Pericyclic reactions

Ref. books:
1. Advanced Organic Chemistry: Part A:
   - F. A. Carey and R. J. Sundberg
2. Reactions and Reagents - O.P. Agarwal

Pericyclic reactions

Reactions of organic compounds:

- a polar reaction

\[
\text{H}^+\text{O}^- \rightarrow \text{CH}_3\text{Br}^- \rightarrow \text{CH}_3\text{OH} + \text{Br}^-
\]

- a radical reaction

\[
\text{CH}_3\text{CH}_2 + \text{Cl}^-\text{Cl}^- \rightarrow \text{CH}_3\text{CH}_2\text{Cl} + \cdot\text{Cl}
\]

Pericyclic reaction

Conjugated polyene $\Delta$ or $h\nu$ cyclic compound

- A pericyclic reaction is a concerted reaction that proceeds through a cyclic transition state.
- Pericyclic reactions require light or heat and are completely stereospecific; that is, a single stereoisomer of the reactant forms a single stereoisomer of the product.
**Pericyclic Reaction I**

An electrocyclic reaction in which a new \(\sigma\) bond is formed between the ends of a conjugated \(\pi\) system.

\[
\text{1,3,5-hexatriene} \xrightarrow{\Delta} \text{1,3-cyclohexadiene}
\]

The product has one fewer \(\pi\) bond than the reactant.

**Pericyclic Reaction II**

A cycloaddition reaction between two compounds with \(\pi\) bonds to form a cyclic product with two new \(\sigma\) bonds.

\[
\text{1,3-butadiene} + \text{ethene} \rightarrow \text{cyclohexene}
\]

The product has two fewer \(\pi\) bonds than the sum of the \(\pi\) bonds in the reactants.

**Pericyclic Reaction III**

A sigmatropic rearrangement where a \(\sigma\) bond is broken in the middle of the \(\pi\) system, and a new \(\sigma\) bond is formed in the product, with the \(\pi\) bonds rearranging.

\[
\text{product and reactant have the same number of } \pi \text{ bonds}
\]

A \(\sigma\) bond is broken at the end of the \(\pi\) system, and a new \(\sigma\) bond is formed in the product, with the \(\pi\) bonds rearranging.
Characteristic features of pericyclic reactions

1. Bonding changes must be concerted i.e; all bonds breaking and bond forming steps are simultaneous but not necessarily synchronous. That means all that bond breaking and making may not occur to the same extent at all states during the formation of transition state.
2. Pericyclic reactions are reversible in nature and follow the microscopic reversibility path.
3. The reaction involves no distinct polar intermediates during the course of the reaction.
4. Reaction proceeds in a single step through the formation of non polar transition state.
5. There is little solvent effect on the rate of pericyclic reactions (unless the reactants themselves happen to be charged species) and normally occur in the gas phase with no solvent.
6. There is no nucleophilic or electrophilic component.

Characteristic features continued

7. Normally no catalyst is needed to promote the reactions. However, many transition metal complexes can catalyze pericyclic reactions by virtue of their d-orbital participation.
8. Pericyclic reactions normally show very high stereoselectivity and regioselectivity.
9. No. of sigma and or pi electrons are important in predicting the stereochemistry of the products.
10. Pericyclic reactions can be promoted by light as well as heat. The stereochemistry of products under two sets of conditions is different and it is just opposite.

Note

- The electrocyclic reactions and sigmatropic rearrangements are intramolecular reactions
- The cycloaddition reactions are usually intermolecular reactions

Common features among the three pericyclic reactions

- are concerted reactions
- are highly stereoselective
- Usually not affected by catalysts

The configuration of the product depends on:

- the configuration of the reactant
- the number of conjugated double bonds or pairs of electrons in the reacting system
- whether the reaction is a thermal or a photochemical reaction
- A photochemical reaction takes place when a reactant absorbs light
- A thermal reaction takes place without the absorption of light
Frontier orbitals and orbital symmetry
Woodward-Hoffman rules

1. Reaction occurs when the HOMO of one reactant overlaps with the LUMO of the other. When different molecules react, it makes no difference whose HOMO or LUMO is selected.

2. Only the terminal $p$ AO's of the interacting molecular orbitals are considered because they overlap to form two new sigma bonds in the resulting ring.

Cycloadditions
Cycloadditions are classified according to the number of $p$ electrons that interact in the reaction:
1. [4+2] or [4n+2]
2. [2+2] or [4n]

Diels-Alder, [4 + 2] cycloaddition

\[
\begin{array}{c}
\text{diene} + \text{dienophile} \rightarrow \text{cyclohexene}
\end{array}
\]

1. diene must be sigma-cis or s-cis
2. syn- addition

Alkene that is attracted to dienes is referred to as dienophile

\[
\text{CO}_2\text{Me} \quad \text{\textbullet} \quad \text{CO}_2\text{Me}
\]

The conformation sigma-cis or s-cis means the two $p$ bonds are cis with respect to the sigma/single bond.

The s-cis conformation of a 1,3-diene permits the formation of a six member ring.
Constructing MO diagram of polyene systems

1. Although there are C-C and C-H sigma bonds present in the molecule, the π MO's can be constructed independently of them. The MO levels of the sigma framework are relatively unaffected.

2. For a conjugated polyene system containing \( n \) (\( n = \text{even} \)) π electrons, there will be \( n/2 \) π bonding molecular orbitals that are filled MOs and \( n/2 \) antibonding MOs that are empty in the ground state electronic configuration of the molecule.

3. The lowest energy MO has zero nodes, the next higher one has one node and the second higher has two nodes and so on. The \( n \)th MO will have \((n-1)\) nodes.

4. The nodal points are found at the most symmetric points in a MO. For example the π MO of butadiene has a node at the center of the bond connecting C2 and C3. It is incorrect to assign this node to the center of the bond connecting C1 and C2.

Note

- A MO is bonding if the number of bonding interactions is greater than the number of nodes.
- A MO is antibonding if the number of bonding interactions is fewer than the number of nodes.
- The normal electronic state of a molecule is known as its ground state.
- The ground state electron can be promoted from its HOMO to its LUMO by absorption of light (excited state).
- In a thermal reaction the reactant is in its ground state; in a photochemical reaction, the reactant is in its excited state.
Rules for Cycloadditions - Suprafacial Cycloadditions

❖ The terminal $\pi$ lobes of the two reactants must have the correct symmetry for bonding to occur.

❖ Suprafacial cycloadditions take place when a bonding interaction occurs between lobes on the same face of one reactant and lobes on the same face of the other reactant.

(a) Suprafacial

Lobes on same face

Or

(b) Antarafacial

Lobes on opposite faces

Lobes on same face

Twist

Rules for Cycloadditions - Antarafacial Cycloadditions

❖ These take place when a bonding interaction occurs between lobes on the same face of one reactant and lobes on opposite faces of the other reactant (not possible unless a large ring is formed).

Cycloaddition: Diels-Alder Reaction (thermal)

An Allowed [4+2] Cycloaddition

[4 + 2] cycloaddition (thermal)

overlapping orbitals have the same color (are in-phase)
Thermal

\[ \text{HOMO} = \psi_2 \]

\[ \text{LUMO} = \psi_3 \]

\[ [4 + 2] \text{ cycloaddition (thermal)} \]

\[ \Delta \]

\[ \text{Forbidden!} \]

\[ [4 + 2] \text{ cycloaddition (thermal)} \]

Photochemical

\[ \text{HOMO}^* = \psi_3 \]

\[ \text{LUMO} = \psi_3 \]

\[ \text{HOMO} = \psi_1 \]

\[ \text{LUMO} = \psi_2 \]

\[ \text{HOMO}^* = \psi_3 \]

\[ \text{Forbidden!} \]

In a photochemical reaction, orbital \text{HOMO}^* (the first excited state) takes place in reaction

\[ \text{HOMO}^* = \psi_3 \]

\[ \text{LUMO} = \psi_3 \]

\[ \text{allowed} \]
### [2+2] Cycloadditions

- Only the excited-state HOMO of one alkene and the LUMO can combine by a suprafacial pathway in the combination of two alkenes.

#### A [2 + 2] Cycloaddition Reaction

\[
\text{alkene} + \text{alkene} \xrightarrow{\Delta} \text{no reaction}
\]

\[
\text{alkene} + \text{alkene} \xrightarrow{h\nu} \text{cycloaddition}
\]

---

**What are the possible products that could result from the thermal cycloaddition of F_2C=CCl_2?**

In order for this to be thermal reaction it cannot be pericyclic, but it occurs in in two steps.

\[
\begin{align*}
2F_2C=CCl_2 &\xrightarrow{\text{heat}} F_2C\cdots Cl_2C\cdots CCl_2 \text{ less stable or does not form} \\
&\xrightarrow{\text{heat}} F_2C\cdots Cl_2C\cdots CCl_2
\end{align*}
\]

---

**Woodward-Hoffmann rule for cycloaddition**

<table>
<thead>
<tr>
<th>No. of electrons</th>
<th>Reactions in ground state (thermal)</th>
<th>Reactions in excited state (photochemical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4n</td>
<td>supra-supra forbidden</td>
<td>supra-supra allowed</td>
</tr>
<tr>
<td>4n+2</td>
<td>supra-supra allowed</td>
<td>supra-supra forbidden</td>
</tr>
</tbody>
</table>

**Antarafacial ring closure is symmetry-allowed, if it occur only with large ring**
Stereochemistry of Cycloadditions

- HOMO of one reactant combines with LUMO of other
- The stereochemistry of the diene or dienophile is retained (stereospecific)

Because a Diels-Alder reaction follows a concerted, suprafacial pathway, the stereochemistry of the diene is retained (stereospecific) in the Diels-Alder product.

Electrocyclic Reactions

- These are pericyclic processes that involve the cyclization of a conjugated polyene
- One \( \pi \) bond is broken, the other \( \pi \) bonds change position, a new \( \sigma \) bond is formed, and a cyclic compound results
- Gives specific stereoisomeric outcomes related to the stereochemistry and orbitals of the reactants
Electrocyclic Reactions

The signs on the outermost lobes must match to interact
- The lobes of like sign can be either on the same side or on opposite sides of the molecule.
- For a bond to form, the outermost $\pi$ lobes must rotate so that favorable bonding interaction is achieved.

Disrotatory orbital rotation
- If two lobes of like sign are on the same side of the molecule, the two orbitals must rotate in opposite directions—one clockwise, and one counterclockwise.
- Woodward called this a disrotatory opening or closure.

Conrotatory orbital rotation
- If lobes of like sign are on opposite sides of the molecule: both orbitals must rotate in the same direction, clockwise or counterclockwise.
- Woodward called this motion conrotatory.
Only the symmetry of the HOMO is important in determining the course of the reaction.

Molecular orbitals 1,3-butadiene (thermal)

Disrotatory ring closure

Conrotatory ring closure

HOMO is symmetric

HOMO is asymmetric

Photochemical electrocyclic reaction

In a photochemical electrocyclic reaction, the important orbital is HOMO * (the first excited state):
Molecular orbitals hexatriene (photochemical)

\[ \text{HOMO*} \]

\[ \text{HOMO} \]

\[ \text{HOMO}^* \]

\[ \text{Butadiene} \]

\[ \text{Cyclobutene} \]

\[ \text{Butadiene} \]

\[ \text{Cyclobutene} \]

\[ \text{SCCH}_3 \]

\[ \text{SCCH}_3 \]

\[ \text{HOMO}^* \]

\[ \text{HOMO} \]

\[ \text{HOMO*} \]

\[ \text{E,E} \]

\[ \text{E,E} \]

\[ \text{1,3} \]

\[ \text{1,3} \]

\[ \text{SCCH}_3 \]

\[ \text{SCCH}_3 \]

\[ \text{E,Z} \]

\[ \text{E,Z} \]

\[ \text{1,3,5} \]

\[ \text{1,3,5} \]

\[ \text{SCCH}_3 \]

\[ \text{SCCH}_3 \]

\[ \text{SCCH}_3 \]

\[ \text{SCCH}_3 \]

\[ \text{HOMO}^* \]

\[ \text{HOMO} \]

\[ \text{HOMO*} \]

\[ \text{E,Z,E} \]

\[ \text{E,Z,E} \]
Electrocyclic interconversions with octatriene

- **(2E,4Z,6E)-2,4,6-Octatriene**
  - Heat
  - cis-5,6-Dimethyl-1,3-cyclohexadiene

- **(2E,4Z,6Z)-2,4,6-Octatriene**
  - Heat
  - trans-5,6-Dimethyl-1,3-cyclohexadiene

Ring closure of conjugated trienes

- Involves lobes of like sign on the same side of the molecule and disrotatory ring closure

Rules for electrocyclic reactions

**Stereochemical rules for electrocyclic reactions**

<table>
<thead>
<tr>
<th>Electron pairs (Total electrons)</th>
<th>Thermal reaction</th>
<th>Photochemical reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Even number (4n)</td>
<td>Conrotatory</td>
<td>Disrotatory</td>
</tr>
<tr>
<td>Odd number (4n+2)</td>
<td>Disrotatory</td>
<td>Conrotatory</td>
</tr>
</tbody>
</table>
Stereochemical rules for electrocyclic reactions

<table>
<thead>
<tr>
<th>Electron pairs (Total electrons)</th>
<th>G. Terminal carbons</th>
<th>Thermal reaction</th>
<th>Photochemical reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Even number (4n)</td>
<td>E,E</td>
<td>Trans</td>
<td>Cis</td>
</tr>
<tr>
<td></td>
<td>E,Z</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odd number (4n+2)</td>
<td>E,E</td>
<td>Cis</td>
<td>Trans</td>
</tr>
<tr>
<td></td>
<td>E,Z</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sigmatropic rearrangements

- A σ-bonded substituent atom or group migrates across a π electron system from one position to another.
- A σ bond is broken in the reactant, the π bonds move, and a new σ bond is formed in the product.

Sigmatropic notation

- Numbers in brackets refer to the two groups connected by the σ bond and designate the positions in those groups to which migration occurs.
- In a [1,5] sigmatropic rearrangement of a diene migration occurs to position 1 of the H group (the only possibility) and to position 5 of the pentadienyl group.
In a [3,3] Claisen rearrangement migration occurs to position 3 of the allyl group and also to position 3 of the vinylic ether.

A [1,5] sigmatropic rearrangement involves three electron pairs (two $\pi$ bonds and one s bond).

Orbital-symmetry rules predict a suprafacial reaction.

5-methylcyclopentadiene rapidly rearranges at room temperature.

Migration of a group across the same face of the $\pi$ system is a suprafacial rearrangement.

Migration of a group from one face of the $\pi$ system to the other face is called an antarafacial rearrangement.
Suprafacial migration of H

- [1,3] Forbidden
- [1,5] Allowed
- [1,7] Forbidden

Suprafacial migration of R

- [1,3] allowed with inversion of configuration
- [1,5] allowed with retention of configuration
- [1,7] allowed with inversion of configuration

= node, number of nodes \( n = n+1 \)
where, \( n = \) orbital energy level
For e.g., for \( \alpha \), no. of nodes \( n = 1 \)
Woodward-Hoffmann rules for sigmatropic rearrangements

<table>
<thead>
<tr>
<th>Number of pair of electrons in the reacting system</th>
<th>Reaction conditions</th>
<th>Allowed mode of ring closure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Even number</td>
<td>Thermal</td>
<td>Antarafacial</td>
</tr>
<tr>
<td></td>
<td>Photochemical</td>
<td>Suprafacial</td>
</tr>
<tr>
<td>Odd number</td>
<td>Thermal</td>
<td>Suprafacial</td>
</tr>
<tr>
<td></td>
<td>Photochemical</td>
<td>Antarafacial</td>
</tr>
</tbody>
</table>

Although, antarafacial ring closure is symmetry-allowed, it can occur only with larger rings (more than six)

Consider the transition state of the reaction,
❖ Sigmatropic rearrangements have cyclic transition states
❖ Rearrangement must be suprafacial if the transition state has six or fewer atoms in the ring

Sigmatropic rearrangements
Migration of hydrogen

- When the total number of electrons = 4n + 2 ➔ Suprafacial
- When the total number of electrons = 4n ➔ Antarafacial

Sigmatropic rearrangements
Migration of hydrogen

A thermal, concerted [1,7]-H shift is sometimes observed in acyclic systems because the 1,3,5-triene system is floppy enough to allow the H to migrate from the top face to the bottom face (making the triene antarafacial component).
Migration of carbon using one lobe

Suprafacial and antarafacial migration of carbon with carbon using the same lobe to bond to its destination position that it uses to bond to its original position.

When carbon uses only one lobe to migrate in a sigmatropic rearrangement, it must migrate suprafacially when an odd number of electron pairs are involved in the migration (symmetric HOMO) and antarafacially when an even number of electron pairs are involved in the migration (antisymmetric HOMO). This type of migration results in retention of configuration at the migrating carbon.

The preference for [1,5]-H shifts over [1,3]-H shifts has been demonstrated in many times. Heating of 3-deuterioindene (I) causes three non-aromatic positions.

Formation of II cannot account for on the basis of [1,3] shifts; migration of D would yield I; migration of H would yield only III.

Migration of carbon using both lobes

Suprafacial and antarafacial migration of carbon with carbon using the opposite lobe to bond to its destination position from the one that it uses to bond to its original position.

When carbon uses both lobes to migrate in a sigmatropic rearrangement, it must migrate antarafacially when an odd number of electron pairs are involved in the migration (symmetric HOMO) and suprafacially when an even number of electron pairs are involved in the migration (antisymmetric HOMO). This type of migration results in inversion of configuration at the migrating carbon.
[1,3] sigmatropic rearrangement of carbon requires inversion of configuration about a chiral center:

![Deuterium-labeled bicyclo[3.2.0]heptene](image)

- Suprafacial migration with retention of configuration of the migrating group would again be forbidden.
- An antarafacial migration with retention, while theoretically allowed would be very unlikely to occur.
- A suprafacial migration forming a new bond to the "back" lobe of the migrating orbital would also be theoretically allowed. This process would result in inversion of the configuration of the migrating group.

**Sigmatropic rearrangements**

**Migration of carbon**

- [1,3] alkyl shift → antarafacial retention or suprafacial inversion
- [1,5] alkyl shift → antarafacial inversion or suprafacial retention
- [1,7] alkyl shift → antarafacial retention or suprafacial inversion

**[3,3] Sigmatropic Rearrangements**

(migration of allyl across allyl)

X = C, Cope Rearrangement
X = O, Claisen Rearrangement
X = C and a hydroxyl attached to that C, Oxy-Cope Rearrangement
4. Cheletropic reactions

Cheletropic reactions are those cycloaddition reactions in which one of the components interacts through a single atom.

It can also be defined as the extrusion of a neutral molecule like CO, C2H4, SO2, C2H2 etc. under thermal or photochemical condition.

5. Group transfer reactions

Group transfer reactions are characterized by transfer of a group or groups from one molecule to another (intermolecular group transfer) or one part of the molecule to another part of the same molecule (intramolecular group transfer). Ene or alder ene reaction is the example of such reaction.