

Syllabus

Part I. Pericyclic Reactions (lectures 1-2)

Part II. Amines (lectures 3-5)

Part III. Phenols and Quinones (lectures 5-6)

Mid-term Exam (lecture 7)

Part IV. Heterocycles (lectures 8-9)

**Part V. Biomolecules: Carbohydrates, Proteins, Nucleic Acids,
and Lipids (lectures 10-13)**

Part VI. Cross-Coupling Rxns , Synthetic Polymers, Drugs...

Final Exam (Nov. 2)

Grading: Assignments & Quizzes: 10 points

Midterm Exam: 30 points

Final Exam: 60 points

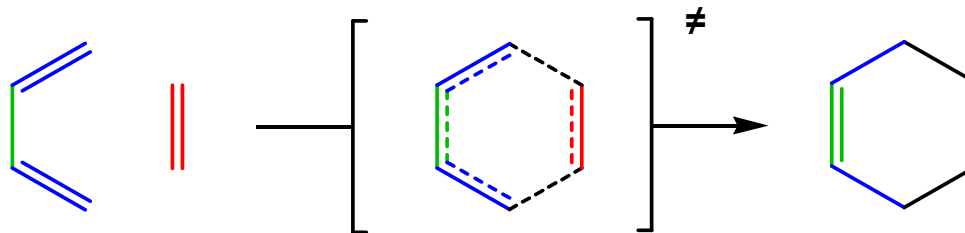
Office hours:

Wednesday 2:00-4:00 PM
@ B437 Chemistry Bldg.

Course FTP: <ftp://dhzhao:engorg@ftp.chem.pku.edu.cn>

Pericyclic Reactions

D-A Reaction: a pericyclic reaction



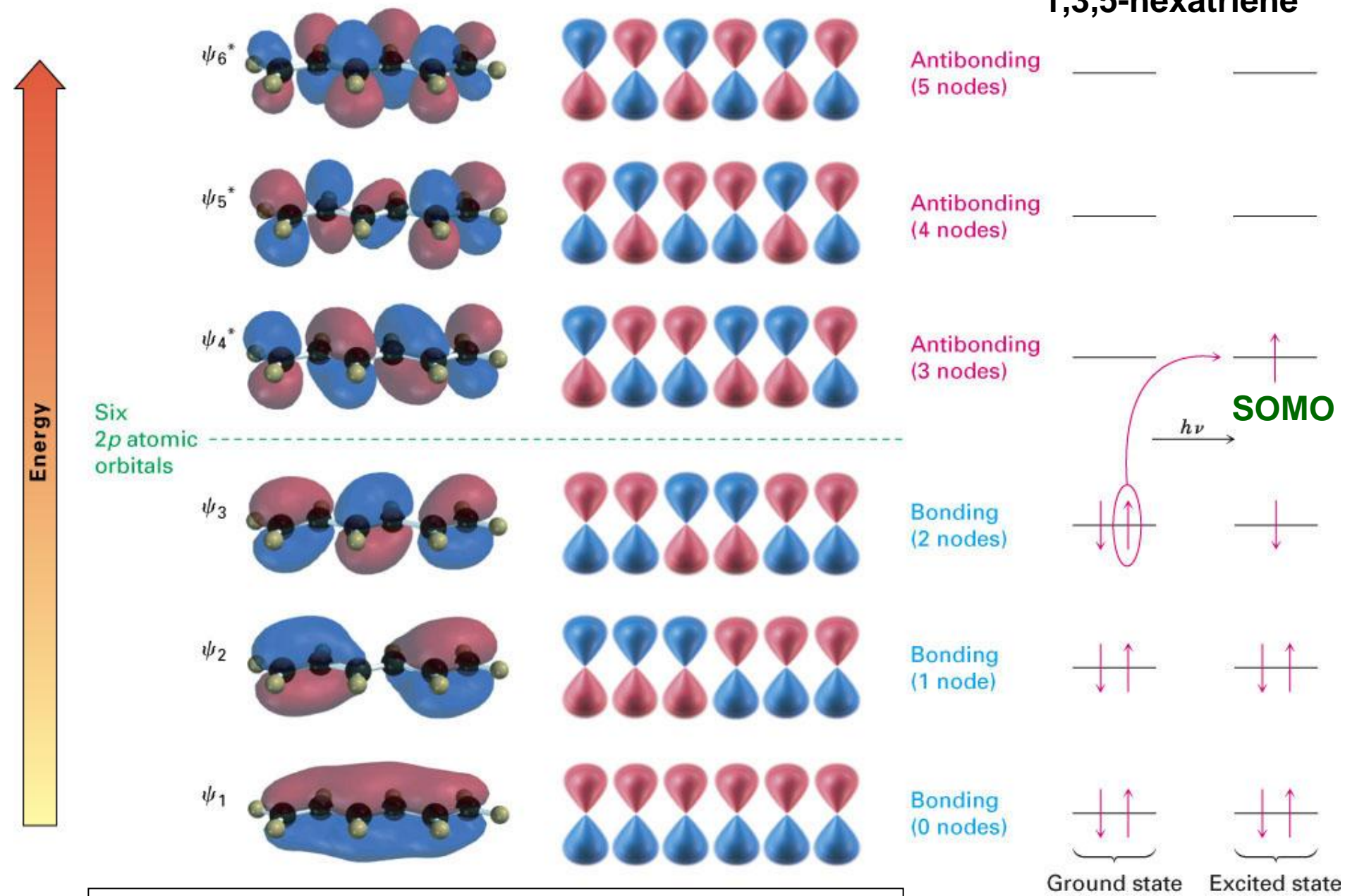
A **pericyclic reaction** occurs by a concerted process through a cyclic transition state involving several simultaneous bond-making and breaking processes.

Concerted (协同) means all bonding changes occur at the same time and in a single step; no intermediates are involved.

Pericyclic reactions is a less common, however, the third major class of organic reaction mechanisms.

What are the other two major classes?

1,3,5-hexatriene



Excitation can be induced by irradiation with UV light

MOs in Pericyclic Reactions

As the MOs increase in energy:

- the number of bonding interactions decreases and the number of nodes increases;
- the MOs alternate from symmetric to asymmetric.

According to *Woodward-Hoffmann* rules, a pericyclic reaction can only take place if the symmetries of the reactant MOs match up with the symmetries of the product MOs.

That means the lobes of reactant MOs must be of the correct algebraic sign for bonding to occur in the transition state leading to product. (* *Fukui*: only **frontier orbitals** need to be considered)

Symmetry-allowed reactions: the symmetries of reactant and product MOs match up (these reactions can usually occur under mild conditions);

Symmetry-disallowed reactions: the symmetries of reactant and product MOs do not correlate (these reactions cannot occur by lower-energy, concerted pathways).

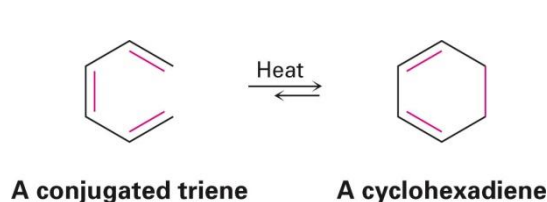
Three main classes of pericyclic reactions:

electrocyclic reactions, cycloadditions, and sigmatropic rearrangements

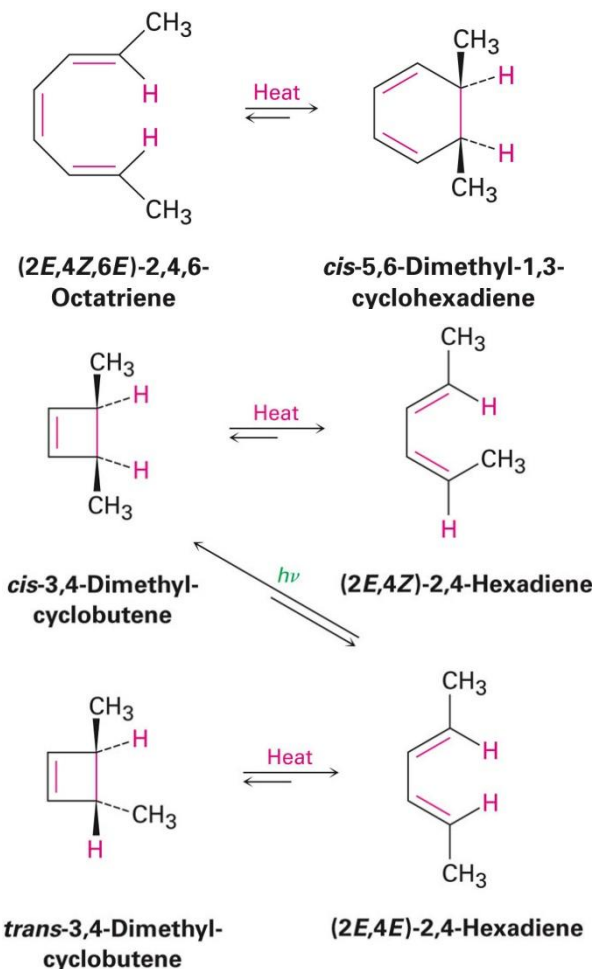
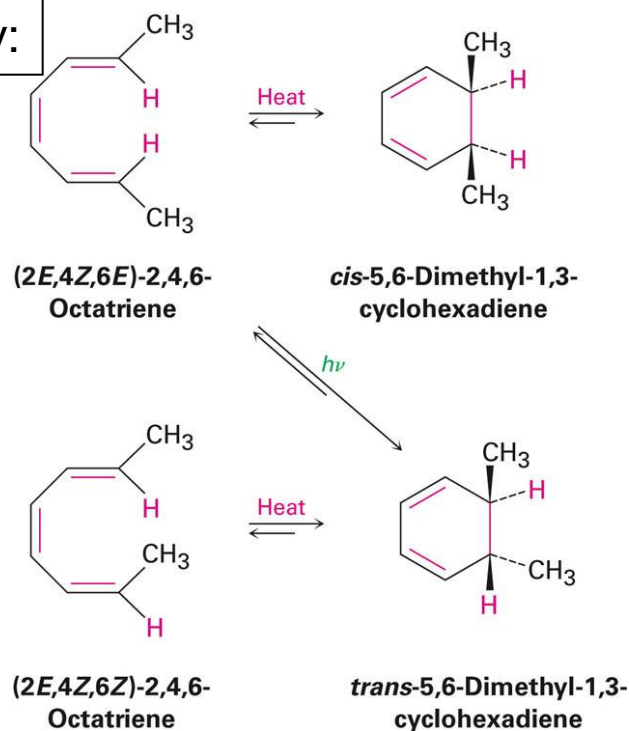
Electrocyclic Reactions

An **electrocyclic** process that involves the **cyclization** of a **conjugated polyene**:

- ✓ One π bond is broken, the other π bonds change position, a new σ bond is formed, and a cyclic compound results;
- ✓ A reversible process;
- ✓ Producing specific stereoisomers related to the orbitals of the reactants

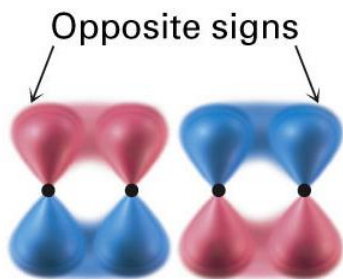


Stereochemistry:

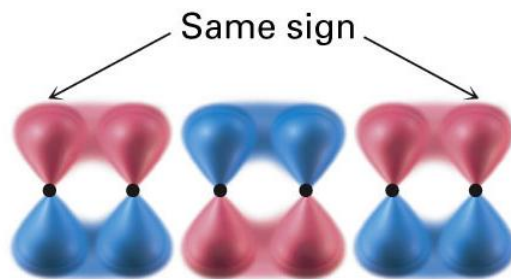


Stereochemistry and Frontier Orbitals

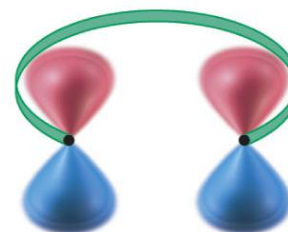
According to *frontier orbital theory*, the **stereochemistry** of an *electrocyclic reaction* is determined by the symmetry of the polyene **HOMO**.



Diene HOMO

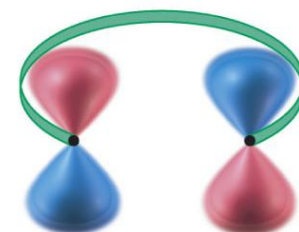


Triene HOMO



Like lobes on same side

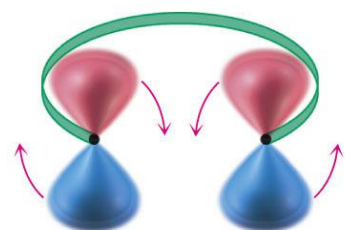
or



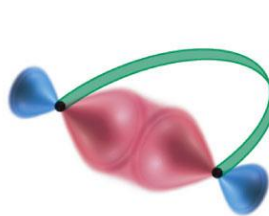
Like lobes on opposite side

For a bond to form, the outermost π lobes must achieve an optimal spatial orientation:

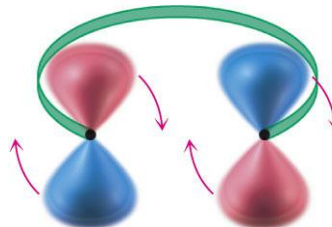
- lobes of like sign overlap: (+) with (+) and (−) with (−) (**constructive** overlapping for bonding orbital);
- head-to-head (**σ bond** formation).



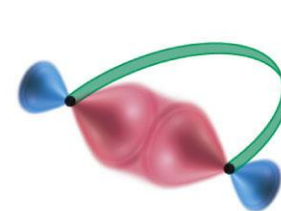
disrotatory



conrotatory

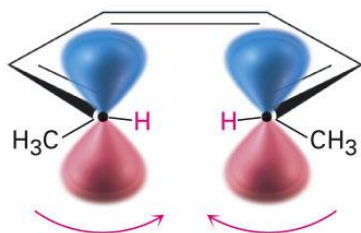


Clockwise Clockwise

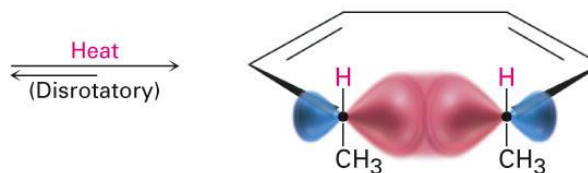


Clockwise Counterclockwise

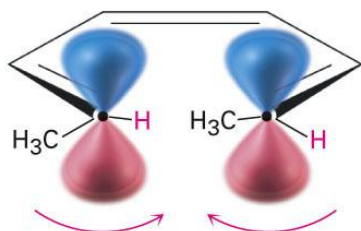
Stereochemistry in Thermal Electrocyclic Reactions



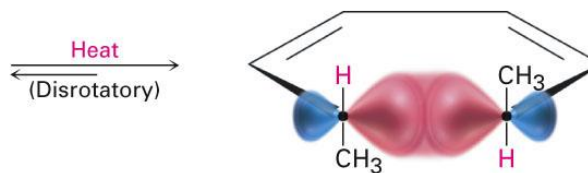
(2E,4Z,6E)-2,4,6-Octatriene



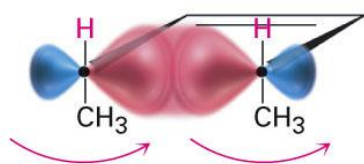
cis-5,6-Dimethyl-1,3-cyclohexadiene



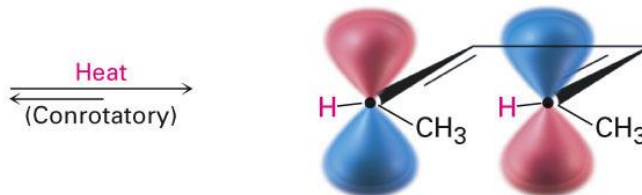
(2E,4Z,6Z)-2,4,6-Octatriene



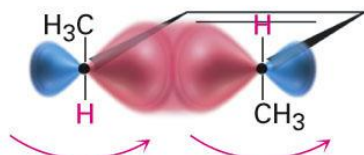
trans-5,6-Dimethyl-1,3-cyclohexadiene



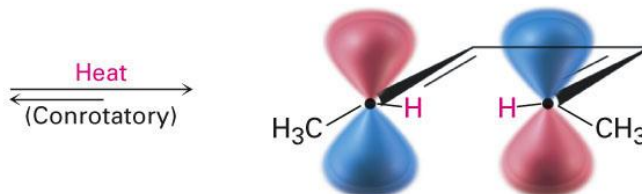
cis-3,4-Dimethylcyclobutene



(2E,4Z)-2,4-Hexadiene

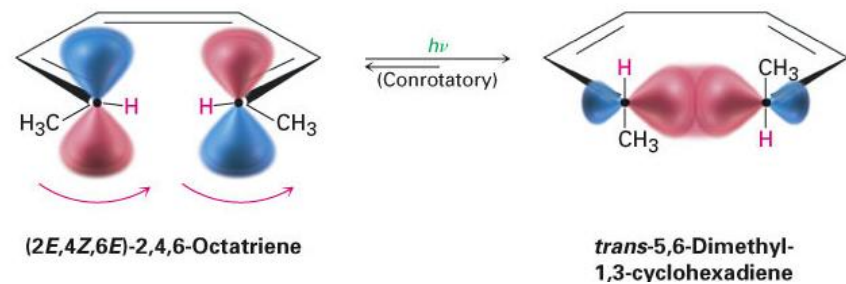
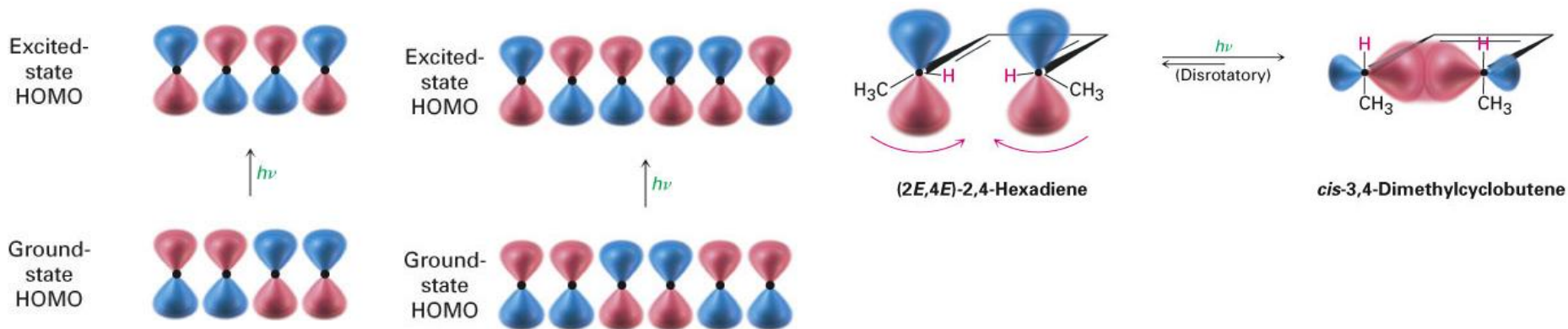


trans-3,4-Dimethylcyclobutene

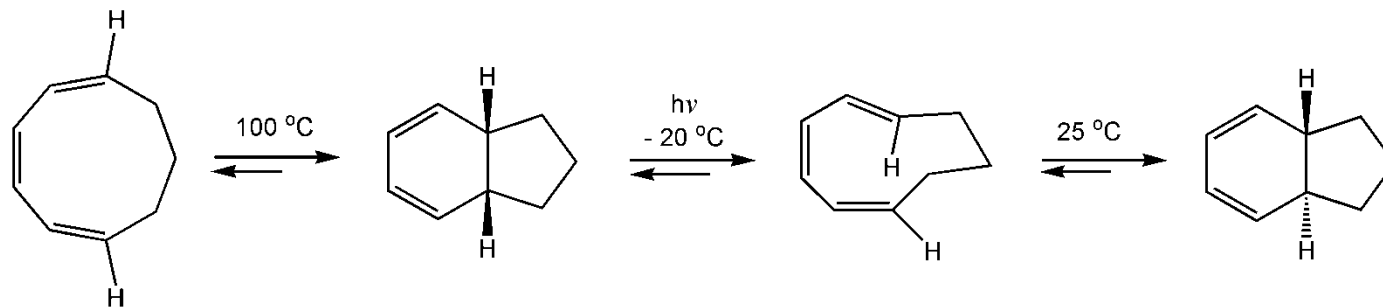
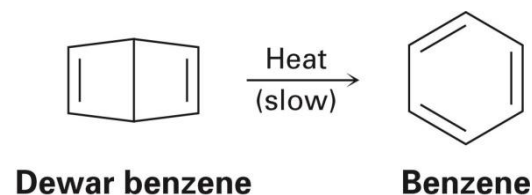


(2E,4E)-2,4-Hexadiene

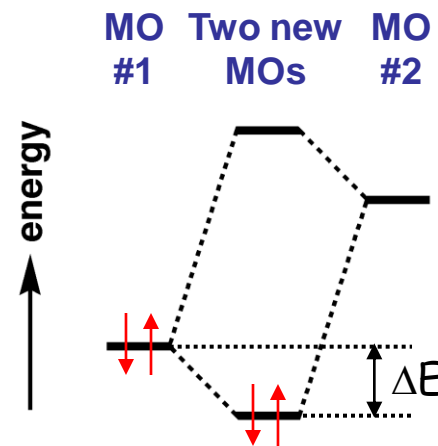
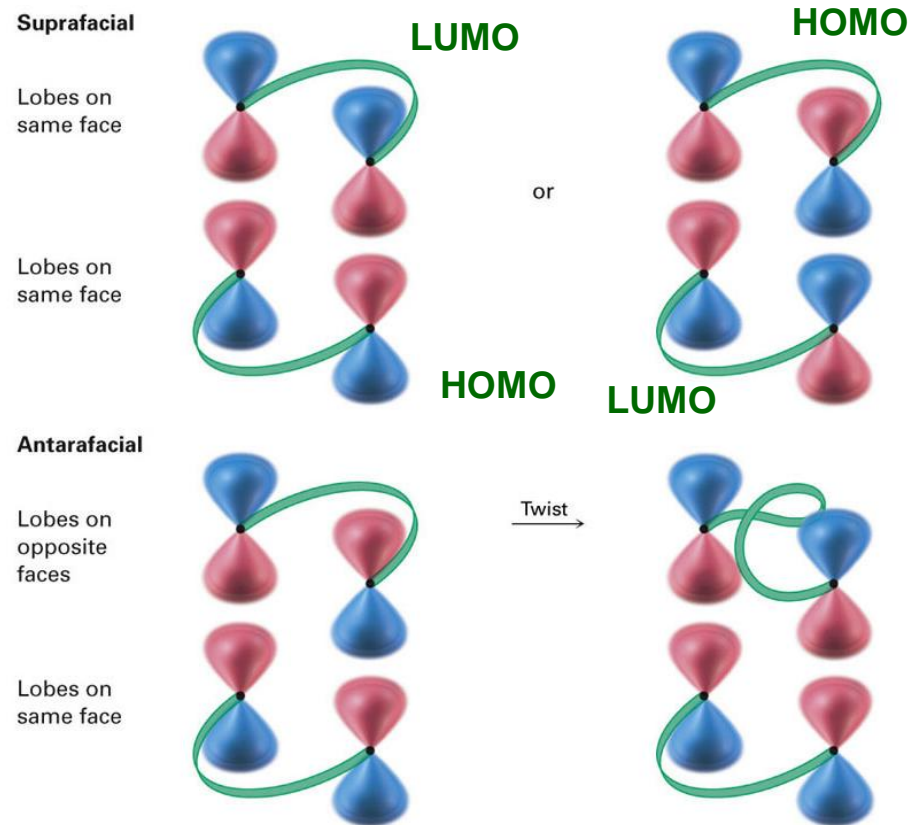
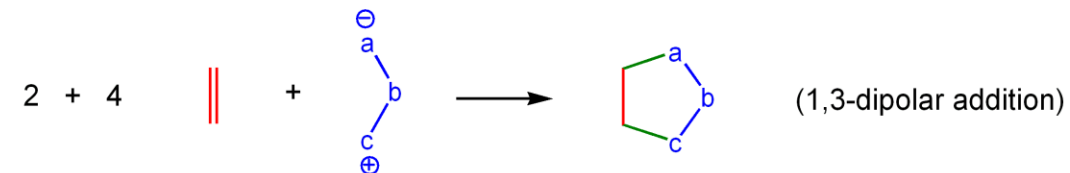
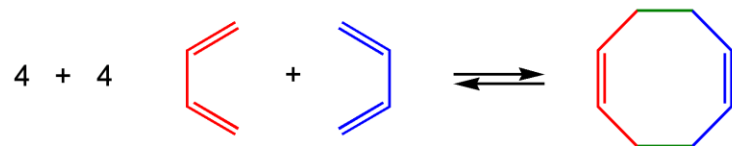
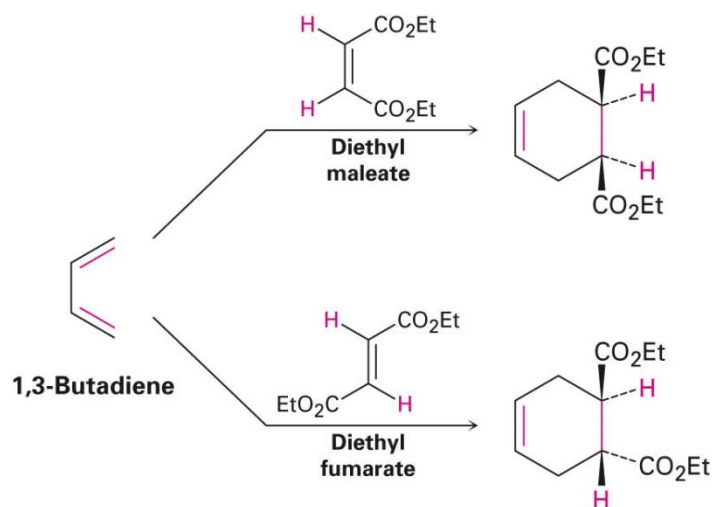
Photochemical Electrocyclic Reactions



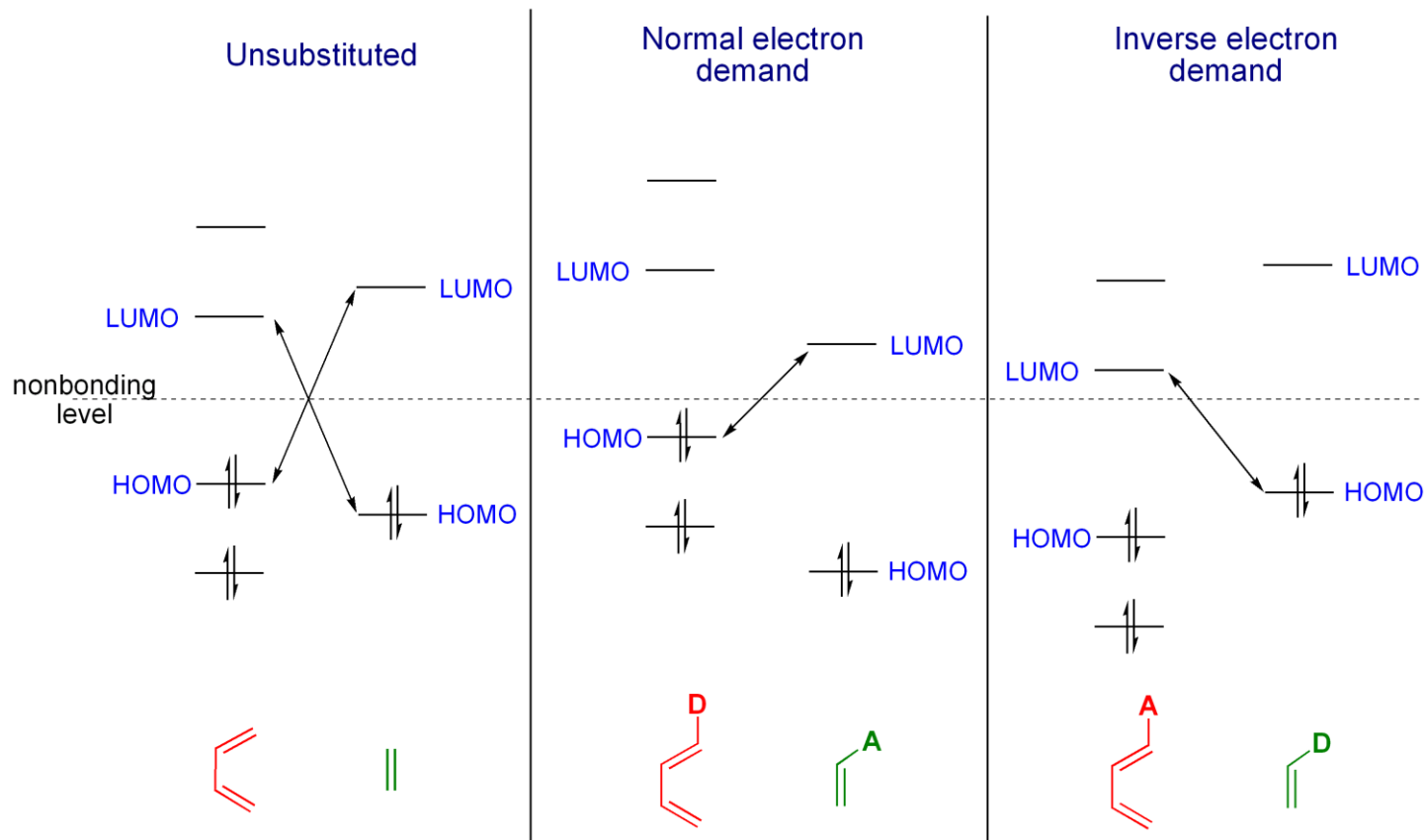
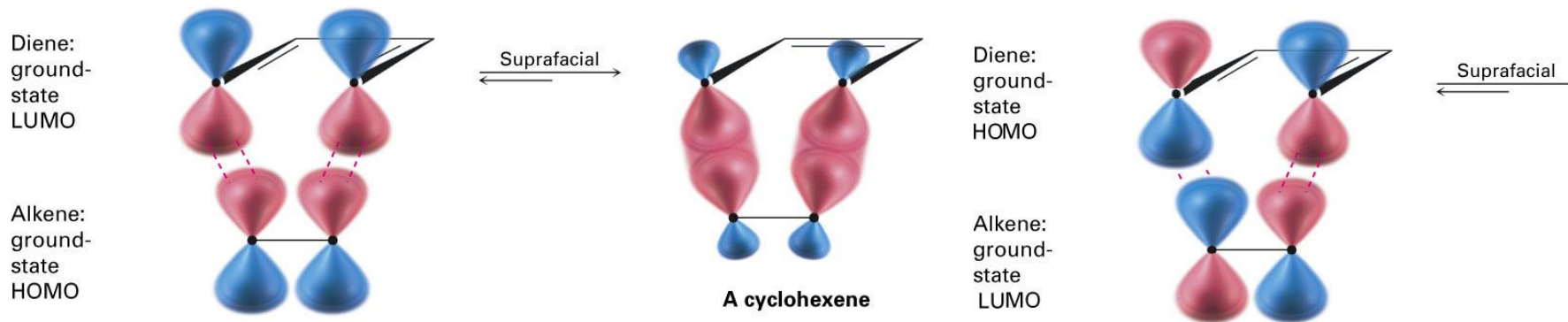
Electron pairs (double bonds)	Thermal reaction	Photochemical reaction
Even number	Conrotatory	Disrotatory
Odd number	Disrotatory	Conrotatory



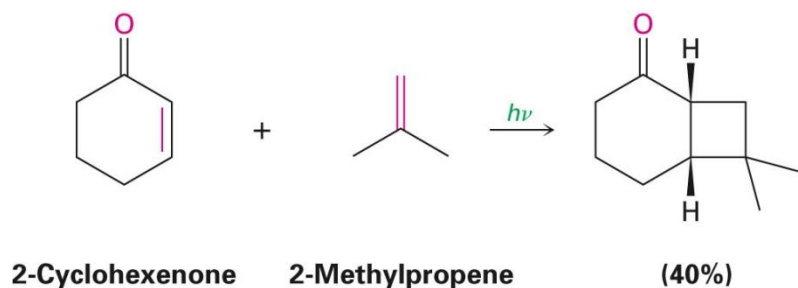
Cycloaddition Reactions



(2+4) Cycloadditions under Thermal Conditions



(2+2) Cycloaddition: A Photochemical Reaction

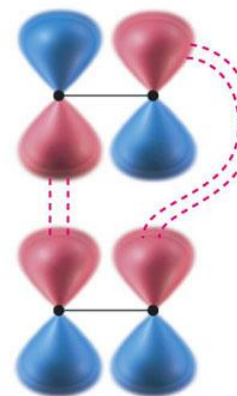


One of the best methods for synthesizing cyclobutane derivatives.

(a) Thermal reaction

Alkene 2:
Ground-state
LUMO

Alkene 1:
Ground-state
HOMO

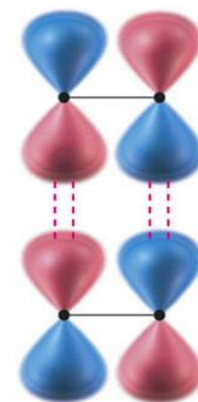


Antarafacial
Strained,
no reaction

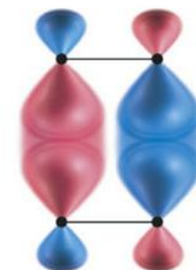
(b) Photochemical reaction

Alkene 2:
Ground-state
LUMO

Alkene 1:
Excited-state
HOMO

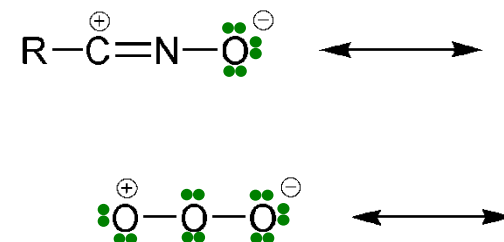
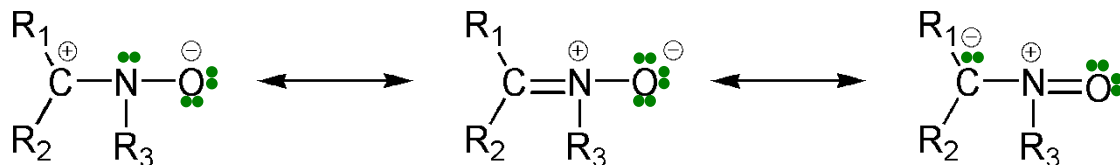
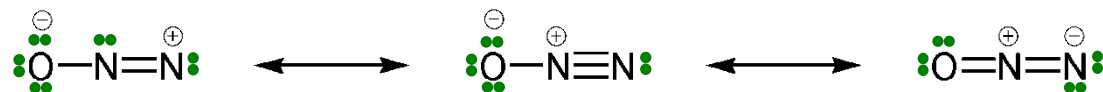
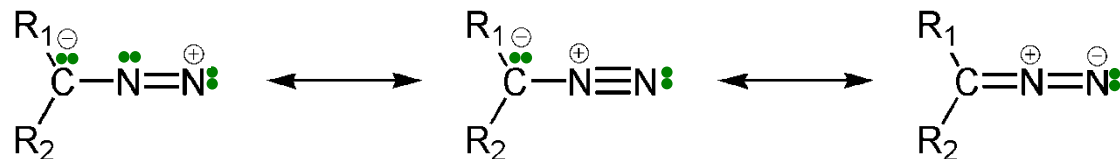


Suprafacial



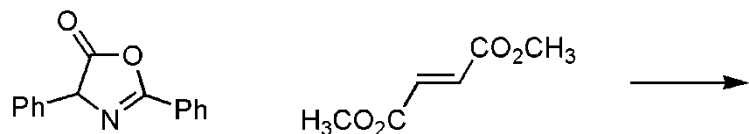
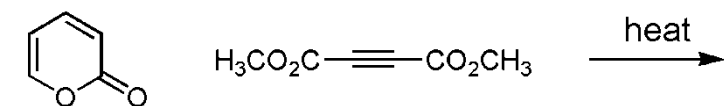
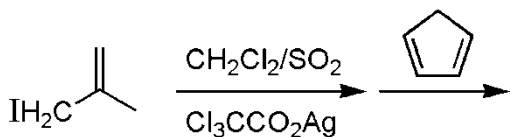
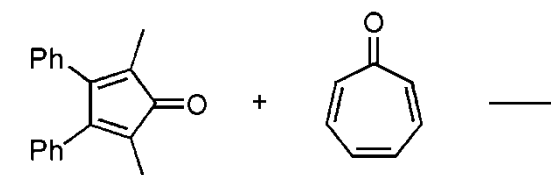
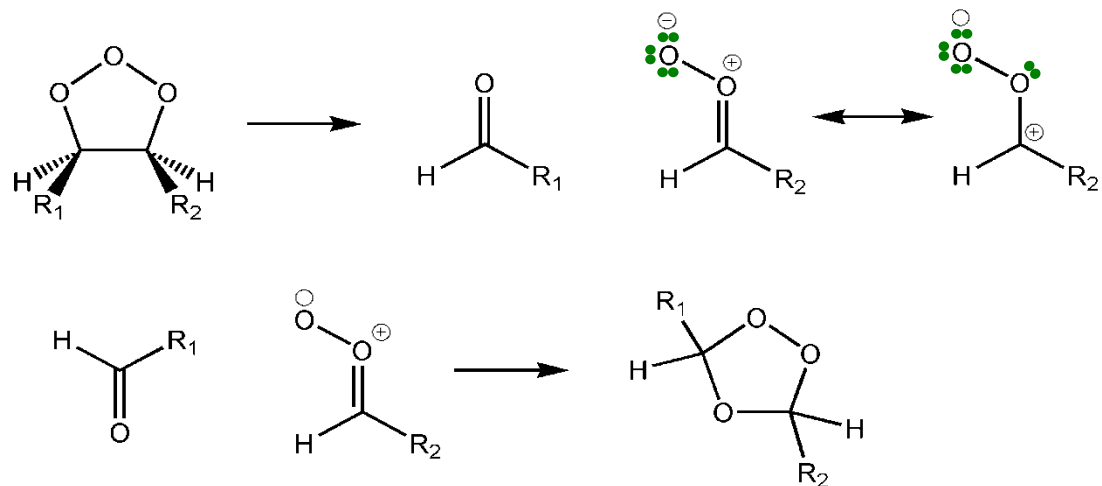
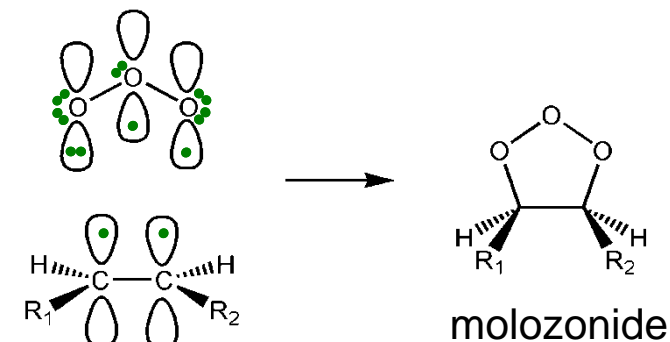
A cyclobutane

Examples of 1,3-dipoles:



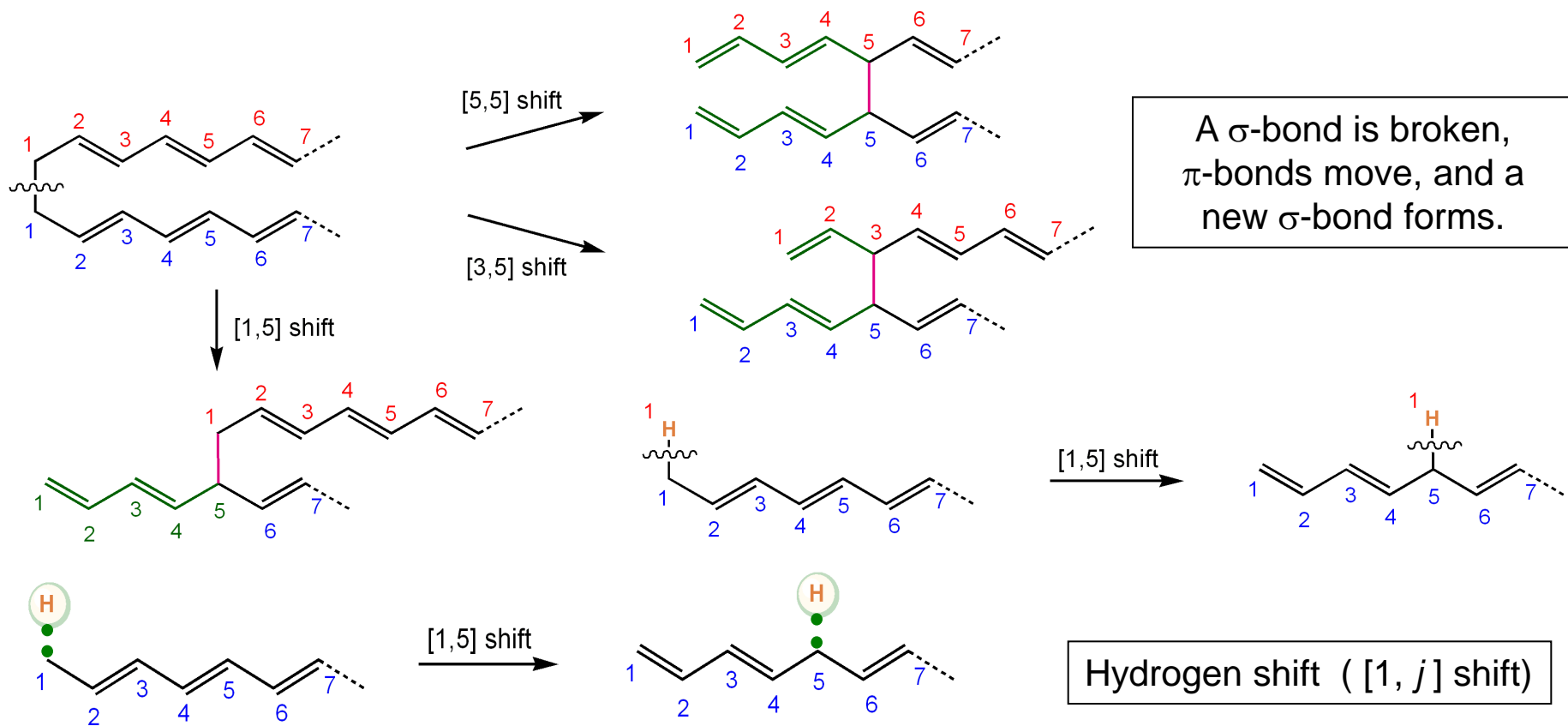
1,3 – Dipolar Addition: Ozonide Formation

Speculate about the HOMO and LUMO interactions in this reaction.

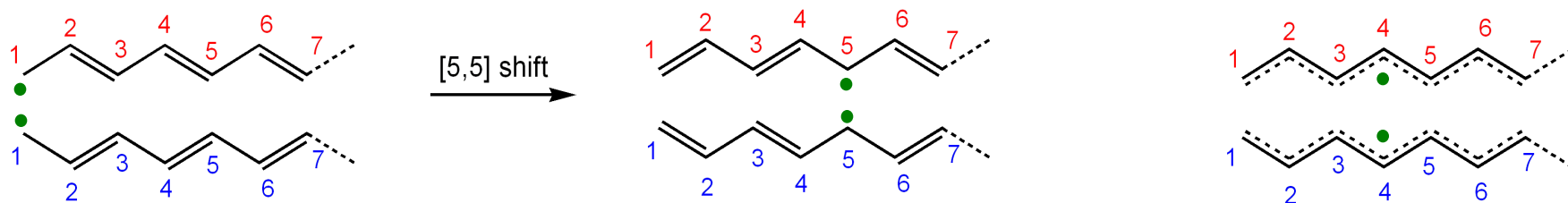


Electron pairs (double bonds)	Thermal reaction	Photochemical reaction
Even number	Antarafacial	Suprafacial
Odd number	Suprafacial	Antarafacial

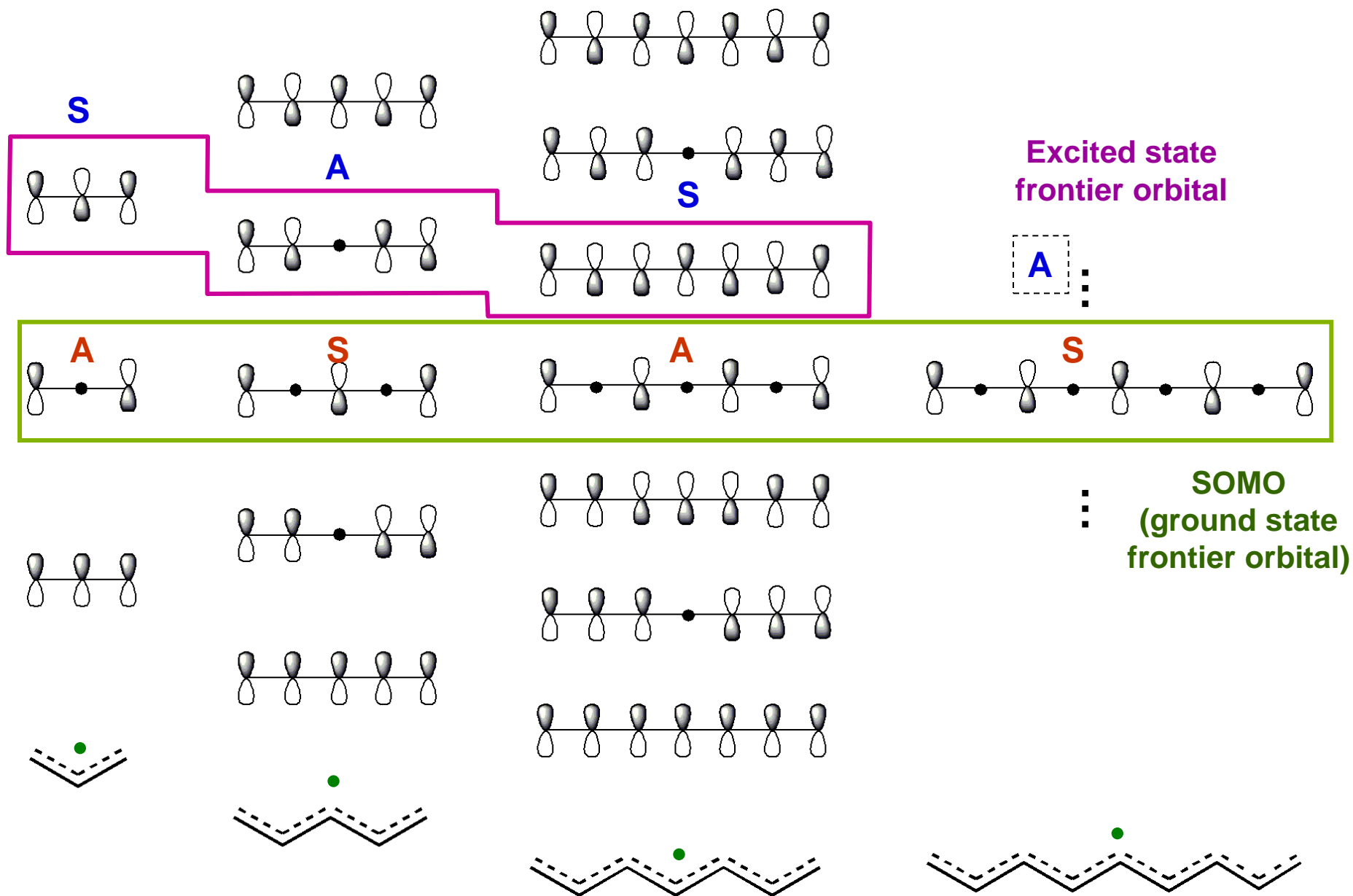
Sigmatropic Rearrangements



- Imagine in sigmatropic rearrangement the migrating σ -bond break to form two "virtual" radicals;
- all the atoms the σ -bond "travel through" must be conjugated.

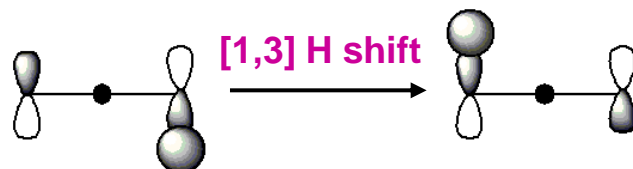


Frontier Orbitals in σ -Tropic Rearrangement

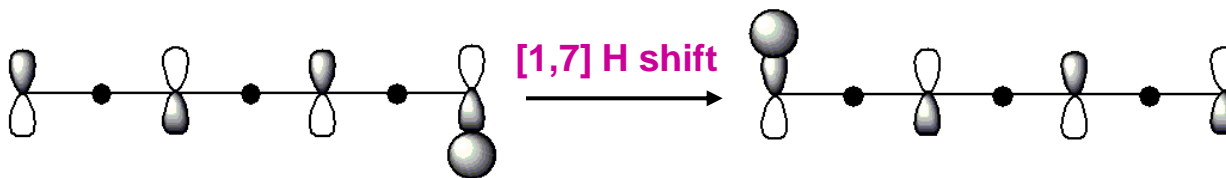


Stereochemistry of Hydrogen Shift

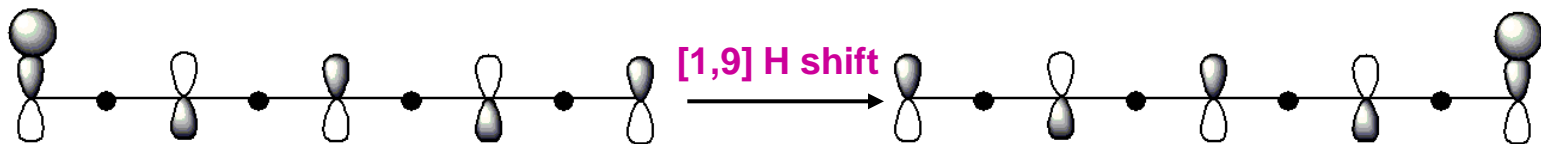
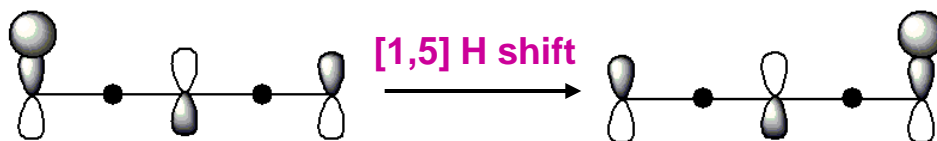
Antarafacial:



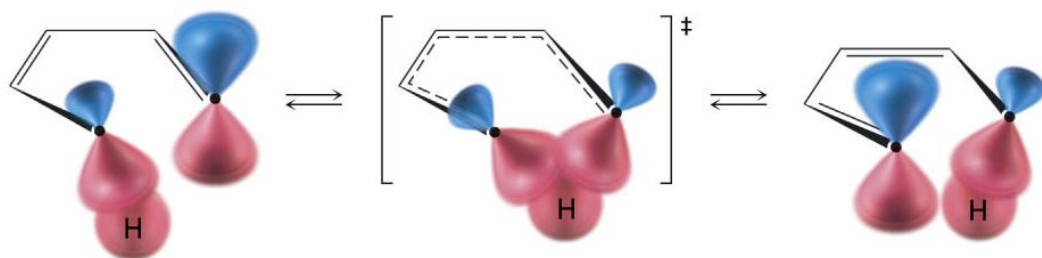
Under thermal conditions



suprafacial:



A cyclic transition state:



Transition state

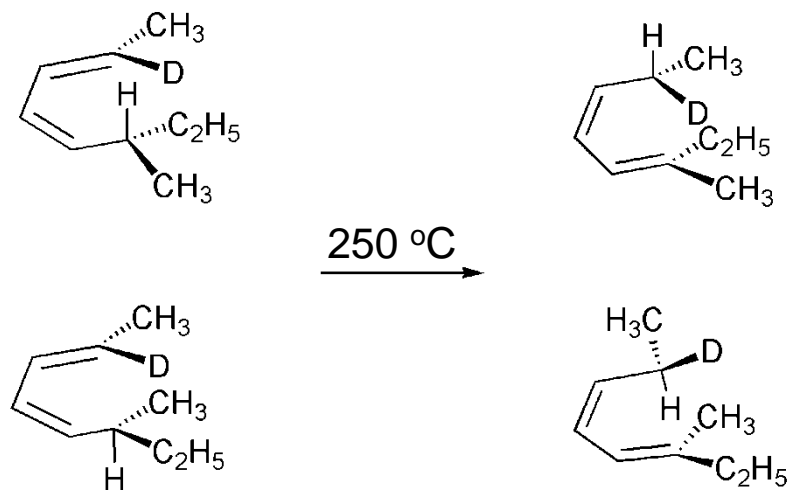
Thermal [1,3] hydrogen shifts so far
are very rare
(antarafacial, cyclic transition state
is highly strained and unfeasible)

What about photochemical reactions?

Stereochemistry of Hydrogen Shift

[1, j] hydrogen shift

[1,5] H shift (suprafacial)

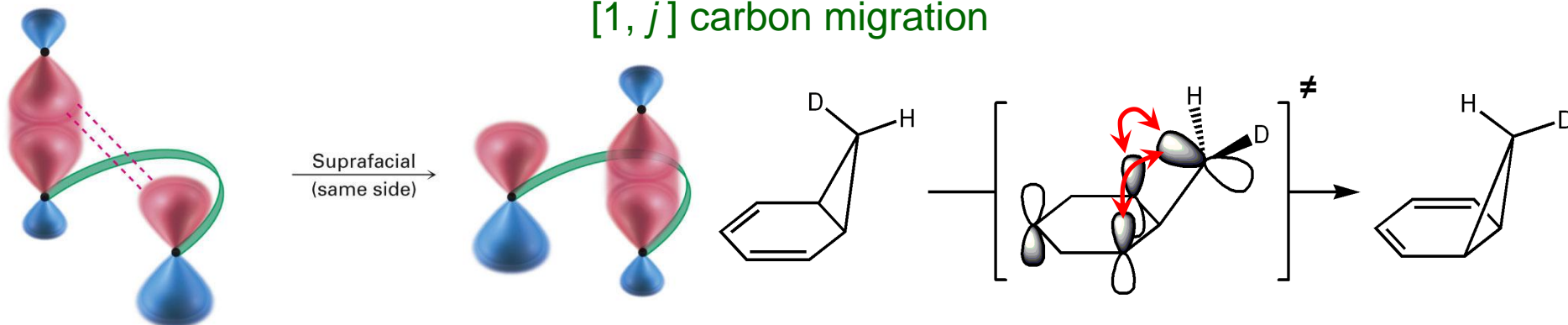


Electron pairs (double bonds)	Thermal reaction	Photochemical reaction
Even number	Antarafacial	Suprafacial
Odd number	Suprafacial	Antarafacial

Carbon Migration

Ground state 6-electron [1,5] rearrangement (suprafacial-suprafacial):

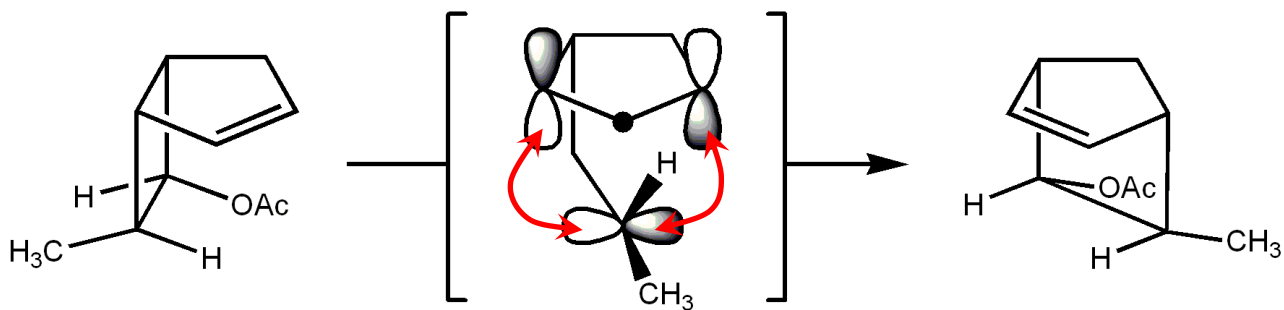
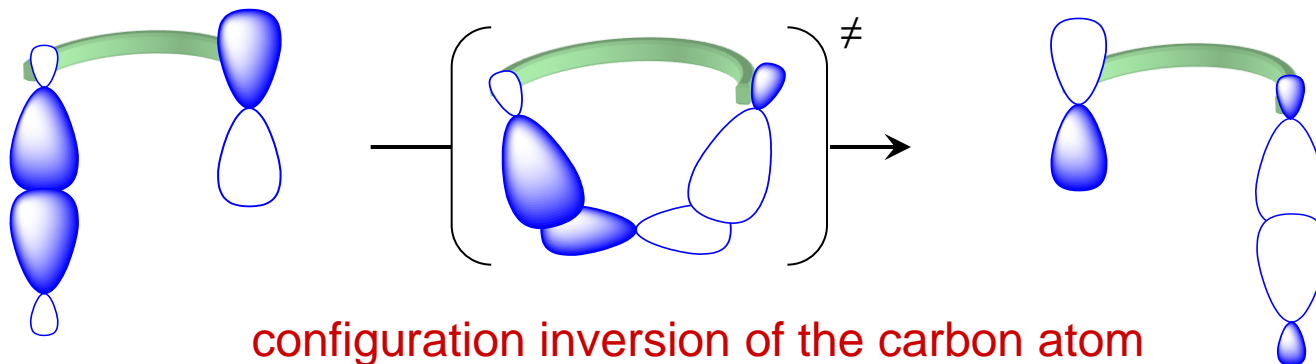
[1, j] carbon migration



Carbon Migration

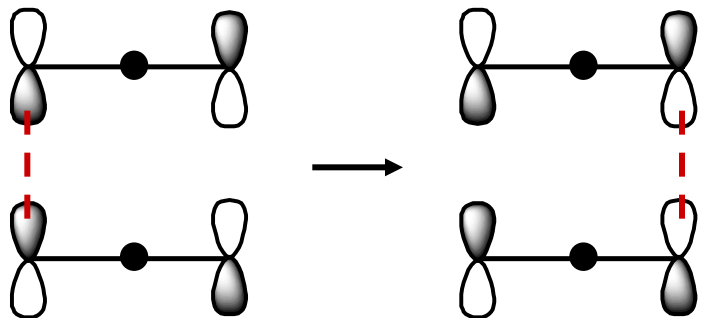
Suprafacial-Antarafacial:

$[1, j]$ carbon migration



4-electron $[1,3]$ rearrangement

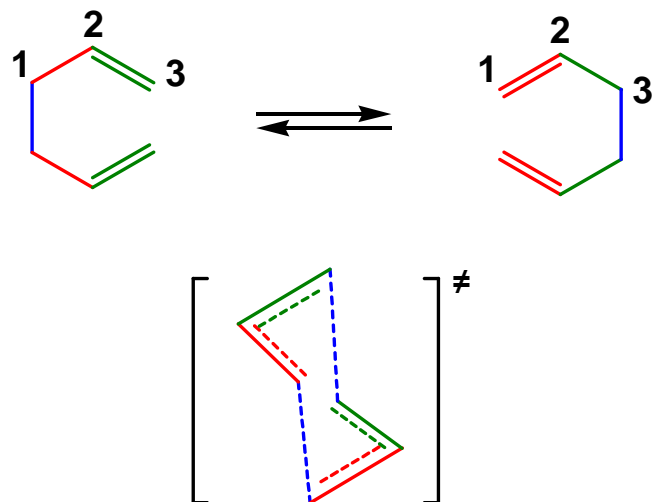
$[i, j]$ carbon migration



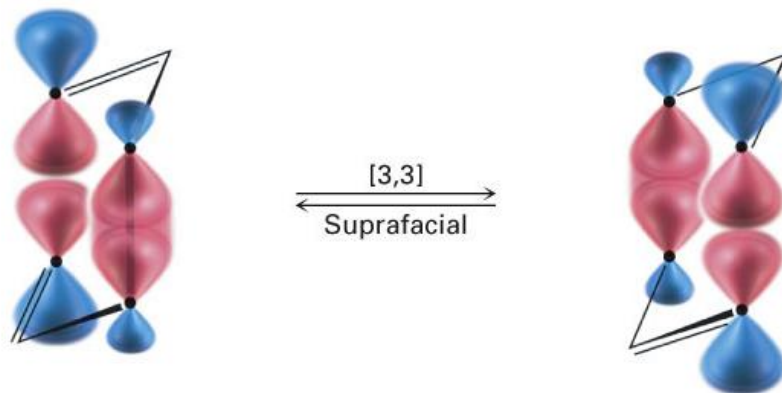
$[3,3]$ -rearrangement is the most common and important class in $[i, j]$ carbon migrations

suprafacial-suprafacial allowed
under thermal conditions
(still requires cyclic transition state)

[3,3] Carbon Migration

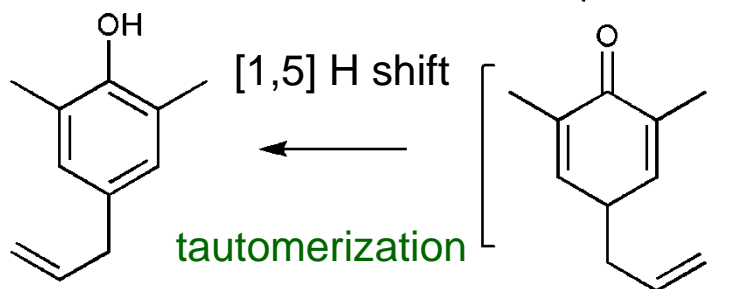
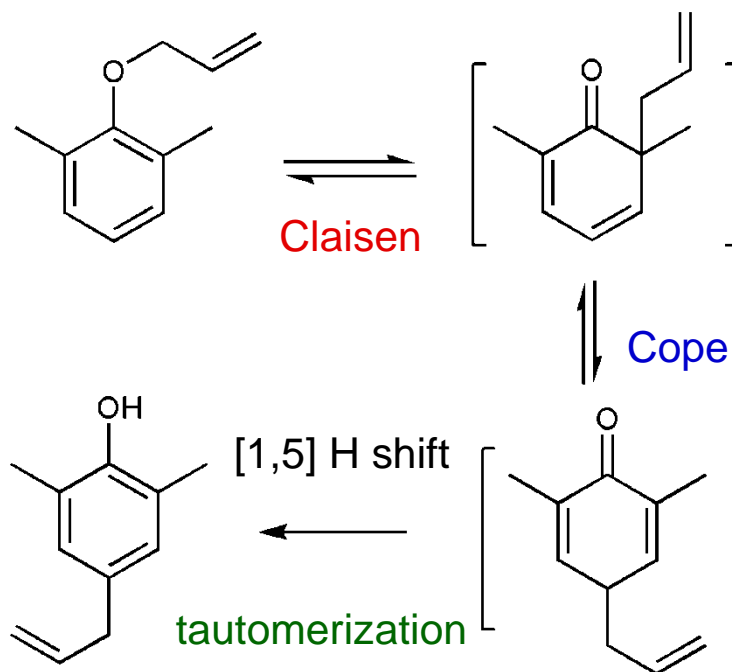
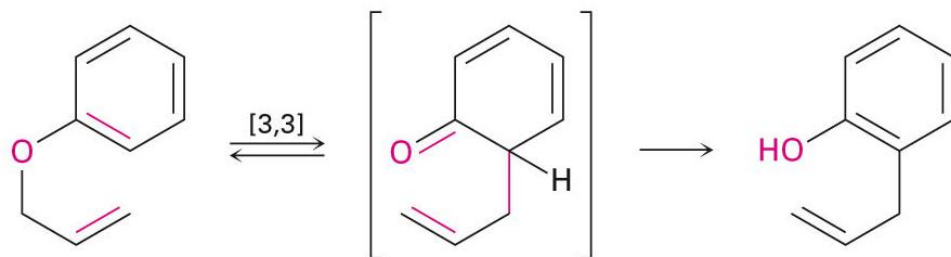
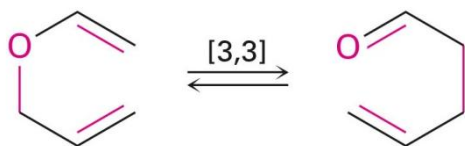


Chair-conformation transition state



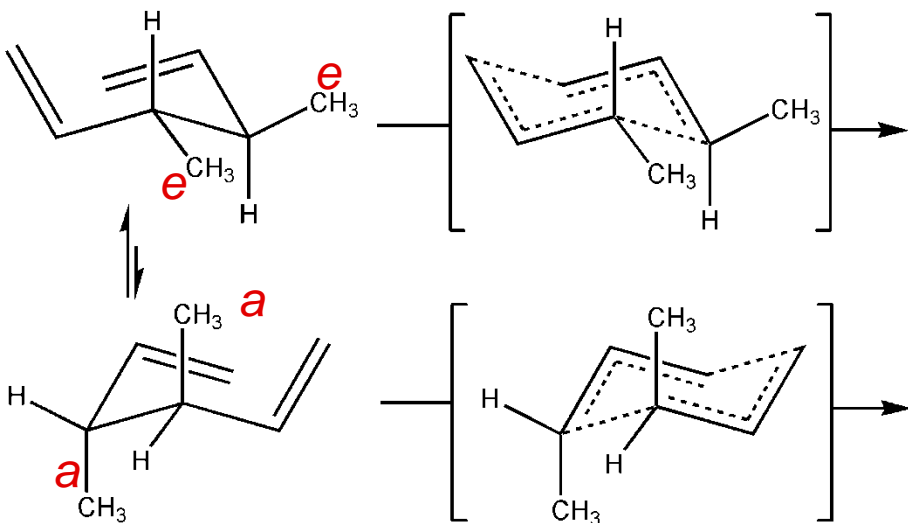
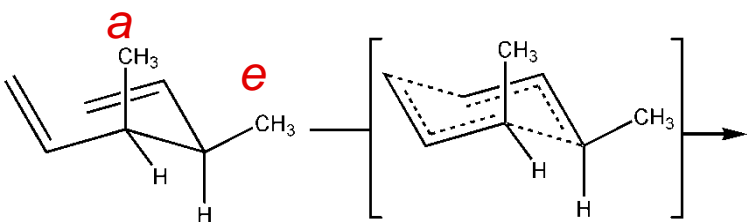
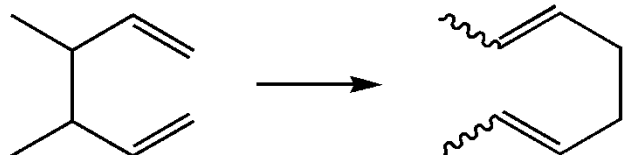
Cope rearrangement

Claisen rearrangement

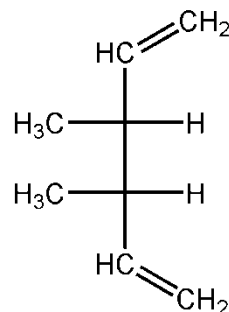


Stereochemistry of [3,3] Carbon Migration

Z or E?



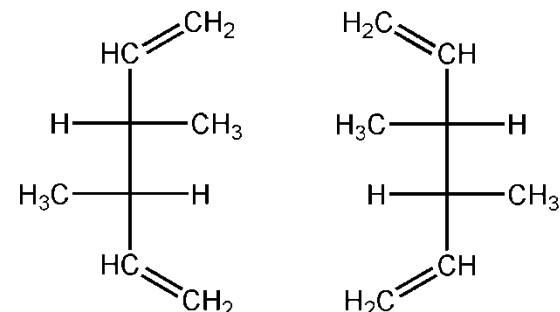
meso



225 °C

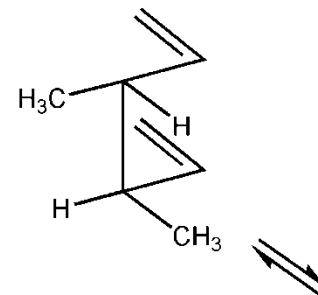
99.7% (*Z,E*)
0.3% (*E,E*)

racemic mixture



100 °C

90% (*E,E*)
10% (*Z,Z*)
< 1% (*Z,E*)



(*Z,E*)