

# Chemistry 2600

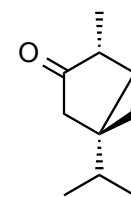
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## Chapter 20

### Cycloaddition Reactions

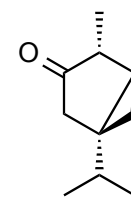
(sections 20.1-20.3, excluding 20.3.3-20.3.4 and 20.3.6.2-20.3.6.3)

# Pericyclic Reactions



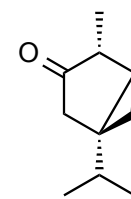
- Pericyclic reactions are those in which electrons move in a cyclic transition state.
- There are 3 classes of pericyclic reactions:
  - Cycloaddition Reactions
  - Sigmatropic Rearrangements
  - Electrocyclic Reactions
- In this chapter we will be looking at the details of cycloaddition reactions.
- Cycloaddition reactions are those in which two separate  $\pi$  components add to each other to form a ring, called a cycloadduct.
- To understand these reactions, it is essential to first understand the molecular orbitals involved.

# $\pi$ Molecular Orbitals (MOs) – A Review



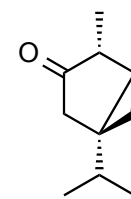
- According to molecular orbital (MO) theory, all  $\pi$ -symmetric orbitals in a  $\pi$ -system combine to give a set of  $\pi$ -MOs in which:
  - The number of  $\pi$ -MOs is equal to the number of  $p$  orbitals which combined to make them.
  - In a linear  $\pi$ -system, # energy levels = #  $\pi$ -MOs.
  - In a cyclic  $\pi$ -system, use the polygon-in-a-circle trick to predict energy levels; the polygon should always point down. *Note that, while benzene has a cyclic  $\pi$ -system, 1,3-cyclohexadiene does not!*
  - The number of delocalized  $\pi$ -electrons is equal to 2 electrons per double bond + 2 electrons per **lone pair that is part of the  $\pi$ -system**. *We are primarily interested in the HOMO and LUMO of any given  $\pi$ -system, so make sure you count your electrons carefully to correctly identify the HOMO and LUMO!*

# $\pi$ Molecular Orbitals (MOs) – A Review

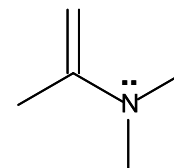
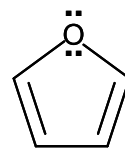


- The shape of each MO can be predicted using symmetry and nodes:
  - The lowest energy  $\pi$ -MO has all  $p$  orbitals aligned in phase, giving no nodes perpendicular to the plane of the  $\pi$ -system.
  - The next  $\pi$ -MO will have one node perpendicular to the plane of the  $\pi$ -system, the next  $\pi$ -MO will have two such nodes, etc.
  - The highest energy  $\pi$ -MO will have every  $p$  orbital out-of-phase with the  $p$  orbitals on neighbouring atoms.
  - As long as the  $\pi$ -system is symmetric (via mirror plane), every MO will be either **symmetric** or **antisymmetric** (with respect to phase).

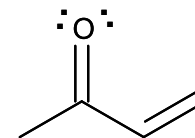
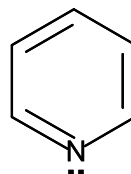
# $\pi$ Molecular Orbitals (MOs) – A Review



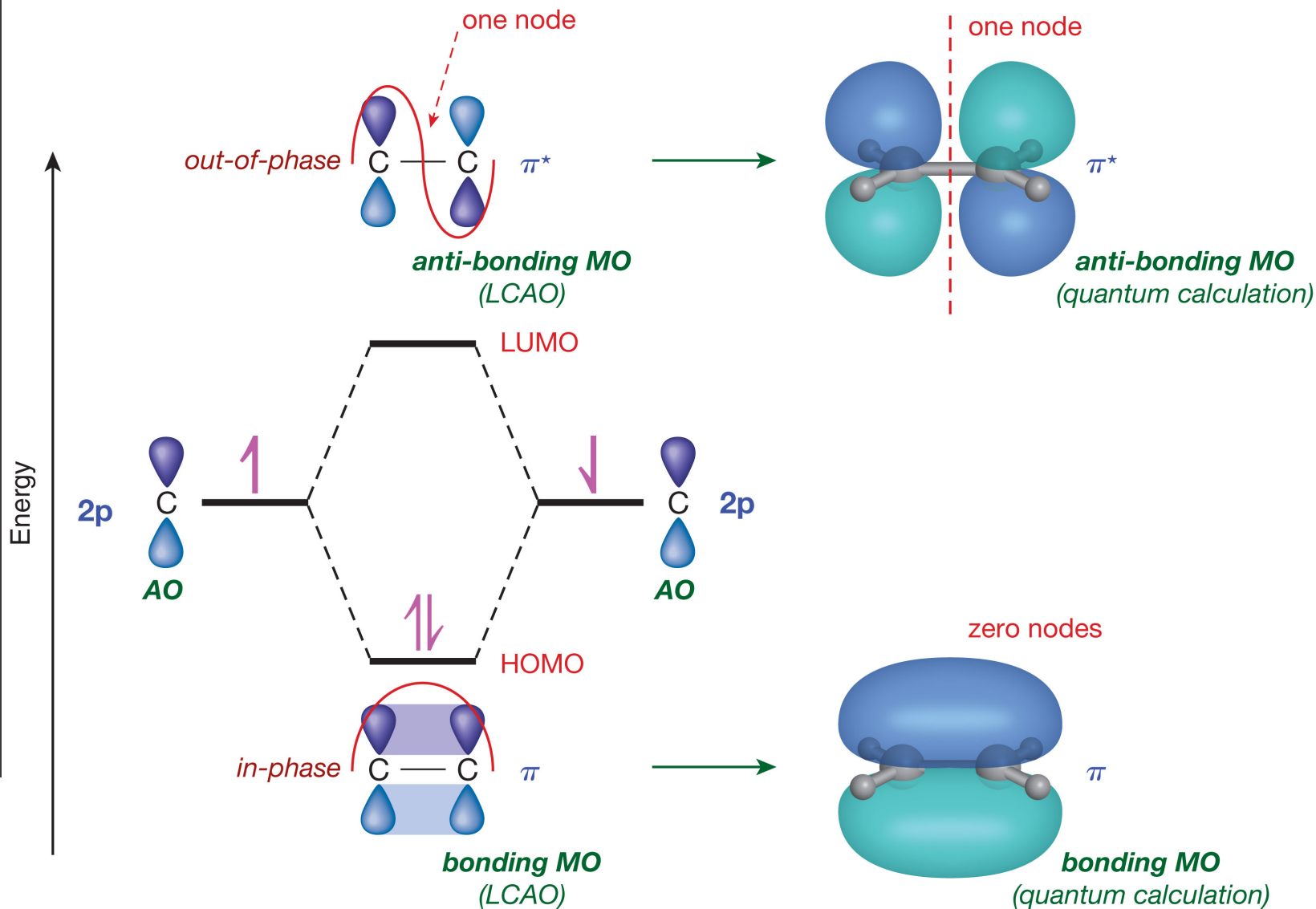
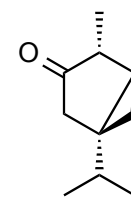
- A  $\pi$ -MO diagram is a simplified MO diagram that is missing the  $\sigma$ -MOs for clarity. You will need to be careful to include the correct number of electrons. Include two electrons for every pi bond on your Lewis structure and two electrons for every lone pair involved in the pi system.
  - A lone pair is involved in the pi system if the atom with the lone pair is bonded to at least one **other** atom which has a pi bond in the pi system. Only one lone pair per atom can be part of the same pi system.



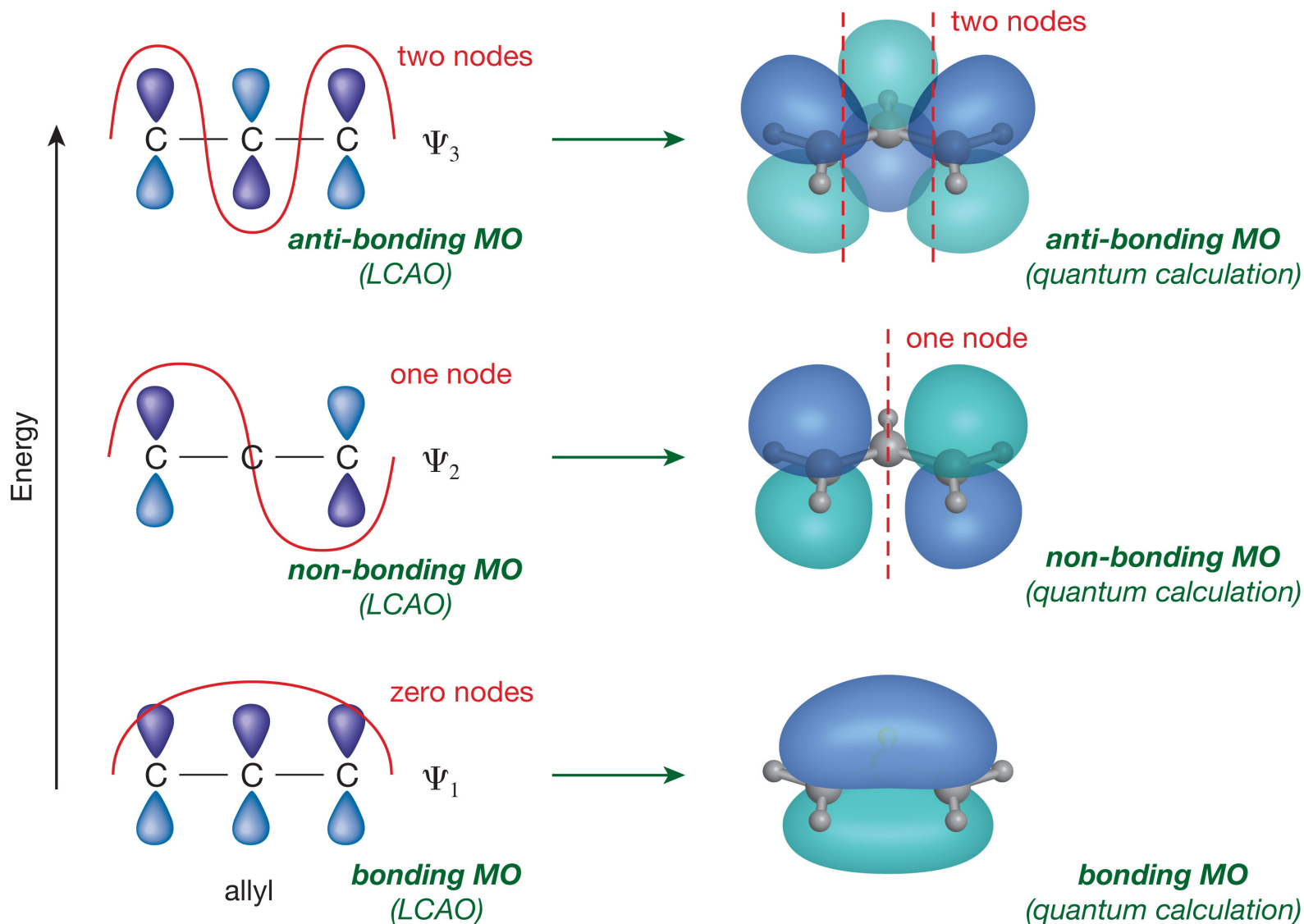
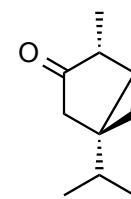
- A lone pair is **not** involved in the pi system if the atom has a pi bond in the pi system.



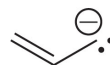
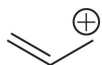
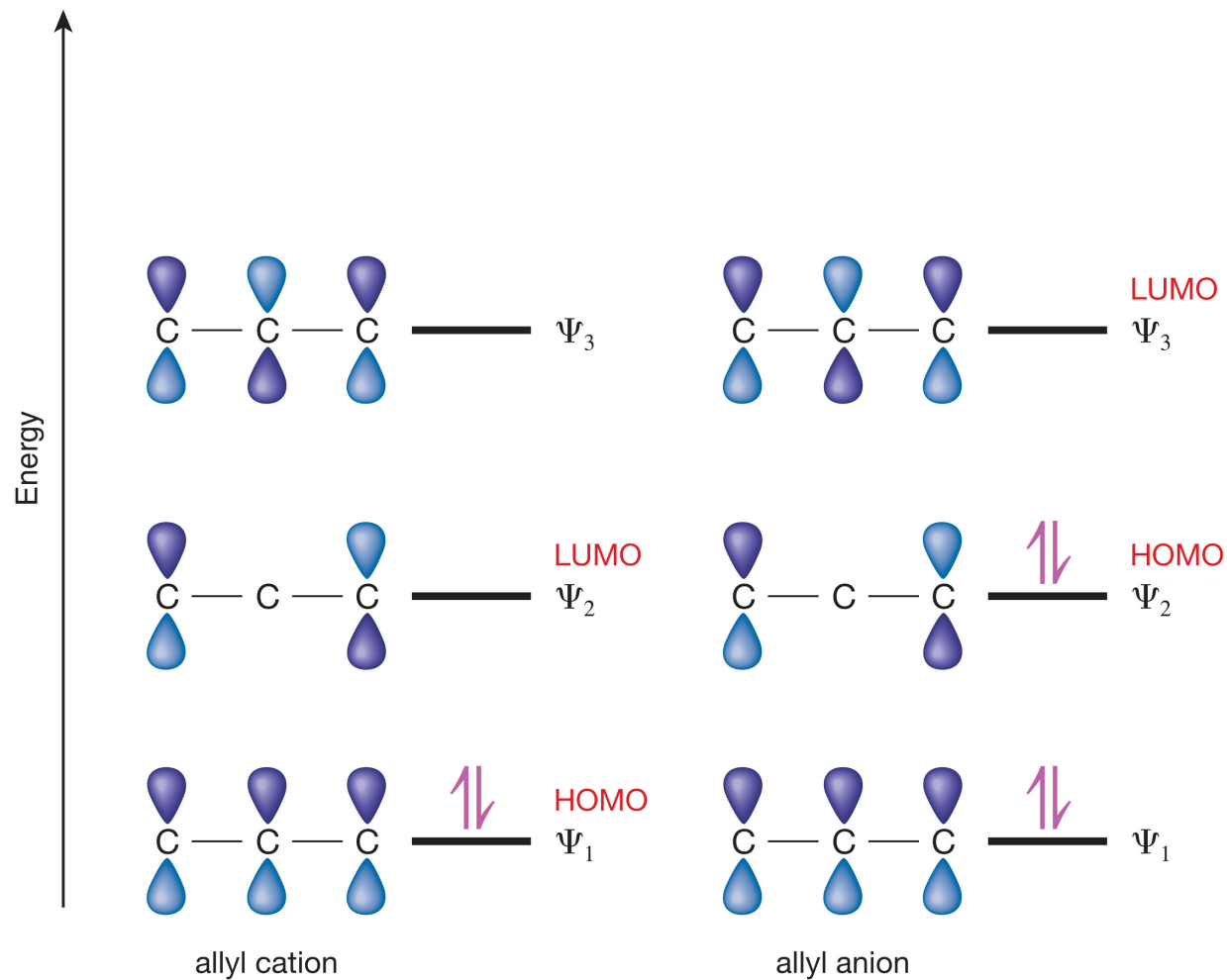
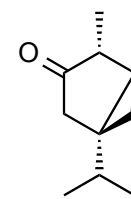
# $\pi$ MOs – 2 Carbon System (Ethylene)



# $\pi$ MOs – 3 Carbon System (Allyl)

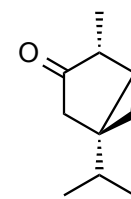


# $\pi$ MOs – 3 Carbon System (Allyl)



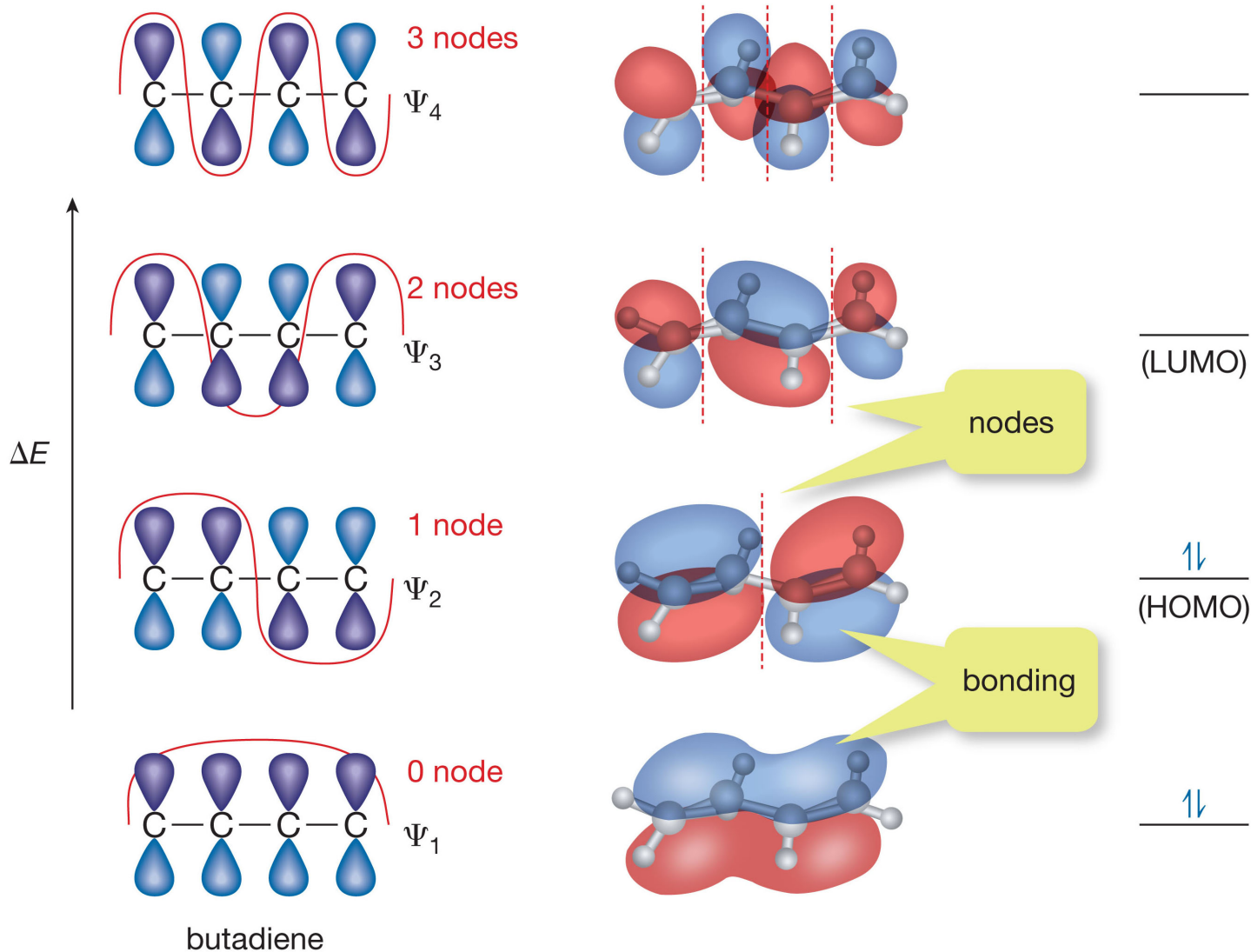
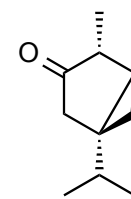


# $\pi$ MOs – 4 Carbon System (Butadiene)

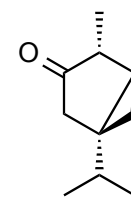


- Draw the valence  $\pi$  MO diagram for 1,3-butadiene:

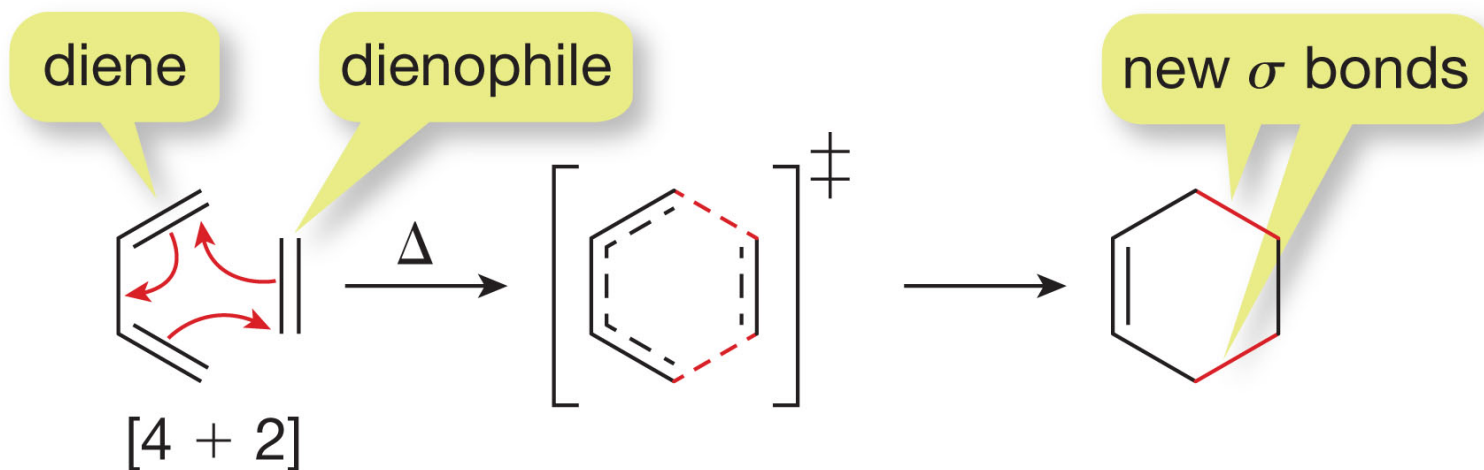
# $\pi$ MOs – 4 Carbon System (Butadiene)



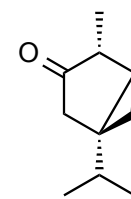
# The Diels-Alder Reaction



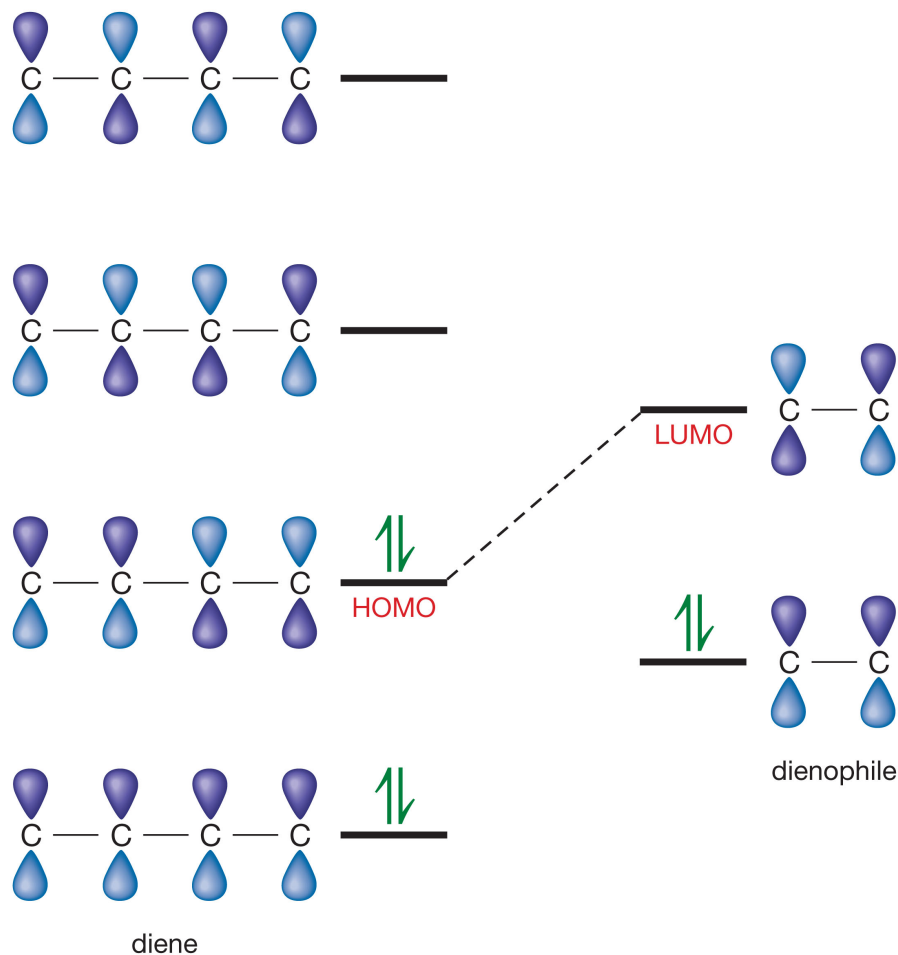
- The **Diels-Alder** reaction is an example of a [4 + 2] cycloaddition reaction. The numbers in brackets refer to the atoms in each reacting functional group that forms the ring.
- The two components of this reaction, a **diene** and a **dienophile**, add together, resulting in a cyclohexene product (the cycloadduct).



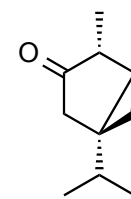
# The Diels-Alder Reaction



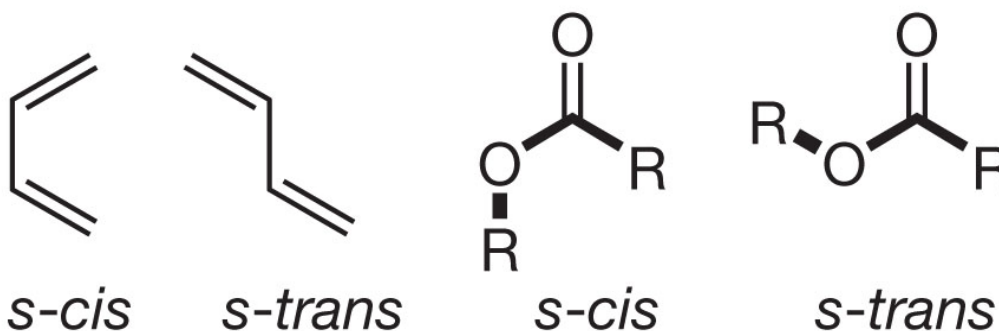
- A typical Diels-Alder reaction involves the overlap of the HOMO of the diene with the LUMO of the dienophile.



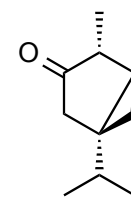
# The Diels-Alder Reaction



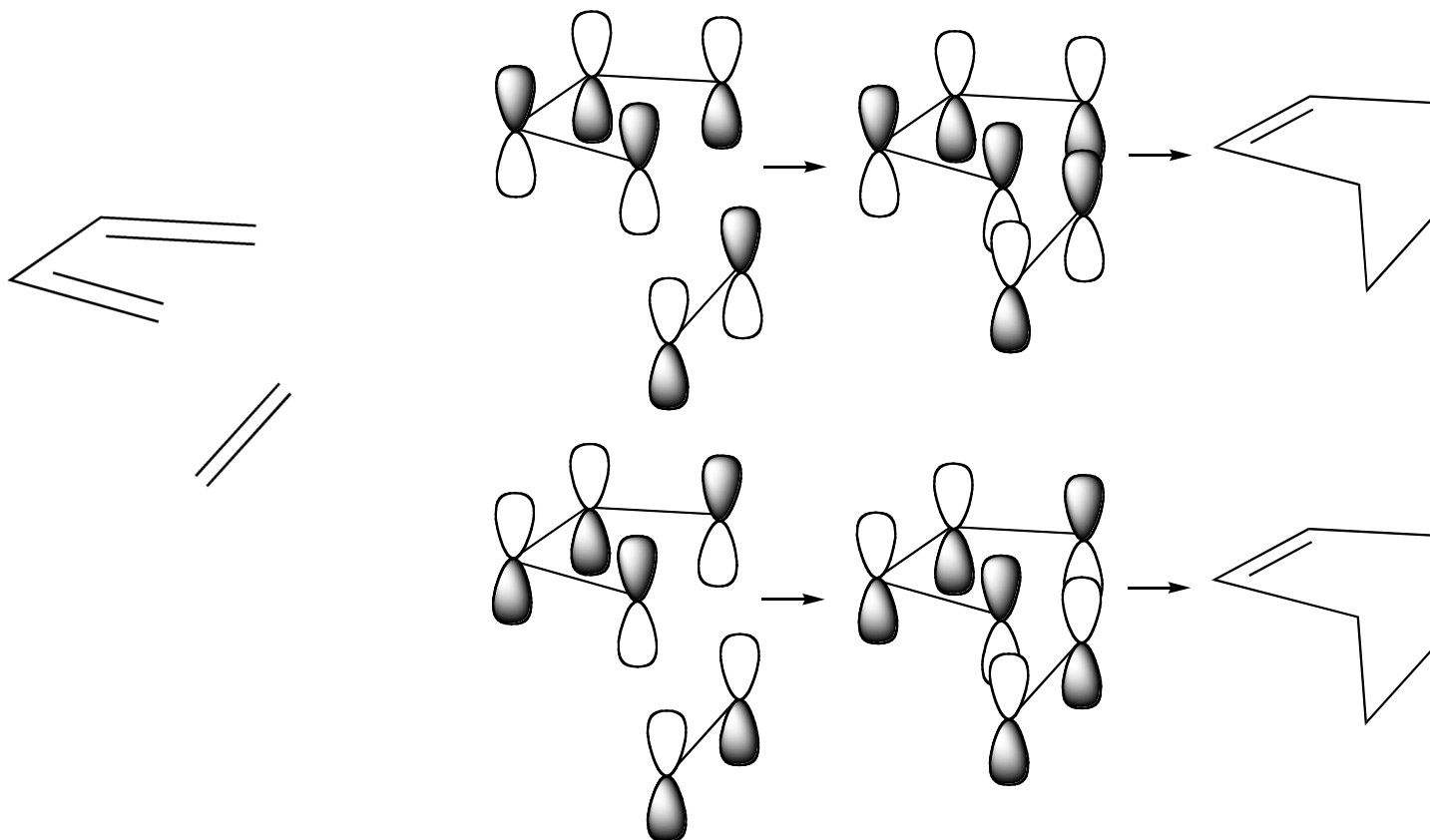
- For the Diels-Alder reaction to take place, the diene must be in its higher *s-cis* conformation.
- The *s-cis* and *s-trans* refer to *cis/trans* isomerism around a single bond where rotation is restricted by conjugation (s stands for sigma bond).



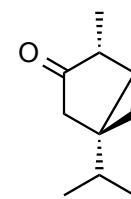
# The Diels-Alder Reaction



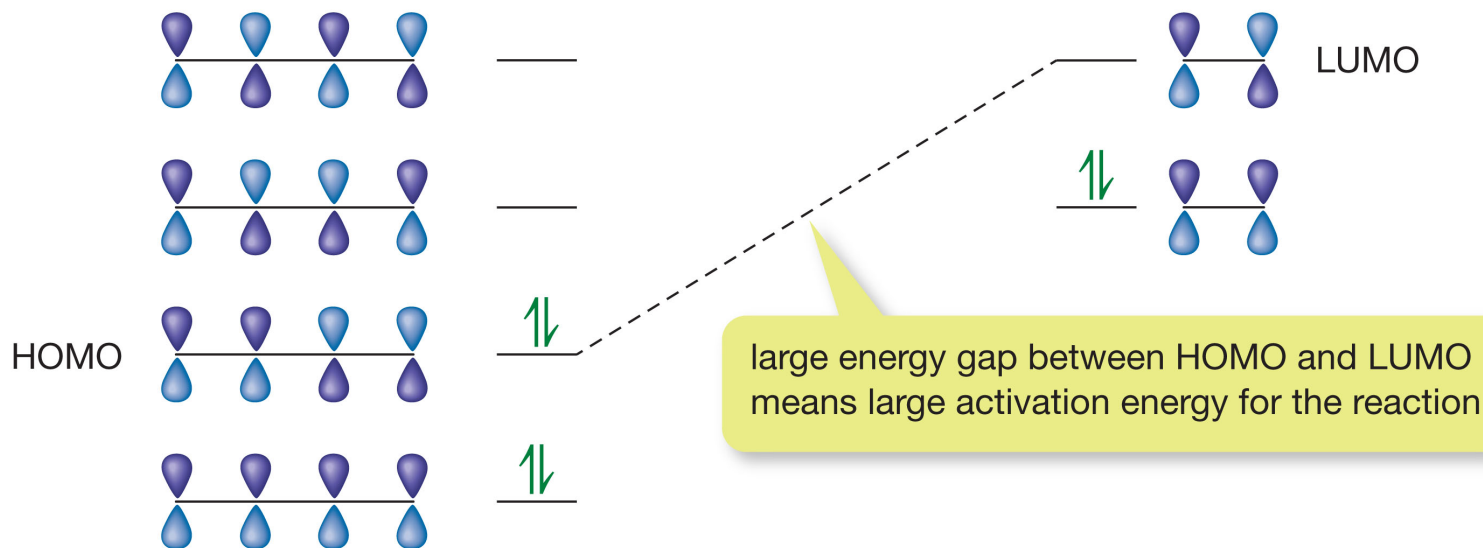
- Additionally, for the Diels-Alder reaction to take place, the symmetries of the interacting diene and dienophile orbitals must match.



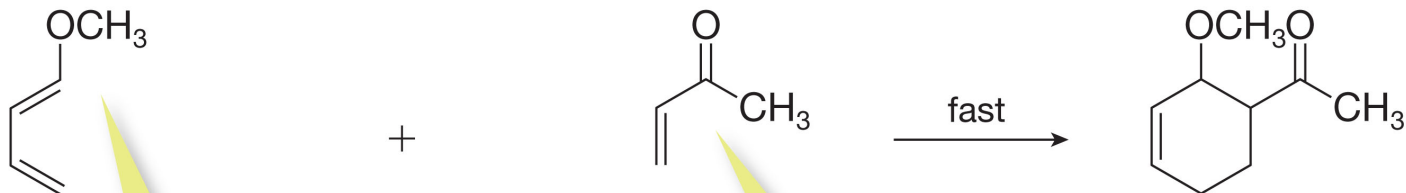
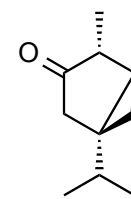
# The Diels-Alder Reaction



- The addition of EDGs to the diene raises the energy of all the  $\pi$  MOs, including the HOMO. Likewise, the addition of the EWGs to the dienophile lowers the energy of the LUMO.
- Either or both of these factors can narrow the HOMO-LUMO gap and increase the rate of the Diels-Alder reaction.

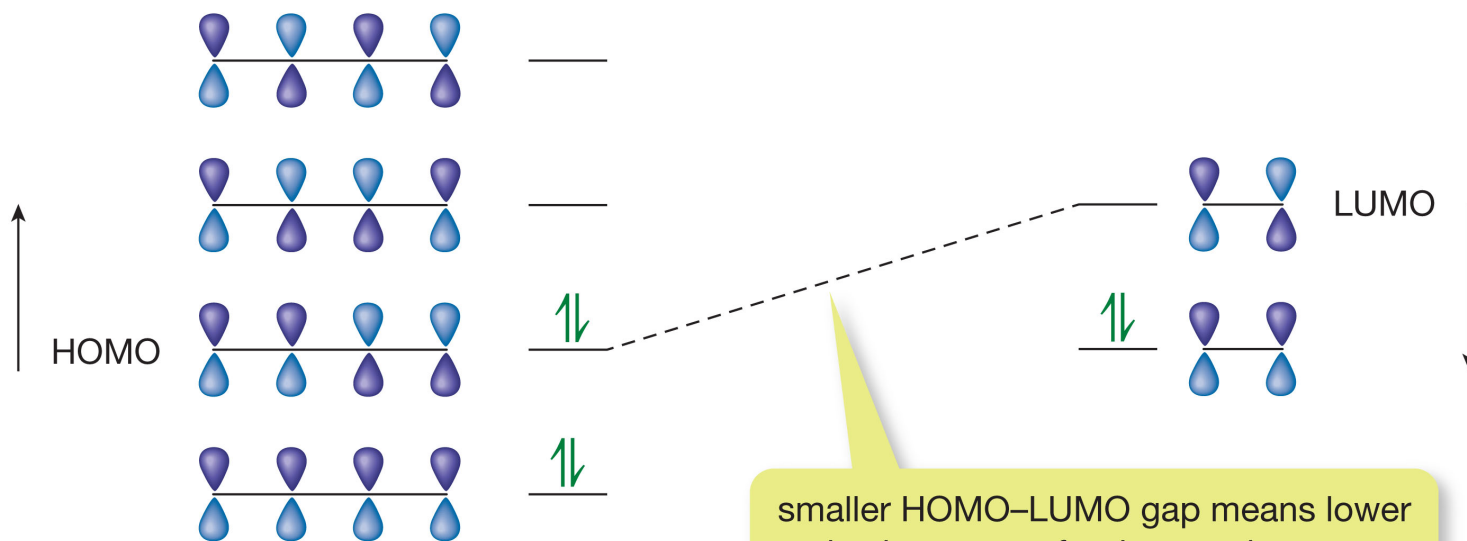


# The Diels-Alder Reaction



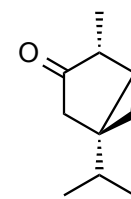
electron-donating group  
raises HOMO energy

electron-withdrawing group  
lowers LUMO energy

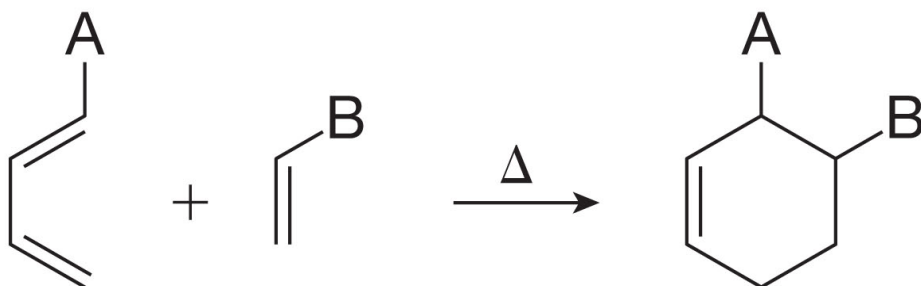




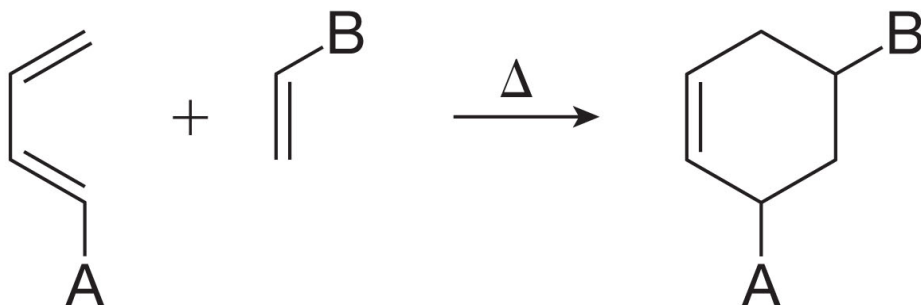
# Regioselectivity



- If the diene and dienophile are both unsymmetrical, the Diels-Alder reaction could give rise to 2 regioisomers based on the relative position of the substituents.

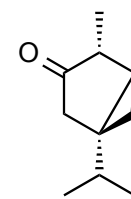


“ortho”  
product

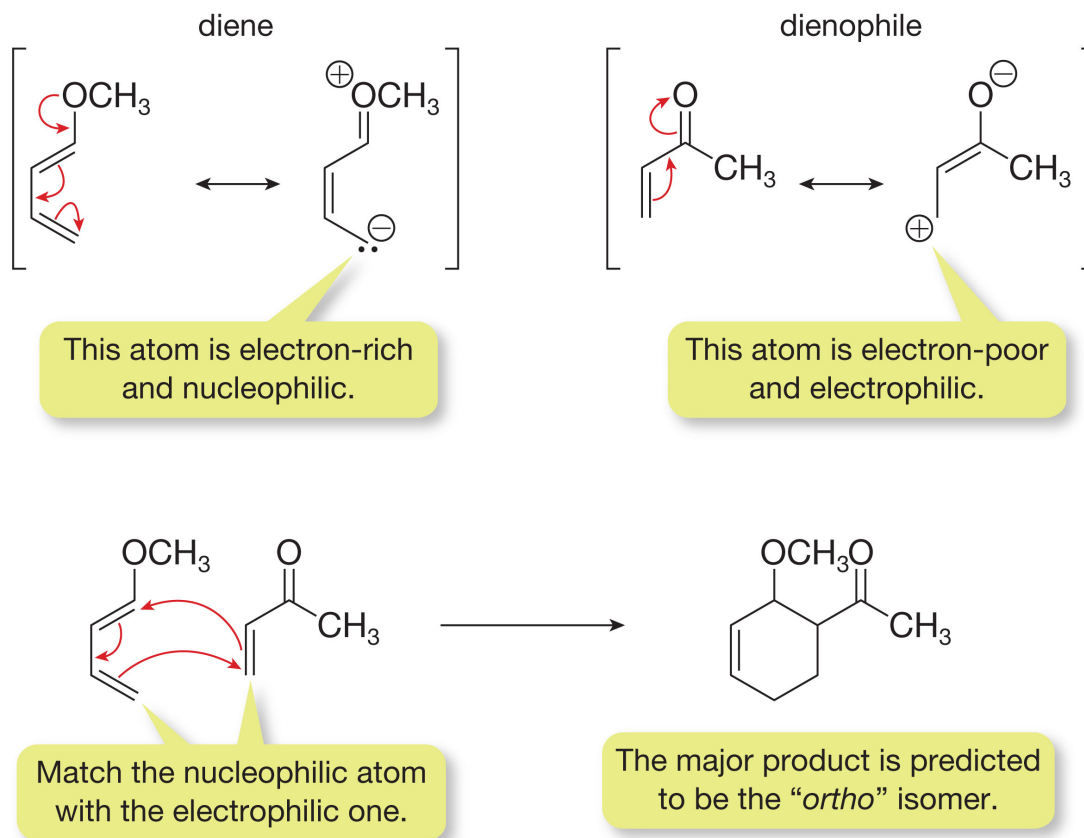


“meta”  
product

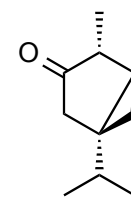
# Regioselectivity



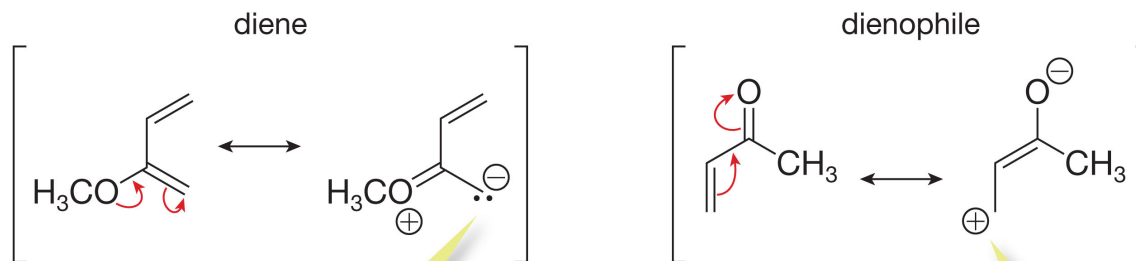
- The regiochemistry of these reactions can often be predicted by looking at the resonance structures of both the diene and dienophile.



# Regioselectivity

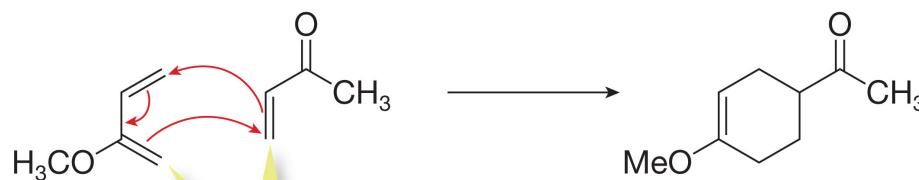
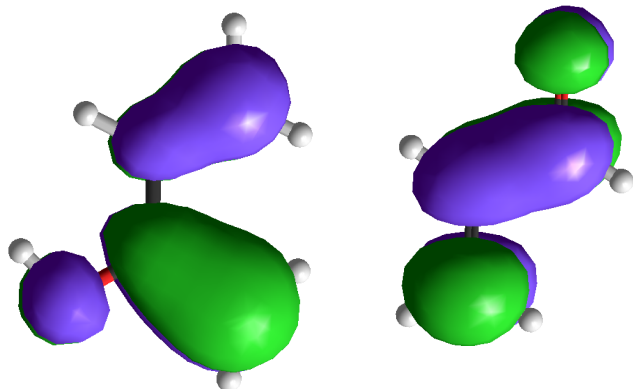


- The same method can be used to predict the regiochemistry of other Diels-Alder reactions



This atom is electron-rich and nucleophilic.

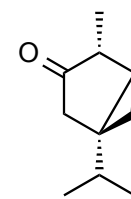
This atom is electron-poor and electrophilic.



Match the nucleophilic atom with the electrophilic one.

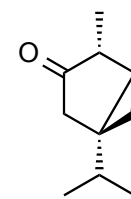
The major product is predicted to be the "para" isomer.

# Stereochemistry



- Three important factors govern the stereochemistry of Diels-Alder reactions:
  - The relative position of the substituents on the diene and the dienophile (*cis/trans*).
  - The orientation of the dienophile as it approaches the diene (*endo/exo*).
  - The direction of approach (top/bottom).
- Because the Diels-Alder reaction is concerted, the relative geometry of any substituents on the diene or dienophile is strictly maintained in the products.

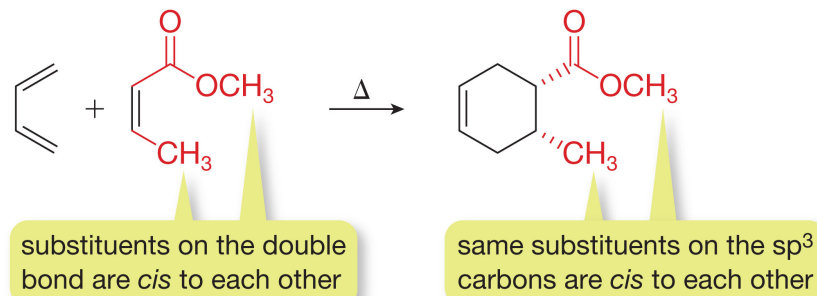
# Stereochemistry – Cis/Trans



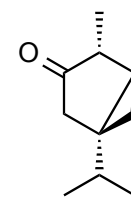
- Diene – The relative position of the terminal substituents is maintained in the product.



- Dienophile – The relative position of dienophile substituents (*cis/trans*) must be maintained in the product.

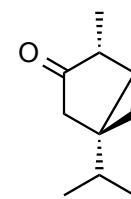


# Stereochemistry – Endo/Exo

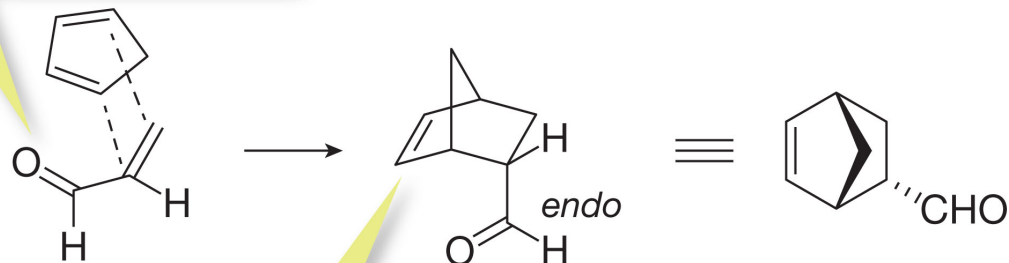


- An unsymmetrical dienophile can approach the diene in one of two ways, giving two possible products (*endo* or *exo* adducts).
  - *Endo* adducts – the substituent on the dienophile is oriented *toward* the alkene of the cycloadduct.
  - *Exo* adducts – the substituent on the dienophile is oriented *away* from the alkene of the cycloadduct.
- Most Diels-Alder reactions favour the formation of the *endo* rather than the *exo* cycloadduct.

# Stereochemistry – Endo/Exo

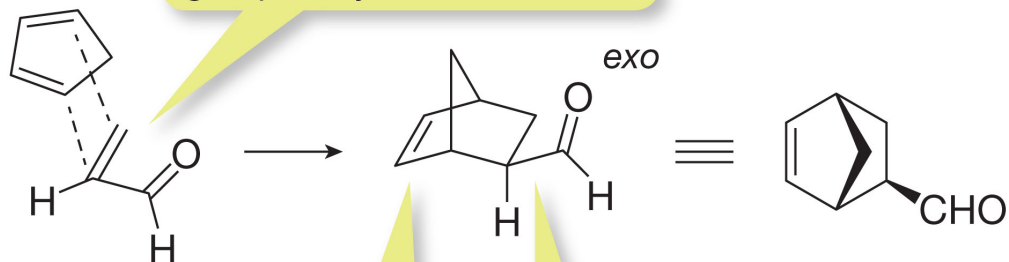


dienophile approaches with the electron-withdrawing group underneath the diene



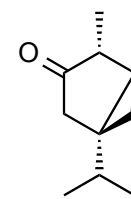
electron-withdrawing group is oriented toward the alkene

dienophile approaches with the electron-withdrawing group away from the diene

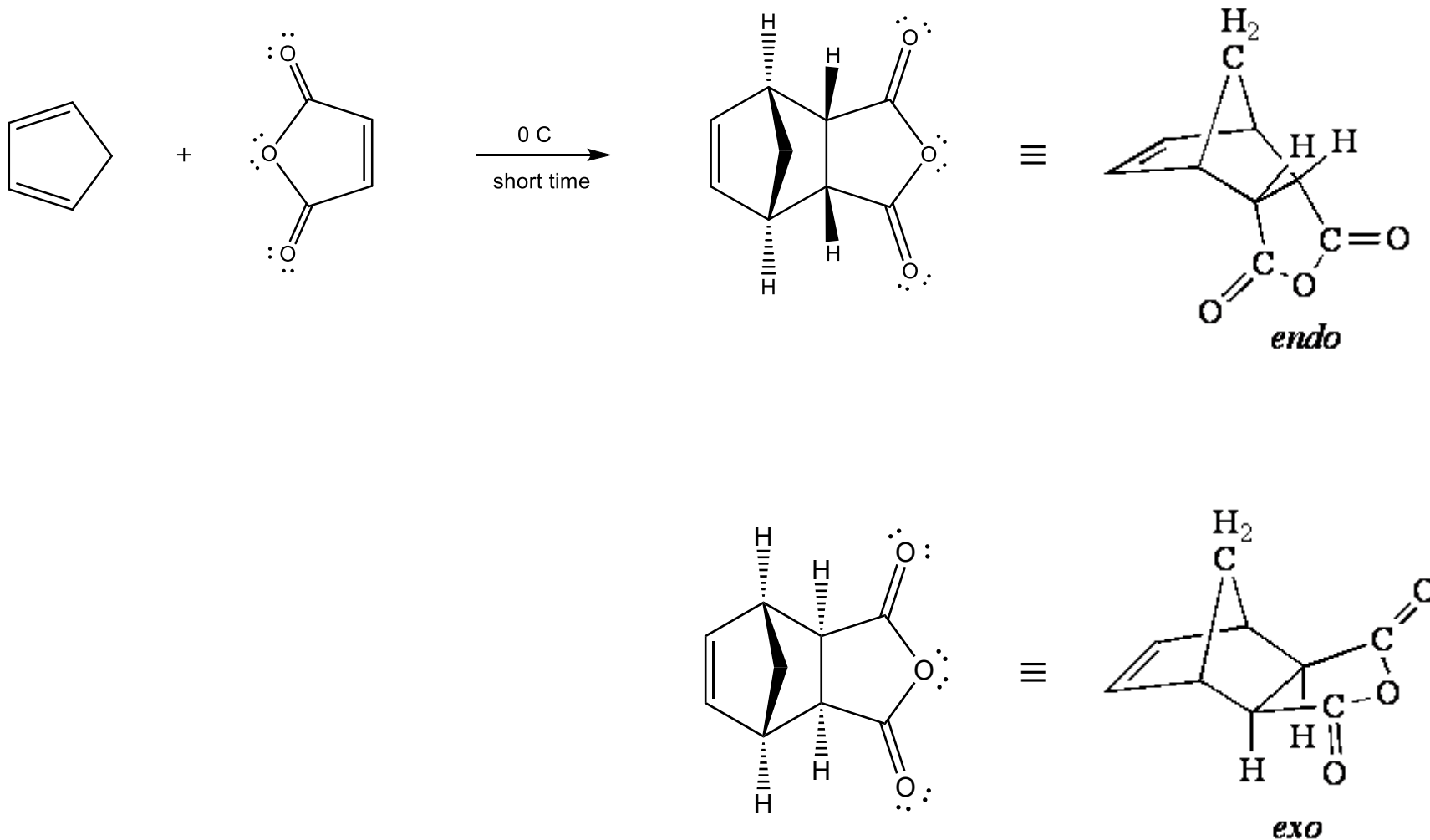


electron-withdrawing group is oriented away from the alkene

# Stereochemistry – Endo/Exo

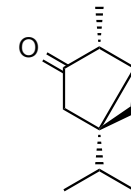


- Another example:

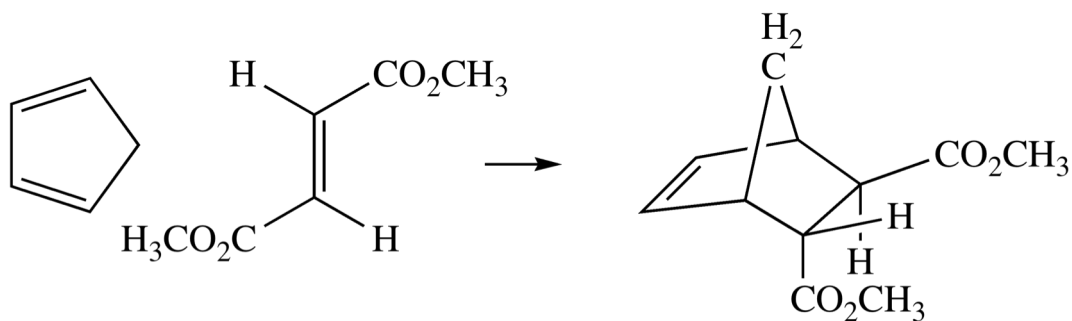




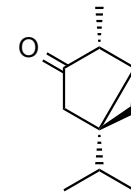
# Stereochemistry – Endo/Exo



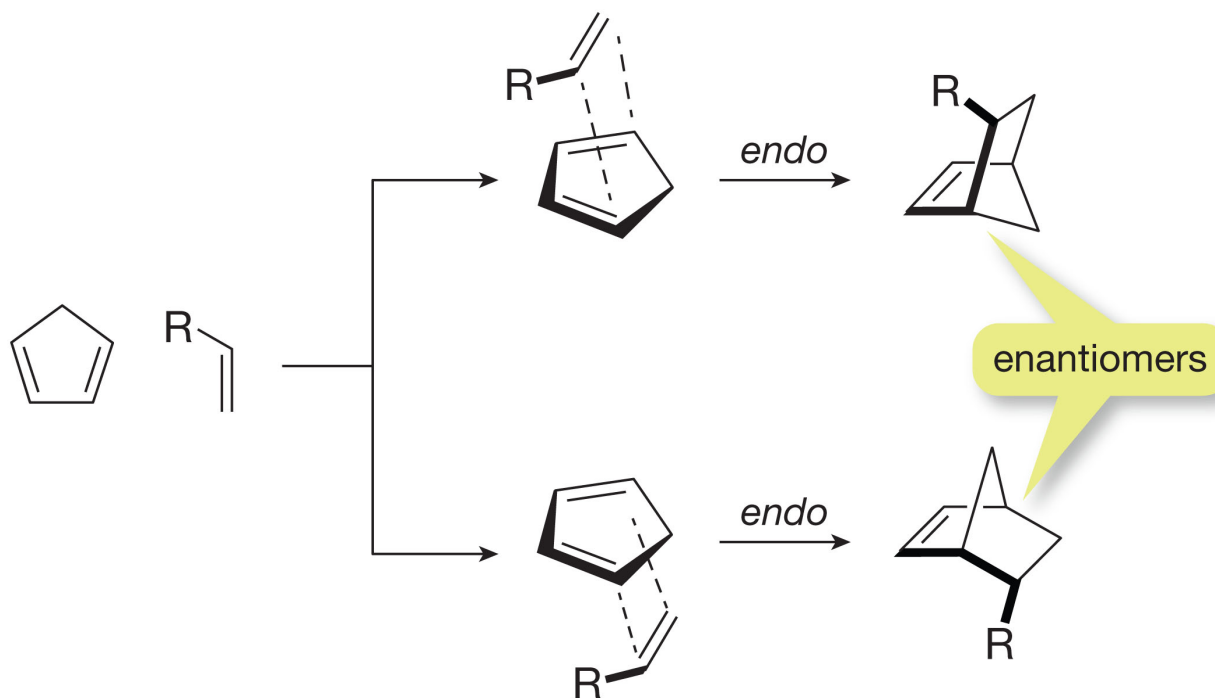
- Endo/exo adducts are not possible from acetylenic or trans disubstituted dienophiles



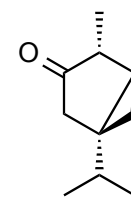
# Stereochemistry – Top/Bottom



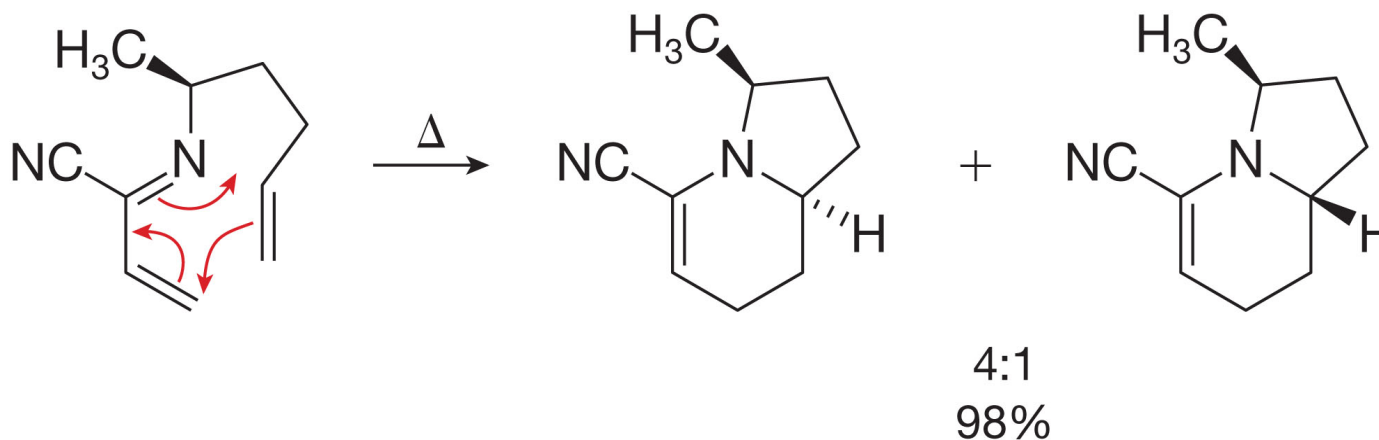
- The direction from which the dienophile approaches the diene controls the formation of Diels-Alder enantiomers.
- In practice, only one enantiomer is drawn with the understanding that a racemate is represented.



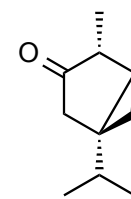
# Hetero-Diels-Alder Reaction



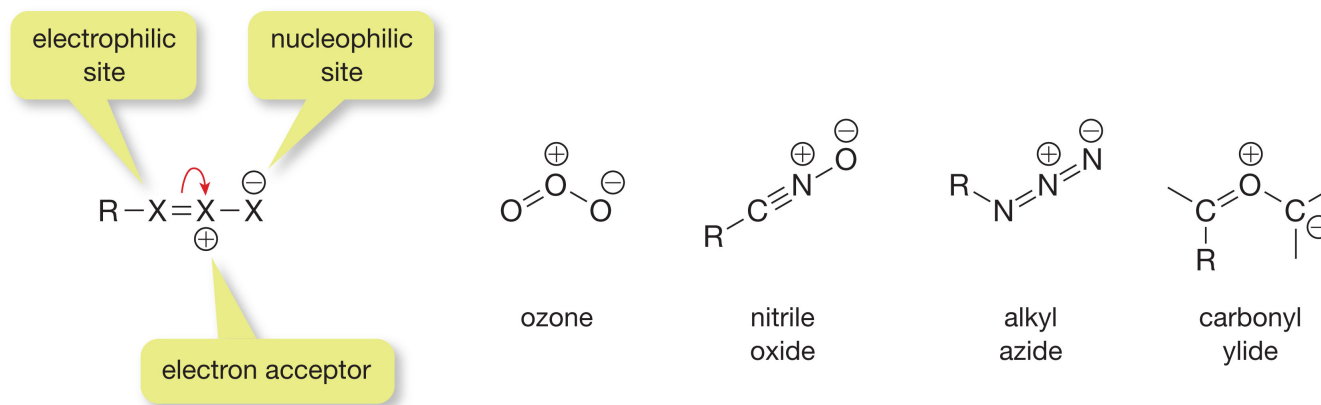
- A hetero-Diels-Alder reaction contains a heteroatom (not carbon) in either the diene or dienophile and forms a heterocycle instead of a cyclohexene.



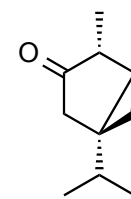
# 1,3-Dipolar Cycloadditions



- 1,3-dipolar cycloaddition reactions are [3 + 2] cycloadditions between **1,3-dipoles** and **dipolarophiles**.
- A 1,3-dipole is a 3 atom functional group that has a nucleophilic site and an electrophilic site at positions 1 and 3 respectively.
- A dipolarophile contains a alkene or alkyne functional group that can react with a 1,3-dipole.

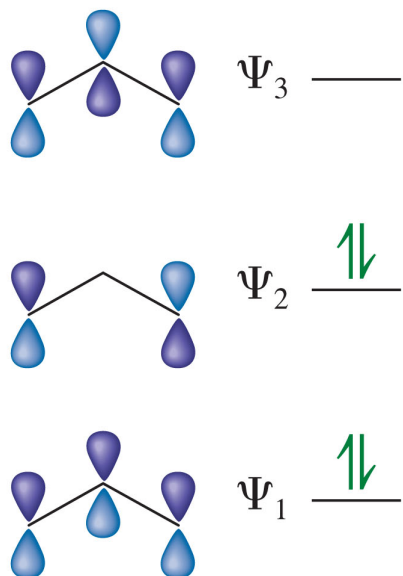


# 1,3-Dipolar Cycloadditions

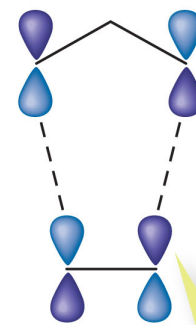
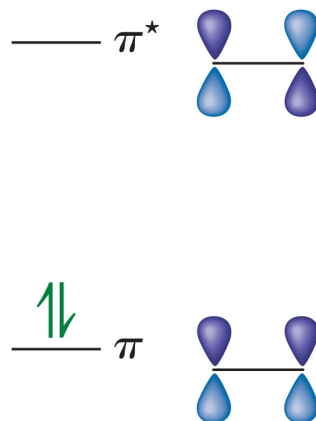


- 1,3-dipolar cycloadditions can be understood by examining the symmetry of their frontier MOs.

1,3-dipole

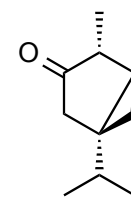


dipolarophile



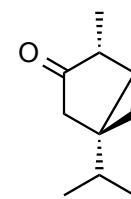
symmetry of frontier orbitals must match

# Ozonolysis

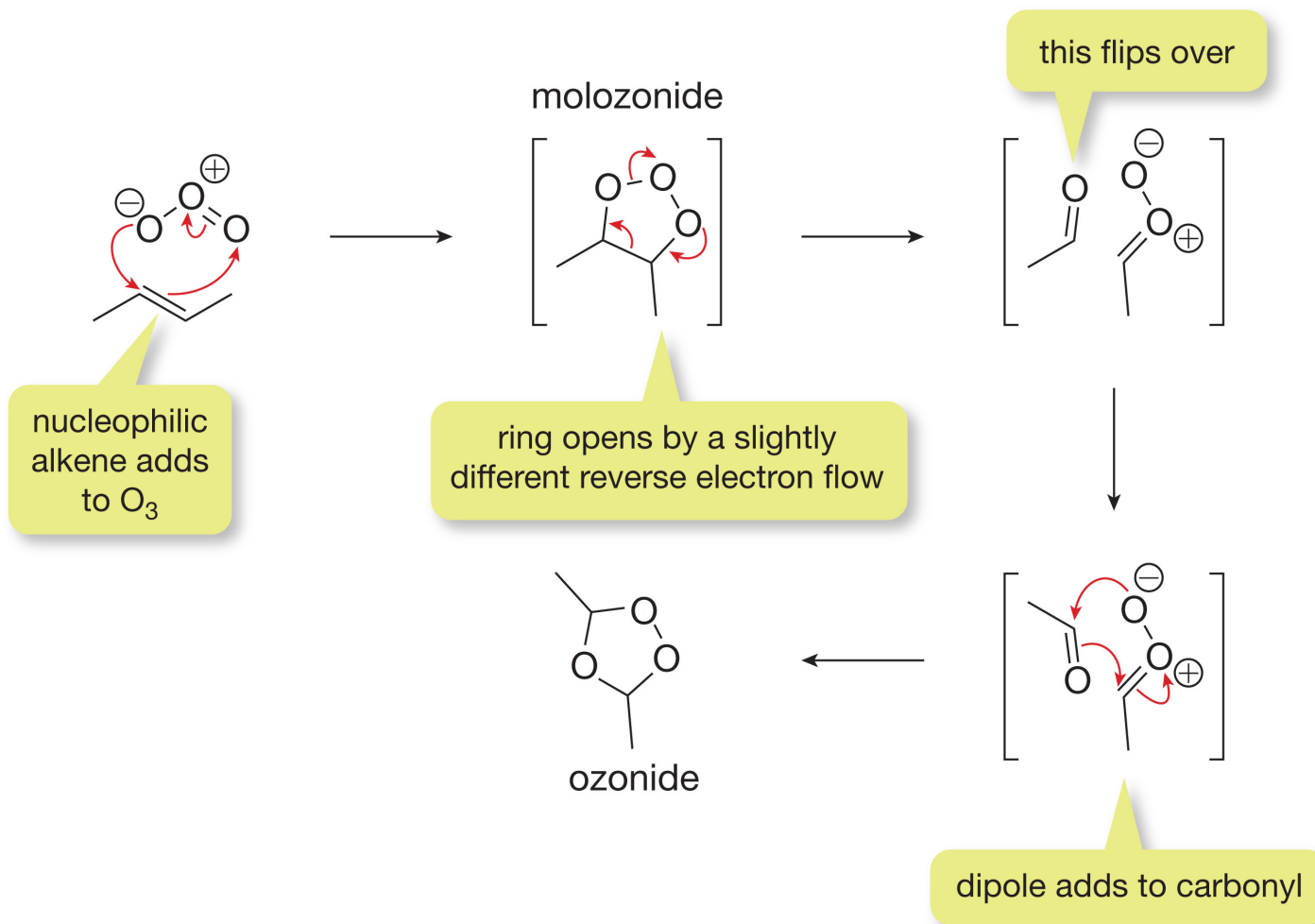


- A common [3+2] cycloaddition is the reaction between ozone and an alkene.
- The product, ozonide, is formed from an initial [3+2] cycloaddition, followed by a ring opening retro [3+2] cycloaddition, followed by a final [3+2] cycloaddition.
- Ozonides are explosive and usually not isolated. Instead, they are immediately worked up under reductive or oxidative conditions to give dicarbonyl or dicarboxylic acids, respectively.

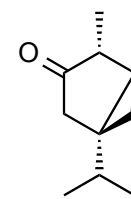
# Ozonolysis



- Initial formation of an ozonide:

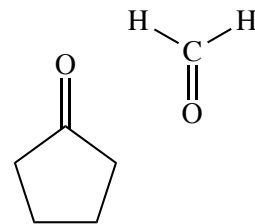
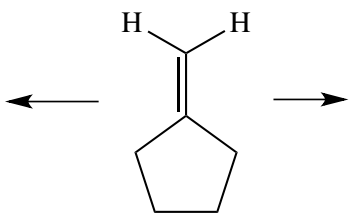
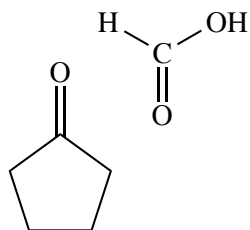
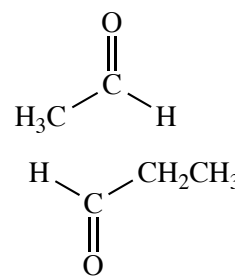
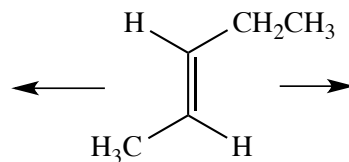
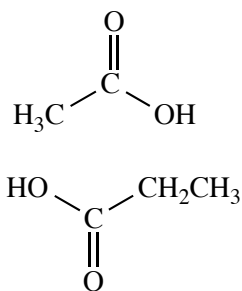
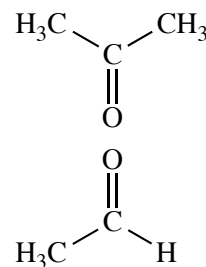
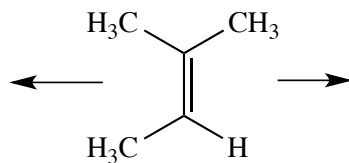
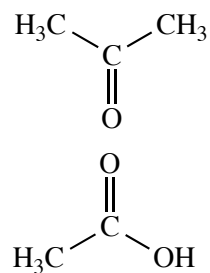


# Ozonolysis



**Oxidative workup** -  $\text{H}_2\text{O}_2$   
- gives carboxylic acid or ketone products

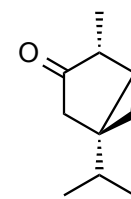
**Reductive workup** - Zn/acetic acid or dimethyl sulfide  
- gives ketone or aldehyde products



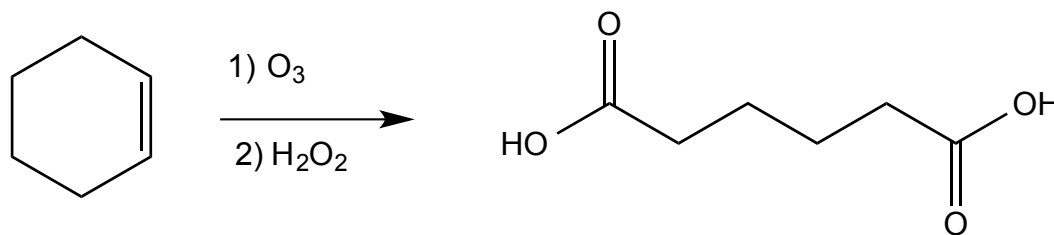
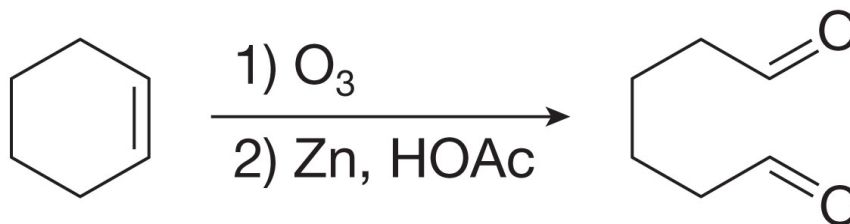
Cycloalkenes and symmetrical alkenes do not give mixtures.



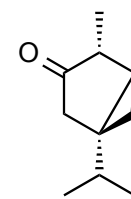
# Ozonolysis



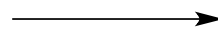
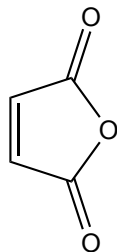
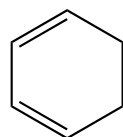
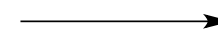
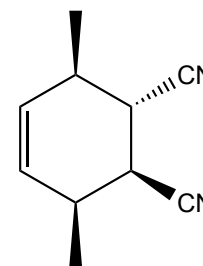
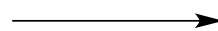
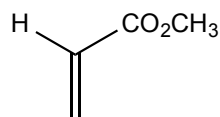
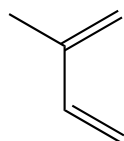
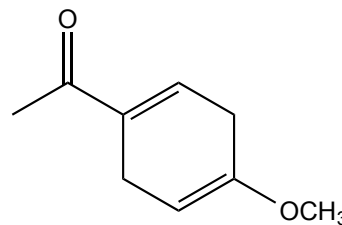
- Ozonolysis results in the cleavage of an alkene and the formation of a dicarbonyl compound, depending on the type of workup.



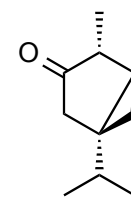
# Practice



- For each of the following reactions, draw the starting materials or the major product. Pay special attention to stereo- and/or regiochemistry.



# Practice



- Draw the ozonolysis products for each of the following alkenes:

