

CYI101
Common CHEMISTRY(Organic)

UNIT –II**Aromaticity****[2L]**

Aromatic, non-aromatic and anti-aromatic compounds

Stereochemistry**[4L]**

Concept of chirality, Axial chirality, enantiomers and diastereomers, specific rotation, optical purity, Racemic modification and resolution, R/S, D/L and E/Z nomenclature

Pericyclic reactions**[4L]**

Definitions, Classifications, photochemical [2+2] and thermal [4+2] cycloaddition, Sigmatropic rearrangement

Macromolecules**[4L]**

Introduction to peptides and proteins. Basics of Polymer Chemistry, Polymerization techniques, natural and synthetic polymer

Recommended Books:

1. Organic Chemistry, J. CLayden, N. Greeves, S. Warren, P. Wothers, Oxford University Press, 2000.
2. Principles of polymerization, George G. Odian, 4th Edn, John Wiley & Sons, Inc., Publication, 2004.

Pericyclic reactions

Pericyclic reaction involves a cyclic redistribution of bonding electrons through a concerted process.

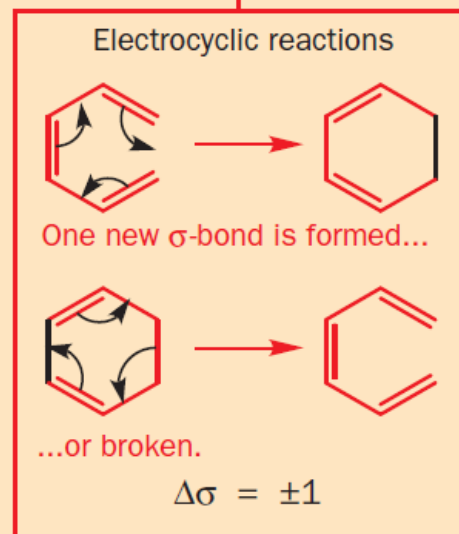
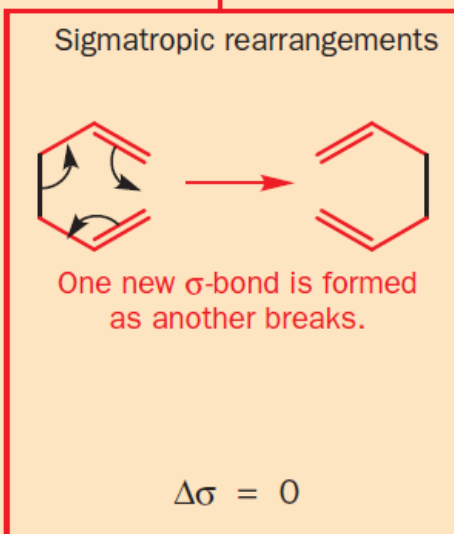
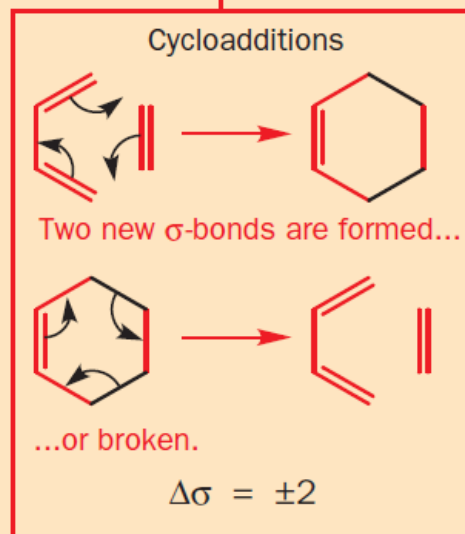
A **pericyclic reaction** is a type of organic reaction wherein the transition state of the molecule has a cyclic geometry, the reaction progresses in a **concerted fashion**, and the bond orbitals involved in the reaction overlap in a continuous cycle at the transition state.

The three principle classes of **pericyclic** reactions are termed:

Cycloaddition, **Electrocyclic**, and **Sigmatropic**

- The types of pericyclic reactions are distinguished by the number of σ bonds made or broken

Types of pericyclic reactions



Cycloaddition Reactions

A concerted combination of two π -electron systems to form a ring of atoms having two new σ bonds and two fewer π bonds is called a cycloaddition reaction.

Three important classifications of cycloaddition reactions

- (i) (4 + 2) Cycloaddition (ii) [2+2] Cycloaddition

The most common cycloaddition reaction is the $[4\pi+2\pi]$ cyclization known as the **Diels-Alder reaction**.



Reaction between a conjugated diene and dienophile

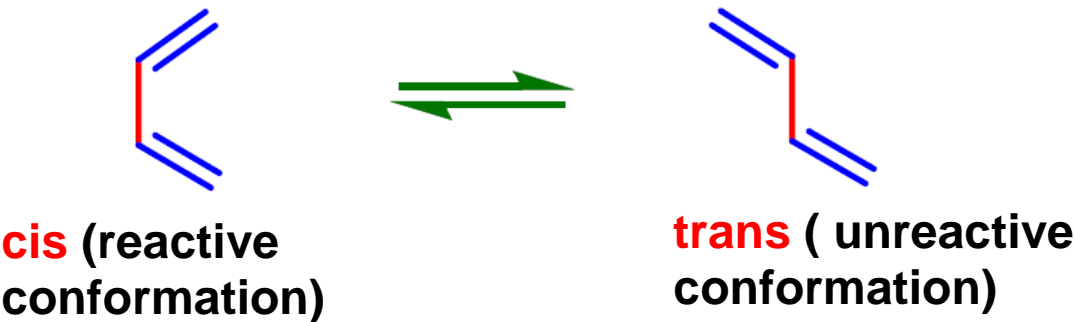
Highly effective method for the formation of cyclohexene ring

Discovered by **Professor Otto Diels** and his student **Kurt Alder** in **1928** and received **Nobel prize** in **1950**

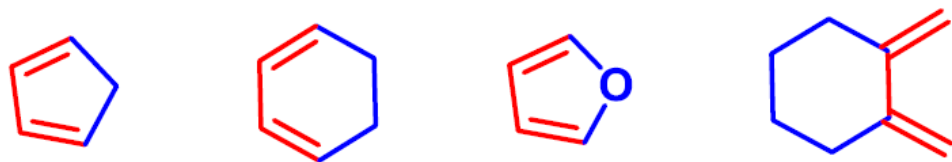
Diene can be open chain or cyclic

- Diene should be **electron rich** and reactivity should be enhanced by electron donating group substituents

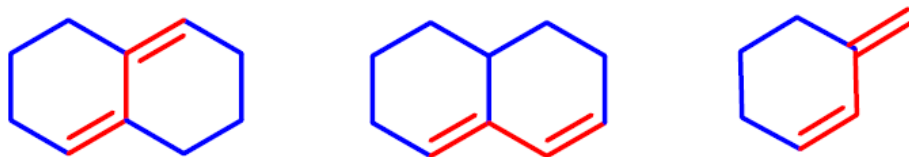
Open chain diene can acquire two conformations



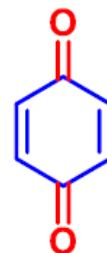
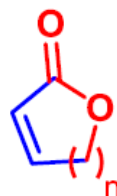
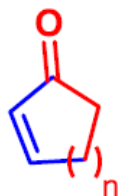
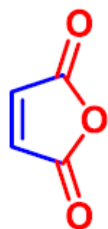
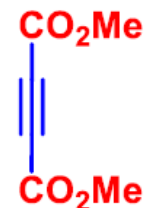
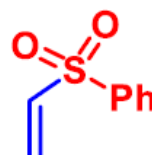
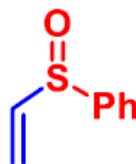
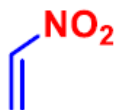
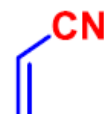
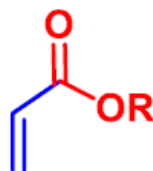
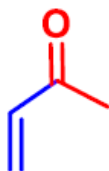
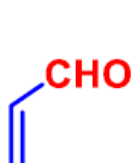
Reactive Diene



Unreactive Diene

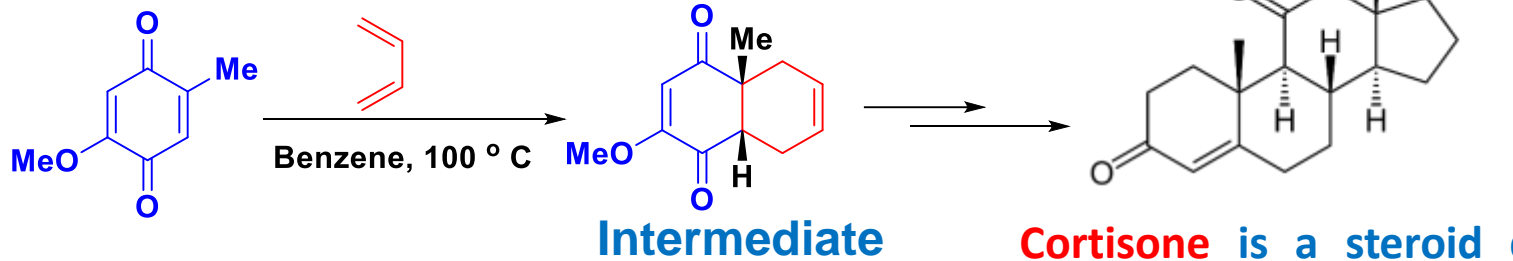


- Dienophile can be open chain or cyclic
- Dienophile should be electron deficient and reactivity enhanced by **electron withdrawing** substituents

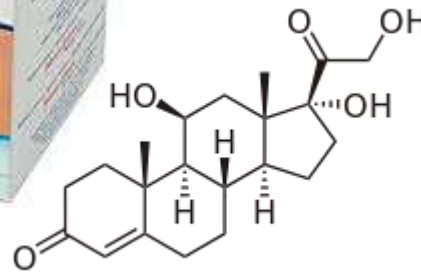


Cortisone

Diels-Alder reaction



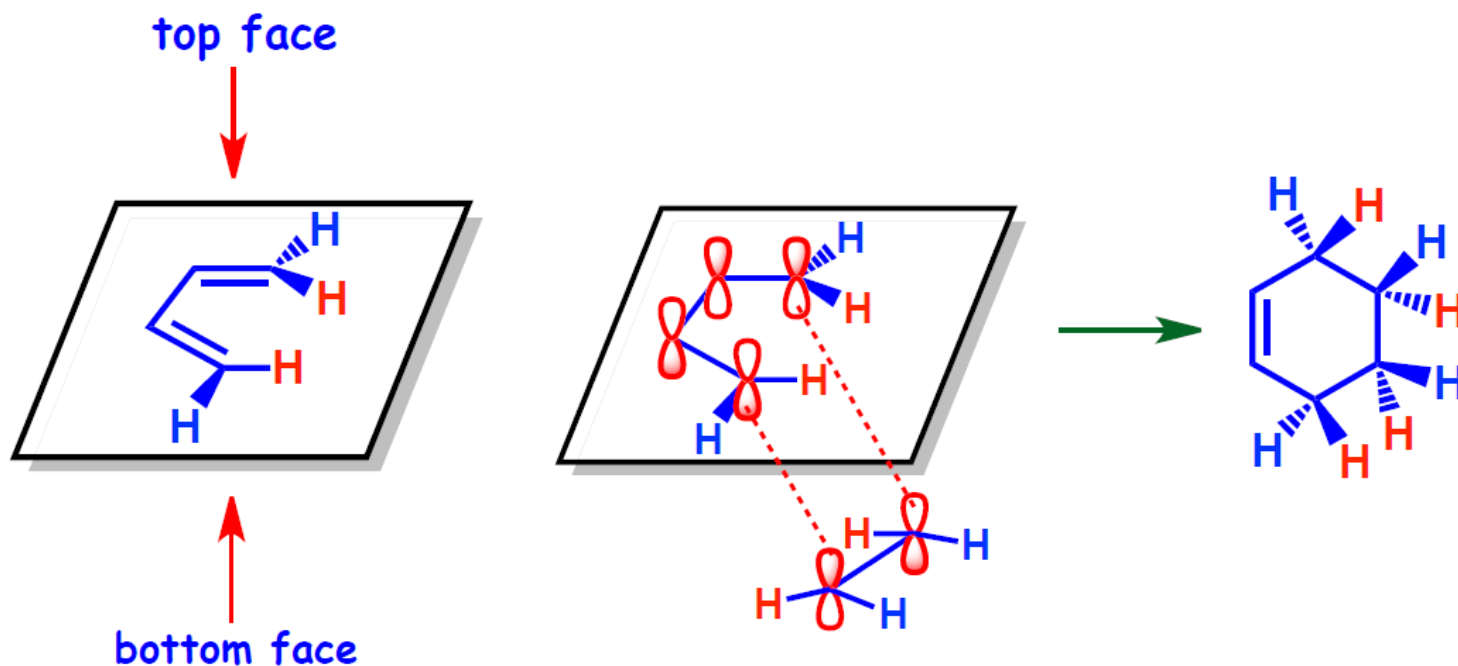
Cortisone is a steroid drug. It helps decrease swelling and inflammation in your body. It works by stopping the release of molecules that cause inflammation. This also stops your body from having an immune response



Hydrocortisone

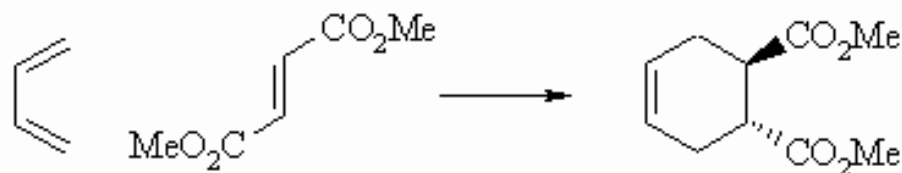
Diels-Alder reaction is stereospecific

- ❖ Relative stereochemical relationship of diene and dienophile is reproduced in the product
 - ❖ Diels-Alder reaction occurs due to the overlapping of p-orbitals of diene and dienophile lying **perpendicular** to the plane of carbon atoms
 - ❖ Hence, a given diene possess two faces namely top face and bottom face
 - ❖ Dienophile can approach either of the faces and lead to racemic mixture
-
- Stereochemistry of both diene and dienophile retained in the product
 - Reaction controls the **relative stereochemistry** at four contiguous centers

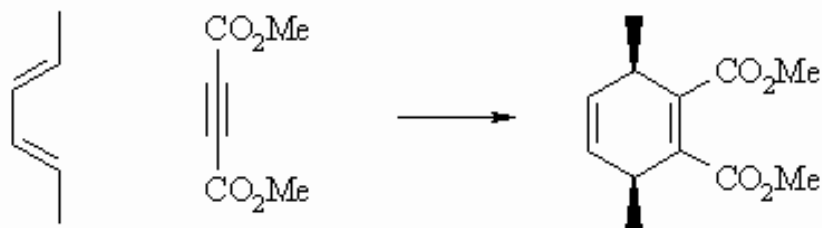




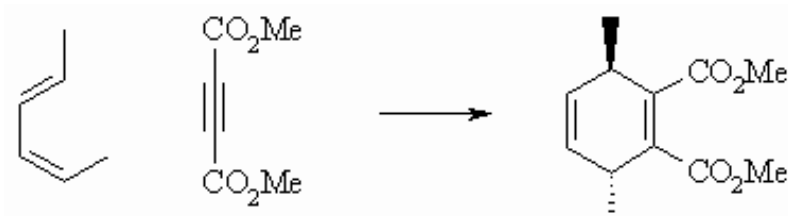
a ***cis***-dienophile gives ***cis***-substituents in the product



a ***trans***-dienophile gives ***trans***-substituents in the product



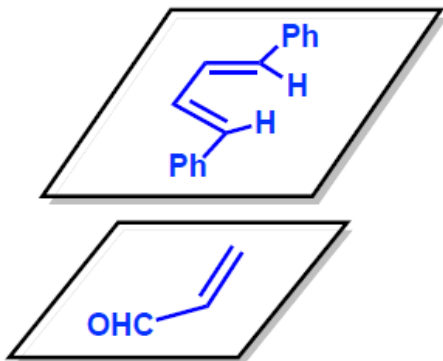
If the diene substituents have the same stereochemistry (here they are both *E*), then both diene substituents end up on the same face of the product.



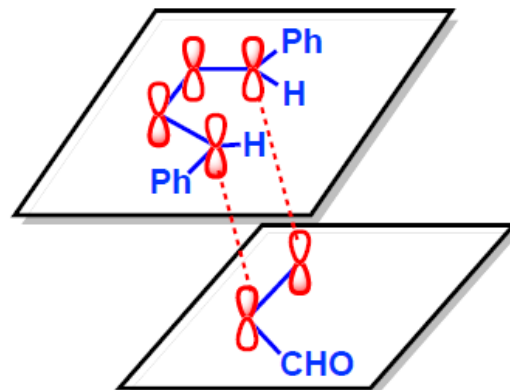
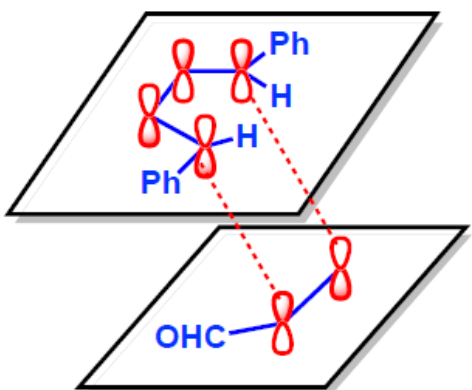
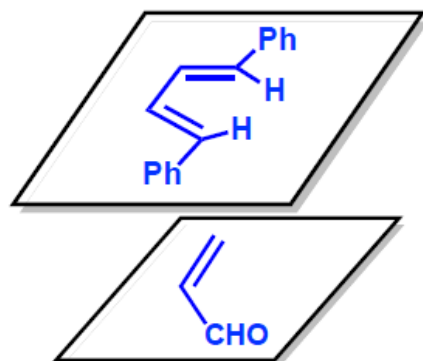
If the diene substituents have opposite stereochemistry (here one is *E* and one is *Z*), then the diene substituents end up on opposite faces of the product.

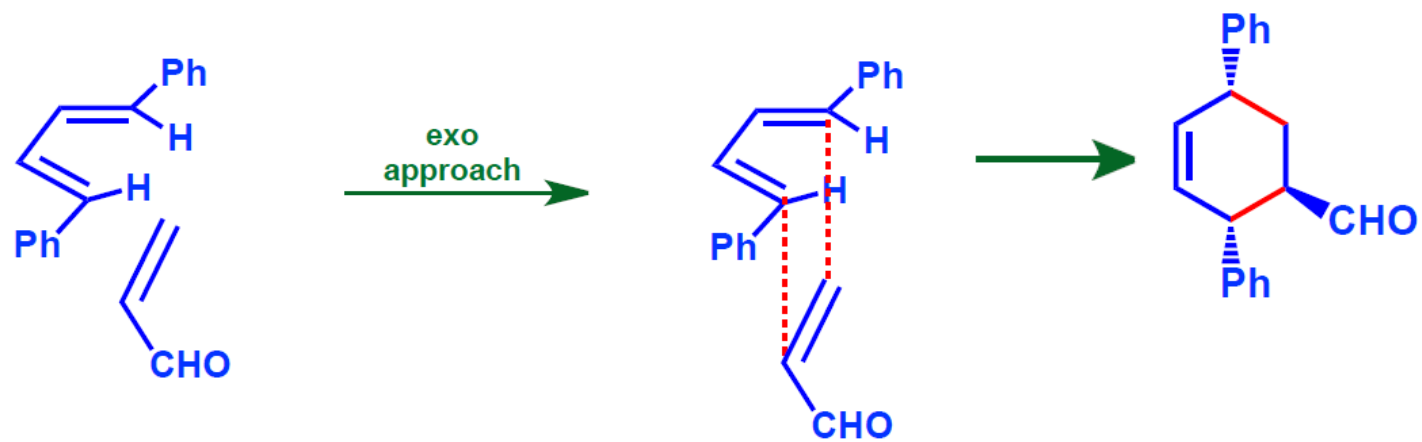
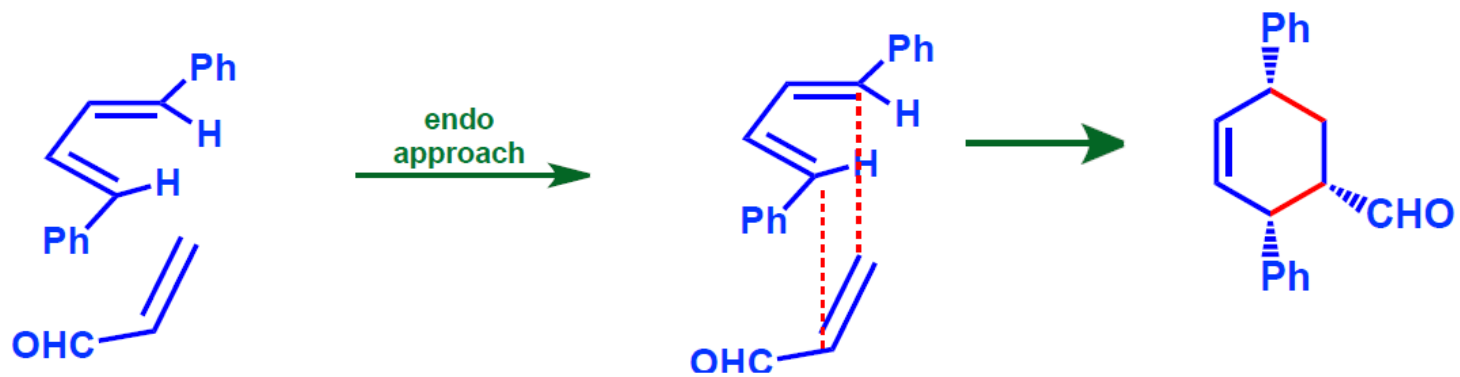
Given the bottom face approach of **dienophile**, substituents on dienophile can take two different orientations with respect to the plane of the diene called **endo** or **exo**

“endo”

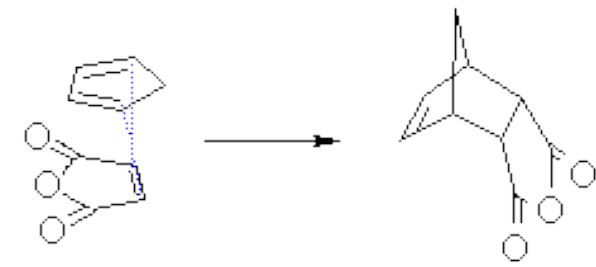
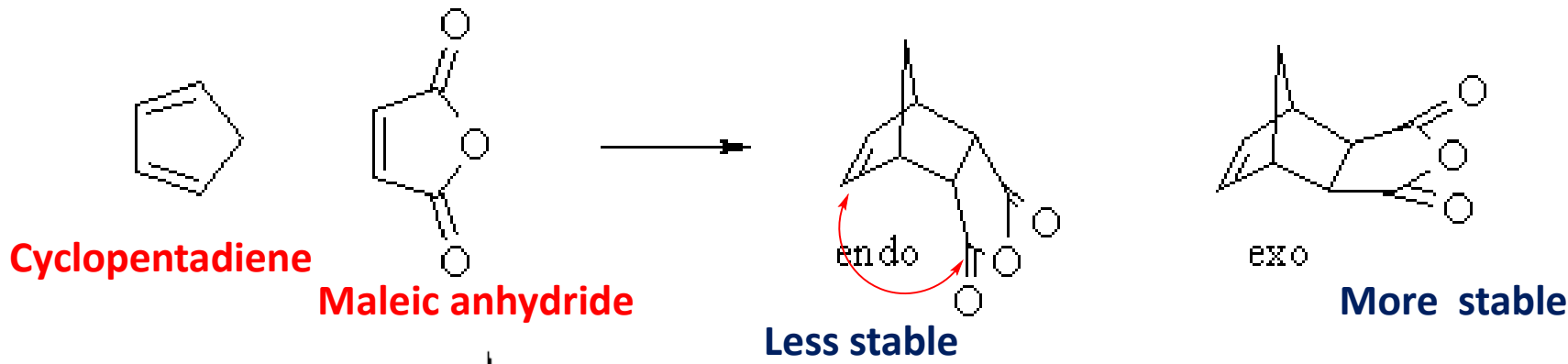


“exo”

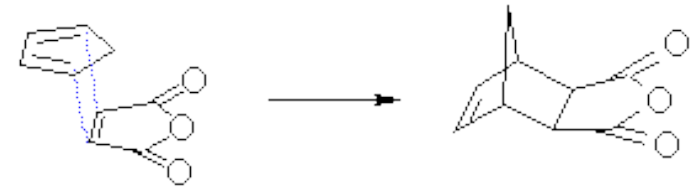




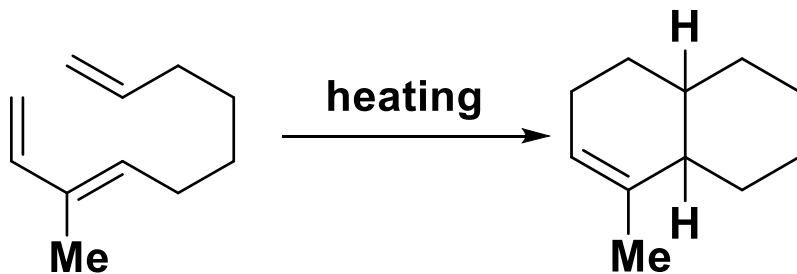
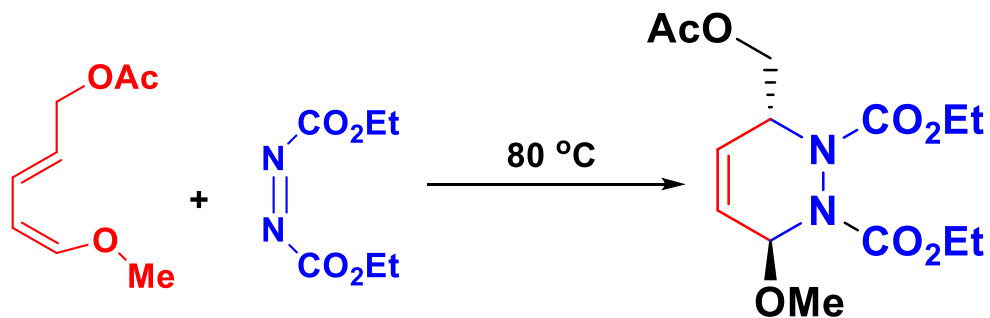
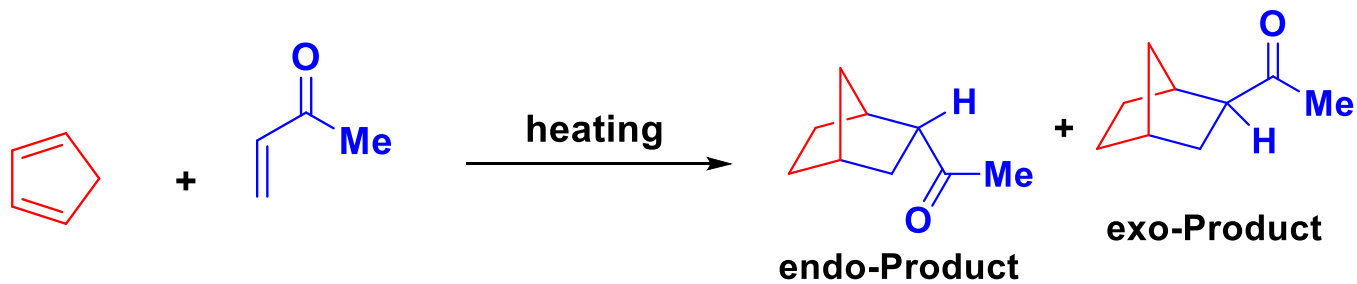
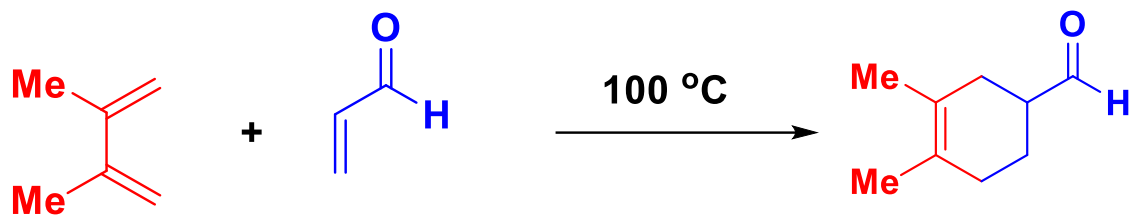
Diels-Alder Reaction



Diene and dienophile aligned directly over each other gives the **endo** product (dienophile **under** or in = **endo**)



Diene and dienophile staggered with respect to each other gives the **exo** product (dienophile exposed or out = **exo**)



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Pericyclic reactions

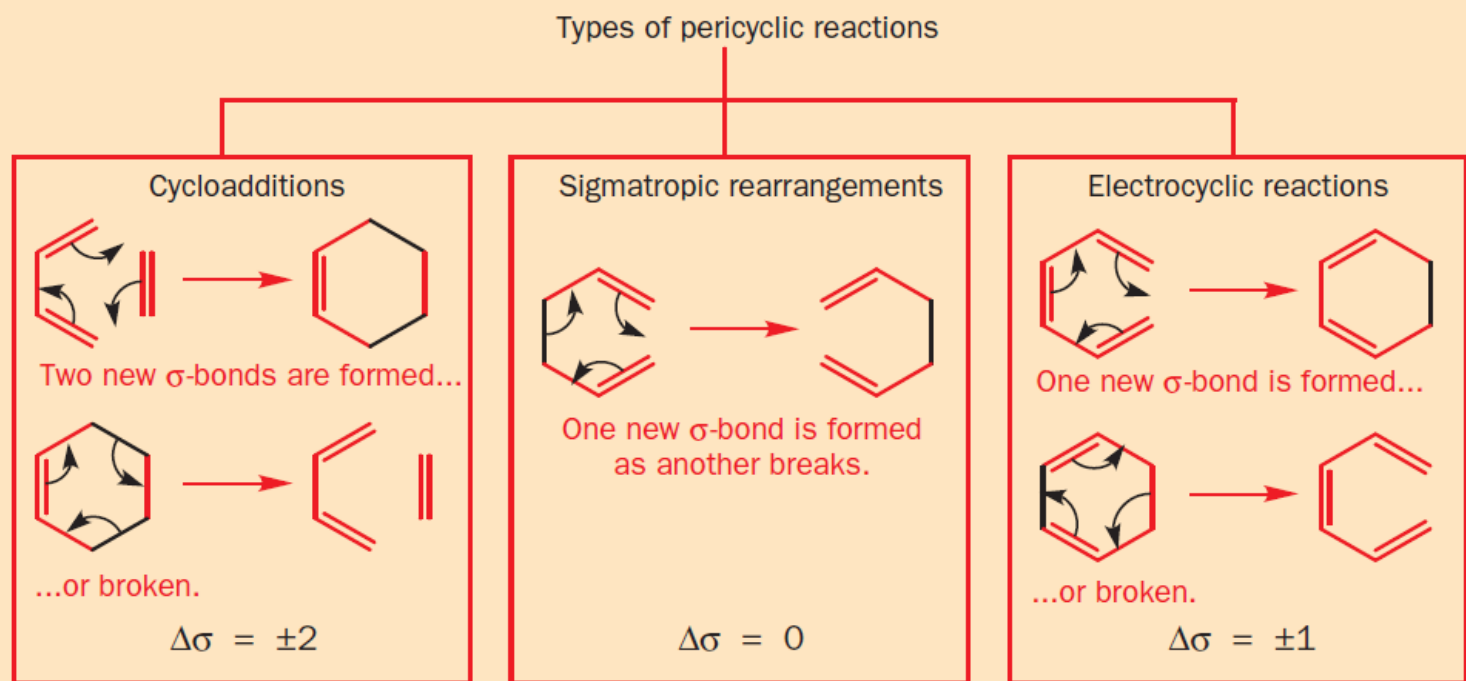
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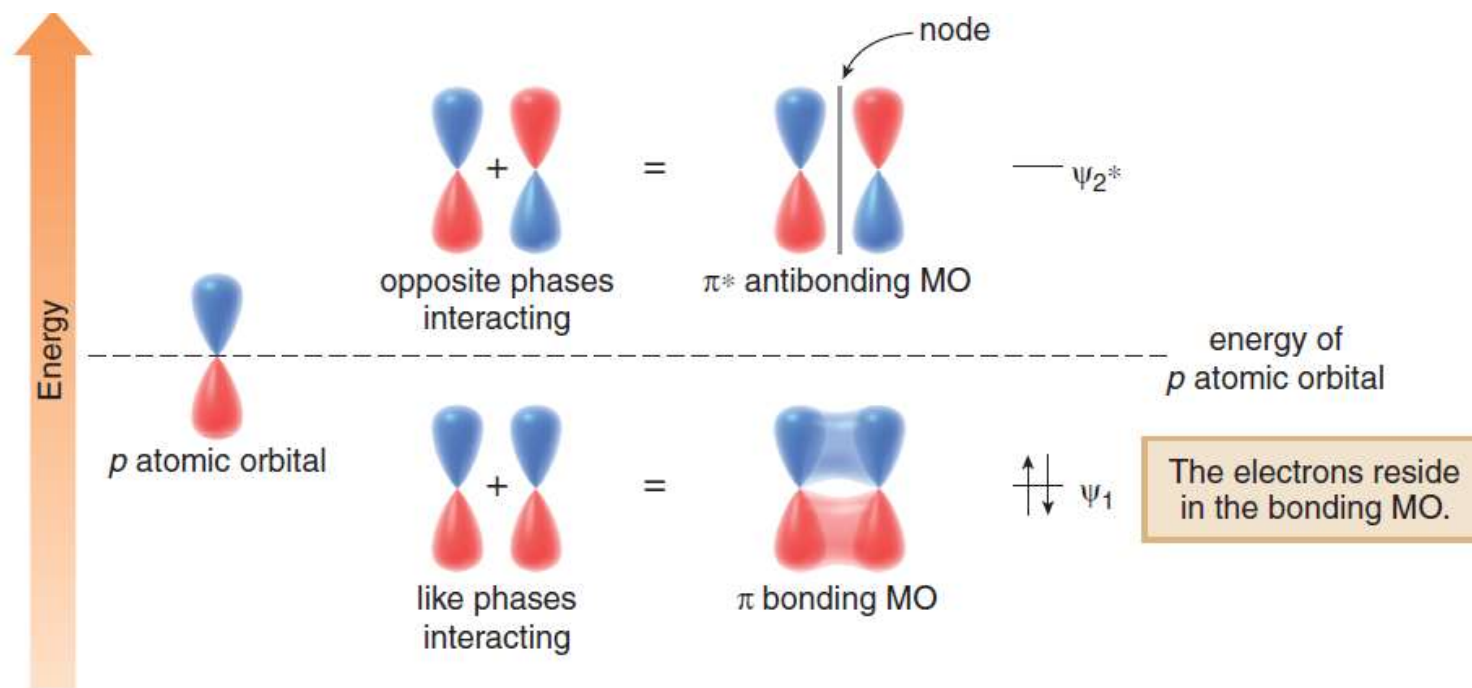
Cycloaddition (4 + 2) (2+2), Electrocyclic, and **Sigmatropic**

- The types of pericyclic reactions are distinguished by the number of σ bonds made or broken



Molecular Orbital (MO) Theory (Ethylene)

MO theory describes bonds as the mathematical combination of atomic orbitals that forms a new set of orbitals called **molecular orbitals (MOs)**. The **number of atomic orbitals used equals the number of molecular orbitals formed**.



The π bond in ethylene ($\text{CH}_2=\text{CH}_2$) is formed by side-by-side overlap of two p orbitals on adjacent carbons. Two p orbitals can combine in two different ways. As shown in Figure C.1, when two p orbitals of similar phase overlap, a π bonding molecular orbital (designated as ψ_1) results. Two electrons occupy this lower-energy bonding molecular orbital. When two p orbitals of opposite phase combine, a π^* antibonding molecular orbital (designated as ψ_2^*) results. A destabilizing node occurs when two orbitals of opposite phase combine.

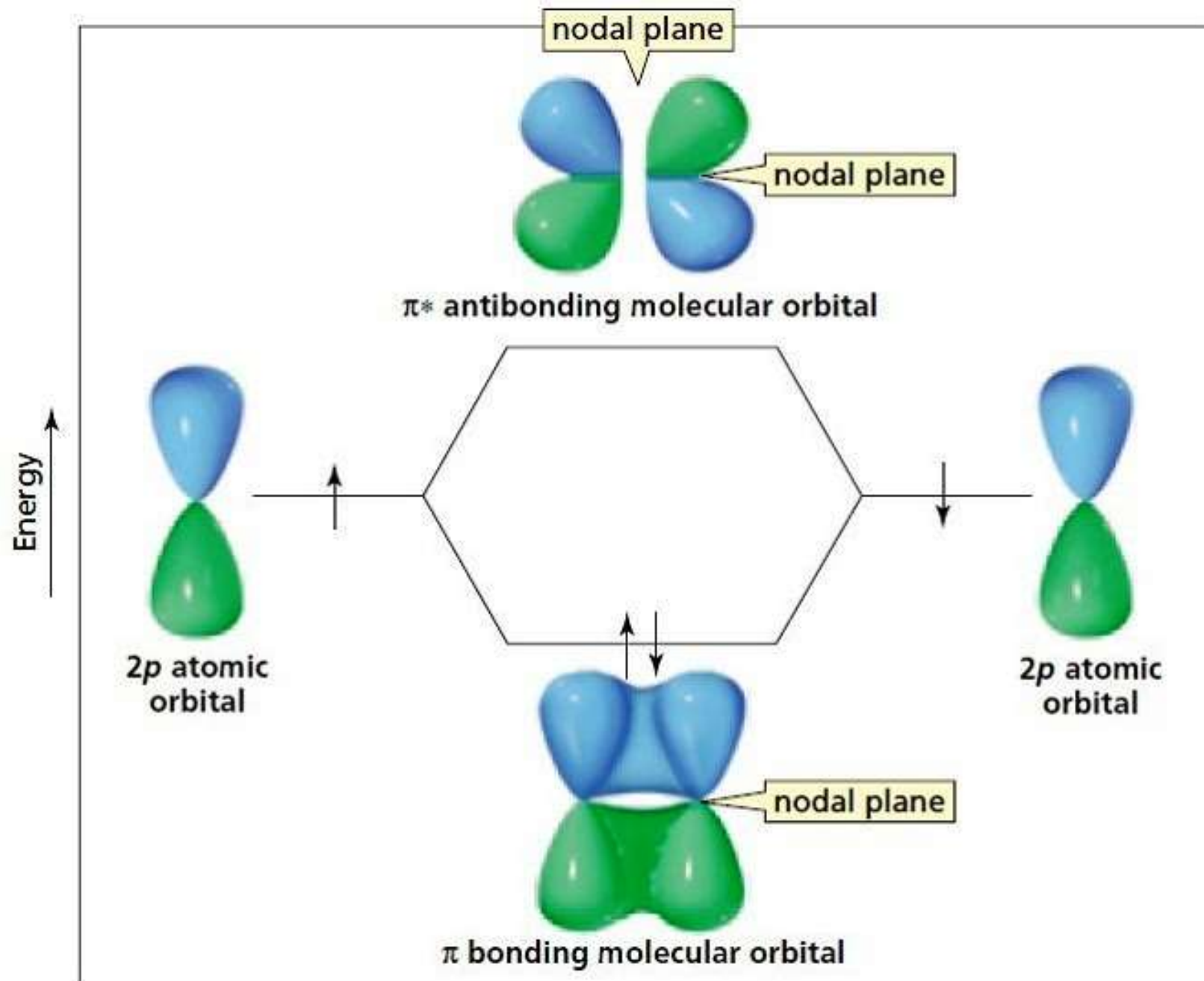
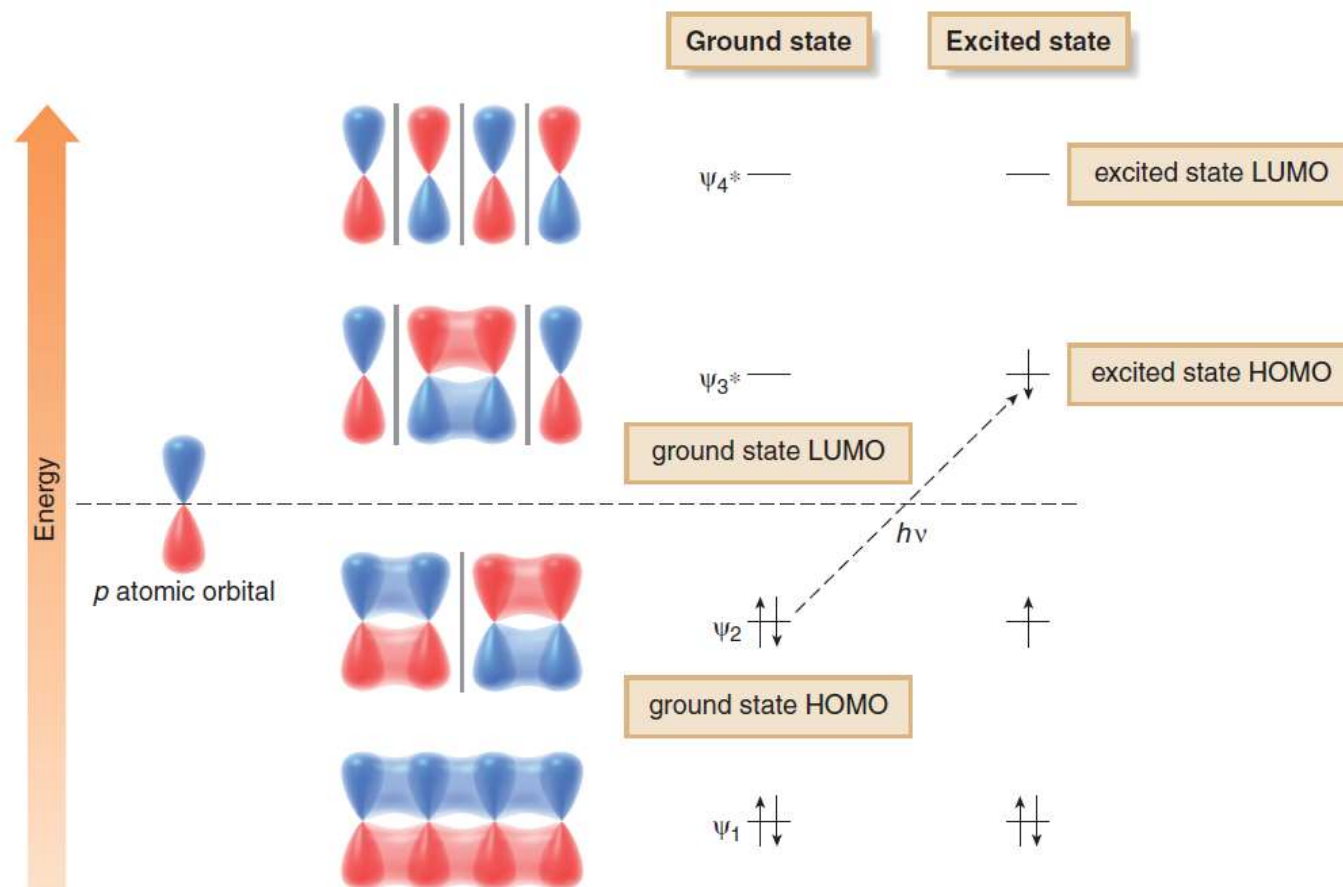


Figure C.2

The four π molecular orbitals of 1,3-butadiene

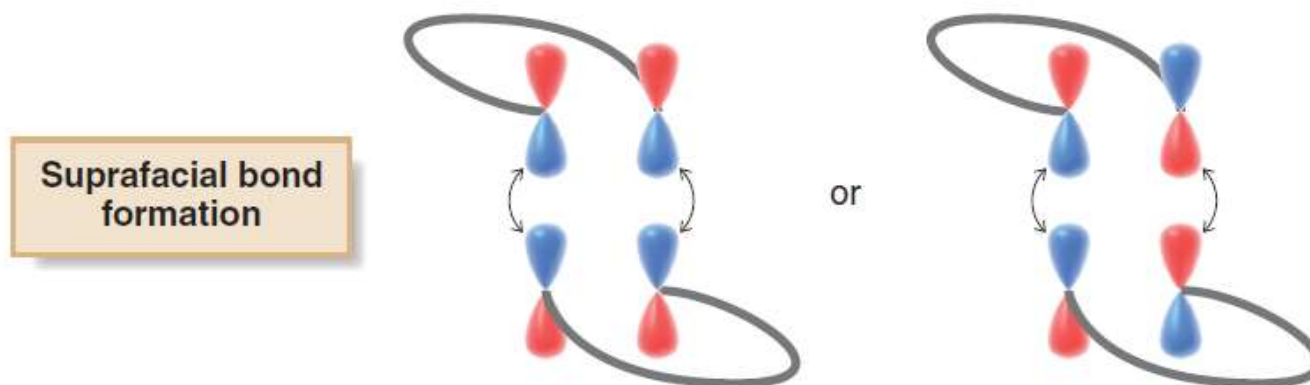


The two π bonds of 1,3-butadiene ($\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$) are formed by overlap of four p orbitals on four adjacent carbons. As shown in Figure C.2, four p orbitals can combine in four different ways to form four molecular orbitals designated as ψ_1 – ψ_4 . Two are bonding molecular orbitals (ψ_1 and ψ_2), and two are antibonding molecular orbitals (ψ_3^* and ψ_4^*). The two bonding MOs are lower in energy than the p orbitals from which they are formed, whereas the two antibonding MOs are higher in energy than the p orbitals from which they are formed.

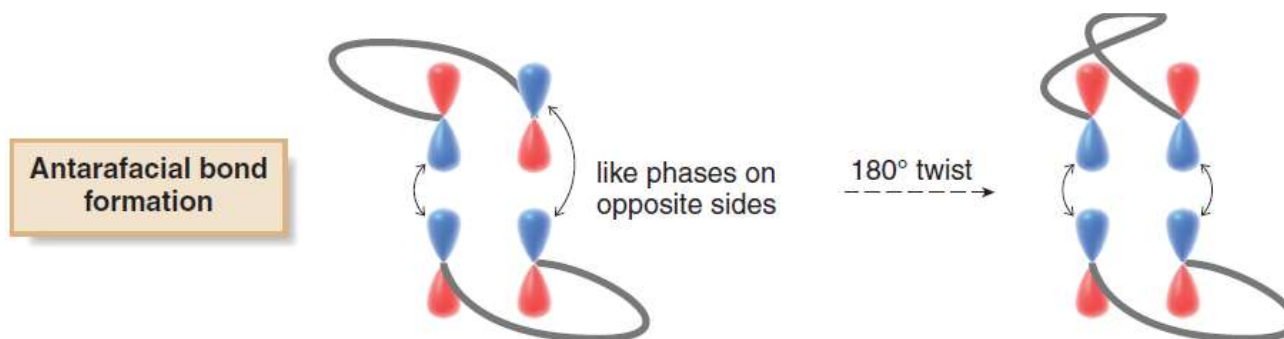
Orbital Symmetry and Cycloaddition Reaction

To understand cycloaddition reactions, let examine the p orbitals of the terminal carbons of both reactants. Bonding can take place only when like phases of both sets of p orbitals can combine. Two modes of reaction are possible.

- A **suprafacial cycloaddition** occurs when like phases of the p orbitals of both reactants are on the same side of the π system, so that two bonding interactions result.



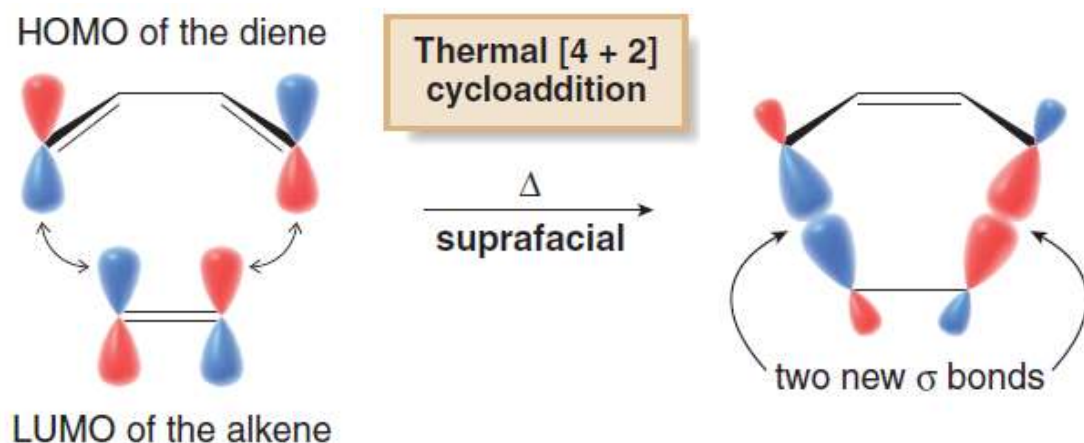
An **antarafacial cycloaddition** occurs when one π system must twist to align like phases of the p orbitals of the terminal carbons of the reactants



Because of the geometrical constraints of small rings, **cycloadditions that form four- or sixmembered rings must take place by suprafacial pathways**

Since cycloaddition involves the donation of electron density from one reactant to another, one reactant donates its **most loosely held electrons**—those occupying its **Highest Occupied Molecular Orbital (HOMO)**—to a **vacant orbital** that can accept electrons—the **Lowest Unoccupied Molecular Orbital (LUMO)**—of the second reactant.

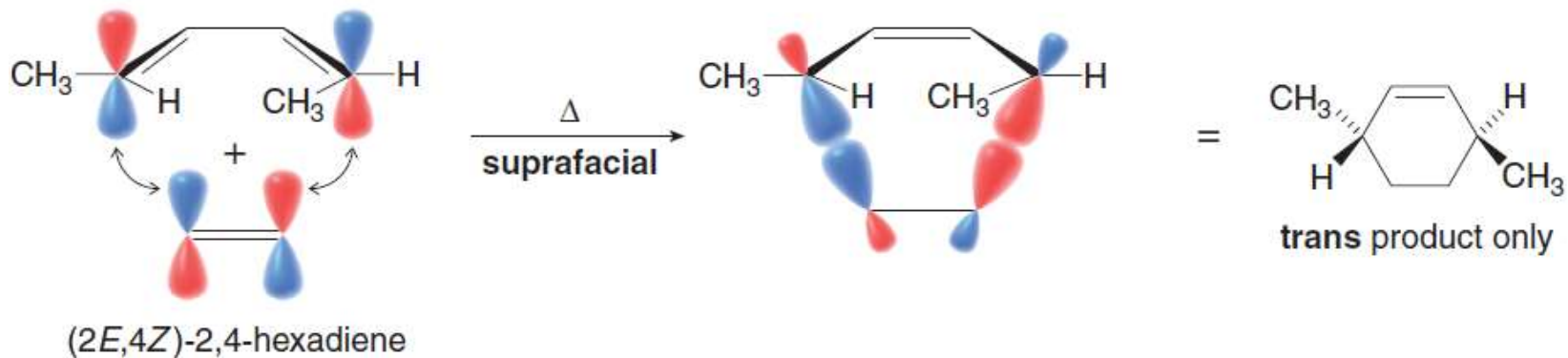
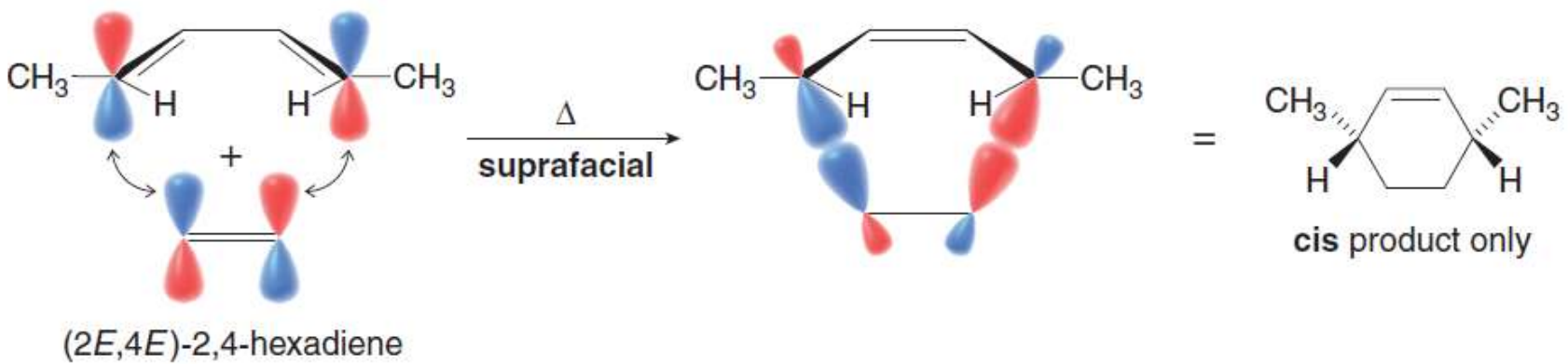
In a **cycloaddition** we examine the bonding interactions of the **HOMO** of one component with the **LUMO** of the second component.



This is a specific example of a general cycloaddition involving an **odd number** of " bonds (three " bonds total, **two from the diene** and **one from the alkene**).

Thermal cycloadditions involving an **odd number** of " bonds proceed by a **suprafacial** pathway

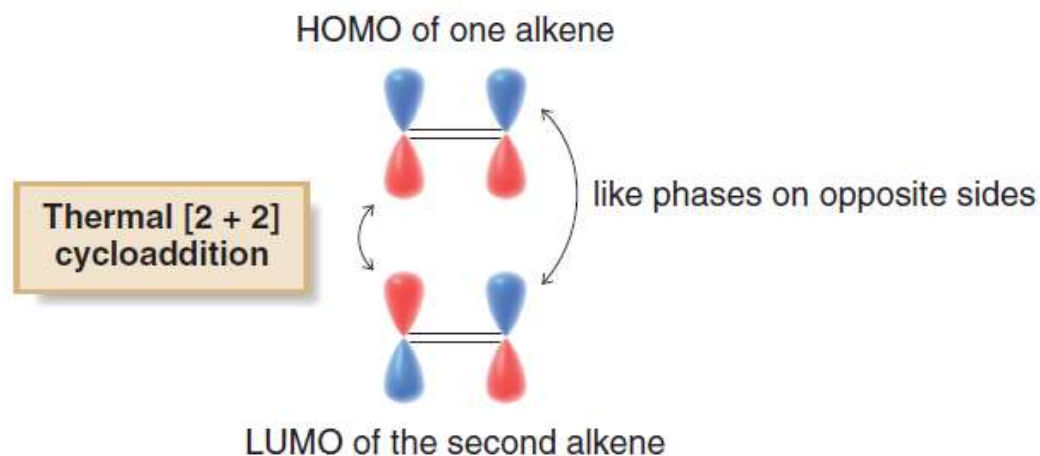
Stereochemistry of the diene is retained in the Diels–Alder product



[2 + 2] Cycloaddition

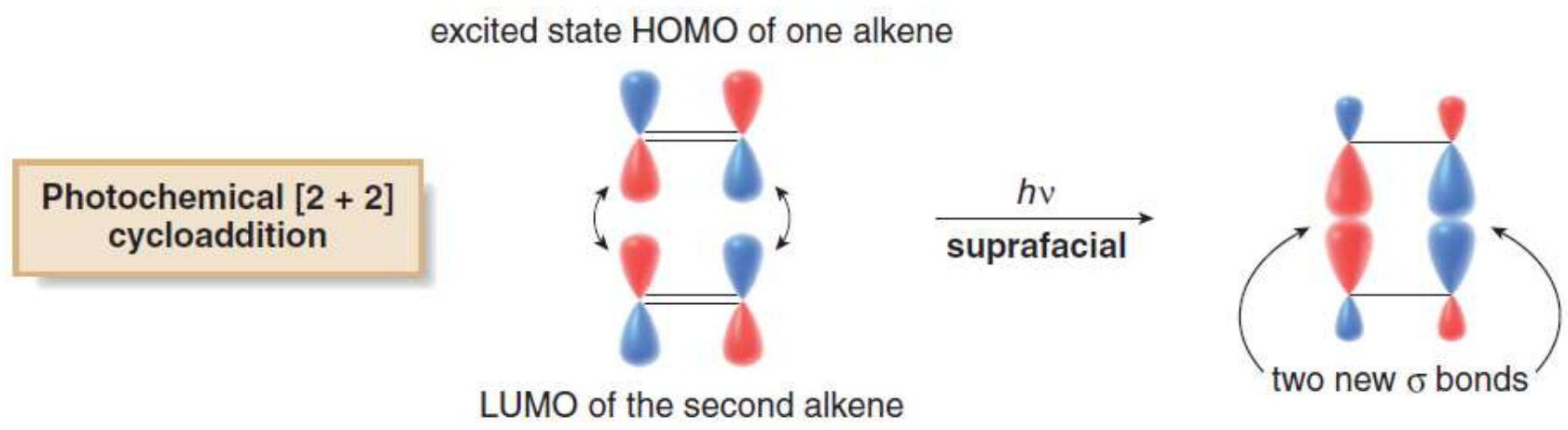
In contrast to a [4 + 2] cycloaddition, a [2 + 2] cycloaddition does *not* occur under thermal conditions, **but does take place photochemically**. This result is explained by examining the **symmetry of the HOMO and LUMO of the alkene reactants**.

In a thermal [2 + 2] cycloaddition, like phases of the *p* orbitals on only one set of terminal carbons can overlap. For like phases to overlap on the other terminal carbon, the molecule must twist to allow for an **antarafacial pathway**. **This process cannot occur to form small rings.**



In a photochemical [2 + 2] cycloaddition, light energy promotes an electron from the ground state HOMO to form the excited state HOMO.

Interaction of this excited state HOMO with the LUMO of the second alkene then allows for overlap of the like phases of both sets of *p* orbitals. Two bonding interactions result and the reaction occurs by a suprafacial pathway.



This is a specific example of a general cycloaddition involving an **even number** of " bonds (two " bonds total, one from each alkene).

Photochemical cycloadditions involving an **even number** of " bonds proceed by a **suprafacial** pathway.

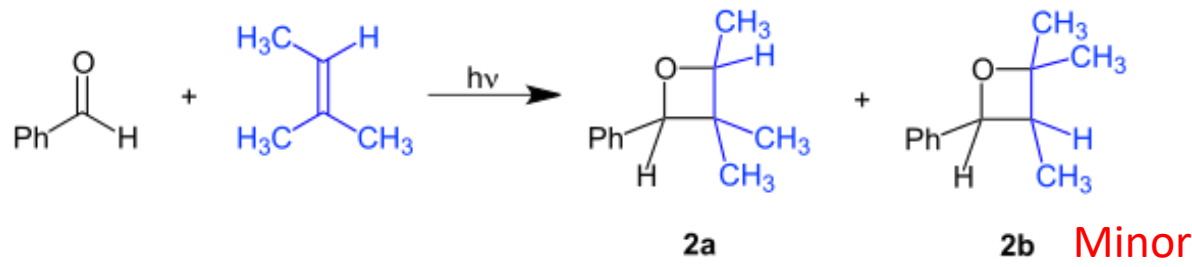
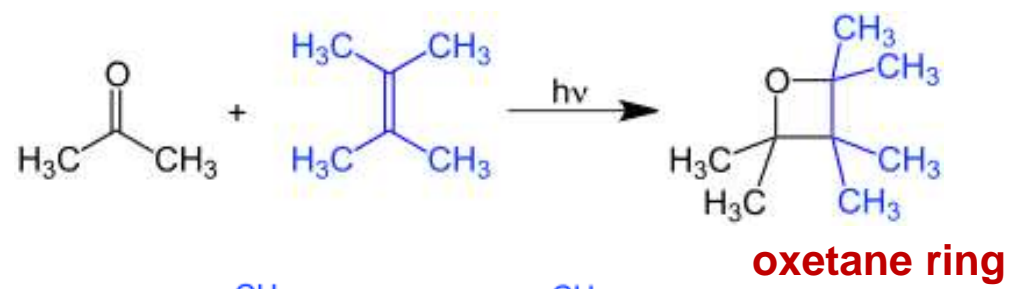
Let summarize the **Woodward–Hoffmann rules** that govern **cycloaddition reactions**. The number of "**bonds refers to the total number of "**bonds from both components of the cycloaddition. For a given number of " bonds, the mode of cycloaddition is always *opposite* in thermal and photochemical reactions.

Table C.2 Woodward–Hoffmann rules for cycloaddition reactions

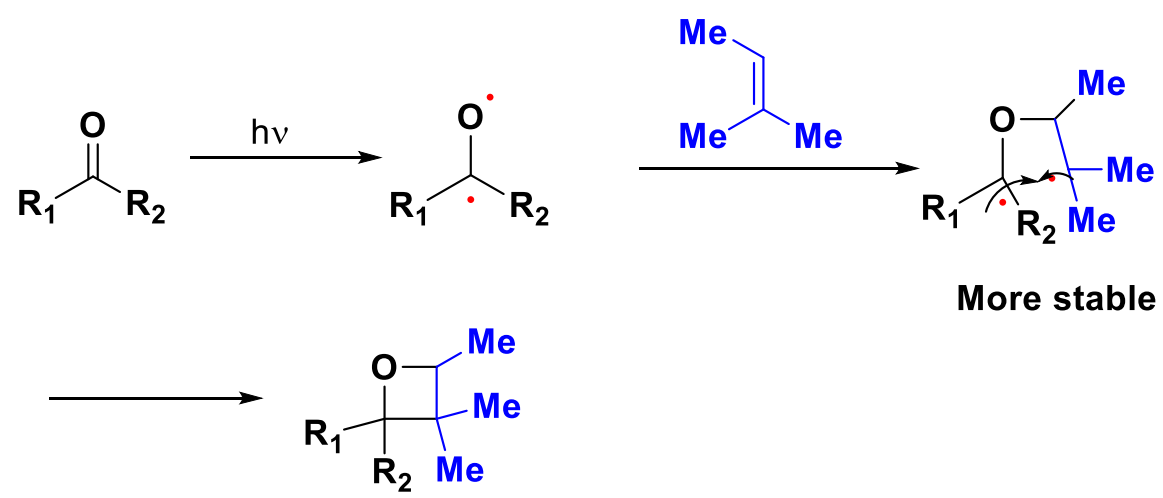
Number of π bonds	Thermal reaction	Photochemical reaction
Even	Antarafacial	Suprafacial
Odd	Suprafacial	Antarafacial

Paternò-Büchi reaction

The **Paternò-Büchi** reaction, named after Emanuele Paternò and George Büchi who established its basic utility and form, is a photochemical **(2+2) cycloaddition** reaction that forms four-membered **oxetane rings** from a **carbonyl and an alkene**

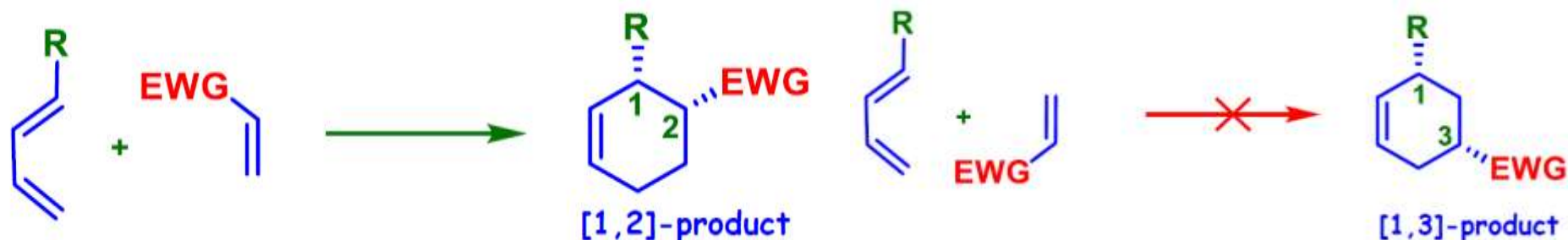


Mechanism

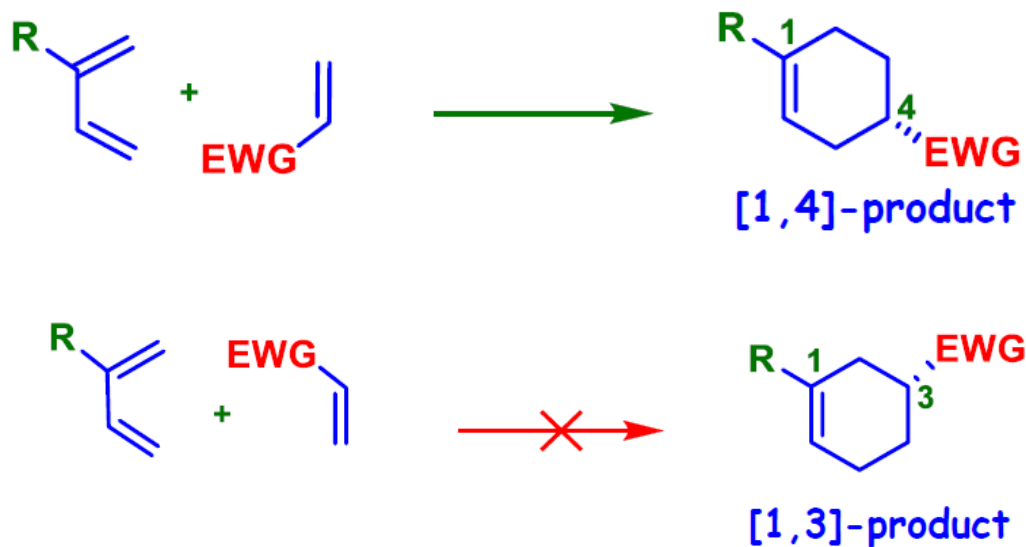


Regiochemistry of Diels-Alder Reaction

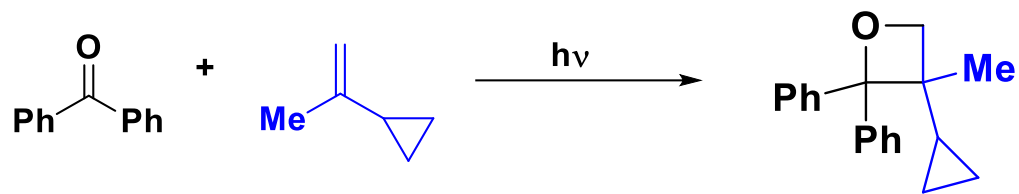
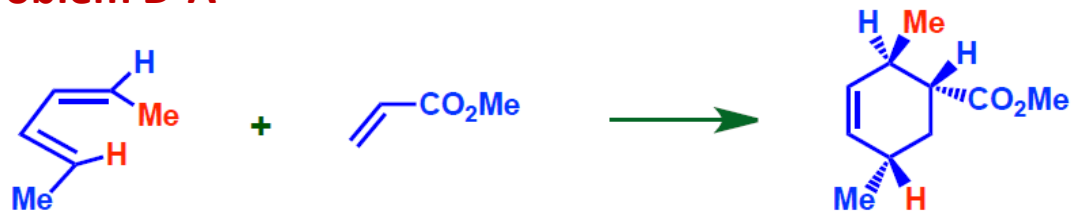
1-substituted diene react to give mainly [1,2]-product



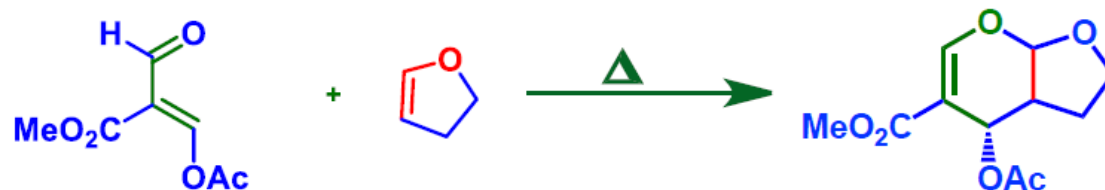
2-substituted diene react to give mainly [1,4]-substituted product



Problem D-A



Hetero Diene: Hetero atom is part of the diene



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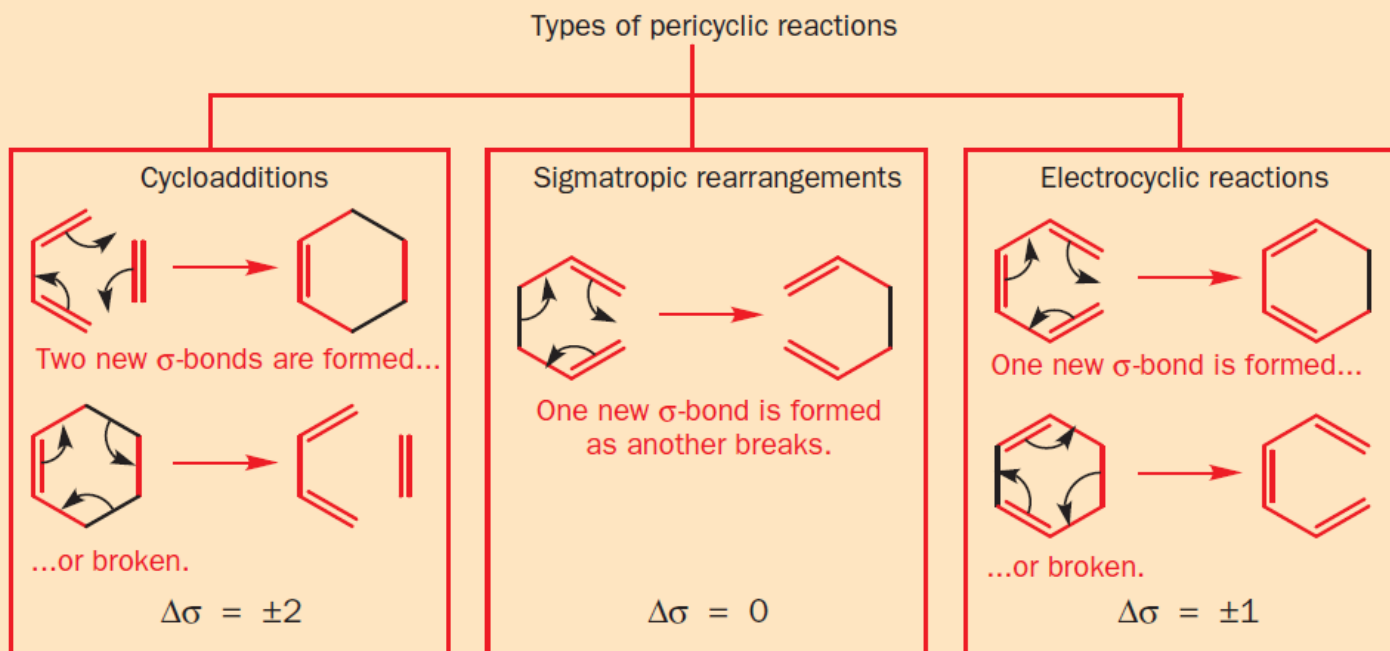
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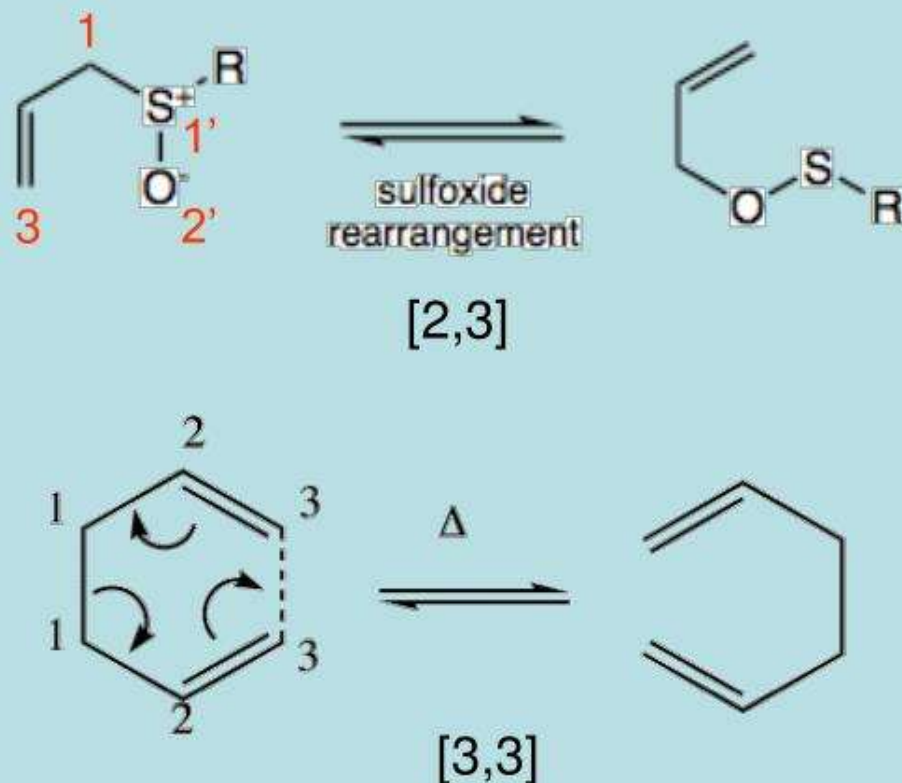
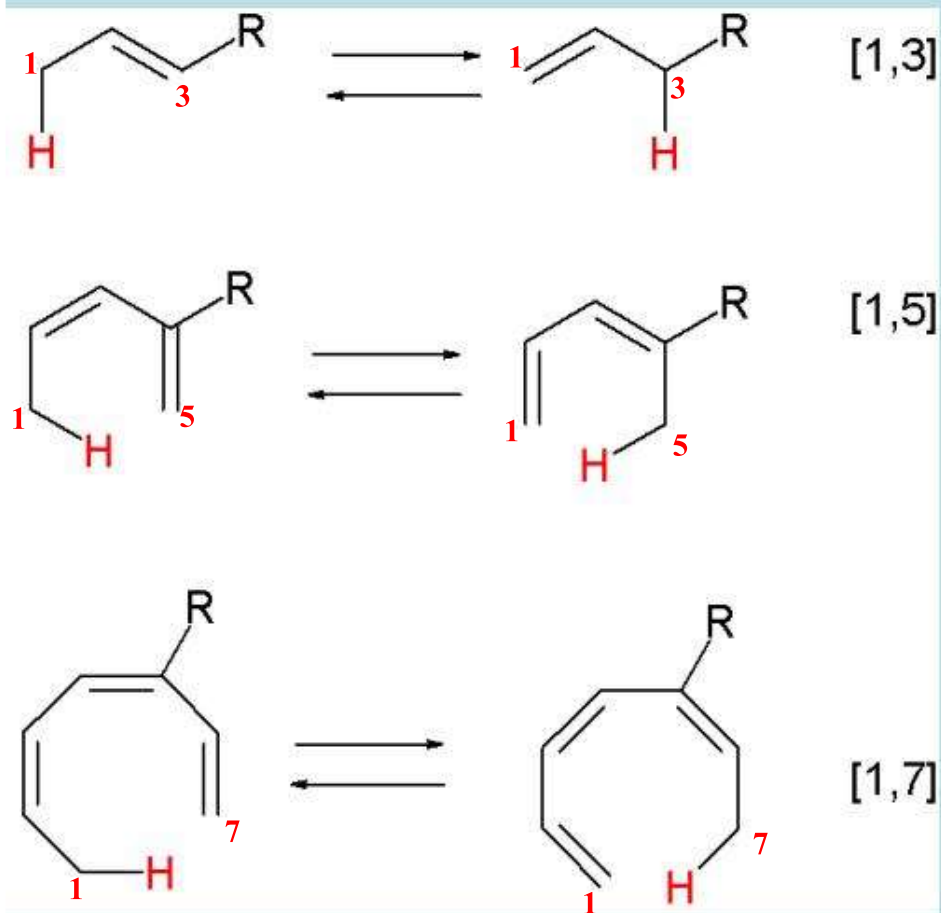
Cycloaddition, **Electrocyclic**, and **Sigmatropic**

- The types of pericyclic reactions are distinguished by the number of σ bonds made or broken



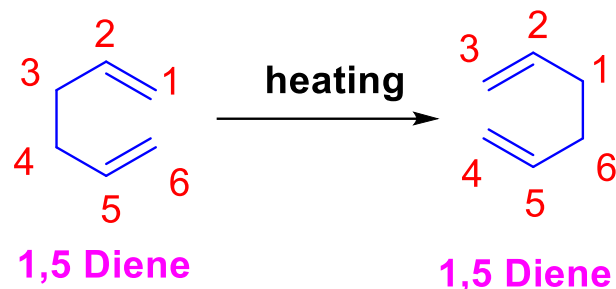
Sigmatropic reaction

Sigmatropic reaction is a pericyclic reaction wherein the net result is one σ bond changed to another σ bond.



[3,3] Sigmatropic Rearrangement

Cope rearrangement



Bond Formed

$\text{C}_1\text{-C}_6$ (σ)

$\text{C}_2\text{-C}_3$ (π)

$\text{C}_4\text{-C}_5$ (π)

Bond Broken

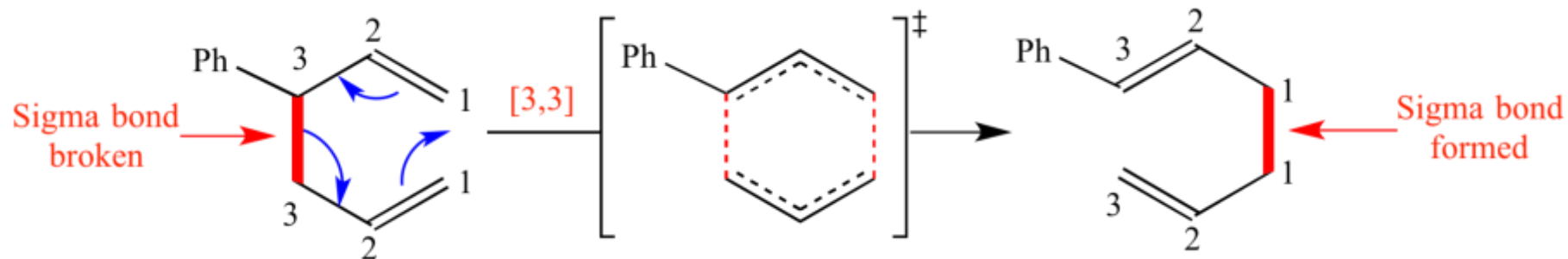
$\text{C}_1\text{-C}_2$ (π)

$\text{C}_3\text{-C}_4$ (σ)

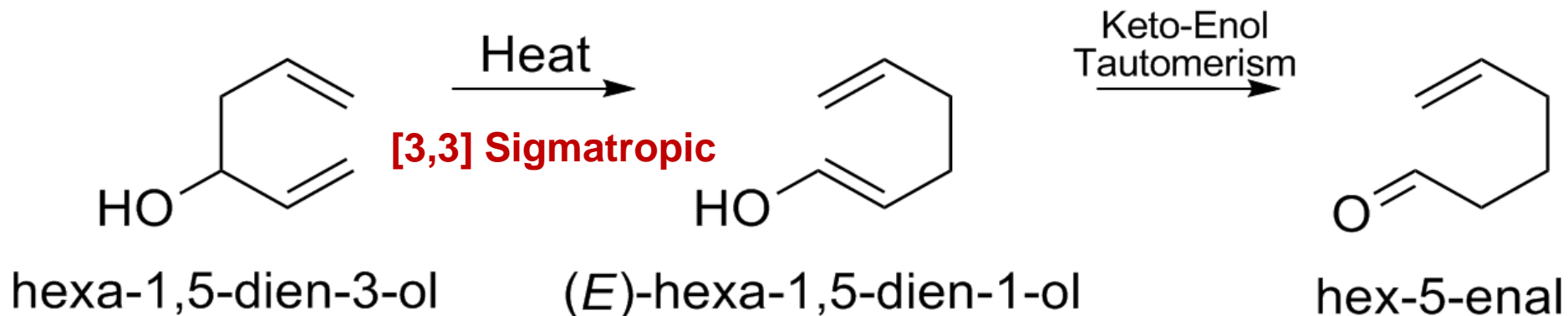
$\text{C}_5\text{-C}_6$ (π)

The **Cope rearrangement** is an organic reaction where a **1,5-diene**, under thermal conditions, is converted to another **1,5-diene** structural isomer. This reaction belongs to a class of reactions termed "**Sigma-tropic rearrangements**" and it is a concerted process where bonds are forming and breaking at the same time.

Mechanism

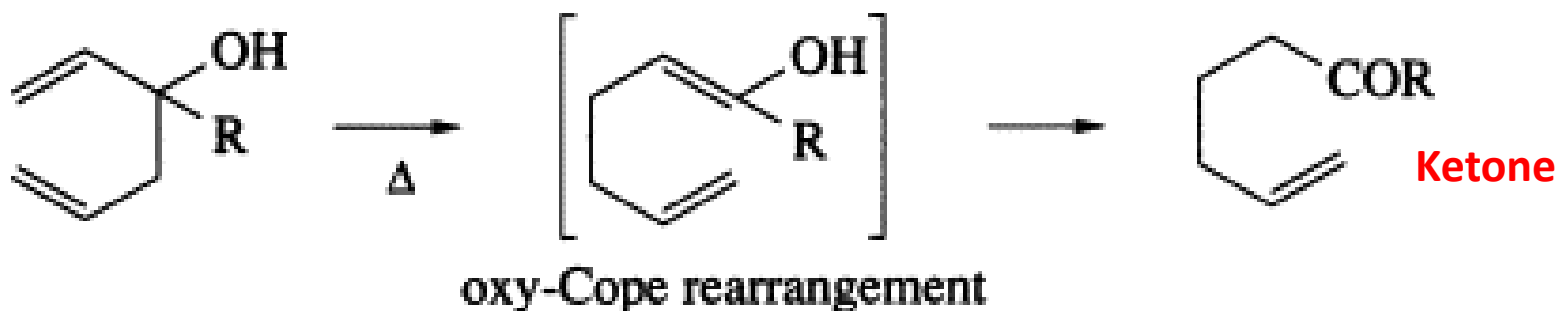


Oxy-Cope Rearrangement

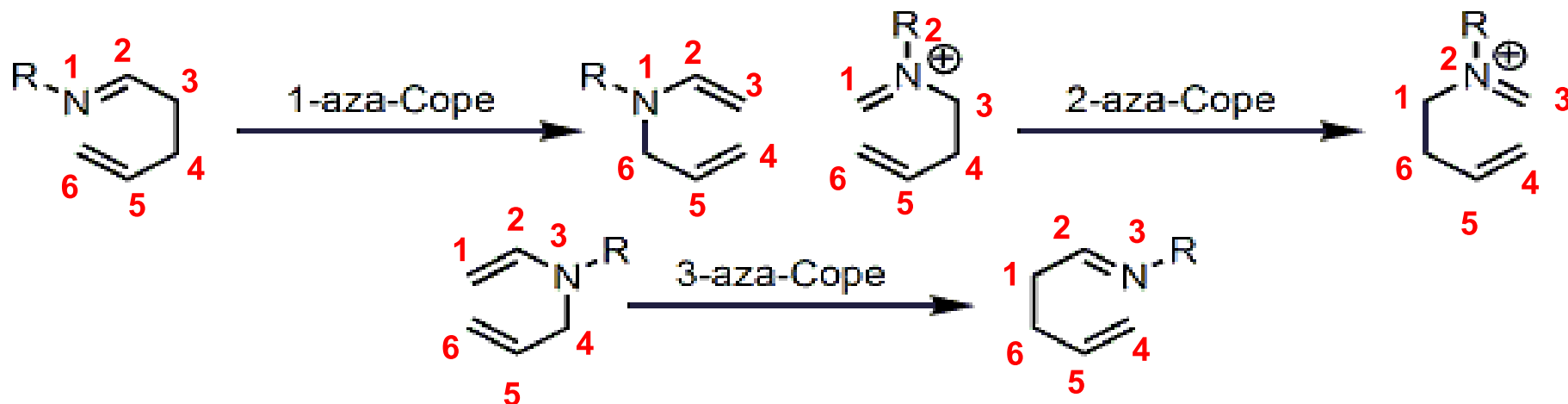


The **oxy-Cope rearrangement** involves reorganization of the skeleton of certain **unsaturated alcohols**, where the **Cope rearrangement** in which **1,5-dien-3-ols** are converted to **unsaturated carbonyl compounds** by a mechanism typical for such a **[3,3]-sigmatropic rearrangement**.

Synthesis of ketone

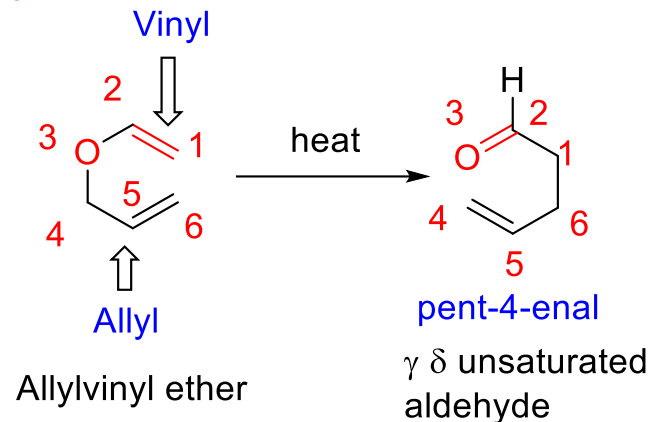


Aza-Cope Rearrangement (Presence of Nitrogen)



The **aza-Cope** rearrangements are examples of **heteroatom (Nitrogen)** versions of the **Cope rearrangement**, which is a **[3,3]-sigmatropic rearrangement** that shifts single and double bonds between **two allylic components**. Aza-Cope rearrangements are generally classified by the position of the **nitrogen in the molecule**

Claisen Rearrangement



Bond Formed

$\text{C}_1\text{-C}_6$

$\text{C}_4\text{-C}_5(\pi)$

$\text{C}_2\text{-O}(\pi)$

Bond Broken

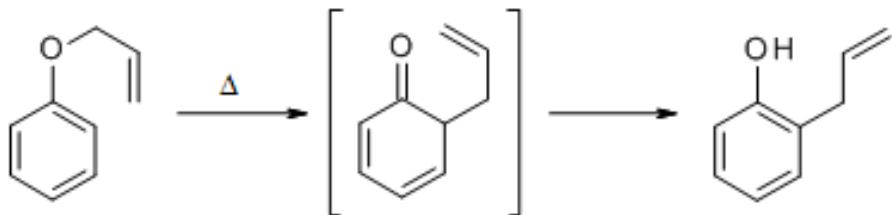
$\text{C}_1\text{-C}_2(\pi)$

$\text{C}_5\text{-C}_6(\pi)$

$\text{C}_4\text{-O}$

The aliphatic Claisen Rearrangement is a **[3,3]-sigmatropic rearrangement** in which an **allyl vinyl ether** is converted thermally to an unsaturated **carbonyl compound**

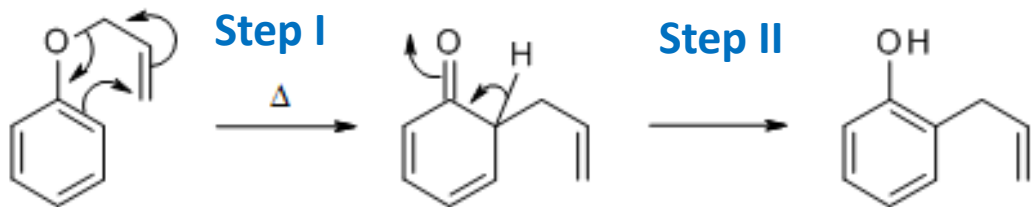
Aromatic



Step 1:

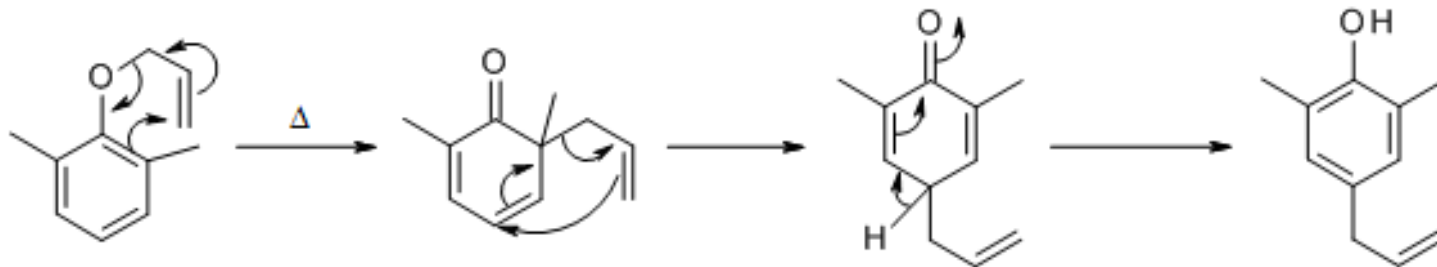
An electrocyclic process. Push those electrons around the 6 membered ring.... Best appreciated by starting the electron flow by having the aromatic **C=C** attacking the allyl **C=C** and displacing an **O** leaving group....

Mechanism



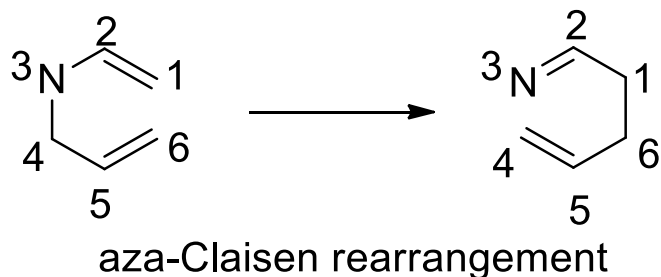
Step 2:

Tautomerisation of the ketone (actually a dienone) to the more stable aromatic enol, the phenol.

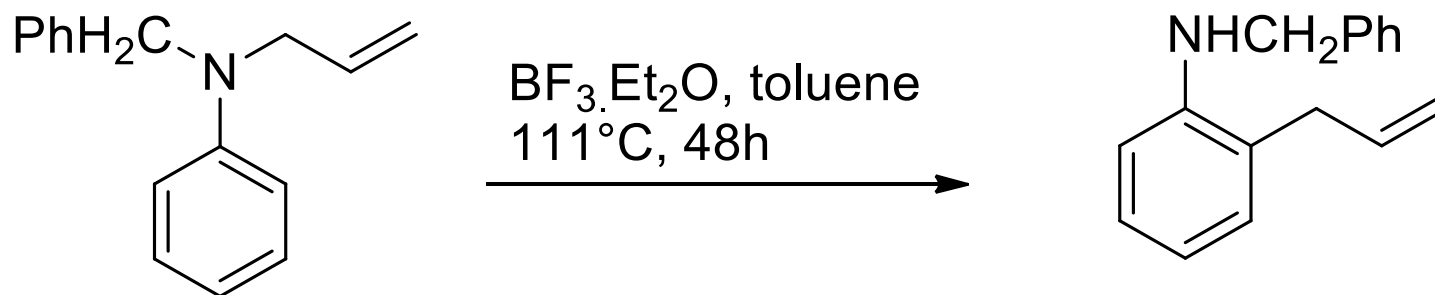


O-substituted

Aza Claisen Rearrangement

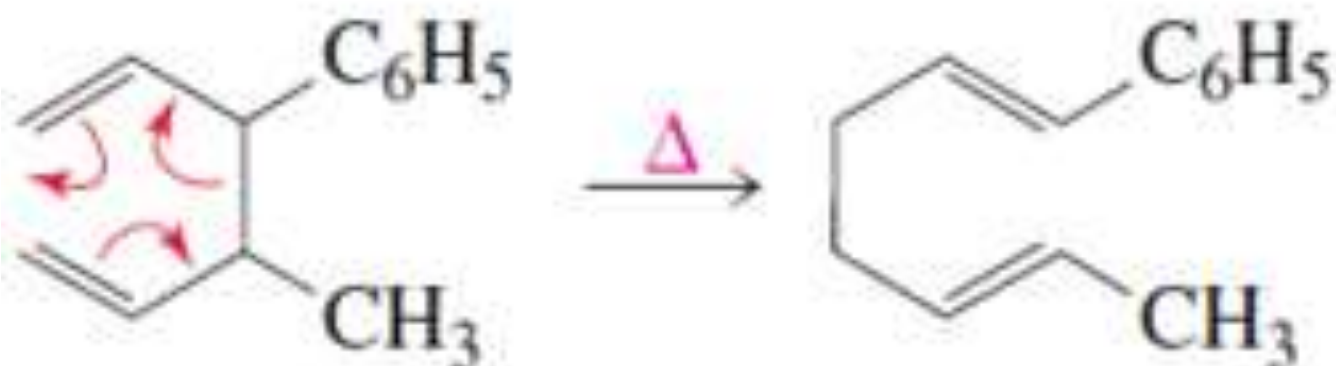


Nitrogen-containing 1,5-dienes undergo [3,3]-sigmatropic rearrangement just like the Claisen rearrangement of 1,5-dienes.



[3,3] Sigmatropic Rearrangement

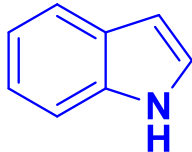
a Cope rearrangement



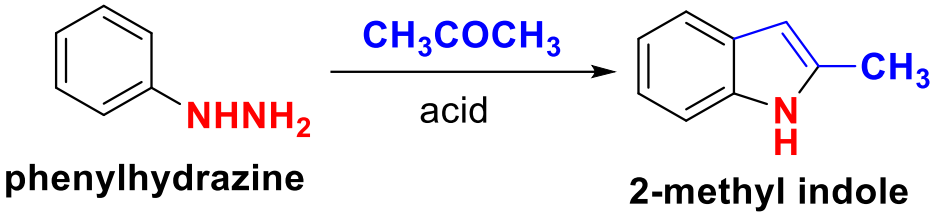
a Claisen rearrangement



[3,3] Sigmatropic Rearrangement : Fischer Indole Synthesis

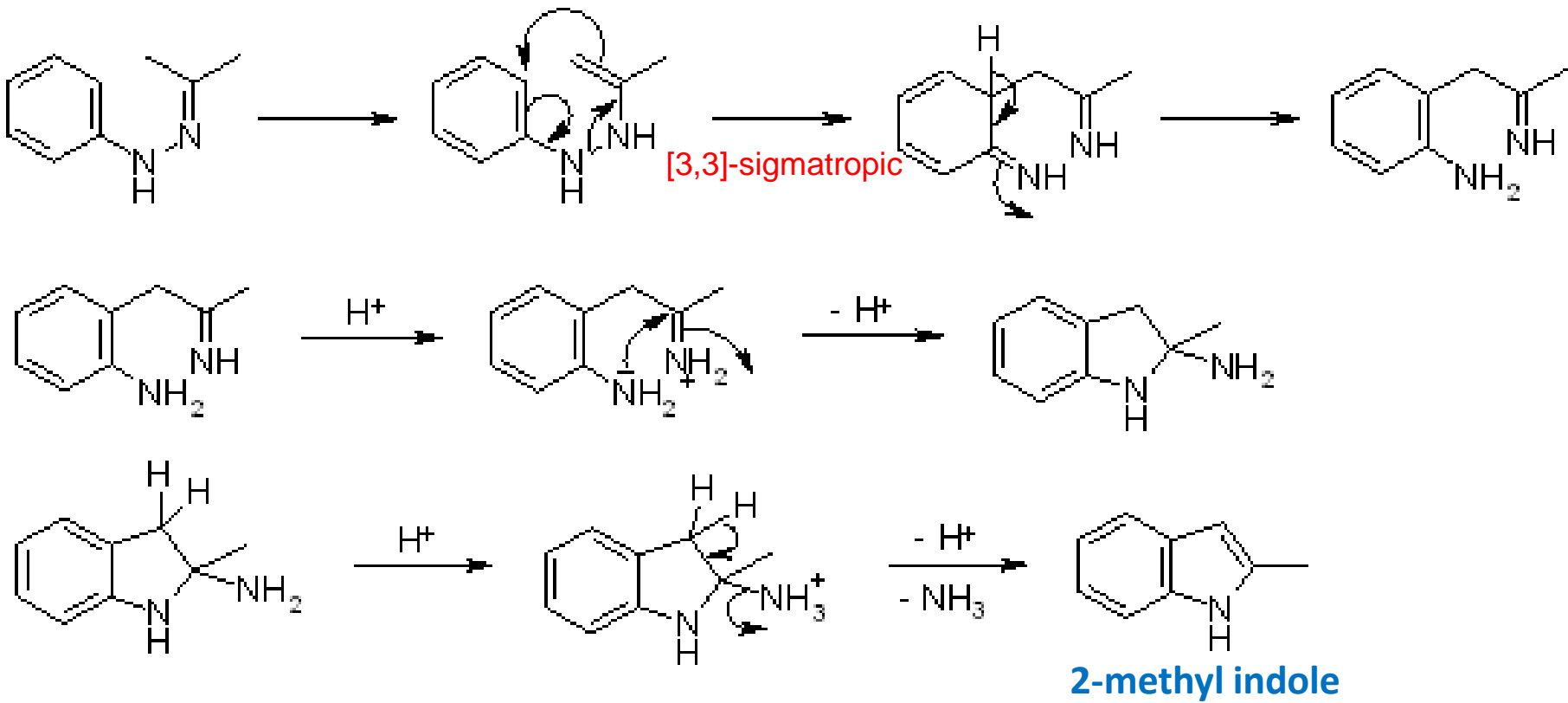


Indole

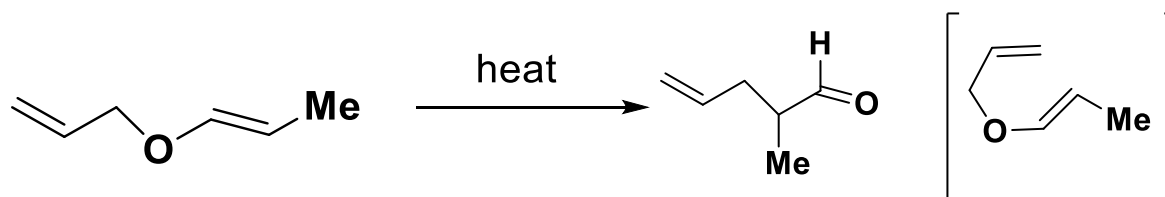
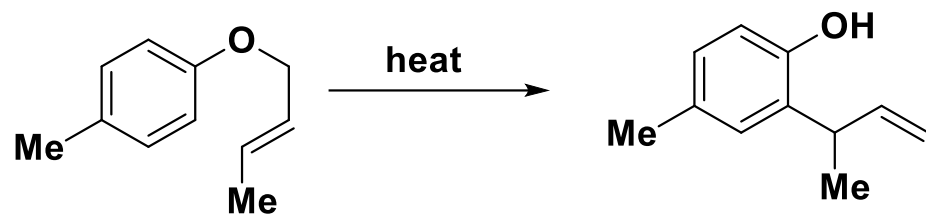
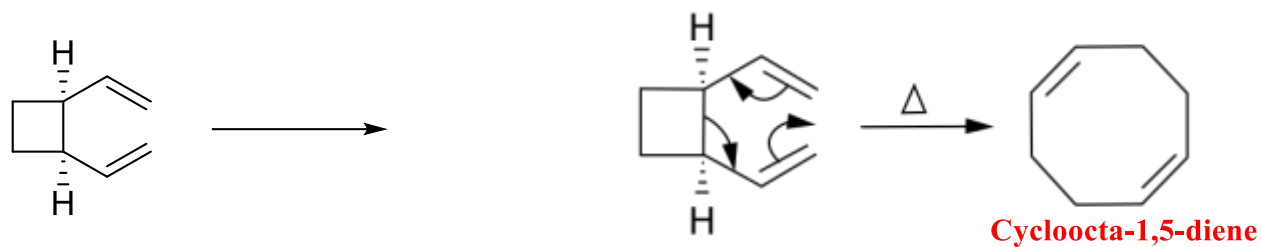
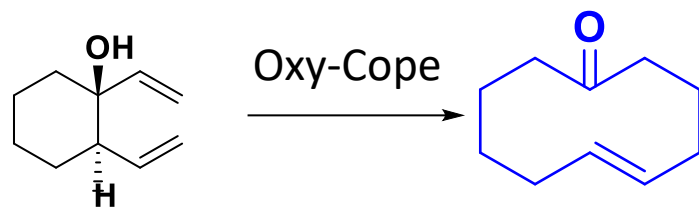


The conversion of aryl hydrazones to indoles; requires elevated temperatures and the addition of Brønsted or Lewis acids.

Mechanism



Chemistry Problem



CYI101
Common CHEMISTRY(Organic)

UNIT –II

Aromaticity

[2L]

Aromatic, non-aromatic and anti-aromatic compounds

Stereochemistry

[4L]

Concept of chirality, Axial chirality, enantiomers and diastereomers, specific rotation, optical purity, Racemic modification and resolution, R/S, D/L and E/Z nomenclature

Pericyclic reactions

[4L]

Definitions, Classifications, photochemical [2+2] and thermal [4+2] cycloaddition, Sigmatropic rearrangement

Macromolecules

[4L]

Introduction to peptides and proteins. Basics of Polymer Chemistry, Polymerization techniques, natural and synthetic polymer

Recommended Books:

1. Organic Chemistry, J. Clayden, N. Greeves, S. Warren, P. Wothers, Oxford University Press, 2000.
2. Principles of polymerization, George G. Odian, 4th Edn, John Wiley & Sons, Inc., Publication, 2004.
3. Advanced Organic Chemistry, Smith & March, 5th Edn, Wiley & Sons

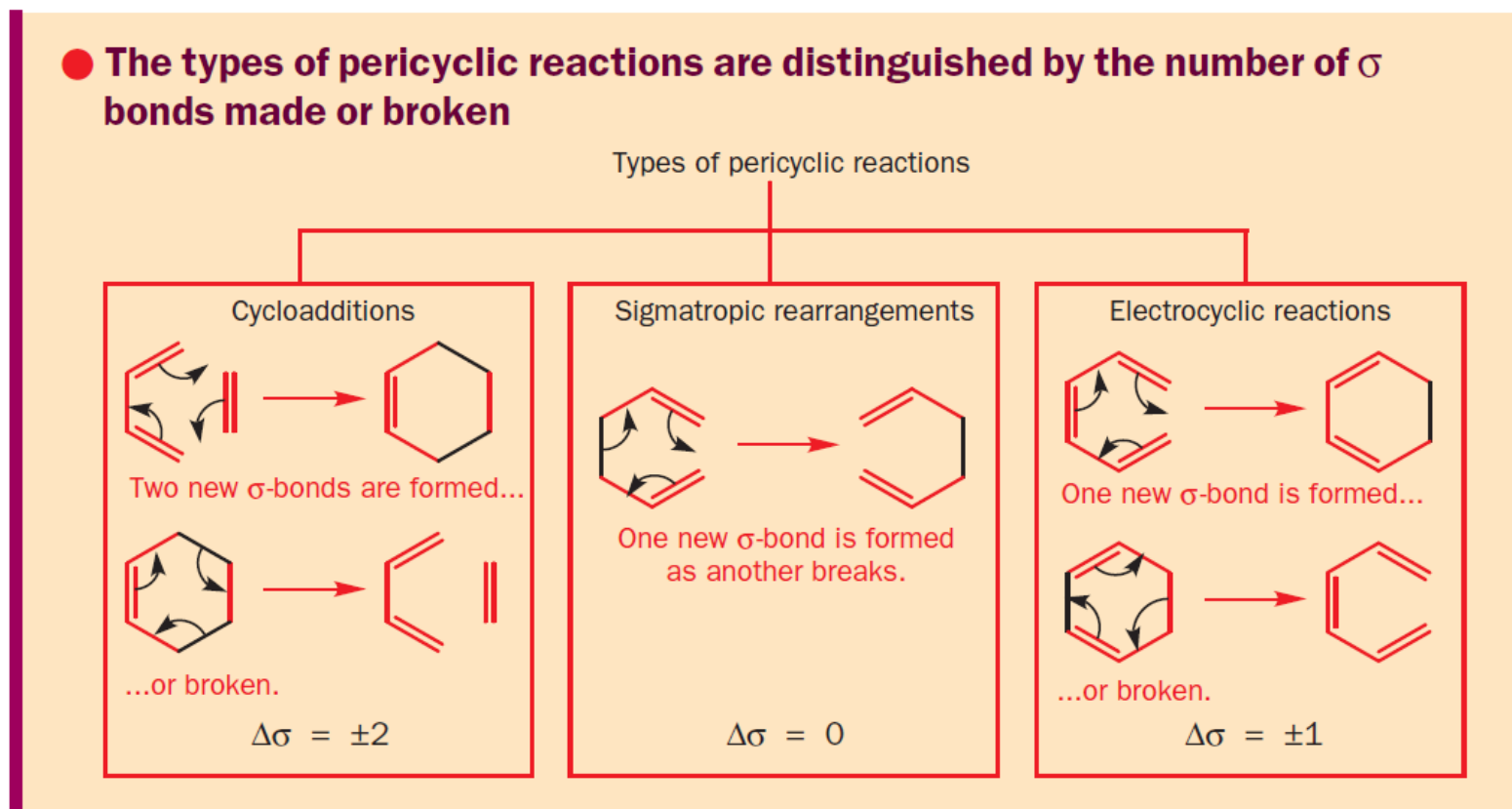
Pericyclic reactions

Pericyclic reaction involves a cyclic redistribution of bonding electrons through a concerted process.

A pericyclic reaction is a type of organic reaction wherein the transition state of the molecule has a cyclic geometry, the reaction progresses in a concerted fashion, and the bond orbitals involved in the reaction overlap in a continuous cycle at the transition state.

The three principle classes of pericyclic reactions are termed:

Cycloaddition, **Electrocyclic**, and **Sigmatropic**



Four major types of pericyclic reactions

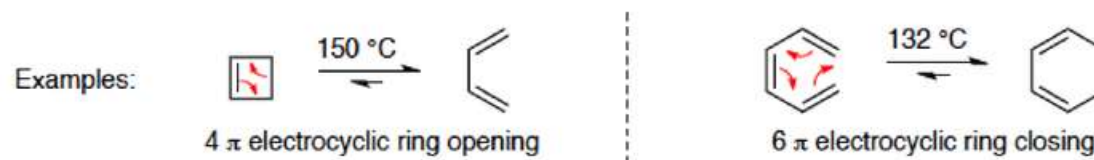
Cycloadditions

Cycloadditions are characterized by formation of a cyclic product when two components come together. In these reactions, two new σ bonds are formed between the ends of the π systems of the two components. The Diels-Alder reaction is one of the most well known example of cycloadditions.



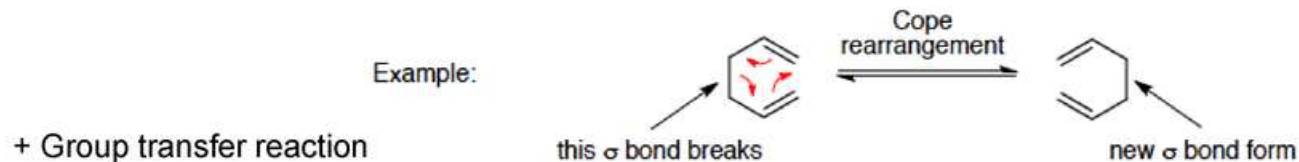
Electrocyclic reactions

Electrocyclic reactions are unimolecular pericyclic reactions characterized by ring closing or ring opening. In an electrocyclic ring closing reaction, a σ bond is formed between the ends of a conjugated π system. In an electrocyclic ring opening reaction (the reverse), a C—C σ bond breaks to give a conjugated π system. Electrocyclic reactions are further described by the number of electrons participated, such as 2π electrocyclic, 4π electrocyclic and etc.



Sigmatropic rearrangements

Sigmatropic rearrangements are also unimolecular pericyclic reactions. They involve breaking a σ bond at one place and forming a new σ bond at another place within the molecule. There is no net change in the number of σ and π bonds in a sigmatropic rearrangement.

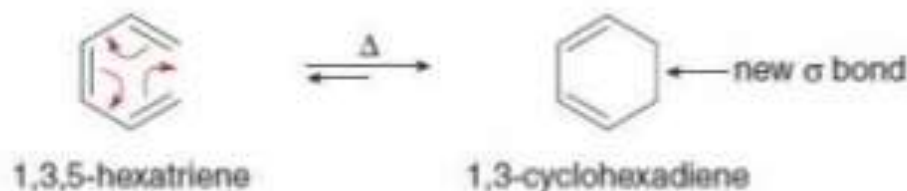


Electrocyclic Reactions

An electrocyclic reaction is a reversible reaction that involves ring closure of a conjugated polyene to a cycloalkene, or ring opening of a cycloalkene to a conjugated polyene.

For example, ring closure of 1,3,5-hexatriene forms 1,3-cyclohexadiene, a product with one more σ bond and one fewer π bond than the reactant. Ring opening of cyclobutene forms 1,3-butadiene, a product with one fewer σ bond and one more π bond than the reactant.

Ring-closing reaction

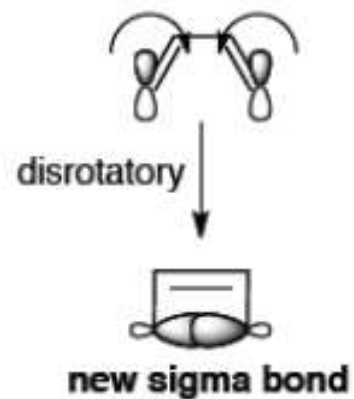
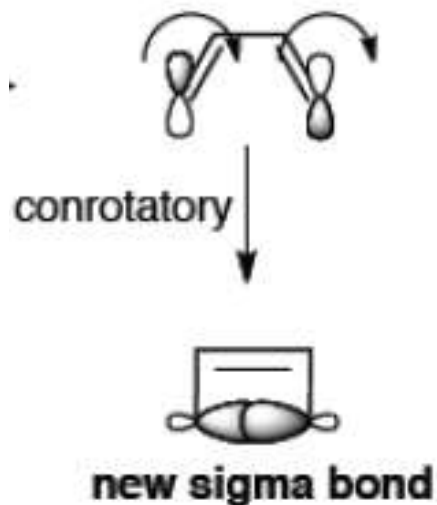


Ring-opening reaction



Conrotatory vs Disrotatory

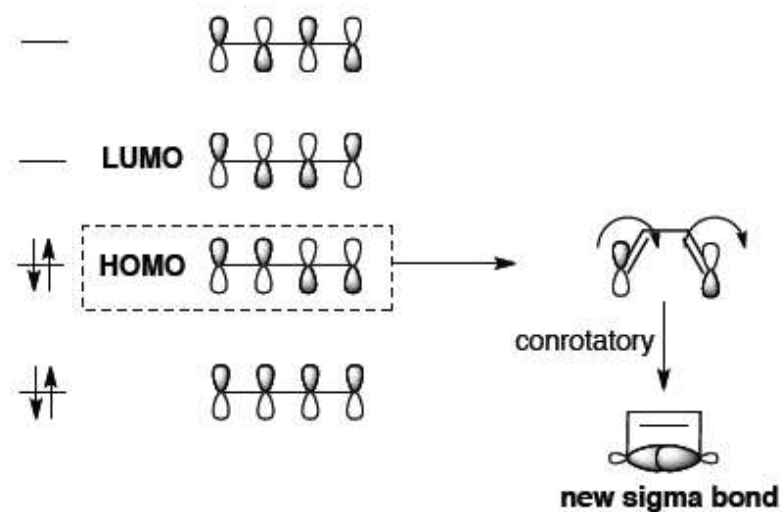
In an electrocyclic reaction the end two orbitals of a **conjugated π -system** have to form a new σ -bond. As you need electrons to form a new σ -bond, the **HOMO of the 1,3-diene** determines the outcome of the reaction. In order to overlap the two end orbitals of the **HOMO** to form the **new σ -bond**, they can be turned in **two different directions**: In **conrotatory mode**, both end groups turn in the same direction (clockwise). In **disrotatory mode**, the groups turn in opposite directions (one clockwise and one counter-clockwise).



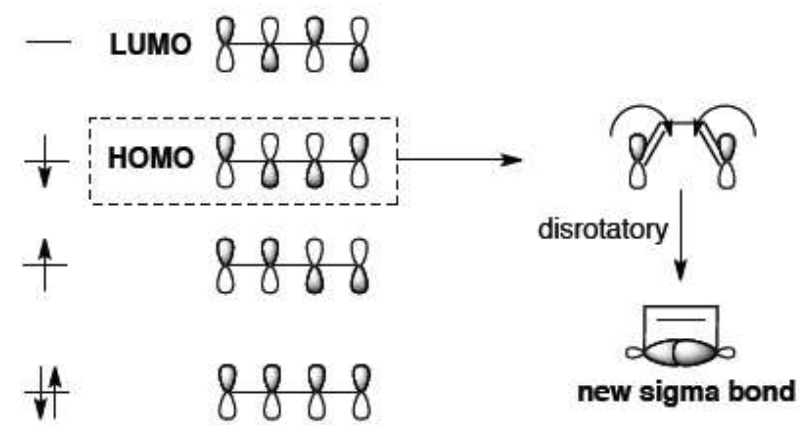
Thermal vs Photochemical

As already showed above, in the thermal electrocyclic ring closure of 1,3-diene the orbitals have to be turned in a **conrotatory fashion** to form the new σ -bond ($4n$, thermal, **conrotatory**). In the photochemical case the disrotation leads to the desired ring closure ($4n$, photochemical, **disrotatory**)

Thermal

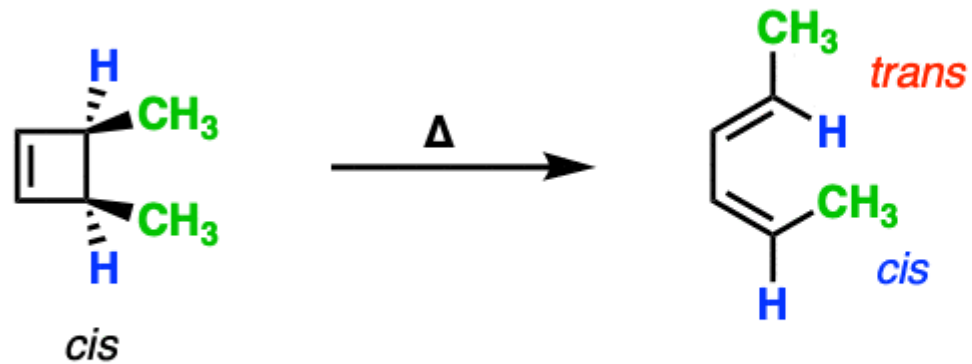


Photochemical



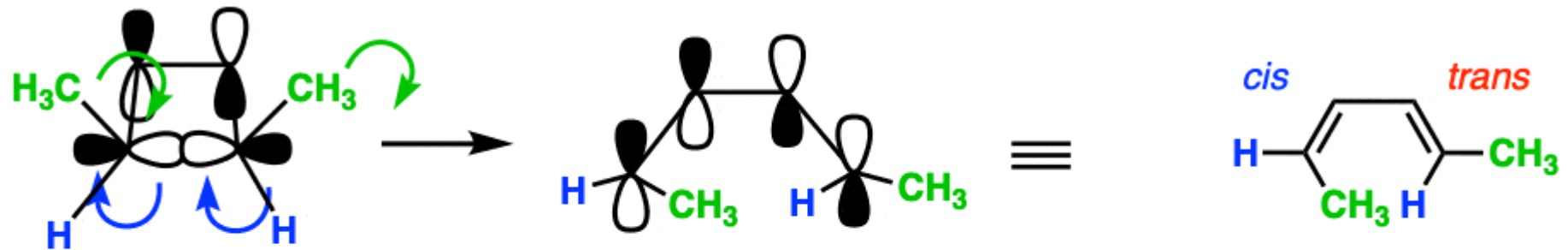
System	Thermal	Photochemical
" $4n$ " electrons	Conrotatory	Disrotatory
" $4n + 2$ " electrons	Disrotatory	Conrotatory

Understanding the stereochemistry of thermal electrocyclic ring-opening



As the carbon rotates (with its lobe) the substituents rotate with it

Front view:

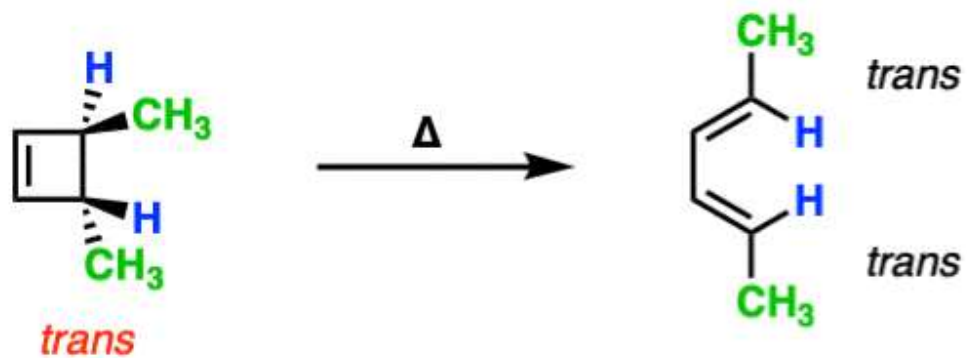


*clockwise
rotation*

*clockwise
rotation*

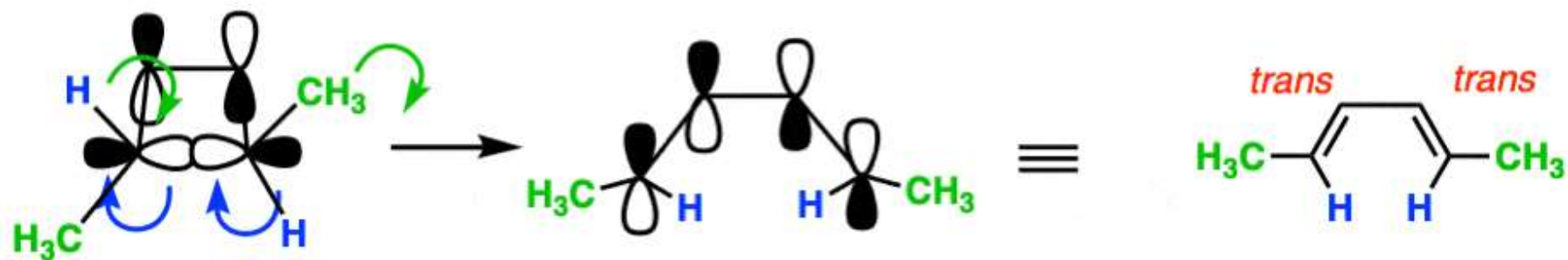
Conrotatory rotation

Another example: *trans*-3,4-dimethylcyclobutene



As the carbon rotates (with its lobe) the substituents rotate with it

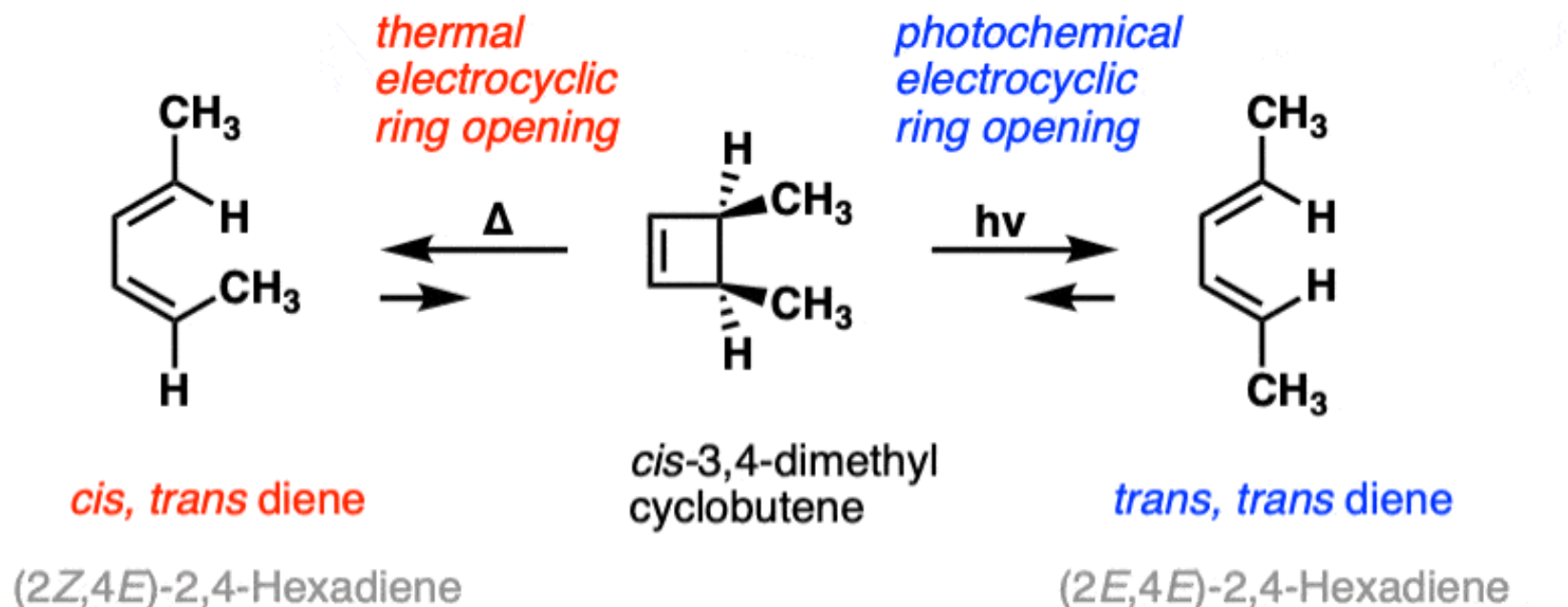
Front view of *trans*-3,4-dimethylcyclobutene



clockwise
rotation clockwise
rotation

Conrotatory rotation

Electrocyclic ring opening: thermal (heat) versus photochemical ($h\nu$) conditions give different products (stereoisomers)



Summary:

π electrons

4

4

conditions

thermal (Δ)

photochemical ($h\nu$)

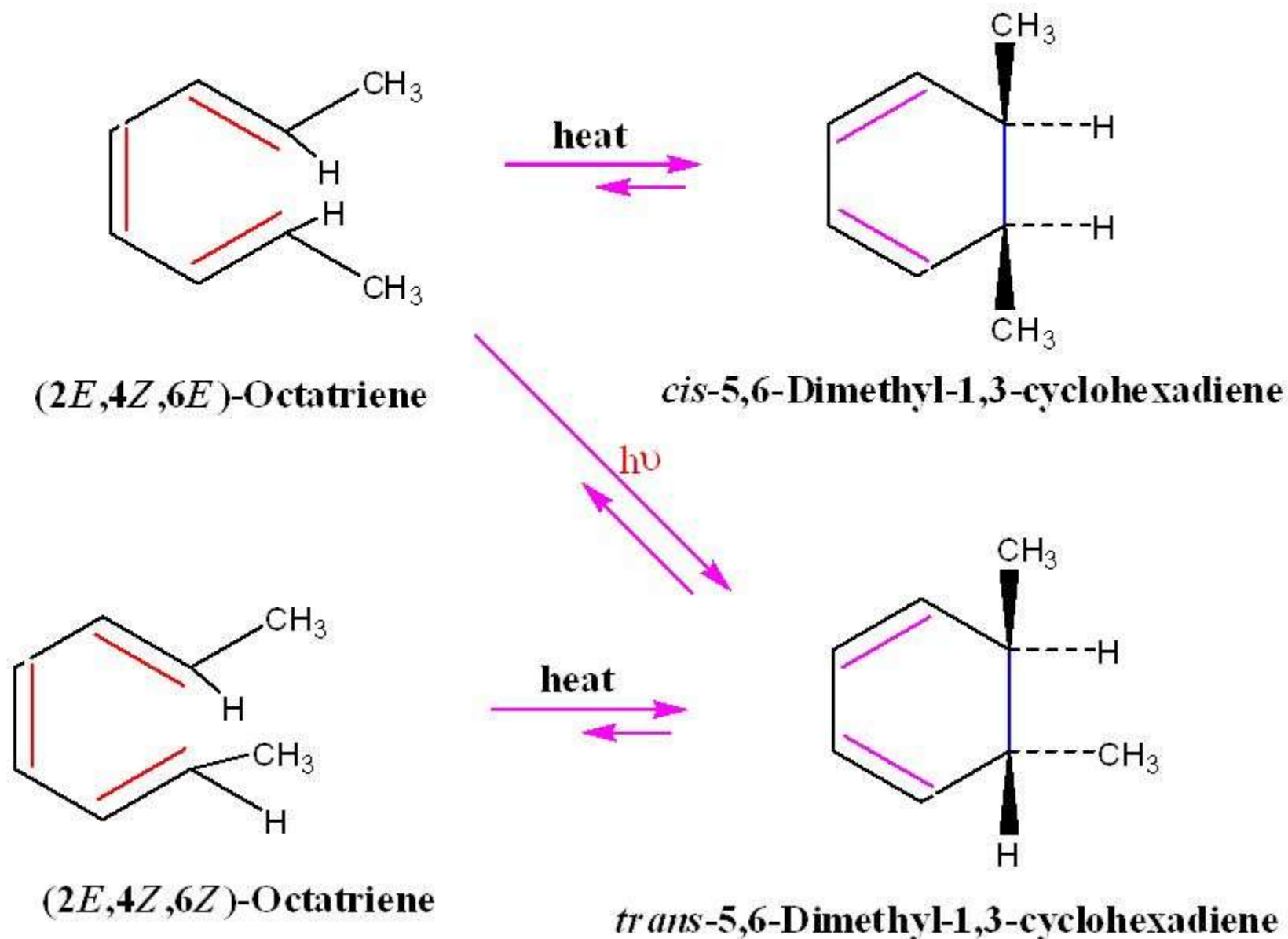
direction

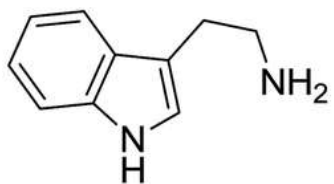
conrotatory

disrotatory

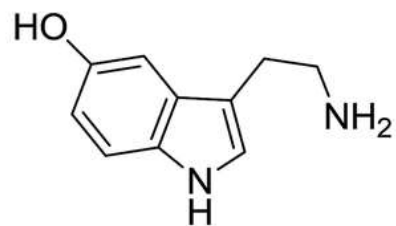
Stereochemistry

The most striking feature of electrocyclic reactions

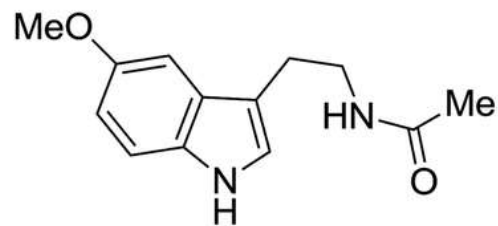




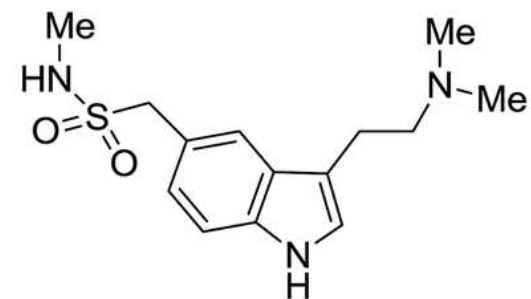
1: Tryptamine



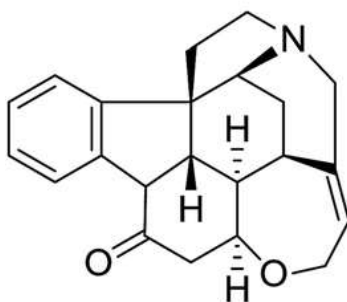
2: Serotonin



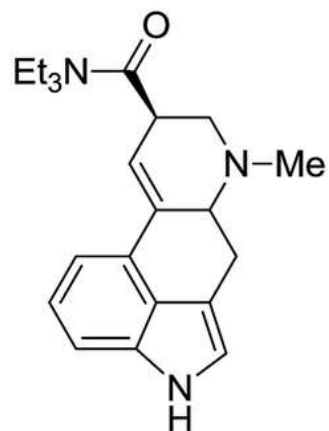
3: Melatonin



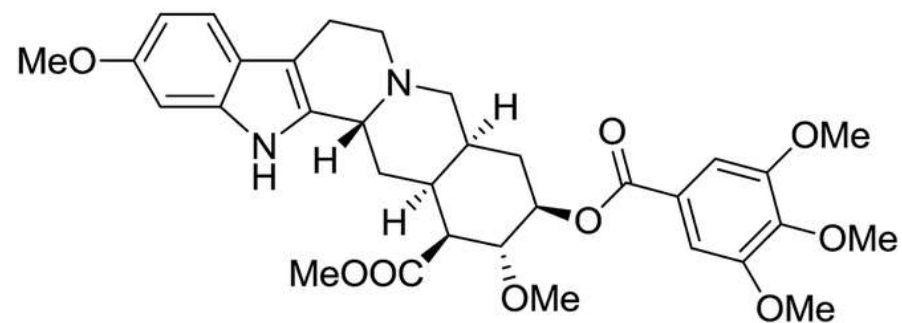
4: Sumatriptan



5: Strychnine

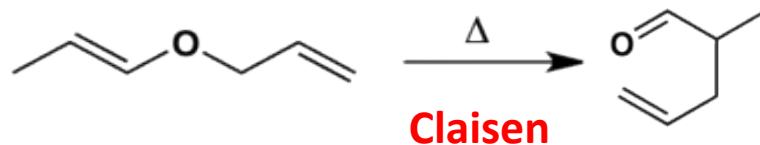


6: LSD

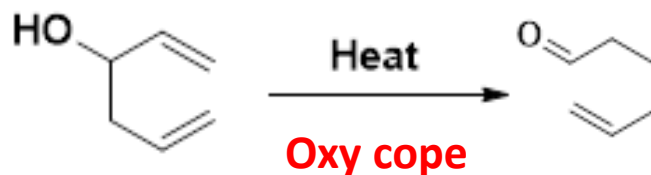


7: Reserpine

Which of unsaturated aldehydes is the sigmatropic rearrangement product obtained by heating the following ether?



Identify the correct product of the following pericyclic reaction



Cope Rearrangement is

- (a) [3,3]-sigmatropic
- (b) [1,3]-sigmatropic
- (c) [1,5]-sigmatropic
- (d) [1,7]-sigmatropic

Paterno-Buchi reaction is

- (a) (4+2) Cycloaddition Reaction
- (b) (2+2) Cycloaddition Reaction
- (c) (3+2) Cycloaddition Reaction
- (d) (6+4) Cycloaddition Reaction

The (4+2) Cycloaddition between Diene and Dienophile known as

- (a) Diels-Alder Reaction
- (b) Oxy Cope Rearrangement
- (c) Aza-Claisen Rearrangement
- (d) Claisen Rearrangement