

# Bicyclic Compounds

- multiple rings that share atoms
- three general types



spirocycle  
(rings share one atom)



fused  
(rings share two adjacent atoms)



bridged  
(rings share non-adjacent atoms)

⊙ = bridgehead

## - Nomenclature

- Parent chain is total number of atoms in the rings
- for spirocycles, add "spiro-" prefix
- for fused & bridged, add "bicyclo-" prefix
- Bridge sizes listed in brackets



spiro[4.4]nonane

put numbers in ascending order



bicyclo[4.3.0]nonane



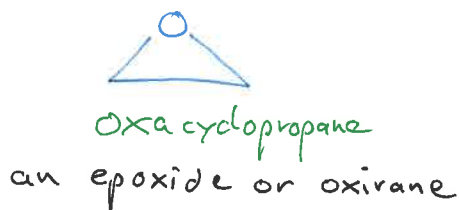
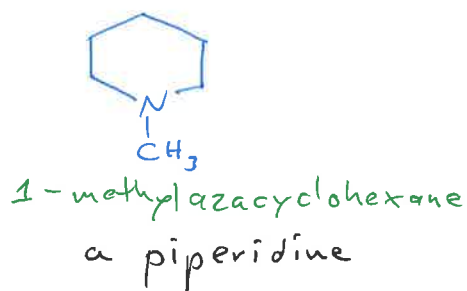
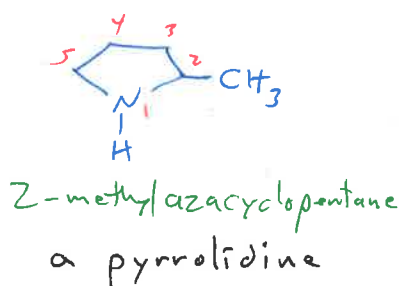
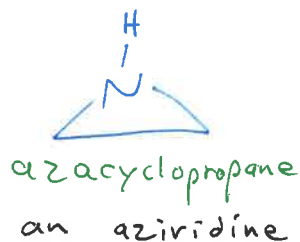
bicyclo[2.2.1]heptane

put numbers in descending order

# Saturated Heterocycles

## - Nomenclature

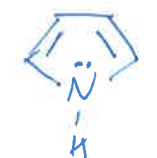
- Parent chain is total number of atoms in the ring
- A prefix is used to "replace" a carbon
  - "aza" for N
  - "oxa" for O
  - "thia" for S
- Numbering starts on the heteroatom



- heterocycles display chemistry typical of the root functional class

# Aromatic Heterocycles

- 5-atom rings



pyrrole

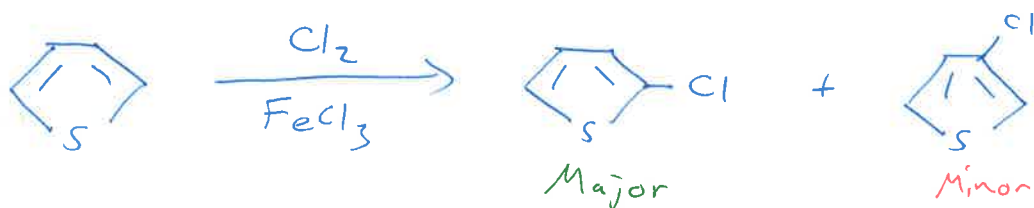


furan

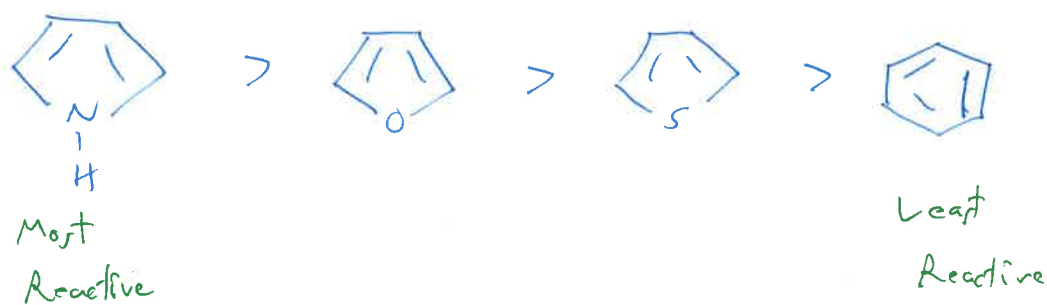


thiophene

- EAS Reactions



- typically favor reaction at 2-position

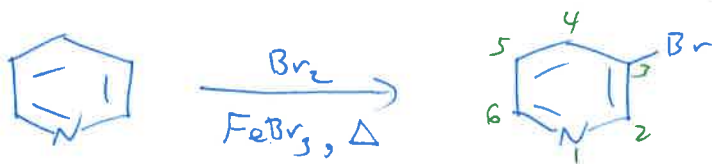


... in EAS

# Pyridine



## - EAS Reactions



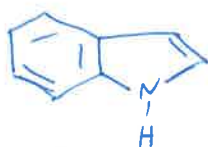
- typically favors EAS at 3-position
- much less reactive than benzene in EAS

## - $S_NAr$



- Halogenated pyridines are very reactive in  $S_NAr$ 
  - does not require nitro group like benzene does
- LG on 2 or 4 position is fastest
  - 3 position is much slower

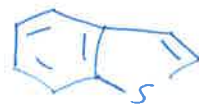
# Bicyclic Aromatic Heterocycles



indole



benzopyran



benzothiophene

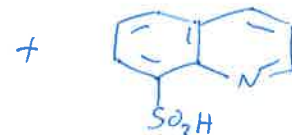
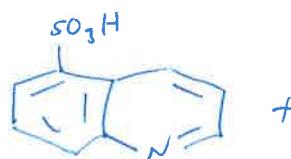
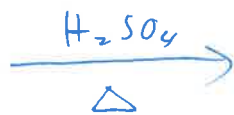
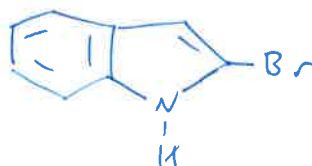
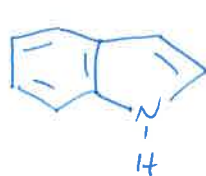


quinoline



isoquinoline

## - EAS Reactions



- The more reactive ring reacts
- Usually displays regioselectivity typical for that ring

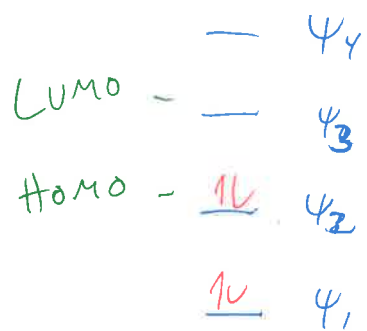
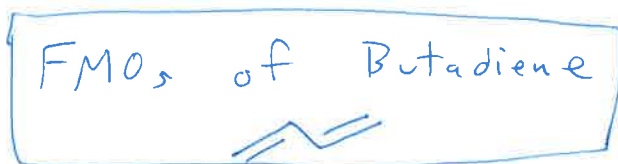
# Pericyclic Reactions

- concerted mechanism
- circular flow of electrons
- have a cyclic transition state
- stereospecific

## Frontier Molecular Orbitals (FMO)

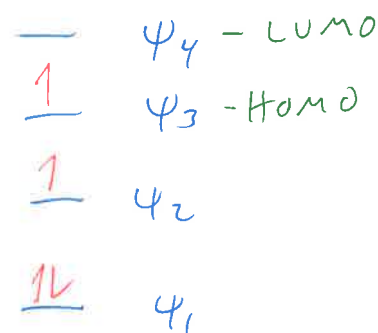
HOMO - Highest Occupied Molecular Orbital

LUMO - Lowest Unoccupied Molecular Orbital



ground state

(thermal conditions)



excited state

(photochemical conditions)

# Electrocyclization Reactions

- Intramolecular reorganization of  $\pi$ -electrons to give a cyclic product

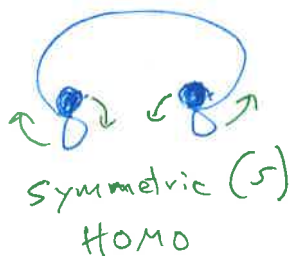


- Ends of the  $\pi$ -system rotate & combine to form a new  $\sigma$  bond

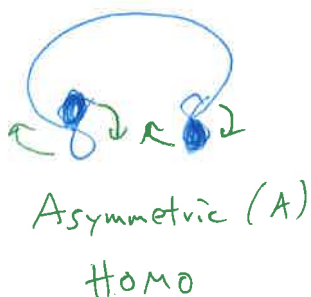
- Closure occurs via the HOMO
- must combine "in-phase"
  - a symmetry allowed process

- Ends of the  $\pi$ -system HOMO can "rotate" two ways:

- conrotatory - (both in same direction)
- disrotatory - (each in an opposite direction)



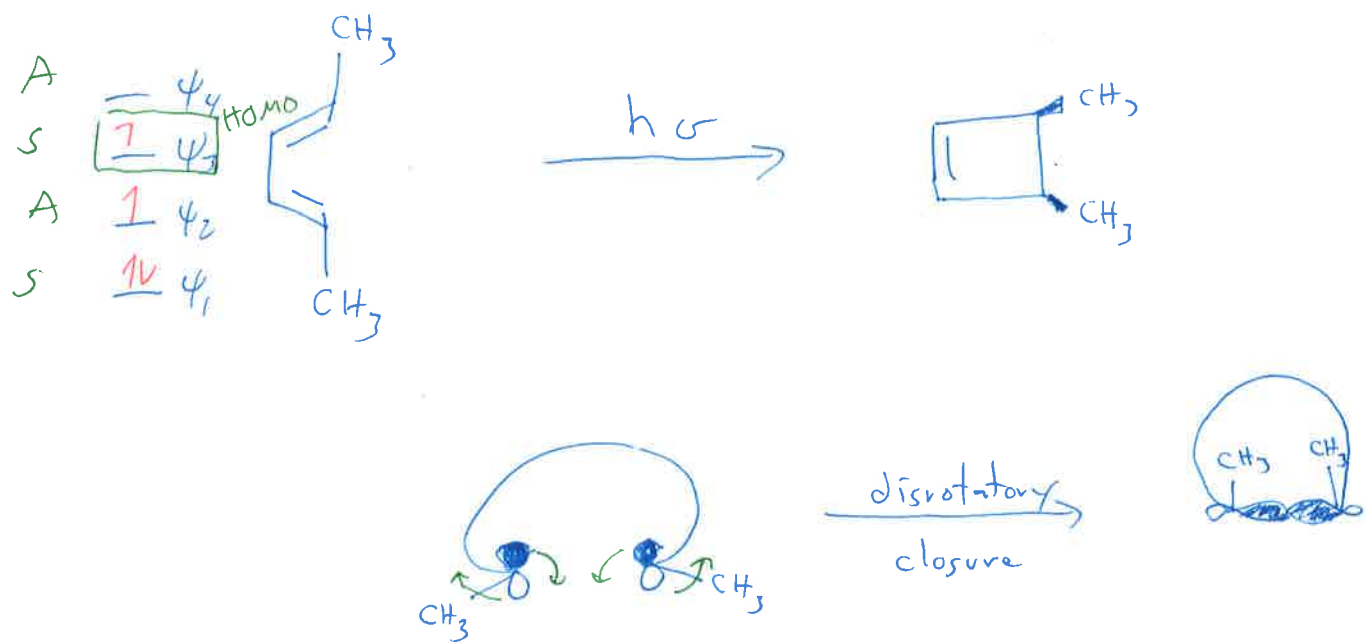
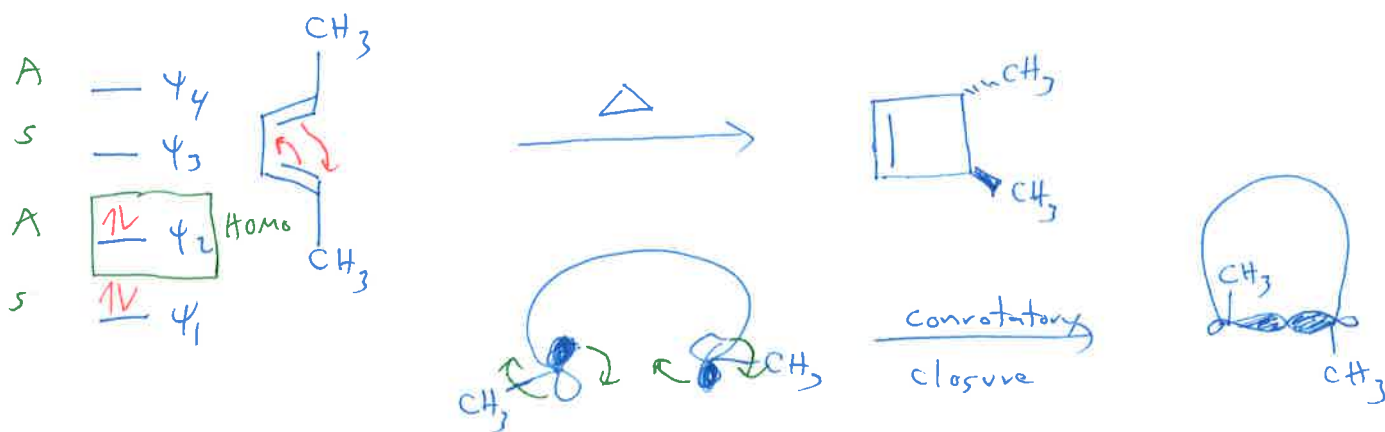
disrotatory  
closure



conrotatory  
closure



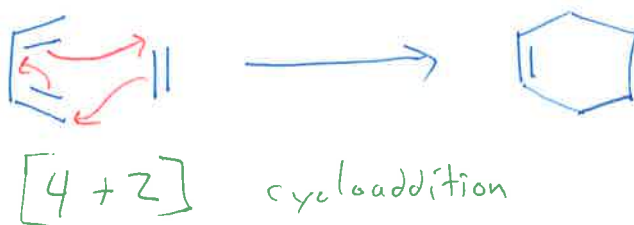
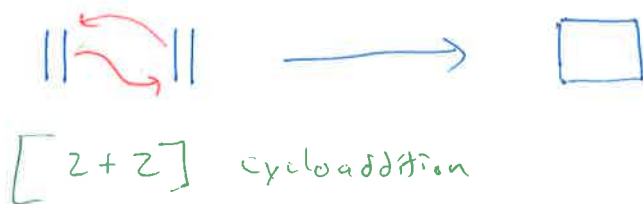
# Examples of Electrocyclization





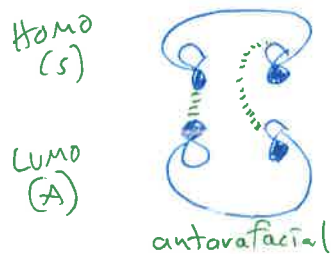
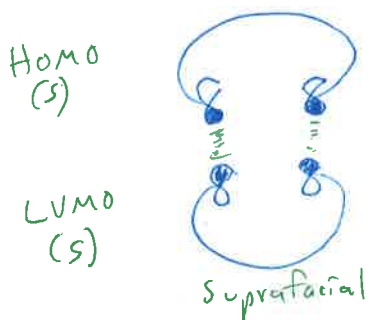
# Cycloaddition Reactions

- Reaction of two  $\pi$ -systems to form a ring



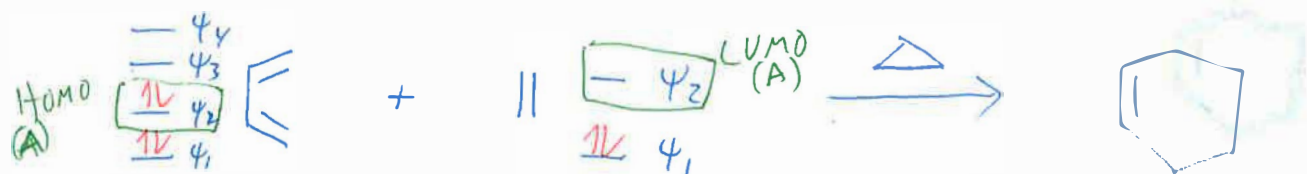
- Ends of two separate  $\pi$ -systems connect to form a ring
  - HOMO of one combines with LUMO of the other
  - must combine "in-phase" (symmetry allowed)
- the two  $\pi$ -systems can combine two ways:

- suprafacial - "syn-like"
- antarafacial - "anti-like"



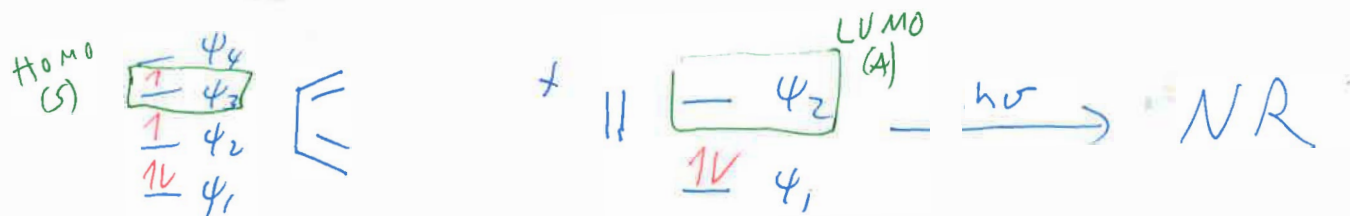
- suprafacial occurs when FMOs match symmetry
- possible for any ring size
- antarafacial occurs when FMOs do not match symmetry
- topologically requires at least 7-atom ring

# Examples of Cycloaddition



HOMO of one  $\pi$ -system & LUMO of the other match symmetry

- suprafacial

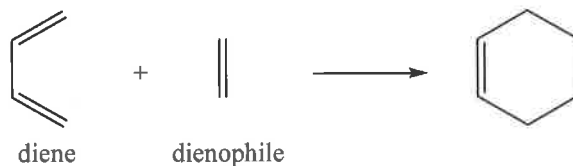


HOMO of one  $\pi$ -system & LUMO of the other do not match symmetry

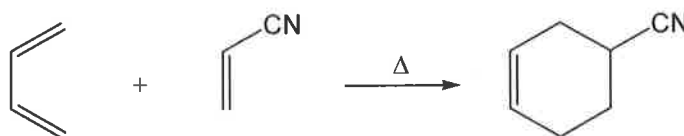
- would be antarafacial, but ring is too small

\* For photochemical cycloadditions, only excite one  $\pi$ -system

## Diels-Alder Reaction

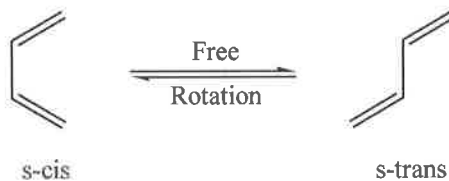


- [4+2] cycloaddition between a conjugated diene and a “dienophile”

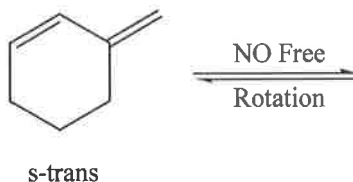


- promoted by electron-withdrawing group on the dienophile (-CN, -NO<sub>2</sub>, -COR)

### - Diene Conformations



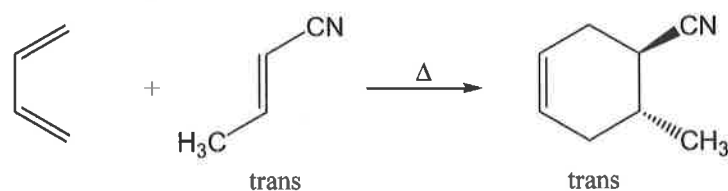
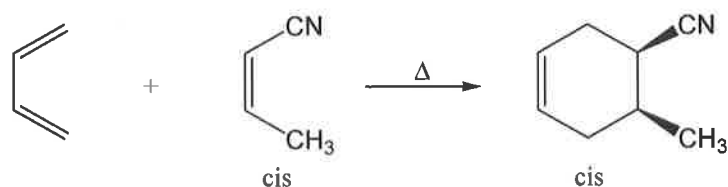
- Diels-Alder only works when the diene can be s-cis



- Locked as s-trans (can't be s-cis)  
- No Diels-Alder reactions

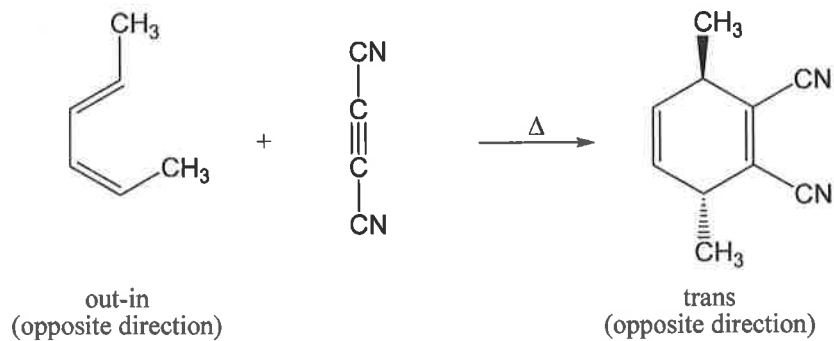
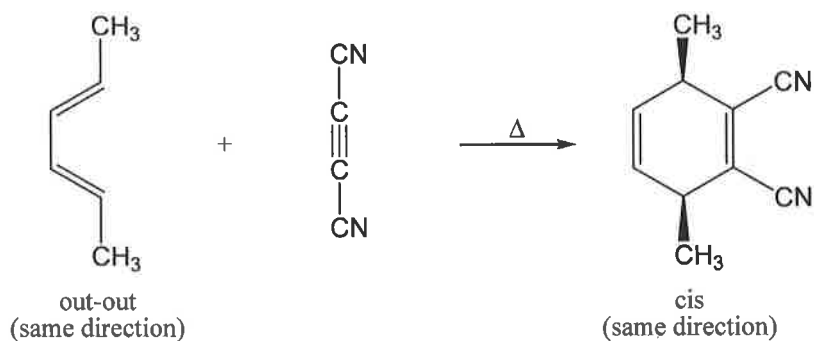
## Stereoselectivity of Diels-Alder

### - The Dienophile



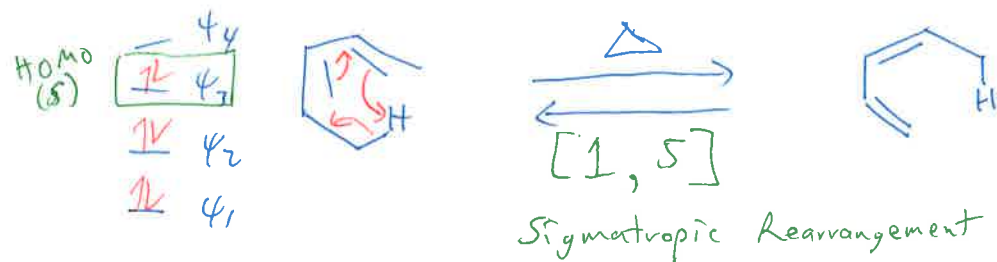
- Dienophile stereochemistry is transferred to product  
*cis*  $\rightarrow$  *cis*                      *trans*  $\rightarrow$  *trans*

### - The Diene



- Diene stereochemistry is also transferred to product  
same  $\rightarrow$  same                      opposite  $\rightarrow$  opposite

# Sigmatropic Rearrangements



- symmetry of HOMO is important

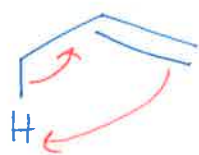
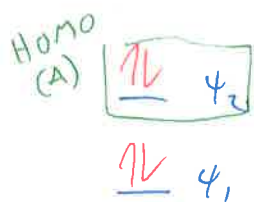


- suprafacial migration requires symmetric HOMO

\* include the one pair of  $\sigma$ -electrons in the  $\pi$ -count



# Examples of Sigmatropic Rearrangement



~~[1,3] sigmatropic rearrangement~~

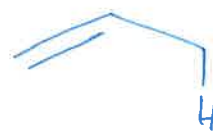
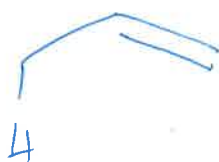
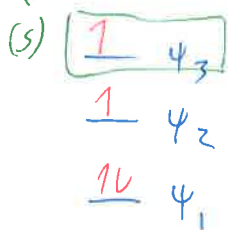


~~antarafacial~~



- antarafacial migration requires an asymmetric HOMO
  - requires 7-atom ring or larger transition state

HOMO (S)



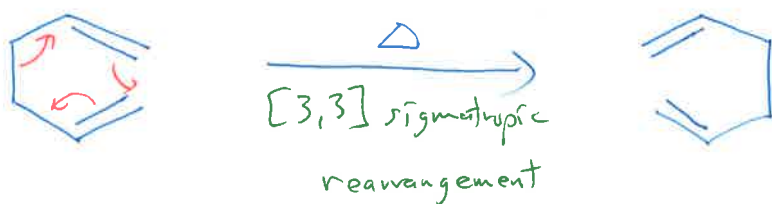
- suprafacial (symmetric HOMO)
  - reaction works

# Claisen Rearrangement



- [3,3] sigmatropic rearrangement of an allyl vinyl ether

# Cope Rearrangement



- [3,3] sigmatropic rearrangement of a 1,5-diene

