Orbital Symmetry and Pericyclic Reactions
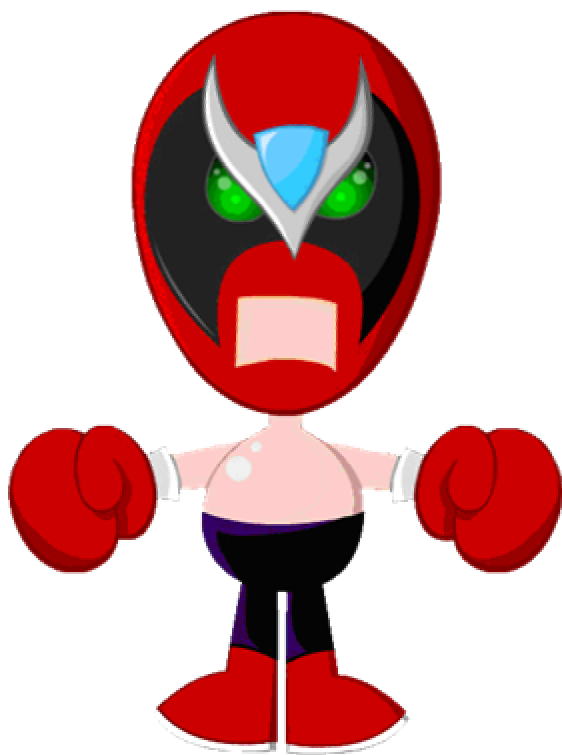
Section Agenda

1) Last. Section. Ever.
2) Handout: Orbital Symmetry and Pericyclic Reactions
3) Office Hours: Thursday, 12/ 16, 3-4PM and 8-9PM, Bauer Lobby (PS#8 due Friday)
4) Exam III on Monday, 12/20. No section that afternoon.
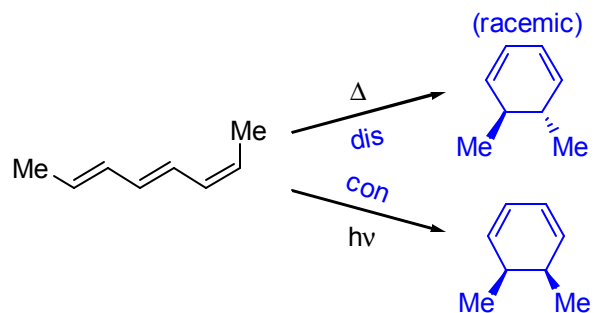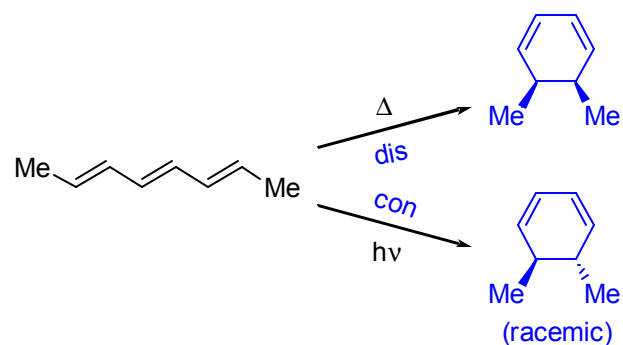5) Stay tuned for extra office hours and review sessions in reading period.

Empty Space

This cartoon character's job is to fill up empty handout space

Skill Drill

Complete the following reactions:

Building Molecular Orbitals (MOs)

- We are about to embark on a journey through the world of pericyclic reactions. You are already familiar with one of these reactions: the Diels-Alder cycloaddition. In all of these reactions, it is of the utmost importance that you know how to draw the MOs of π systems.

Simple Rules

- Atomic orbitals must overlap if they are to interact to form a set of molecular orbitals. There are no exceptions—orthogonal orbitals will not interact.

- You will get n molecular orbitals (MOs) for every n atomic orbitals (AOs) that interact.

- The most stable MOs have the most bonding character. The highest energy MOs have the most antibonding character. The energy of an MO is directly proportional to the number of nodes. Thus, as the number of nodes increases, the antibonding character increases and the orbital is less stable.

- The electron density at an atom is equal to the square of the MO's coefficient at that atom. Locations with bigger coefficients are depicted by drawing bigger orbital lobes.

- The + and − designations, also shown as green and blue, have *nothing* to do with charge. They are designations for the sign of that orbital's wavefunction. When orbitals of the same wavesign interact, there is constructive interference resulting in a bonding interaction. When orbitals of the opposite wavesign interact, there is destructive interference resulting in an antibonding interaction.

- Nodes are locations in the system where the bonding interactions are completely cancelled by antibonding interactions. Molecular orbitals have zero electron density at nodes. Reactions will not occur at these locations.

- Molecular orbitals for equivalent atoms are symmetric. Note how the MOs below either have a mirror plane of symmetry (a "symmetric" MO = **S**) or a C_2 axis of symmetry (an "antisymmetric" MO = **A**).

- Note patterns in MO diagrams to help you draw them and to figure out "shortcuts" in problem solving

    - In the lowest energy MO, all of the wavesigns are the same
    - In the highest energy MO, all of the wavesigns alternate
    - The termini alternate between having the same wavesign and opposite wavesigns
    - The number of nodes increases by one as you climb higher in energy
    - For linear systems with an odd number of AOs, some nodes will lie at atoms in the chain

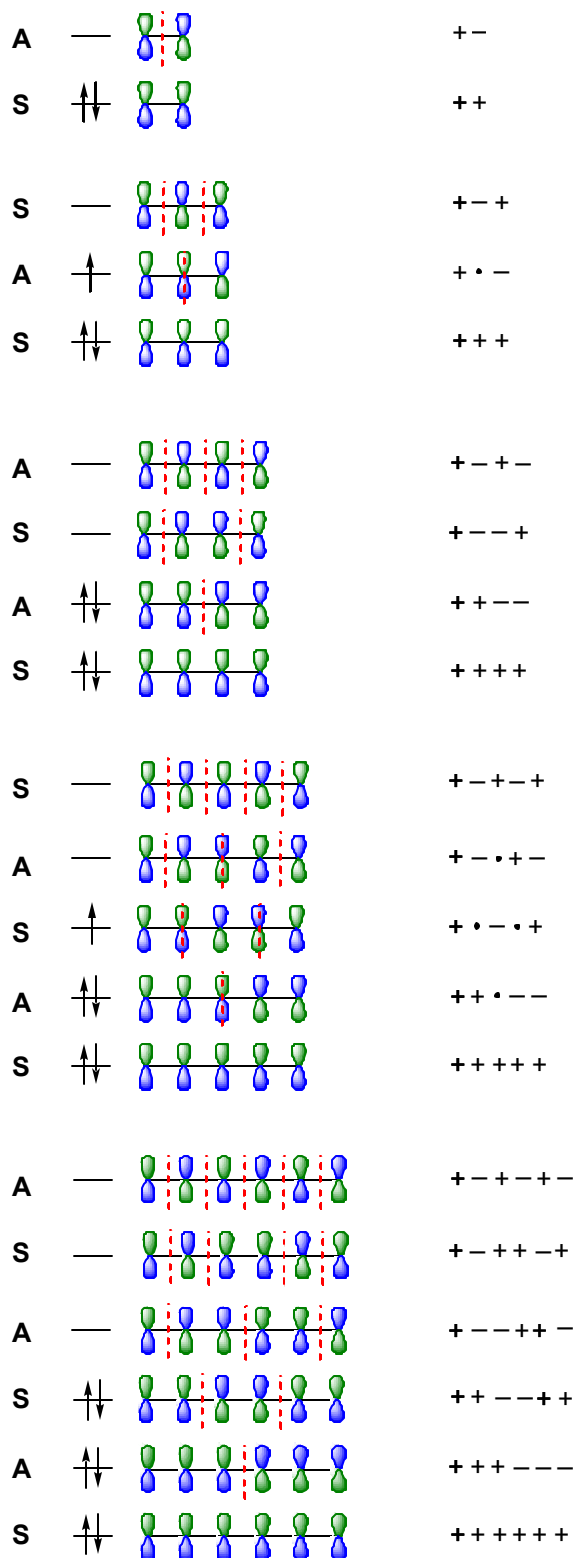Electronic Perturbations of Molecular Orbitals

Placing electron donating groups (EDGs) or electron withdrawing groups (EWGs) on a π system will shift or "perturb" the relative energies of the molecular orbitals.

- EDGs will push more electron density into the π system and will correspondingly raise the energies of the molecular orbitals

- EWGs will pull electron density out of the π system and will correspondingly lower the energies of the molecular orbitals

- Lewis acids that complex with extended π systems also lower the energies of the MOs. These metals typically serve as catalysts by lowering the energy of a reactive LUMO such that it is more accessible.
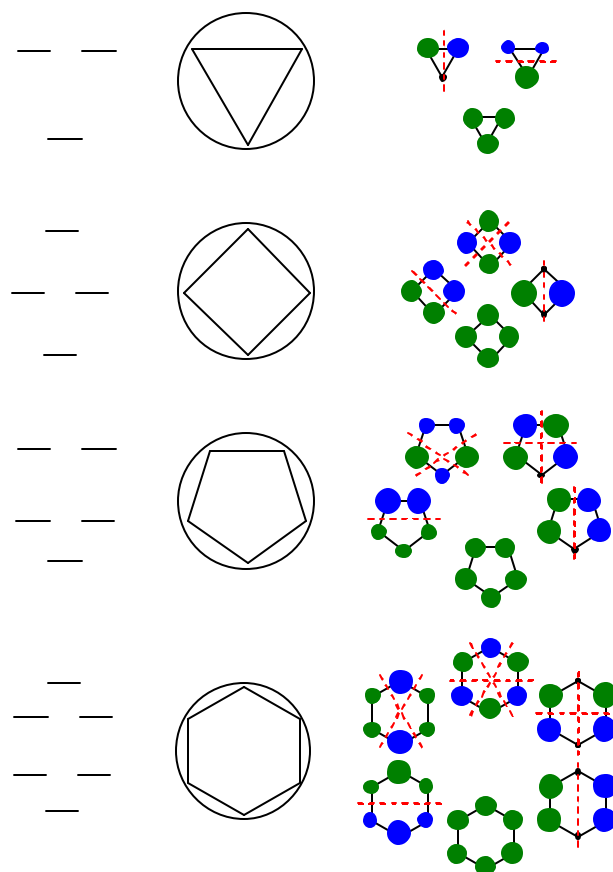
Determining which atoms will become enriched or depleted in electron density can be accomplished by using an electron pushing model.

Graphical Depictions of Molecular Orbitals

<u>Linear Systems</u>

A   + −

S   + +

S   + − +

A   + • −

S   + + +

A   + − + −

S   + − − +

A   + + − −

S   + + + +

S   + − + − +

A   + − • + −

S   + • − • +

A   + + • − −

S   + + + + +

A   + − + − + −

S   + − + + − +

A   + − − + + −

S   + + − − + +

A   + + + − − −

S   + + + + + +

<u>Cyclic Systems</u>

<u>Frost Circles</u>

- Frost circles are the fastest method to arrive at the molecular orbitals for conjugated cyclic systems.

- You simply inscribe the polygon in a circle "vertex down," such that one of the corners touches the bottom of the circle.

- Each vertex of the polygon represents the energy level of a molecular orbital.

- For Chem 30, you need only worry about the relative position of the MOs and not the quantitative energy difference between the MOs. However, the reason Frost circles are so powerful is that they can be used to get these energies.

Pericyclic Reactions

Pericyclic reactions have cyclic transition states with electron flow that is governed by the rules of orbital symmetry.

Classification of Pericyclic Reactions

1) **Electrocyclic reactions** involve the closure of linear π systems to rings and the reverse reaction, the opening of these rings.

   - You must be able to classify an electrocyclic reaction by # of electrons, as conrotatory/disrotatory, and as photochemical/thermal

2) **Cycloadditions** are reactions where two π systems react to form cyclic/ringed compounds

   - You must be able to classify a cycloaddition reaction by [m + n] and as photochemical/thermal.

3) **Sigmatropic rearrangements** involve the movement of a σ bond across a π system

   - You must be able to classify a sigmatropic reaction by [m,n] and photochemical/thermal

- These reactions involve making and breaking or shifting σ and π bonds. The key shared element is that in order for these reactions to occur, the wavesigns of the molecular orbitals have to match. When they do, the reaction is said to be "symmetry allowed." When not, "symmetry forbidden."

- Draw all of the reactions as occurring in cyclic conformations when you are drawing arrow pushing mechanisms. These reactions are called peri<u>cyclic</u> for a reason.

- Beware of the reverse, "retro reactions." If the forward reaction is "symmetry allowed," then so is the reverse reaction.

- Beware of tandem reactions, where two or more pericyclic reactions occur in "one pot." When you irradiate a mixture, both photochemical and thermal processes can occur.
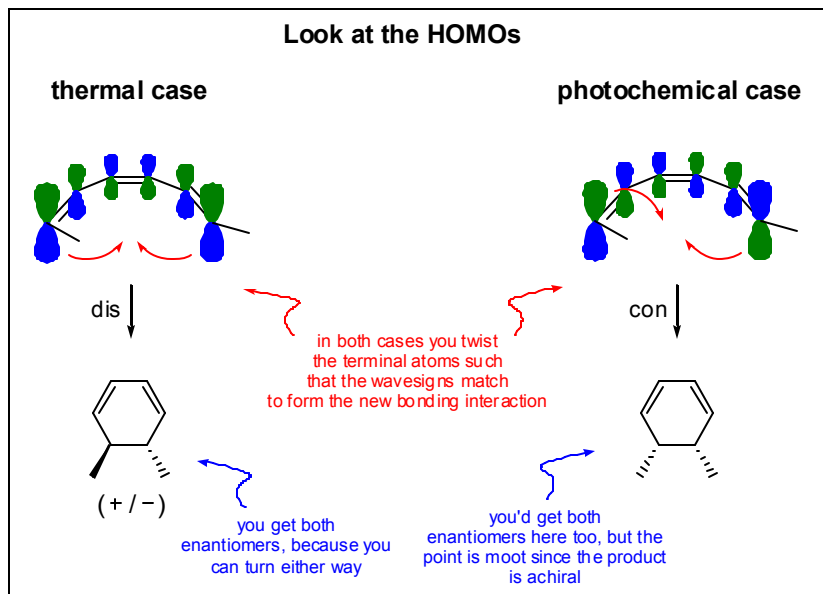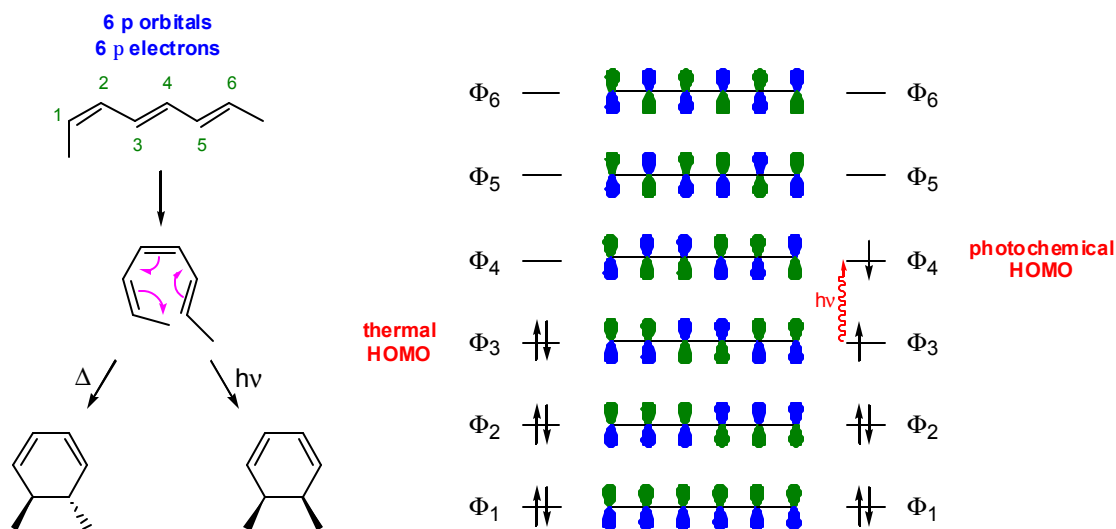
Electrocyclic Reactions

- In an electrocyclic reaction, a linear π system is closed when a π bond is exchanged for a σ bond. The reverse reaction is also electrocyclic.

The simplest approach is to analyze the "forward" ring closure reaction:

Approach

1) Identify the conjugated system, count the number of π electrons and number of p orbitals in the chain
2) Construct the MO diagram, then fill in the electrons to identify the HOMO
3) Push electrons to obtain a correct 2D Lewis structure of the product
4) Determine stereochemistry in the product by twisting the terminal atoms so that the wavesigns match.
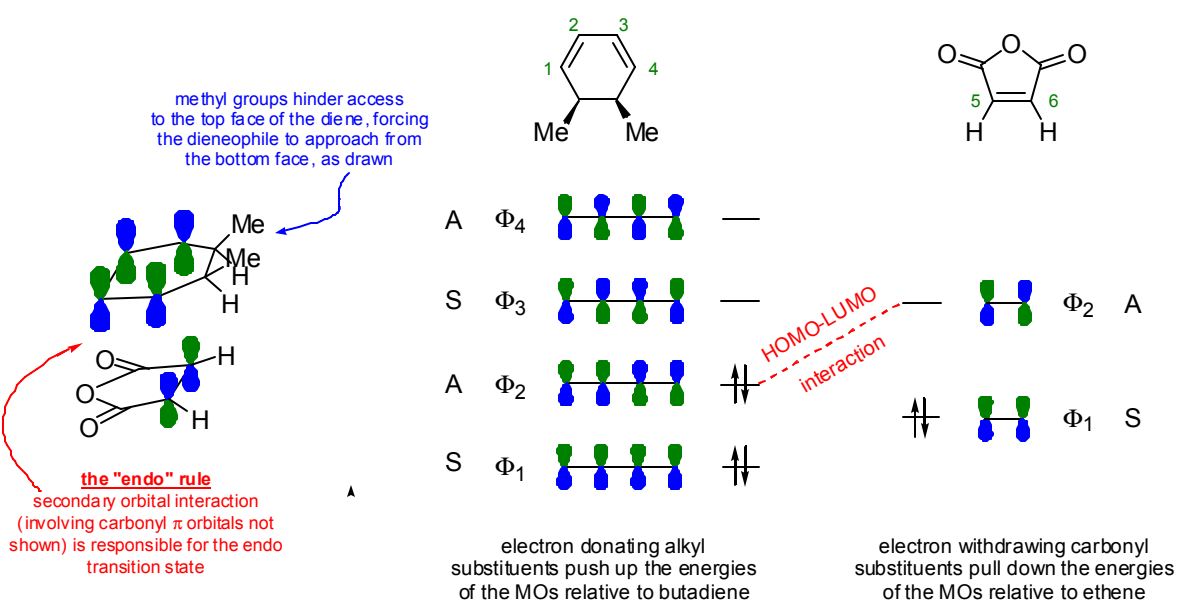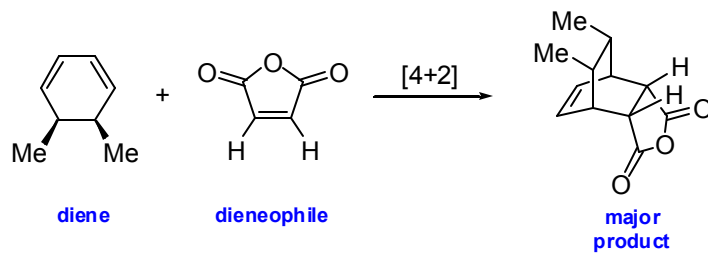
6 p orbitals
6 p electrons

Φ_6 — — Φ_6

Φ_5 — — Φ_5

Φ_4 — **photochemical HOMO** Φ_4

$h\nu$

thermal HOMO Φ_3 Φ_3

Φ_2 Φ_2

Φ_1 Φ_1

Δ $h\nu$

Look at the HOMOs

thermal case   **photochemical case**

dis   con

in both cases you twist
the terminal atoms such
that the wavesigns match
to form the new bonding interaction

$(+/-)$

you get both
enantiomers, because you
can turn either way

you'd get both
enantiomers here too, but the
point is moot since the product
is achiral

Cycloaddition Reactions

- In a cycloaddition reaction, two π systems react such that four π electrons go into forming two σ bonds to join the termini of the systems.
- The reaction will only proceed if the wavesigns match at the termini of the π systems

Approach

1) Identify the two π systems (can be intramolecular)
2) Sketch out the molecular orbitals for the systems
3) Choose which system will serve as the HOMO and LUMO
4) Regiochemistry and Stereochemistry: analyze both substitutent and secondary orbital effects

diene **dieneophile** **major product**

methyl groups hinder access to the top face of the diene, forcing the dieneophile to approach from the bottom face, as drawn

the "endo" rule
secondary orbital interaction (involving carbonyl π orbitals not shown) is responsible for the endo transition state

HOMO-LUMO interaction

electron donating alkyl substituents push up the energies of the MOs relative to butadiene

electron withdrawing carbonyl substituents pull down the energies of the MOs relative to ethene
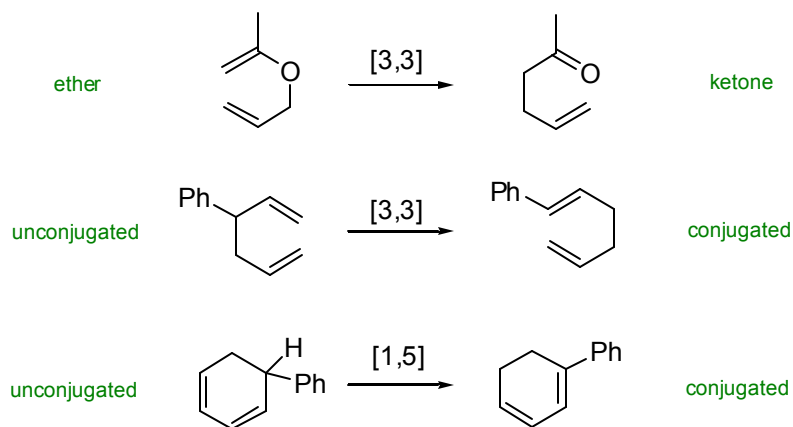
- Cycloadditions will proceed only if the symmetries of the HOMO and LUMO are the same

- As discussed previously, substituents and Lewis acids catalysts will change the energies of the MOs. Anytime the relative energy of the HOMO and LUMO are changed, the reaction rate will also change. The closer they become in energy, the faster the reaction. The HOMO typically has electron donating substituents; the LUMO typically has electron withdrawing substituents.

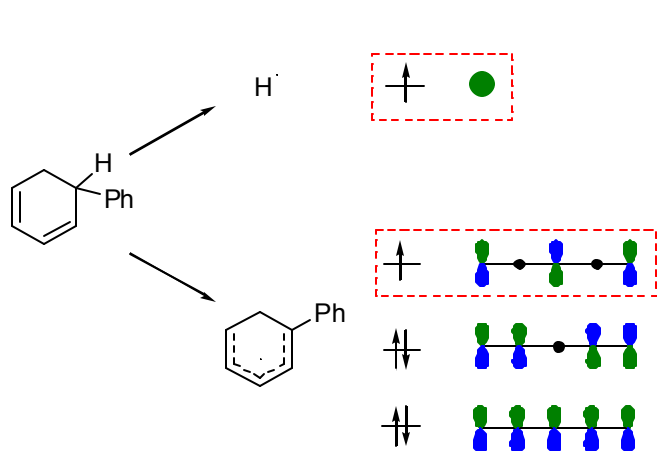- Endo selectivity can lead to the more sterically crowded product:

major **minor**
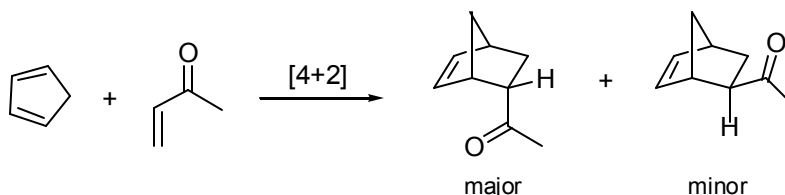
Sigmatropic Rearrangements

- In sigmatropic reactions it appears as if a σ bond has "moved" to a different location on a π system
- Suprafacial rearrangement: The bond moves along the same face of the π system
- Antarafacial rearrangement: The bond crosses to the other face of the π system

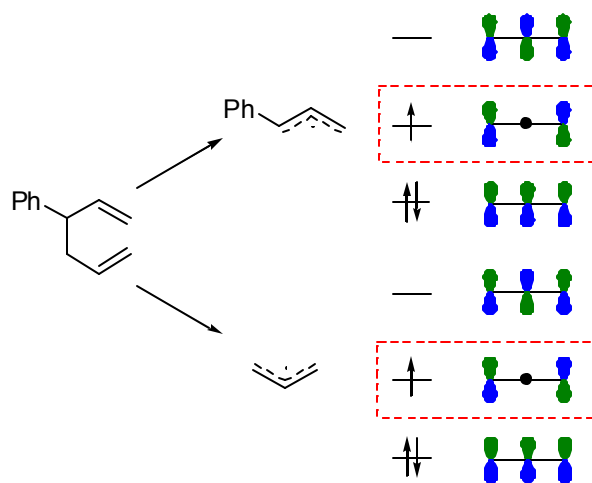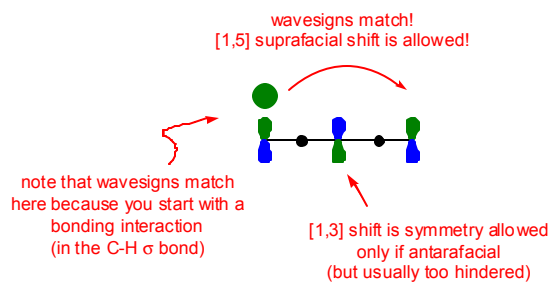- Look for a driving force, such as conjugation or the formation of stronger bonds

ether   [3,3] →   ketone

unconjugated   [3,3] →   conjugated

unconjugated   [1,5] →   conjugated

Molecular Orbital Analysis

Linear Shifts [1,n]

Cope and Claisen Rearrangements [3,3]

Look at SOMOs

wavesigns match!
[1,5] suprafacial shift is allowed!

note that wavesigns match here because you start with a bonding interaction (in the C-H σ bond)

[1,3] shift is symmetry allowed only if antarafacial (but usually too hindered)

Look at SOMOs

wavesigns match!
[3,3] suprafacial shift is allowed!

note that wavesigns match here because you start with a bonding interaction (in the C-C σ bond)

7
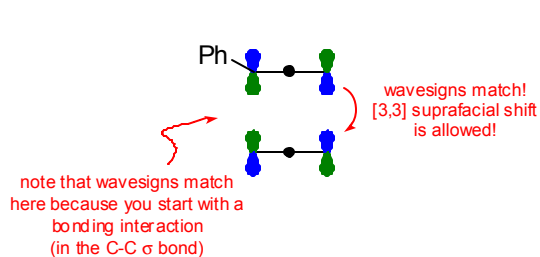
## The Claisen Rearrangement – Stereochemistry and [3,3] Shifts

- The Claisen rearrangement is a [3,3] sigmatropic shift in which an ether is converted into a ketone.

- Concerted mechanism (one step). Usually proceeds through a chair-like transition state, as it does in the case of the enzyme chorismate mutase, but the reaction can also (but very rarely) proceed through a boat-like transition state. The transition state geometry determines the stereochemistry of the product.

- The ketone is more stable than the ether, but always remember that the reverse reaction can occur. Be on the lookout!

General Case

ether

ketone
(more stable)

bond
rotations

chair
transition state

boat
transition state
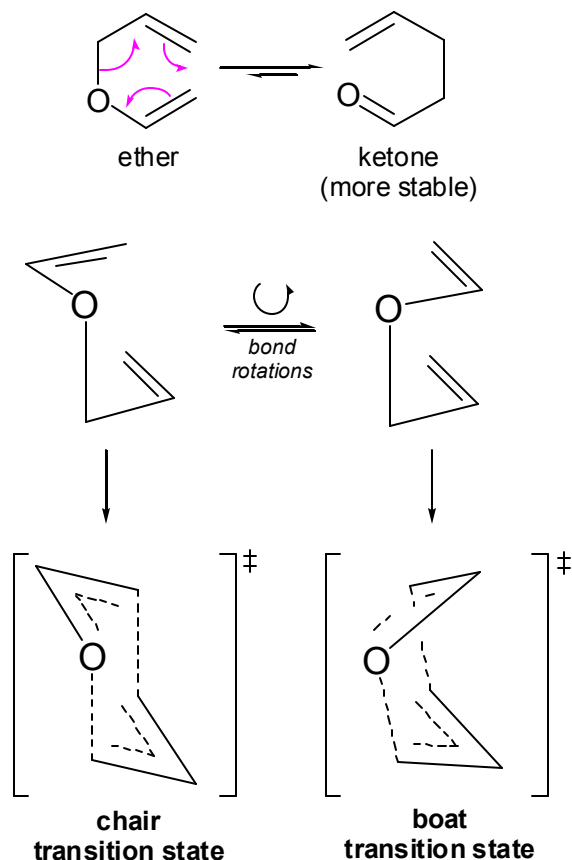
Step-by-Step Problem Solving

1) Recognize the bound allyl systems are the giveaway sign for a [3,3] sigmatropic rearrangement
2) Label all stereocenters as (*R* or *S* and *E* or *Z*)
3) Draw a cyclic conformation and "push arrows" to give you the bond connectivity in the product (with ambiguous stereochemistry)
4) The most favored transition states for these reactions are chairs. There are two chair conformations which you should draw.
5) Double check to ensure that you have retained the *R*/*S*+*E*/*Z* stereochemistry on your 3D chair drawings
6) The most favored transition state corresponds to the chair with the least strain (typically places the bulkiest substituents at equatorial positions).
7) Push arrows to yield the product in its 3D chair form
8) Label all newly generated stereocenters as *R*/*S* or *E*/*Z*
9) Transfer as wedges and dotted lines on to a Lewis structure of the product

Example: Stereochemical Issues