships



homotopic protons

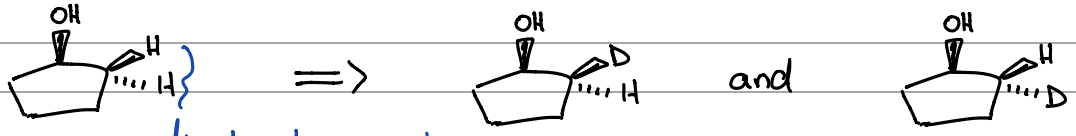
↳ have same NMR signal

Identical

enantiotopic protons

↳ have same NMR signal unless a shift reagent is used.

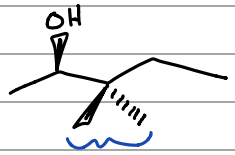
enantiomers



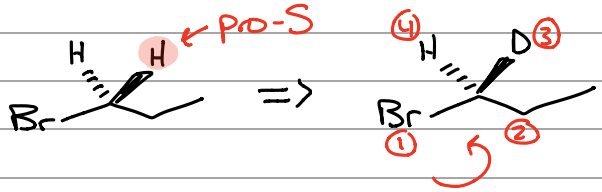
diastereotopic protons

↳ have distinct ^1H NMR signals

diastereomers

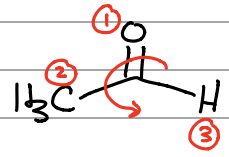


diastereotopic CH_3 groups

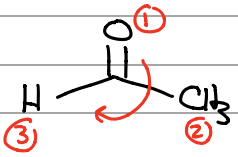


Prochiral Face

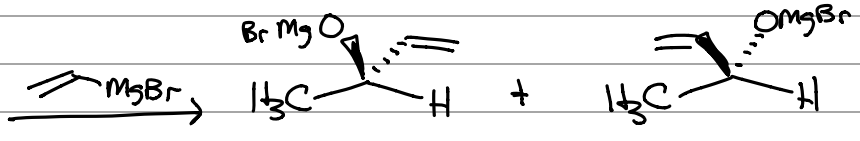
- Assign the 3 groups like R/S



Si face



Re face



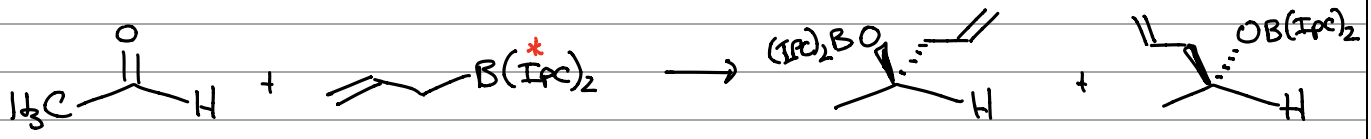
Re attack

Si attack

(1:1)

Enantiomers

Rxn of an achiral molecule w/ a Chiral reagent



diisopinocampheylborane

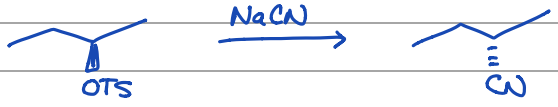
Diastereomers formed in different amounts

Stereospecific and Stereoselective Rxns

Stereospecific rxn - Stereochem of the starting material dictates the stereochem of the product.

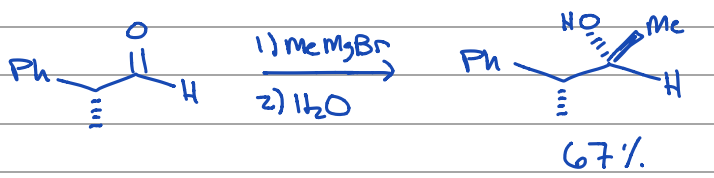
Stereoselective rxn - rxn that produces an excess of one stereoisomer

S_N2 Rxn



Stereospecific + Stereoselective

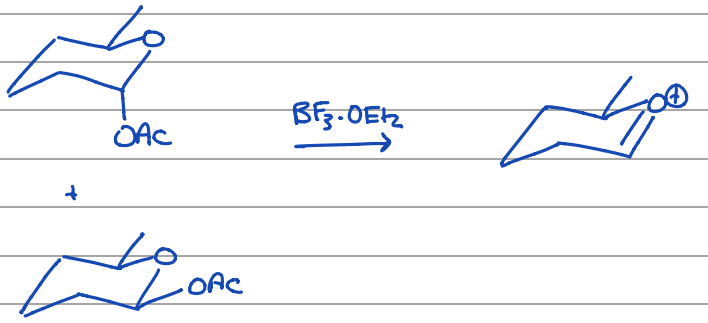
* Any Stereospecific rxn is Stereoselective



67%

33%

Stereospecific + Stereoselective

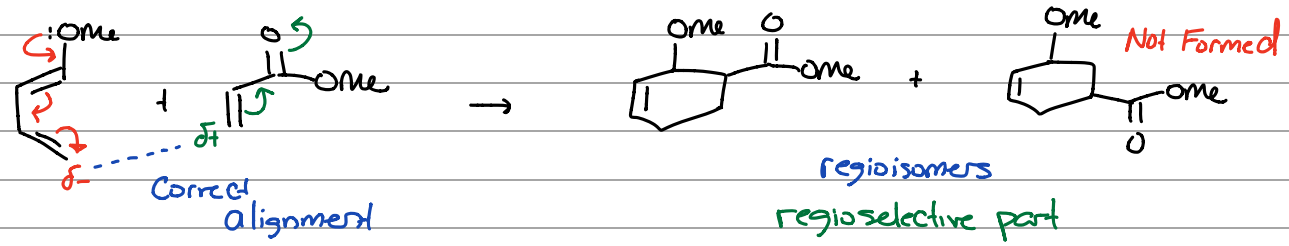


Sole Product

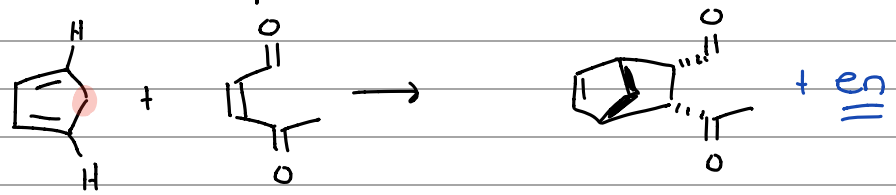
Stereoselective rxn (not stereospecific)

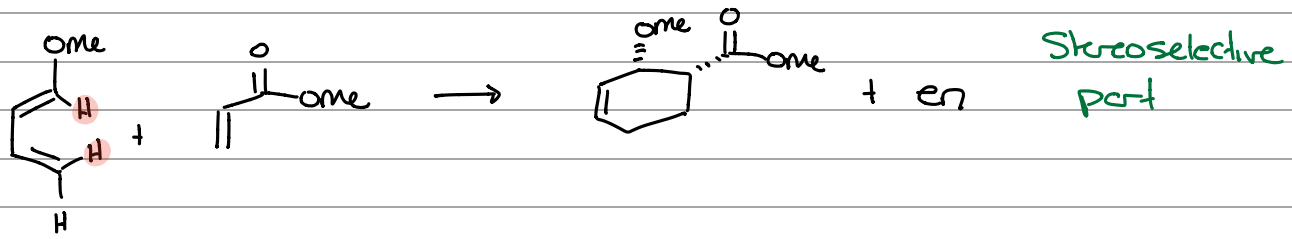
Diels-Alder Rxn

Regioselective & Stereoselective



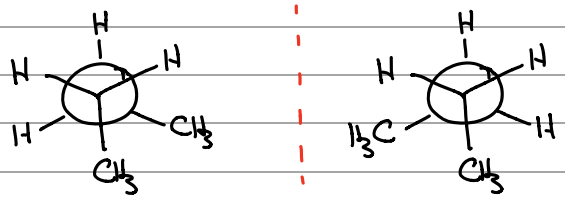
Use endo rule to predict stereoisomers





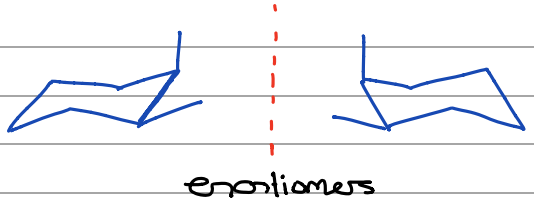
Time Scale Implications

Time scale is important for all Stereochemical concepts



But is achiral because the barrier to rotation is so low you can't freeze out a single conformation

enantiomers



achiral because a fast ring flip interconverts the enantiomeric forms

enantiomers