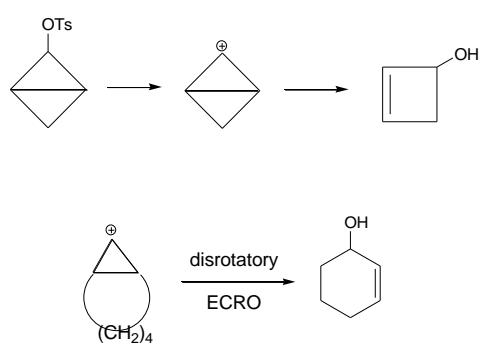
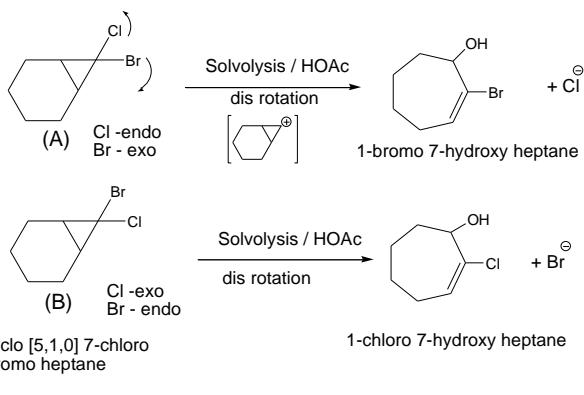
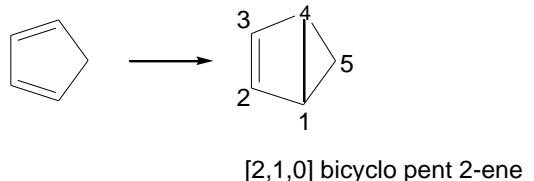
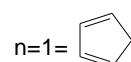
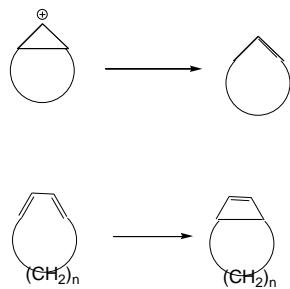
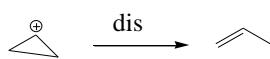


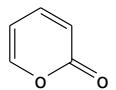
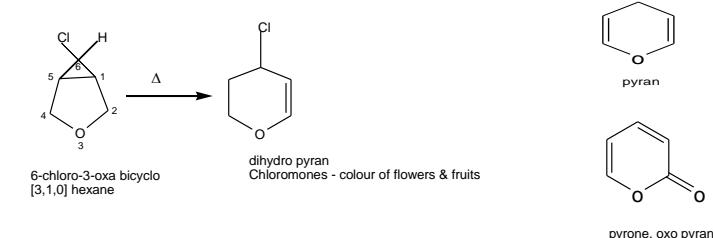
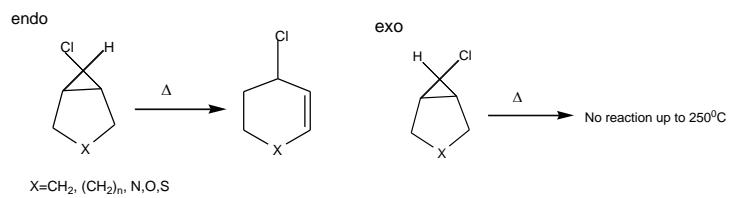
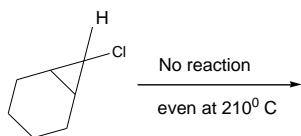
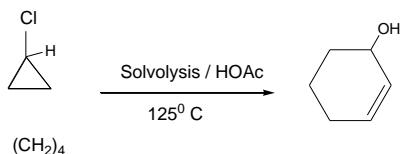
Examples of Electrocyclic Reaction

	Thermal(Δ)	Photochemical($h\nu$)
$4n$	conrotatory	disrotatory
$4n + 2$	disrotatory	conrotatory

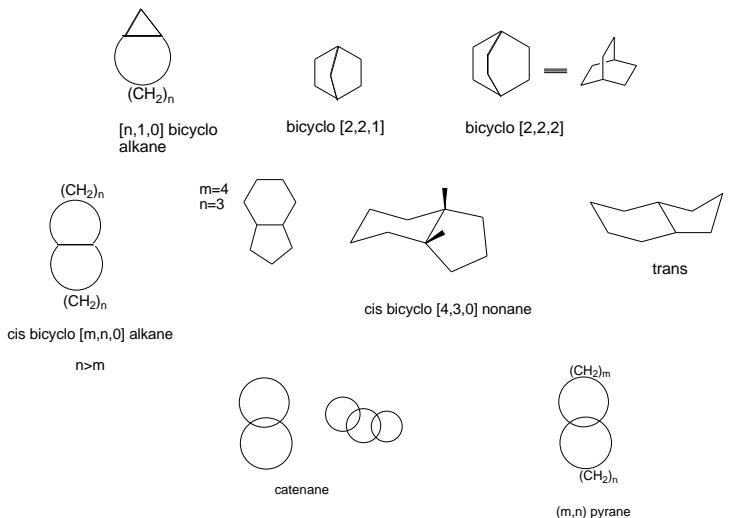
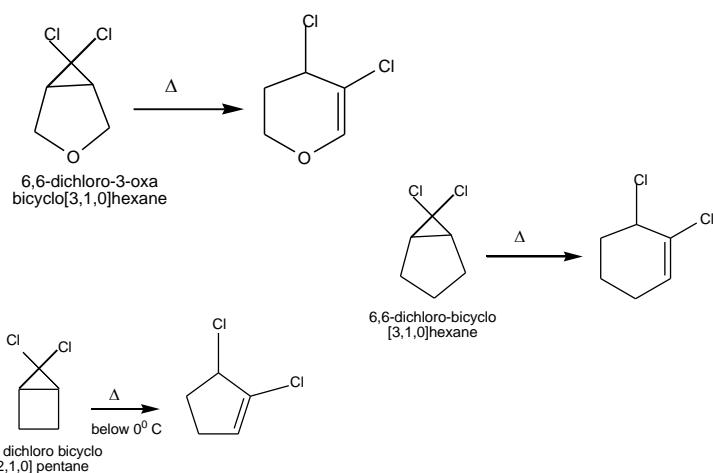


The driving force in solvolysis is ring expansion of small membered ring

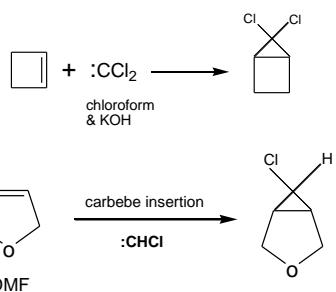
Endo group participates in solvolysis



This conclusively show the endo preference of EC ring opening reaction

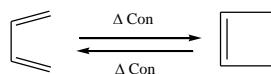


Ring strain is very high --- relief of ring strain plays key role

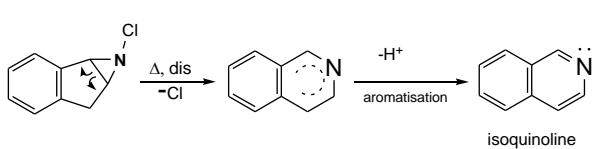
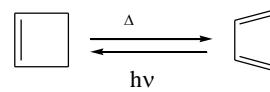


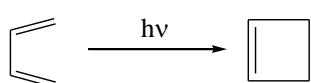
4π systems are conrotatory under thermal condition

Butadiene \rightleftharpoons Cyclobutene

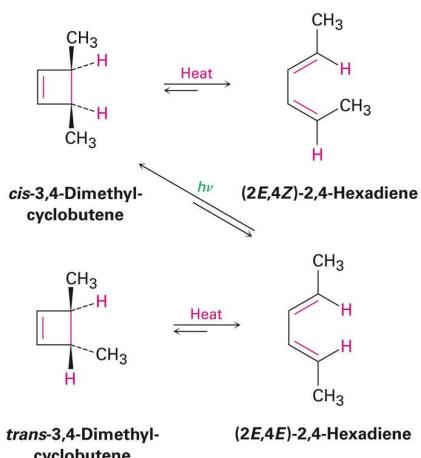
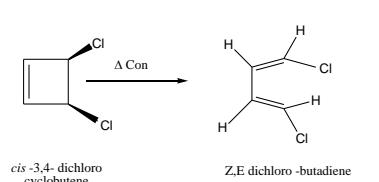
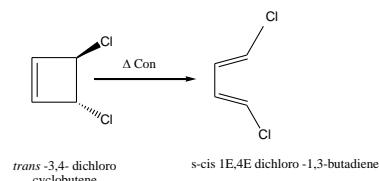
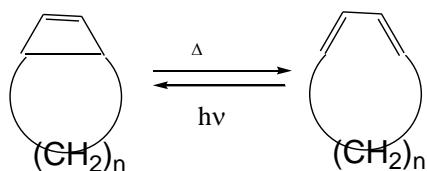


thermal cleavage of cyclobutene to butadiene is preferred
 the reverse reaction is not so favoured



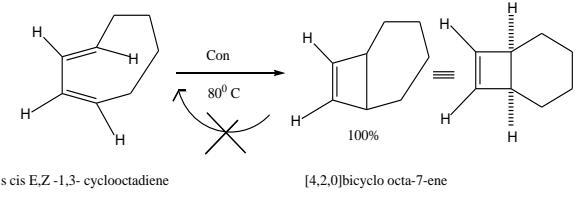


more favoured system



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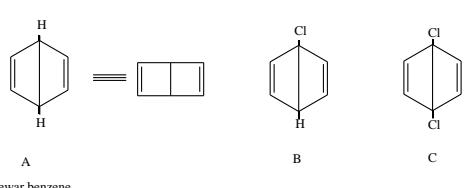
The reverse process is sometimes preferred



[4,2,0]bicyclo octa-7-ene

It must be cis at fused points (can't be trans)

Cyclobutene is highly strained but when a 5 or 6 membered ring is fused to it, it gets extra ordinary stability and resists to undergo ring cleavage.



Dewar benzene
fused cyclobutene

B undergoes cleavage most easily

	ΔH KJ/mol
	→ A 96
	→ B 80
	→ C 127

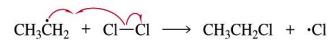
Reactions of Organic Compounds

Unit 3: Pericyclic Reaction

a polar reaction



a radical reaction



A pericyclic reaction, a reaction that occurs as a result of reorganizing the electrons in the reactant(s)

Concerted Reaction

- Concerted reaction is always a **single step process** and proceeds via **transition state** and does not proceed through any **intermediate**.
- Not affected by solvent, cationic/ anionic species.
- Bond breaking and bond formation are **synchronous** process.
- All pericyclic reactions are concerted but all concerted reactions are not pericyclic.
- e.g. $\text{S}_{\text{N}}2$ reactions are not pericyclic but are concerted.
- $\text{S}_{\text{N}}2$ reactions are affected by bases, acids, solvents, reactants etc.

• Any concerted process, going from reactant(s) to product involving cyclic transition state is said to be pericyclic process.

Such process of transformation of reactant(s) to product maintains conservation of orbital symmetry between reactant(s) and product.

• The symmetries of molecular orbitals of the reactants pass on to the product molecular orbital while maintaining the bonding order. Such reactions proceed via cyclic transition state and is said to be pericyclic and also said to be symmetry allowed process. Such reactions are controlled (generally proceed) by heat (raising or lowering of temperature).

Syllabus

- Molecular orbital symmetry, Frontier orbitals of ethylene, 1,3- butadiene, 1,3,5- hexatriene and allyl system. Classification of pericyclic reactions. Woodward-Hoffmann correlation diagrams. FMO and PMO approach.
- Electrocyclic reaction – conrotatory and disrotatory motions, $4n$, $4n+2$ and allyl systems.
- Cycloaddition – antarafacial and suprafacial additions, $4n$ and $4n+2$ systems, $2+2$ addition of ketenes, 1,3 –dipolar cycloadditions and chelotropic reactions.
- Sigmatropic rearrangements - suprafacial and antarafacial shifts of H, sigmatropic shifts involving carbon moieties, 3,3- and 5,5- sigmatropic rearrangements. Claisen, Cope and aza-Cope rearrangements, Fluxional tautomerism. Ene reaction. Regioselectivity, periselectivity.

Atomic Orbitals

- Heisenberg Uncertainty Principle states that it is impossible to define what time and where an electron is and where it is going next. This makes it impossible to know exactly where an electron is traveling in an atom.
- Since it is impossible to know where an electron is at a certain time, a series of calculations are used to approximate the volume and time in which the electron can be located. These regions are called Atomic Orbitals. These are also known as the quantum states of the electrons.
- Only two electrons can occupy one orbital and they must have different spin states, $\frac{1}{2}$ spin and $-\frac{1}{2}$ spin (easily visualized as opposite spin states).
- Orbitals are grouped into subshells.
- This field of study is called quantum mechanics.

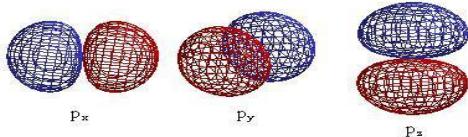
Atomic Subshells

- These are some examples of atomic orbitals:
 - s subshell: (Spherical shape) There is one S orbital in an s subshell. The electrons can be located anywhere within the sphere centered at the atom's nucleus.



<http://www.chm.davidson.edu/ronut/che115/AO.htm>

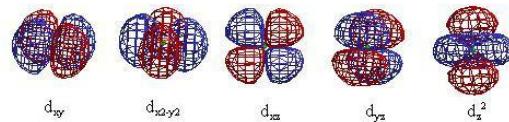
- p Orbitals: (Shaped like two balloons tied together) There are 3 orbitals in a p subshell that are denoted as p_x , p_y , and p_z orbitals. These are higher in energy than the corresponding s orbitals.



<http://www.chm.davidson.edu/ronut/che115/AO.htm>

Atomic Subshells (cont'd)

- d Orbitals: The d subshell is divided into 5 orbitals (d_{xy} , d_{xz} , d_{yz} , d_z^2 and $d_{x^2-y^2}$). These orbitals have a very complex shape and are higher in energy than the s and p orbitals.



d_{xy} d_{xz} d_{yz} $d_{x^2-y^2}$ d_z^2

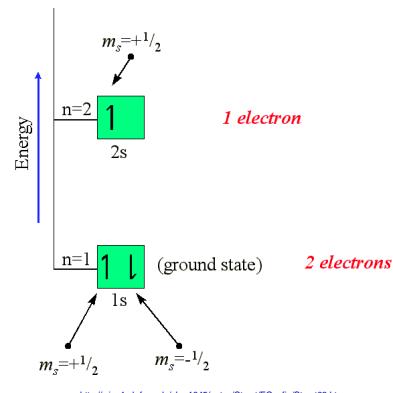
Electronic Configuration

- Every element is different.
 - The number of protons determines the identity of the element.
 - The number of electrons determines the charge.
 - The number of neutrons determines the isotope.
- All chemistry is done at the electronic level (that is why electrons are very important).
- Electronic configuration is the arrangement of electrons in an atom. These electrons fill the atomic orbitals
- Atomic orbitals are arranged by energy level (n), subshells (l), orbital (m_l) and spin (m_s).

Lithium Electronic Configuration

- The arrows indicate the value of the magnetic spin (m_s) quantum number (up for $+1/2$ and down for $-1/2$)
- The occupation of the orbitals would be written in the following way:*

$1s^2 2s^1$
or, "1s two, 2s one".



<http://wine1.sbfsu.edu/chm1045/notes/Struct/EConfig/Struct08.htm>

Electronic Configurations – Box Diagram

Element	Total Electrons	Orbital Diagram	Electron Configuration
		1s 2s 2p 3s	
H	1	1	$1s^1$
He	2	1 1	$1s^2$
Li	3	1 1 1	$1s^2 2s^1$
Be	4	1 1 1 1	$1s^2 2s^2$
B	5	1 1 1 1 1	$1s^2 2s^2 2p^1$

<http://wine1.sbfsu.edu/chm1045/notes/Struct/EConfig/Struct08.htm>

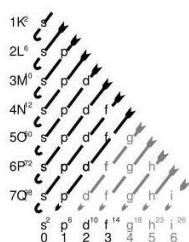
- The two electrons in Helium represent the complete filling of the first electronic shell. Thus, the electrons in He are in a very stable configuration
- For Boron (5 electrons) the 5th electron must be placed in a $2p$ orbital because the $2s$ orbital is filled. Because the $2p$ orbitals are equal energy, it doesn't matter which $2p$ orbital is filled.

Electronic Configuration

- Electronic configurations can also be written in a short hand which references the *last completed orbital shell* (i.e. all orbitals with the same principle quantum number 'n' have been filled)
 - The electronic configuration of Na can be written as $[Ne]3s^1$
 - The electronic configuration of Li can be written as $[He]2s^1$
- The electrons in the stable (Noble gas) configuration are termed *the core electrons*
- The electrons in the outer shell (beyond the stable core) are called *the valence electrons*

Electron Configuration

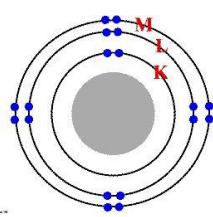
Two ways to remember the order of electrons



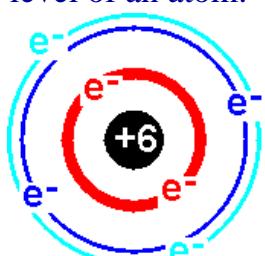
http://en.wikipedia.org/wiki/Image:Electron_orbitals.svg

Valence Electrons

- The **valence electrons** are the electrons in the last shell or energy level of an atom.



The lowest level (K), can contain 2 electrons.
The next level (L) can contain 8 electrons.
The next level (M) can contain 8 electrons.



www.uoregon.edu

Examples of Electronic Configuration

- Ne $\rightarrow 1s^2 2s^2 2p^6$ (10 electrons)
- F $\rightarrow 1s^2 2s^2 2p^5$ (9 electrons)
- F⁻ $\rightarrow 1s^2 2s^2 2p^6$ (10 electrons)
- Mg $\rightarrow 1s^2 2s^2 2p^6 3s^2$ (12 electrons)
- Mg²⁺ $\rightarrow 1s^2 2s^2 2p^6$ (10 electrons)
- Notice – different elements can have the same number of electrons

Molecular Orbital Theory

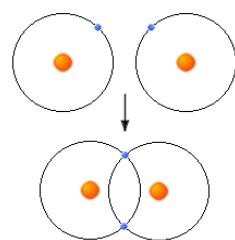
The goal of molecular orbital theory is to describe molecules in a similar way to how we describe atoms, that is, in terms of orbitals, orbital diagrams, and electron configurations.

Forming a Covalent Bond

- Molecules can form bonds by sharing electrons
 - Two shared electrons form a single bond
- Atoms can share one, two or three pairs of electrons
 - forming single, double and triple bonds
- Other types of bonds are formed by charged atoms (ionic) and metal atoms (metallic).

Atomic and Molecular Orbitals (cont'd)

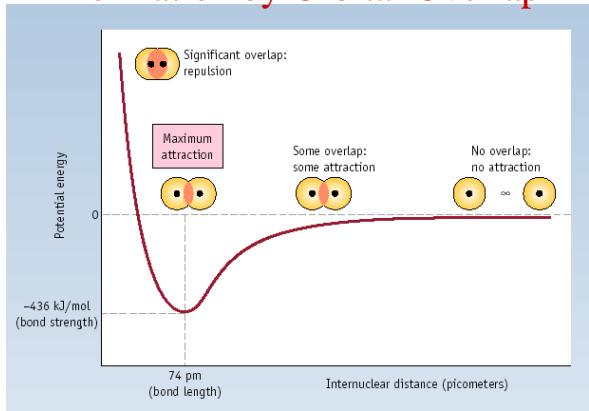
- Orbital Mixing**
 - When atoms share electrons to form a bond, their atomic orbitals mix to form molecular bonds. In order for these orbitals to mix they must:
 - Have similar energy levels.
 - Overlap well.
 - Be close together.



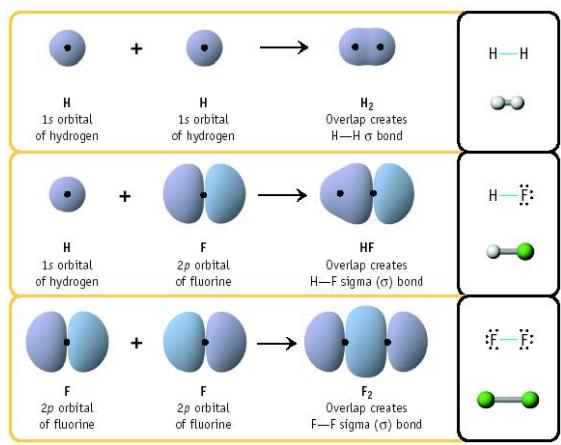
http://library.thinkquest.org/27819/ch2_2.shtml

This is an example of orbital mixing. The two atoms share one electron each from their outer shell. In this case both 1s orbitals overlap and share their valence electrons.

Energy Diagram of Sigma Bond Formation by Orbital Overlap

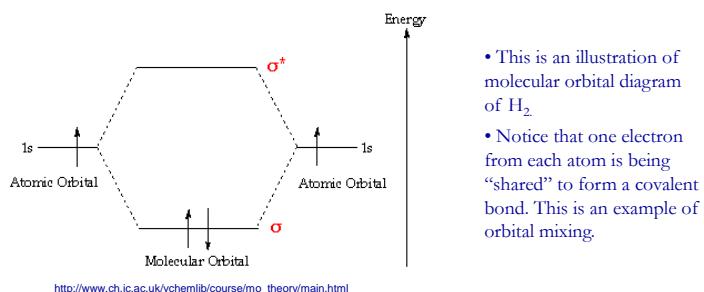


Examples of Sigma Bond Formation



Atomic and Molecular Orbitals

- In atoms, electrons occupy **atomic orbitals**, but in molecules they occupy similar **molecular orbitals** which surround the molecule.
- The two 1s atomic orbitals combine to form two molecular orbitals, one bonding (σ) and one antibonding (σ^*).



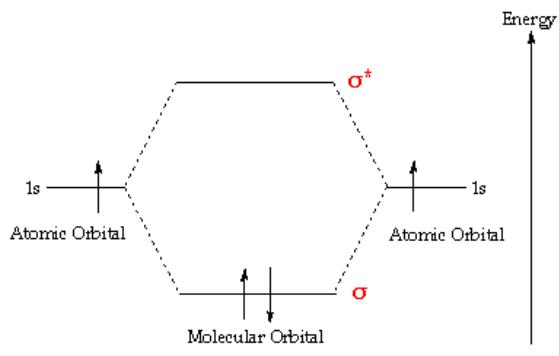
Molecular Orbital Theory

- Each line in the diagram represents an orbital.
- The molecular orbital volume encompasses the whole molecule.
- The electrons fill the molecular orbitals of molecules like electrons fill atomic orbitals in atoms

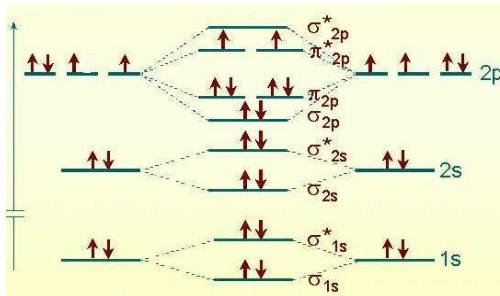
Molecular Orbital Theory

- Electrons go into the lowest energy orbital available to form lowest potential energy for the molecule.
- The maximum number of electrons in each molecular orbital is two. (Pauli exclusion principle)
- One electron goes into orbitals of equal energy, with parallel spin, before they begin to pair up. (Hund's Rule.)

Molecular Orbital Diagram (H₂)

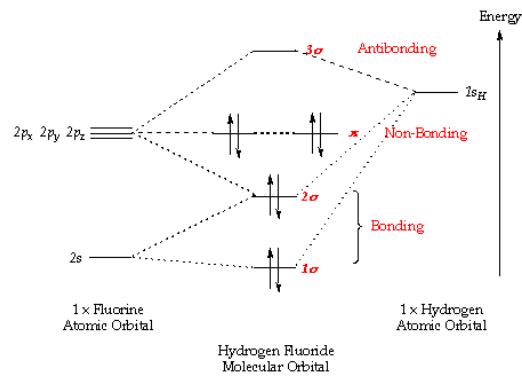


MO Diagram for O₂



<http://www.chem.uncc.edu/faculty/murphy/1251/slides/C19b/sld027.htm>

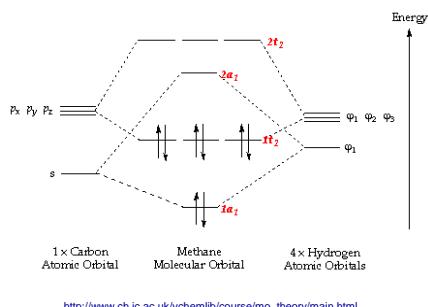
Molecular Orbital Diagram (HF)



http://www.ch.ic.ac.uk/vchemlib/course/mo_theory/main.html

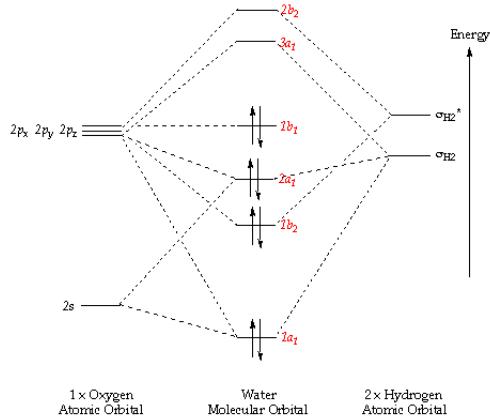
Molecular Orbital Diagram (CH₄)

So far, we have only look at molecules with two atoms. MO diagrams can also be used for larger molecules.



http://www.ch.ic.ac.uk/vchemlib/course/mo_theory/main.html

Molecular Orbital Diagram (H₂O)



Conclusions

- Bonding electrons are localized between atoms (or are lone pairs).
- Atomic orbitals overlap to form bonds.
- Two electrons of opposite spin can occupy the overlapping orbitals.
- Bonding increases the probability of finding electrons in between atoms.
- It is also possible for atoms to form ionic and metallic bonds.

Why Sharing Electron Forms Covalent Bond?



Without Electrons, Internuclei Repulsion Forces Pushes Nuclei Apart.



Sharing Electrons (in some area around the nuclei) Generates Attractive Force to Bind Nucleus Together.

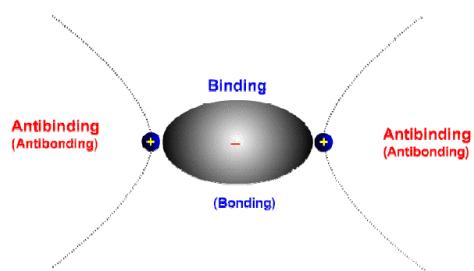
Why Sharing Electron Forms Anti-Bond?

In Some Area, Sharing Electrons Generates Repulsive Force.



Bonding and Antibonding

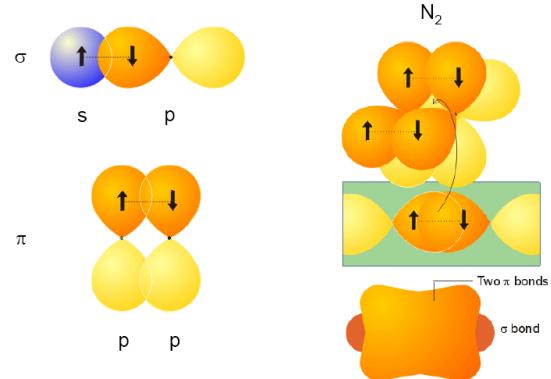
Region Around The Nuclei has **Binding** (bonding) and **Antibinding** (antibonding) Zones.



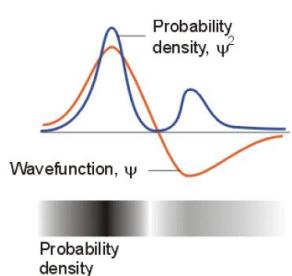
Valence Bond Theory

- **VB Theory** is a quantum mechanical model describes the distribution of electrons in bonds. Developed from **Lewis** theory and the **VSEPR** model.
- Usually provides bonding picture with **localized view**.
- Simple VB theory cannot explain bonding in polyatomic molecules. The concept of **Hybridization** is developed to explain different geometry variations. Describes molecular geometry easier.
- Using **Delocalization** and **Resonance** to explain extended distribution of electrons over many atoms in a substance.

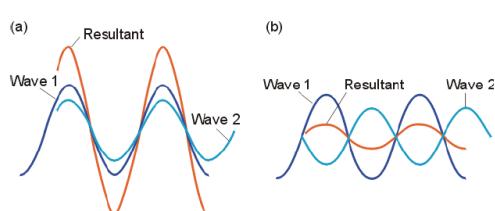
Valence Bond Theory



Square of a Wavefunction is Probability Density



Constructive and Destructive Interference

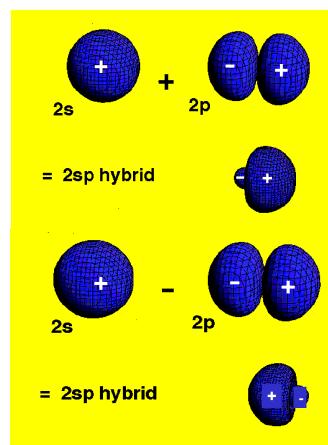


Hybridization

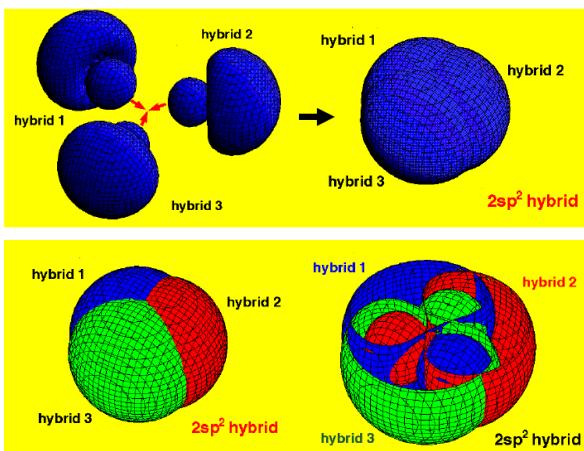
- Linear Combination of Atomic Orbitals of an Atom forms a new set of orbitals.
- Hybridization divides the electron density distribution of an atom into new areas.

$$\begin{aligned}
 \Psi(sp)A &= (1/2)^{1/2}(\psi(s) + \psi(p)) \\
 \Psi(sp)B &= (1/2)^{1/2}(\psi(s) - \psi(p)) \\
 \Psi(sp^2)A &= (1/3)^{1/2}\psi(s) + (2/3)^{1/2}\psi(px) \\
 \Psi(sp^2)B &= (1/3)^{1/2}\psi(s) - (1/6)^{1/2}\psi(px) + (1/2)^{1/2}\psi(py) \\
 \Psi(sp^2)C &= (1/3)^{1/2}\psi(s) - (1/6)^{1/2}\psi(px) - (1/2)^{1/2}\psi(py) \\
 \Psi(sp^3)A &= (1/2)(\psi(s) + \psi(px) + \psi(py) + \psi(pz)) \\
 \Psi(sp^3)B &= (1/2)(\psi(s) + \psi(px) - \psi(py) - \psi(pz)) \\
 \Psi(sp^3)C &= (1/2)(\psi(s) - \psi(px) + \psi(py) - \psi(pz)) \\
 \Psi(sp^3)D &= (1/2)(\psi(s) - \psi(px) - \psi(py) + \psi(pz))
 \end{aligned}$$

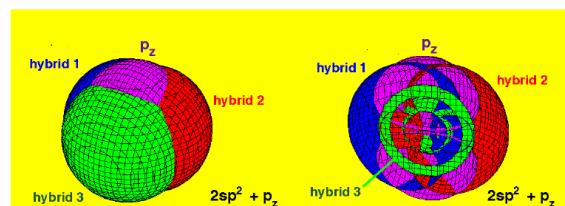
Hybridization sp



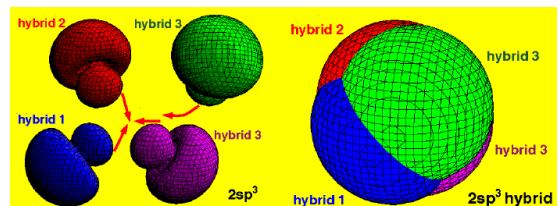
Hybridization sp^2



Hybridization $sp^2 + p$



Hybridization sp^3



Rules of Molecular Orbitals

Molecular Orbital Theory

- Electrons occupy orbitals that spread through the entire molecule.
- Providing bonding pictures with non-localized view.
- Deals with entire area surrounding a molecule.

Rules for forming bonding and antibonding MOs

number of total molecular orbitals = number of total atomic orbitals
atomic orbitals have the right symmetry
atomic orbitals overlap well
atomic orbitals have similar energy

Rules for filling electrons are the same for MOs and AOs.

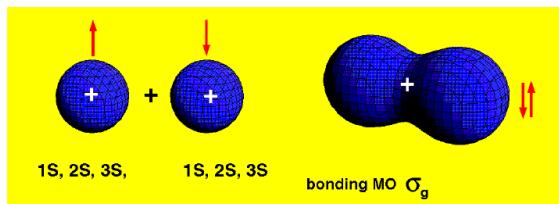
start filling from the lowest energy orbital
follows Pauli exclusion principle and Hund's rule

Provides molecular energy information

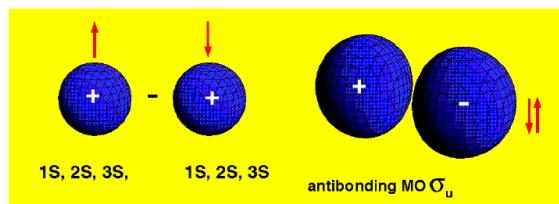
Explains magnetic behavior

Can provide molecular structural explanation, but more difficult to comprehend than VB theory

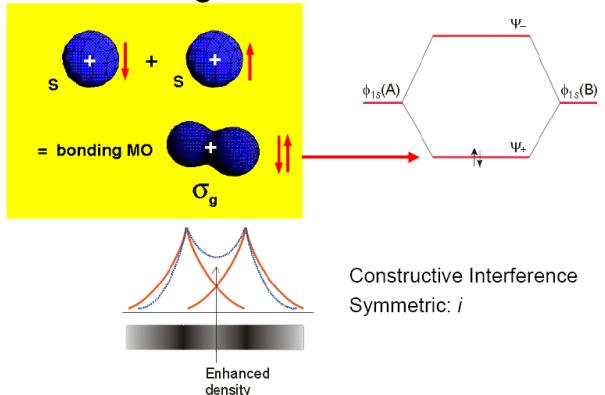
Bonding Molecular Orbitals



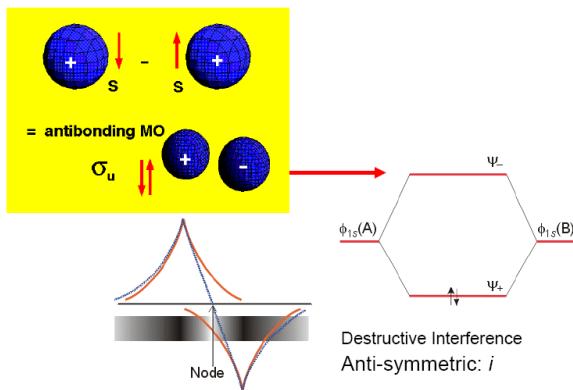
Antibonding Molecular Orbitals



Bonding Molecular Orbitals

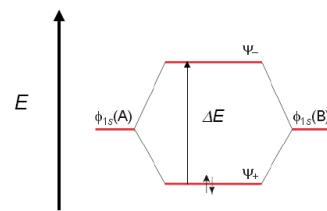


Antibonding Molecular Orbitals



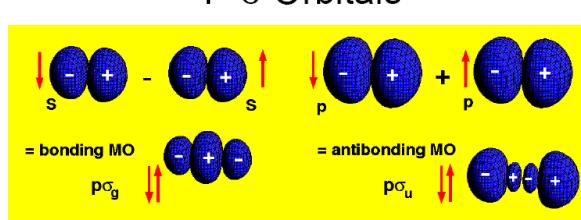
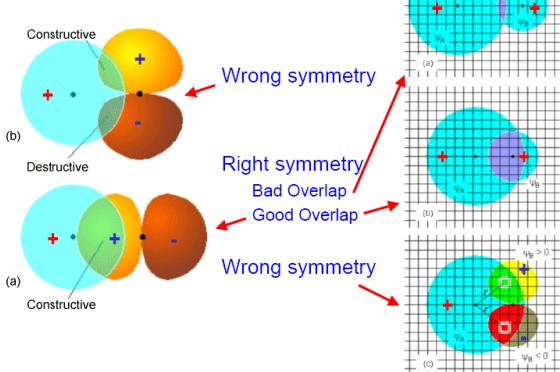
Molecular Orbital Energy Level Diagram

- Better Overlap \Rightarrow Higher ΔE
- Bond Order = $\frac{1}{2}(\# \text{ of B.O. e}^- - \# \text{ of A.O. e}^-)$
- Diamagnetic: all e^- paired
- Paramagnetic: with e^- unpaired

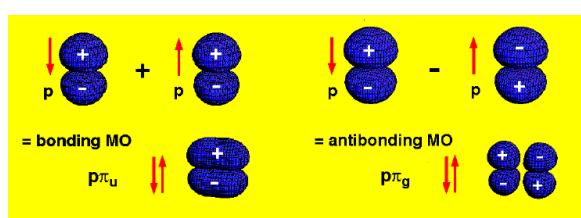


	B.O.	Magnetic Property
H_2^+	$\frac{1}{2}$	P
H_2	1	D
H_2^-	$\frac{1}{2}$	P
He_2	0	-

Overlap of MOs

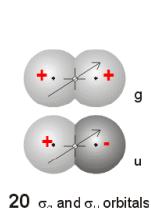


P σ Orbitals



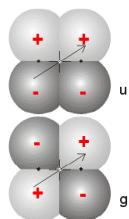
MO Symmetry

g: gerade
u: ungerade

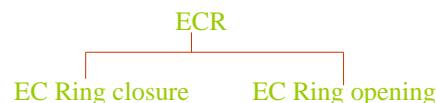


B.MO

A.MO



- Electrocyclic Reaction (ECR) is a class of pericyclic reaction and is intramolecular.

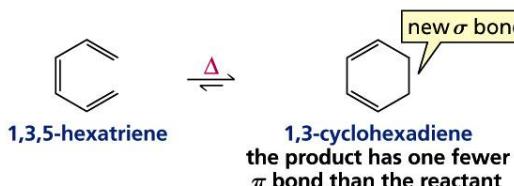


- These reactions are highly stereospecific in character
- These reactions are initiated either by heat (Δ) or by light ($h\nu$)
- Stereospecificity is also pointed by Δ or $h\nu$
- If same reaction is carried out by Δ and $h\nu$ generally different stereo products are obtained.
- Not generally affected by catalyst
- Ring closure and/or ring opening can take place either by disrotatory process or by con rotatory process but not by both – very exclusive.

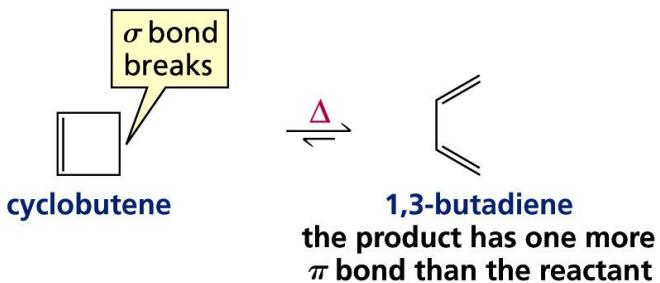
Electrocyclic Reaction

Electrocyclic Reaction

an electrocyclic reaction

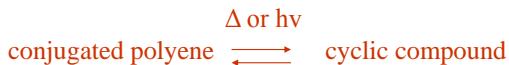


Electrocyclic Reactions Are Reversible

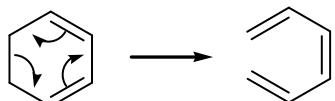
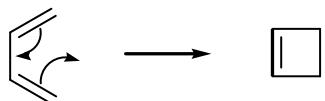


An intramolecular reaction in which a new σ bond is formed between the ends of a conjugated π system

Electrocyclic reactions:



The mechanism is **concerted!**

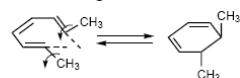


electrocyclic reaction

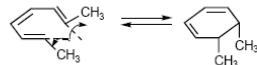
A **molecular rearrangement** that involves the formation of a σ -bond between the termini of a fully **conjugated** linear π -electron system (or a linear fragment of a π -electron system) and a decrease by one in the number of π -bonds, or the reverse of that process. For example:



The stereochemistry of such a process is termed 'conrotatory' or **antarafacial** if the substituents at the interacting termini of the conjugated system both rotate in the same sense, e.g.



or 'disrotatory' (or **suprafacial**) if one terminus rotates in a clockwise and the other in a counter-clockwise sense, e.g.



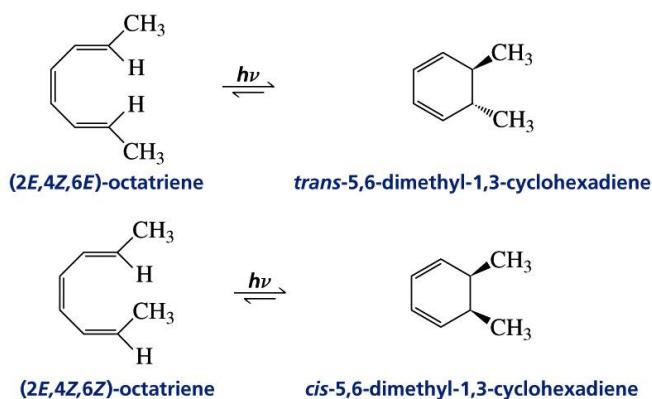
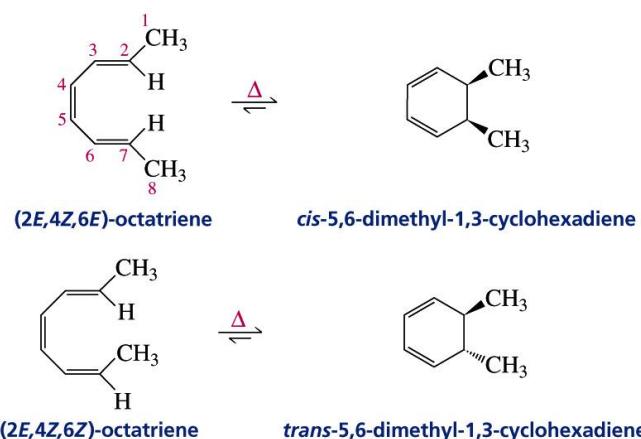
See also **pericyclic reaction**.

1994, 66, 1108

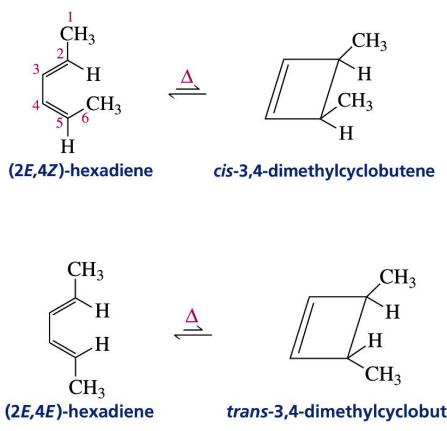
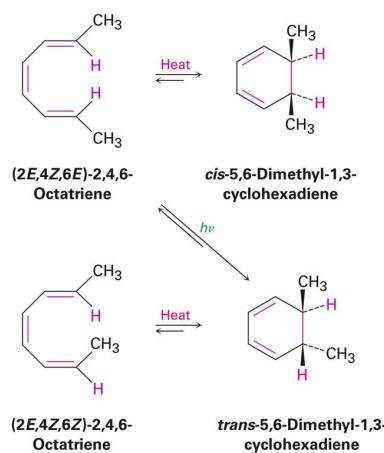
IUPAC Compendium of Chemical Terminology

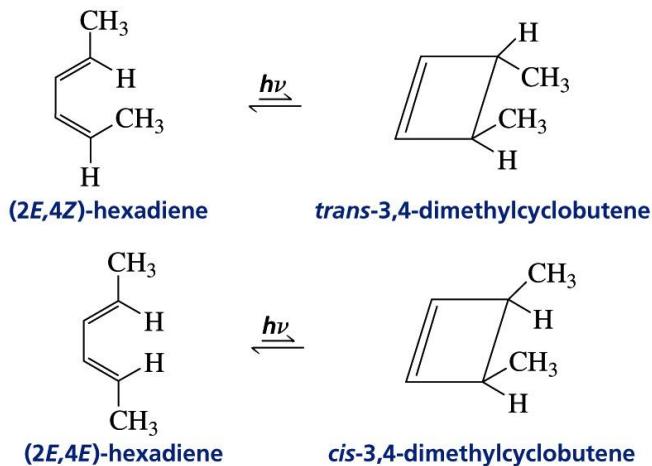
2nd Edition (1997)

An electrocyclic reaction is completely stereoselective

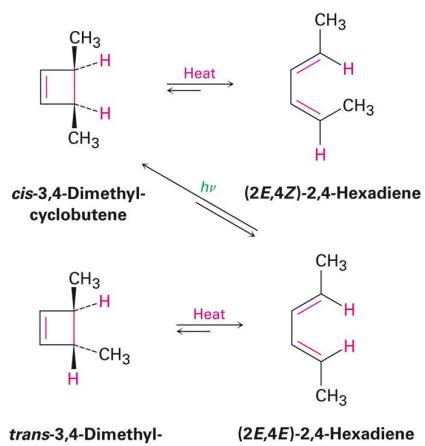


Electrocyclic Interconversions with Octatriene



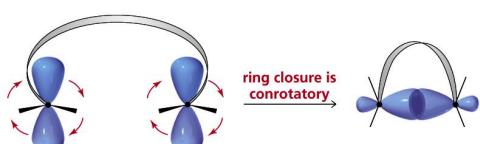


Electrocyclic Interconversions with Dimethylcyclobutene



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To form the new σ bond in the electrocyclic reaction, the π orbitals at the end of the conjugated system must overlap head-to-head



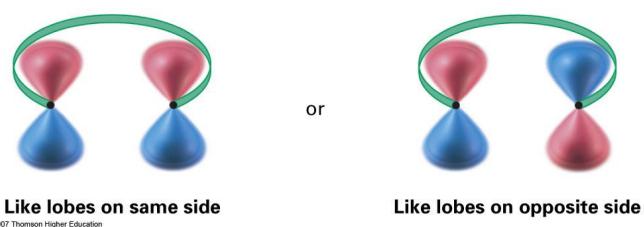
Follows C_2 symmetry



Follows mirror symmetry

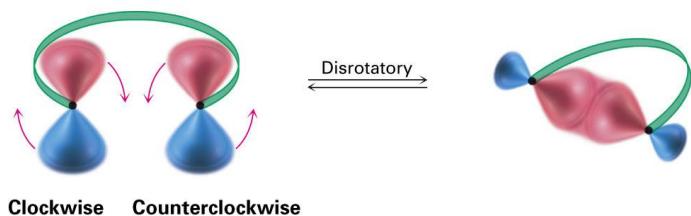
The Signs on the Outermost Lobes Must Match to Interact

- 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 π lobes must rotate so that favorable bonding interaction is achieved

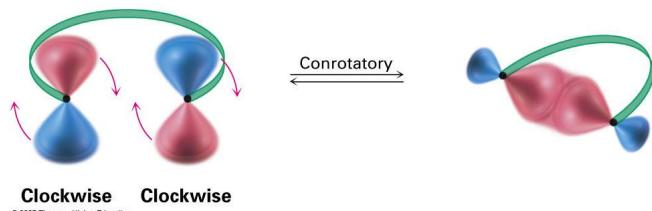


Conrotatory Orbital Rotation

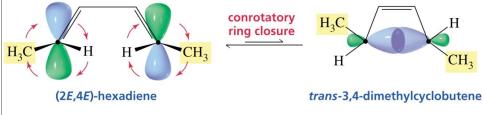
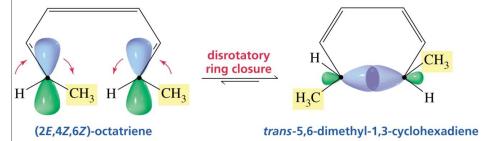
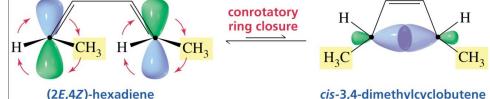
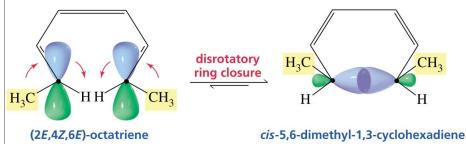
- If two lobes of like sign are on the same side of the molecule, the two orbitals must rotate in opposite directions—one clockwise, and one counterclockwise
- Woodward called this a disrotatory (dis-roh-tate'-or-ee) opening or closure



- 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 (con-roh-tate'-or-ee)

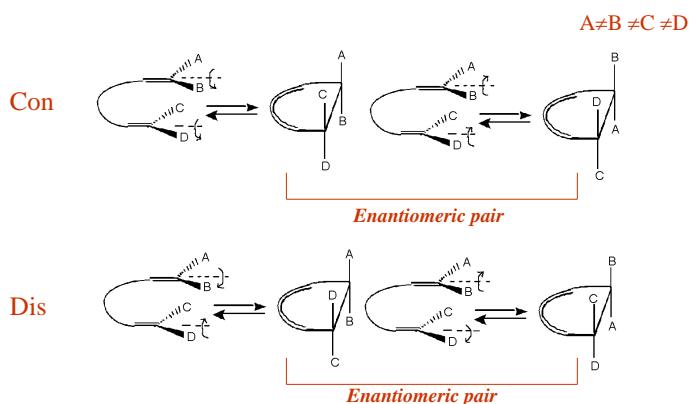


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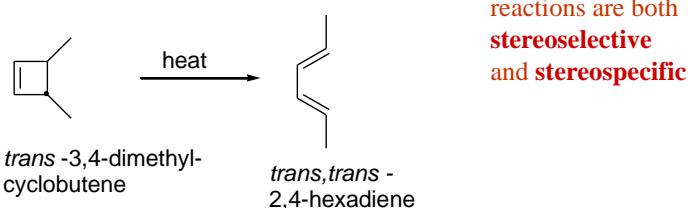
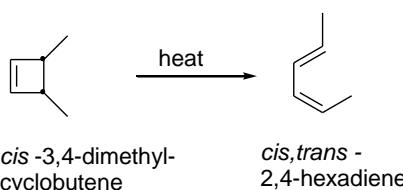
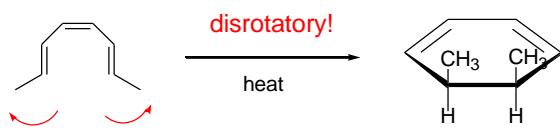
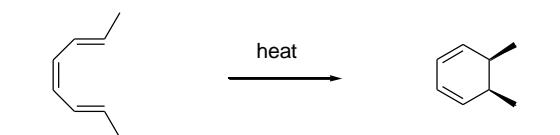
Steric Course of Electrocyclic ring closure

For different substituents at termini both dis and con motion give two types of product.

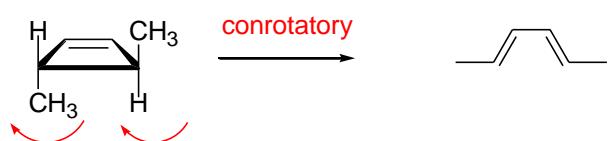


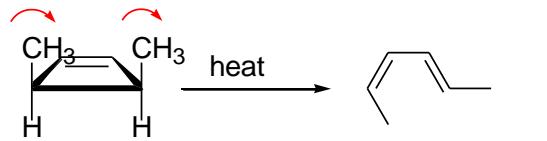
So we get racemic mixture in both cases.

If any one of the two substituents are same then two dis (or two con) products cannot be differentiated.



Electrocyclic reactions are both
stereoselective and **stereospecific**





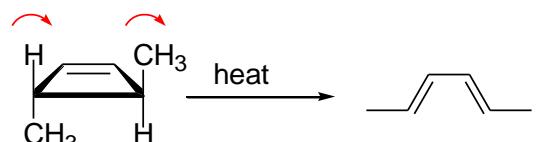
cis-3,4-dimethylcyclobutene *cis,trans*-2,4-hexadiene

geometric isomers

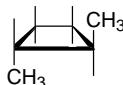


trans-

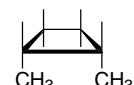
cis-



trans-3,4-dimethylcyclobutene *trans,trans*-2,4-hexadiene



trans-



cis-

Woodward – Hofmann Rules for Electrocyclic Reactions:

	Thermal(Δ)	Photochemical($h\nu$)	
4n	conrotatory	disrotatory	
4n + 2	disrotatory	conrotatory	

- If a $4n$ system proceeds by **con rotatory** process by **thermal condition** the same system proceeds by **dis rotatory** process under **photochemical condition**.
- Similarly $4n+2$ proceeds by **dis rotatory** process under **thermal condition**, it proceeds by **con rotatory** process under **photochemical condition**.

In other words,

- Thermolysis of $4n$ system** undergoes **electrocyclic ring closure** by **con rotatory process** whereas **thermolysis of a $4n+2$ system** proceeds by **dis rotatory process**.
- On the other hand the **photolysis of the $4n$ system** proceeds by **dis rotatory** while the **$4n+2$ system** proceeds by **con rotatory process**.

Frontier Molecular Orbital Theory

History

In 1952, Kenichi Fukui published a paper in the *Journal of Chemical Physics* titled "A molecular theory of reactivity in aromatic hydrocarbons." Though widely criticized at the time, he later shared the Nobel Prize in Chemistry (1981) with Roald Hoffmann for his work on reaction mechanisms. Hoffmann's work focused on creating a set of rules for pericyclic reactions in organic chemistry, based on orbital symmetry, which he coauthored with Robert Burns Woodward entitled, "The Conservation of Orbital Symmetry."



The Woodward-Hoffmann Rules

	Ground state (thermal)	Excited state (photochemical)
$4n \pi e$	Conrotatory	Disrotatory
$4n + 2 \pi e$	Disrotatory	Conrotatory

• Explanations for the Woodward-Hoffmann Rules

- FMO Theory (Fukui)
- Aromatic Transition States (Dewar-Zimmerman)
- Conservation of Orbital Symmetry (Woodward-Hoffmann)

Theory

Frontier Molecular Orbital Theory

Fukui's own work looked at the frontier orbitals, and in particular the effects of the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO) on reaction mechanisms, which led to it being called Frontier Molecular Orbital Theory (FMO Theory). He used these interactions to better understand the conclusions of the Woodward-Hoffmann rules.

Fukui realized that a good approximation for reactivity could be found by looking at the frontier orbitals (HOMO/LUMO). This was based on three main observations of molecular orbital theory as two molecules interact:

1. The occupied orbitals of different molecules repel each other.
2. Positive charges of one molecule attract the negative charges of the other.
3. The occupied orbitals of one molecule and the unoccupied orbitals of the other (especially the HOMO and LUMO) interact with each other causing attraction.

From these observations, frontier molecular orbital (FMO) theory simplifies reactivity to interactions between the HOMO of one species and the LUMO of the other. This helps to explain the predictions of the Woodward-Hoffmann rules for thermal pericyclic reactions, which are summarized in the following statement:

"A ground-state pericyclic change is symmetry-allowed when the total number of $(4q+2)_s$ and $(4r)_a$ components is odd"

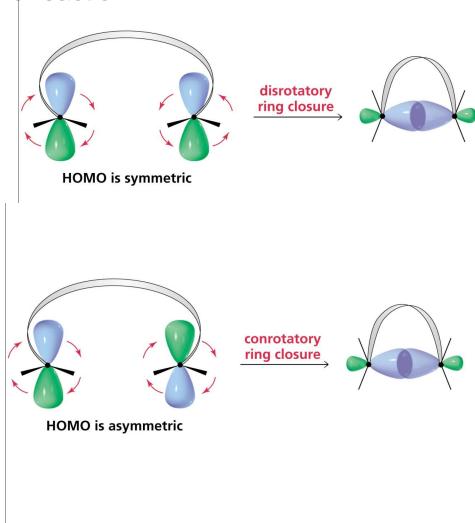
$(4q+2)_s$ refers to the number of aromatic, suprafacial electron systems; likewise, $(4r)_a$ refers to antiaromatic, antarafacial systems. It can be shown that if the total number of these systems is odd then the reaction is thermally allowed.

A symmetry-allowed pathway is one in which in-phase orbitals overlap

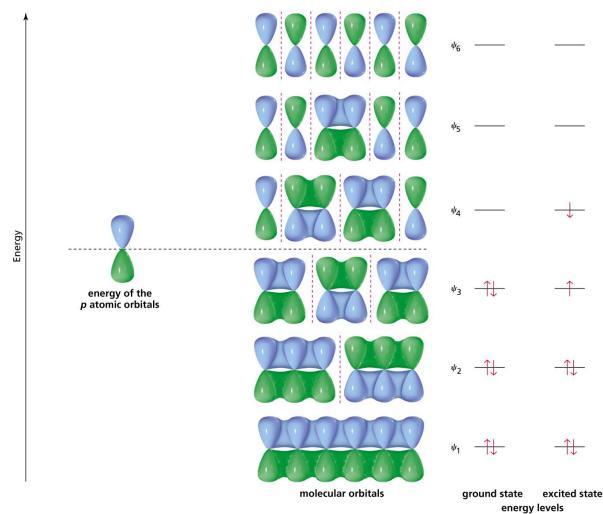
If a reaction is symmetry-forbidden, it cannot take place by a concerted pathway

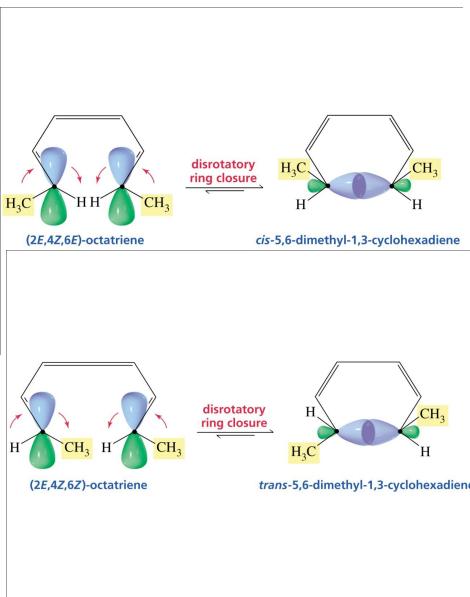
The symmetry of the HOMO of the compound undergoing ring closure controls the stereochemical outcome of an electrocyclic reaction

Only the symmetry of the HOMO is important in determining the course of the reaction

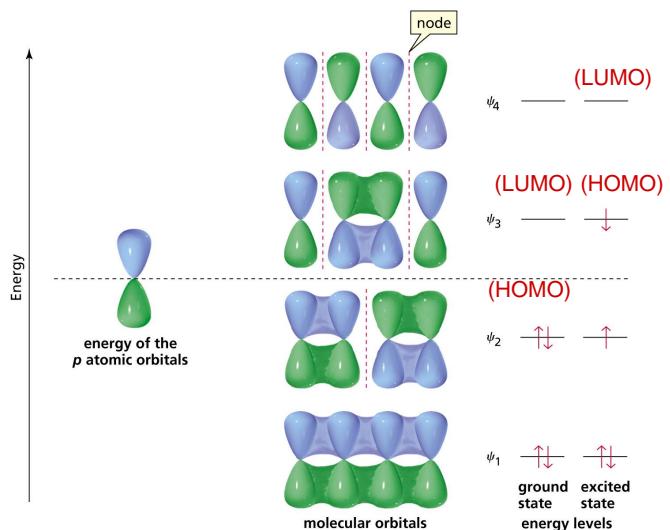


A Molecular Orbital Description of 1,3,5-hexatriene



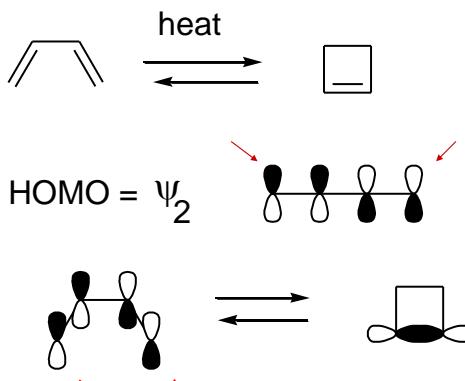
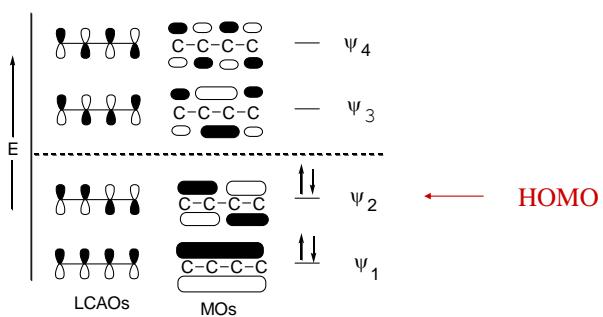


Four p atomic orbitals interact to give the four p MOs of 1,3-butadiene

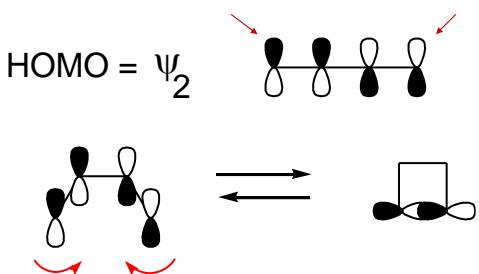


In the concerted electrocyclic reactions, symmetry must be conserved for bonding to take place.

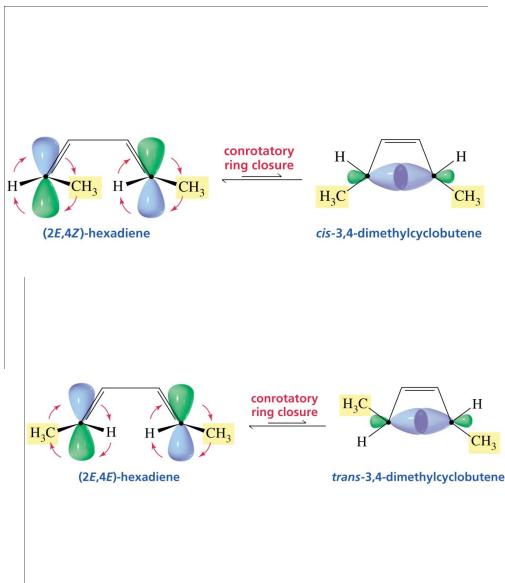
The molecular orbital involved = highest occupied molecular orbital in the polyene. **HOMO**



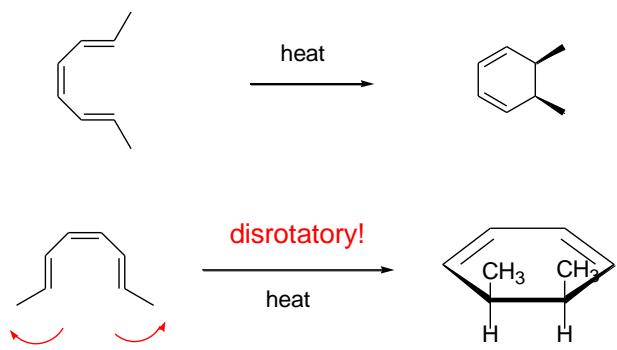
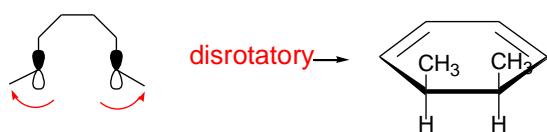
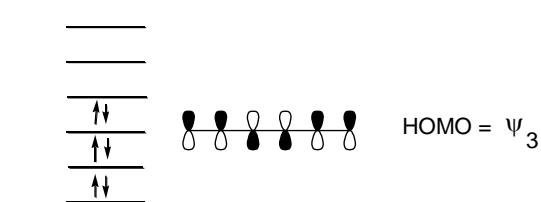
motion must be **conrotatory** for bonding



disrotatory motion would result in antibonding



HOMO (polyene) = ? 6 AO \rightarrow 6 MO 6 e⁻

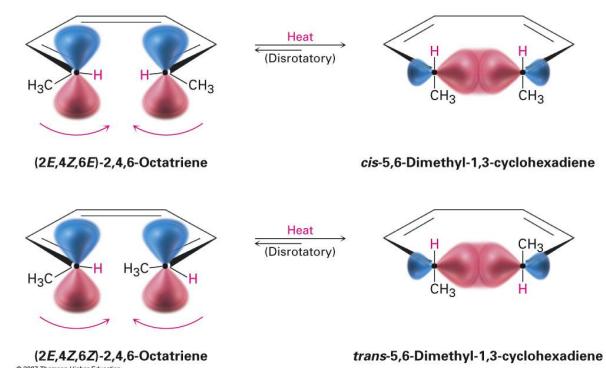


Stereochemistry of Thermal Electrocyclic Reactions

- Determined by the symmetry of the polyene HOMO
- The ground-state electronic configuration is used to identify the HOMO
- (Photochemical reactions go through the excited-state electronic configuration)

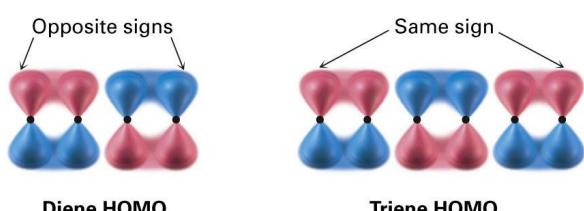
Ring Closure of Conjugated Trienes

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



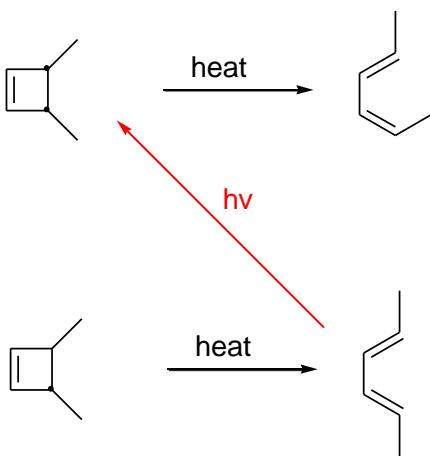
Contrast: Electrocyclic Opening to a Diene

- Conjugated dienes and conjugated trienes react with opposite stereochemistry
- Different symmetries of the diene and triene HOMOs
- Dienes open and close by a conrotatory path
- Trienes open and close by a disrotatory path

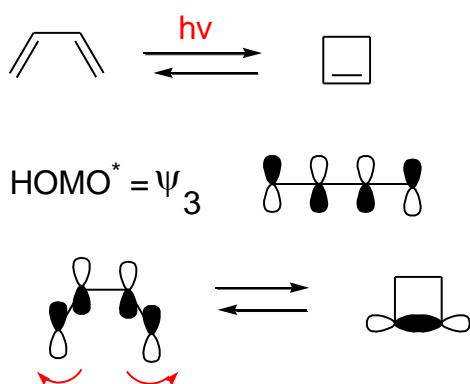
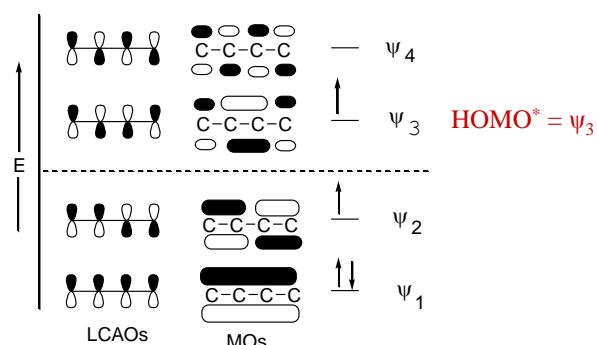


Photochemical Electrocyclic Reactions

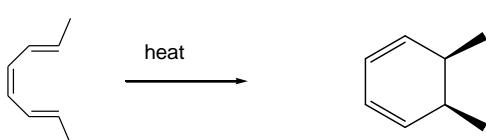
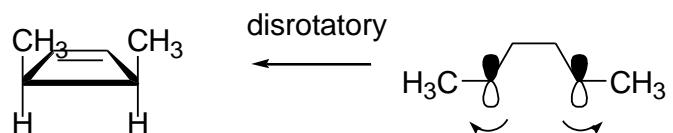
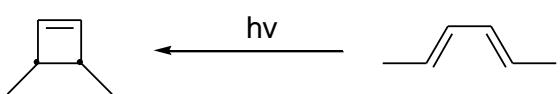
- Irradiation of a polyene excites one electron from HOMO to LUMO
- This causes the old LUMO to become the new HOMO, with changed symmetry
- This changes the reaction stereochemistry (symmetries of thermal and photochemical electrocyclic reactions are always opposite)



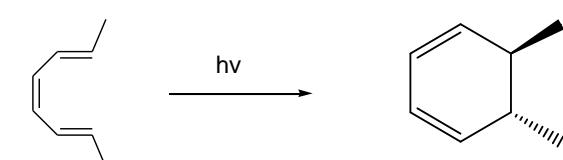
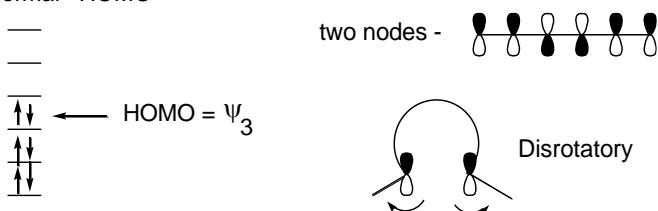
In a photochemical electrocyclic reaction, the important orbital is **HOMO*** (the first excited state):



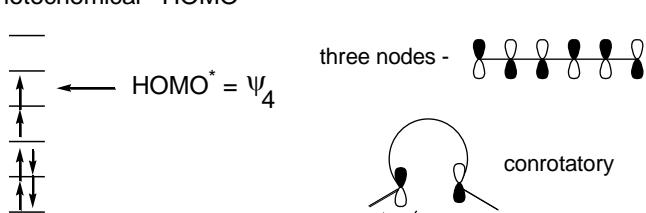
motion must be **disrotatory** for bonding



polyene 6 AOs - 6 MO's 6 e⁻
thermal HOMO



polyene 6 AOs - 6 MO's 6 e⁻
photochemical HOMO*



Rules for Electrocyclic Reactions

Aromatic Transition States (the Dewar-Zimmerman model)

Perturbational Molecular Orbital (PMO) approach

Hückel-Möbius method

Table 30.1 | Stereochemical Rules for Electrocyclic Reactions

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

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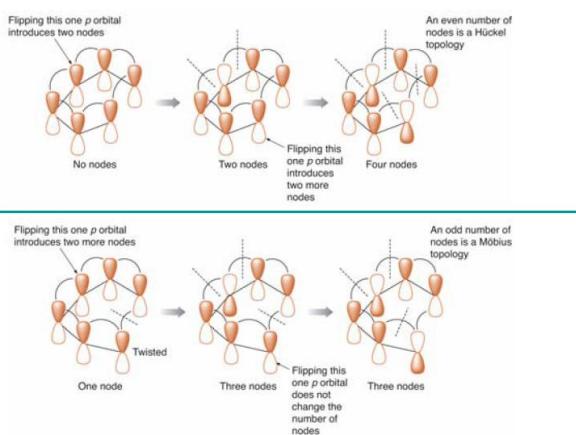
Hückel transition state: the p orbitals around a ring have zero or an even number of phase inversions.

Möbius transition state: the p orbitals around a ring have an odd number of phase inversions.

In a Hückel system, $4n + 2$ electrons, aromatic; $4n$ electrons, antiaromatic.

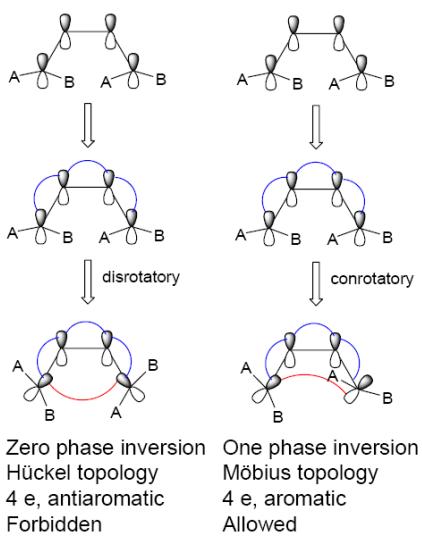
In a Möbius system, $4n$ electrons, aromatic; $4n + 2$ electrons, antiaromatic.

53



How to apply the Dewar-Zimmerman model?

- (1) Draw all the p, s and sp^3 hybridized orbitals (orbital phases can be assigned arbitrarily).
- (2) Connect all the orbitals that interact in the starting materials before the reaction begins.
- (3) Allow the reaction proceed to a postulated transition state.
- (4) Connect the lobes that begin to interact.
- (5) Determine the aromatic or antiaromatic transition state.



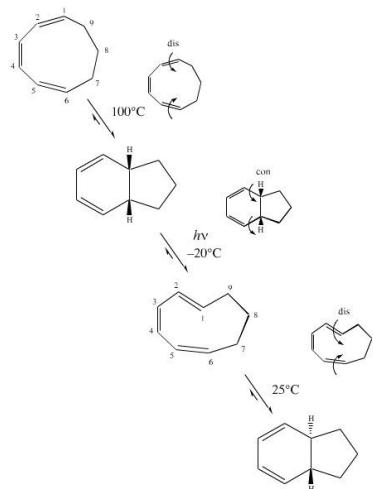
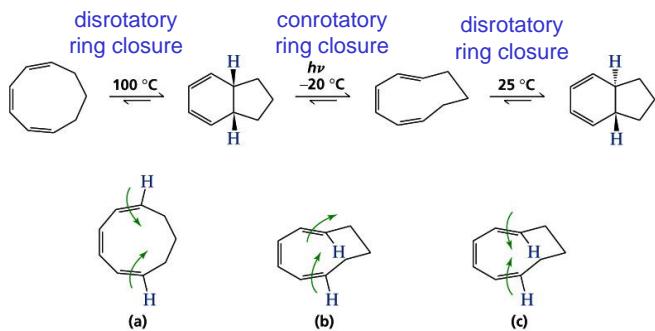
Selection rules for ECR by PMO method

Array of π e involved	Number of Nodes	Type of aromaticity	Δ allowed	hv allowed
4q	0 or even	antiaromatic	-	dis
	odd	aromatic	con	-
4q+2	0 or even	aromatic	dis	-
	odd	antiaromatic	-	con

Determining the stereochemistry of the product of an electrocyclic reaction

Hence, the Woodward-Hoffmann rules can also be phrased as: *Reactions are allowed if they proceed by aromatic transition states and are forbidden if they proceed by antiaromatic transition states.*

Note: the Dewar-Zimmerman is probably the easiest model used to explain pericyclic reactions. For further reading, see. H. E. Zimmerman, *Acc. Chem. Res.* **1971**, 4, 272.



Pericyclic Reactions

Lecture 2

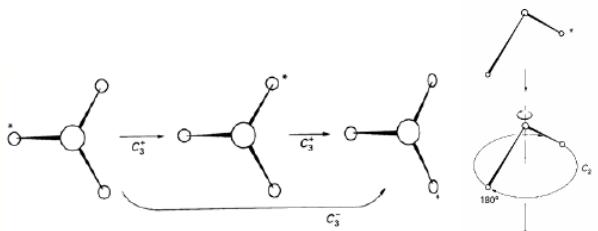
Symmetry concepts

- The study of symmetry in molecules is an adaptation of mathematical group theory.
- Molecular symmetry** in chemistry describes the symmetry present in molecules and the classification of molecules according to their symmetry. Molecular symmetry is a fundamental concept in chemistry, as it can predict or explain many of a molecule's chemical properties, such as its dipole moment and its allowed spectroscopic transitions (based on selection rules such as the Laporte rule).

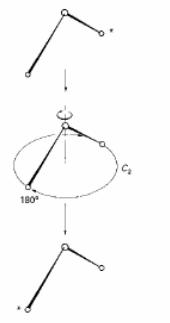
- While various frameworks for the study of molecular symmetry exist, group theory is the predominant one. This framework is also useful in studying the symmetry of molecular orbitals, with applications such as the Hückel method, ligand field theory, and the Woodward-Hoffmann rules. Another framework on a larger scale is the use of crystal systems to describe crystallographic symmetry in bulk materials.
- Many techniques exist for the practical assessment of molecular symmetry, including X-ray crystallography and various forms of spectroscopy. Spectroscopic notation is based on symmetry considerations.

- **Symmetry axis:** an axis around which a rotation by $360/n$ results in a molecule indistinguishable from the original. This is also called an *n*-fold **rotational axis** and abbreviated C_n . Examples are the C_2 in water and the C_3 in ammonia. A molecule can have more than one symmetry axis; the one with the highest *n* is called the **principal axis**, and by convention is assigned the z-axis in a Cartesian coordinate system.

Rotation axes



4.2 A threefold rotation and the corresponding C_3 axis in NH_3 . There are two rotations associated with this axis, one through 120° (C_3^+) and the other through -120° (C_3^-).



4.1 An H_2O molecule may be rotated through any angle about the bisector of the HOH bond angle, but only a rotation of 180° , C_2 , leaves it apparently unchanged.

Rotation axes examples 1

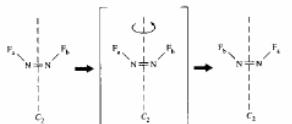


Fig. 3.6 The two-fold rotational axis in *cis*-dinitrogen difluoride.

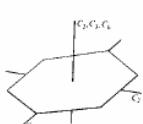


Fig. 7.1 Symmetry elements of a planar hexagon.

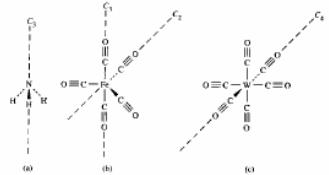


Fig. 3.7 Additional molecules having *n*-fold axes: (a) ammonia, (b) pentacarbonyliron, (c) hexacarbonylf tungsten.

Rotation axes examples 2

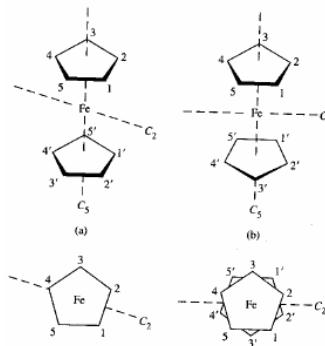
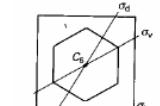
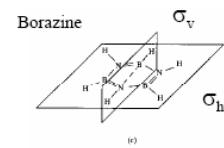
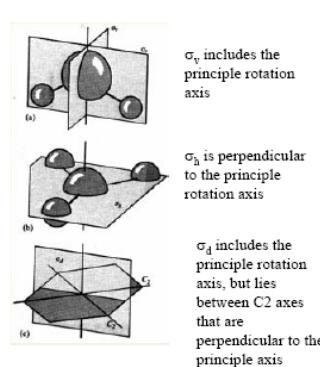


Fig. 3.8 Molecules containing five-fold rotational axes: (a) eclipsed ferrocene, side and top view; (b) staggered ferrocene, side and top view. Each molecule has five C_5 axes, only one of which is shown. Upon rotation about the C_5 axis, the atoms interchange: $1 \rightarrow 1'$, etc.

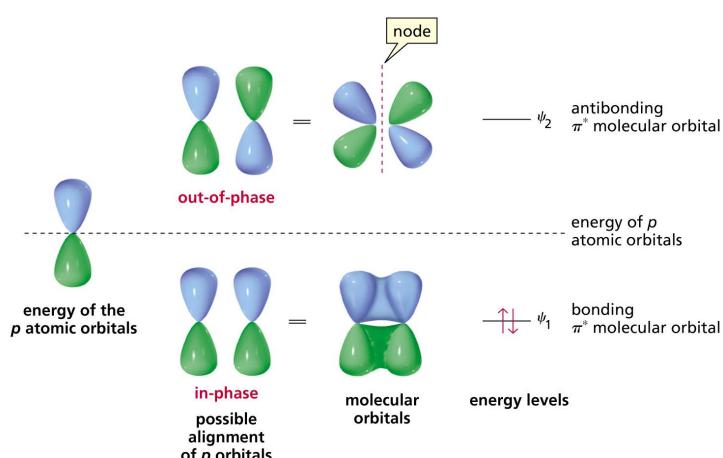
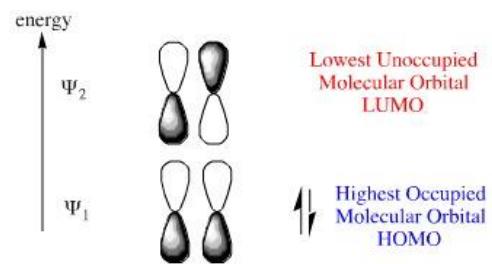
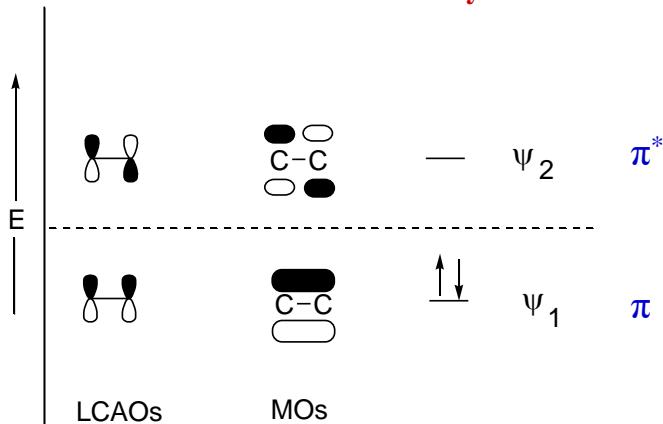
- **Plane of symmetry:** a plane of reflection through which an identical copy of the original molecule is given. This is also called a **mirror plane** and abbreviated σ . Water has two of them: one in the plane of the molecule itself and one perpendicular to it. A symmetry plane parallel with the principal axis is dubbed *vertical* (σ_v) and one perpendicular to it *horizontal* (σ_h). A third type of symmetry plane exists: if a vertical symmetry plane additionally bisects the angle between two 2-fold rotation axes perpendicular to the principal axis, the plane is dubbed *dihedral* (σ_d). A symmetry plane can also be identified by its Cartesian orientation, e.g., (xz) or (yz).

Mirror planes

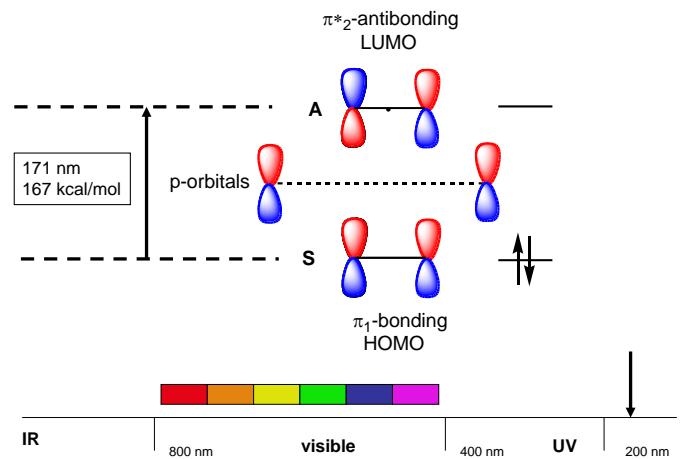


4.4 Some of the symmetry elements of the benzene ring. There is one horizontal reflection plane (σ_h) and two sets of vertical reflection planes (σ_v and σ_d): one example of each is shown.

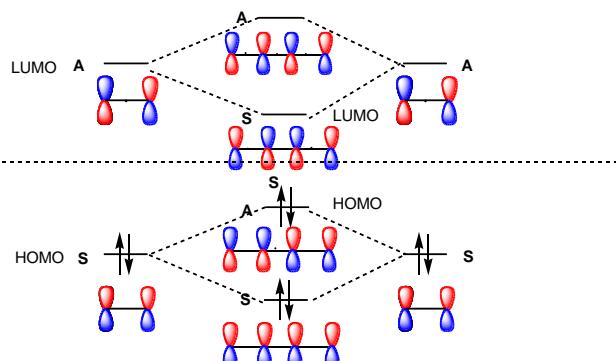
π - molecular orbitals for ethylene



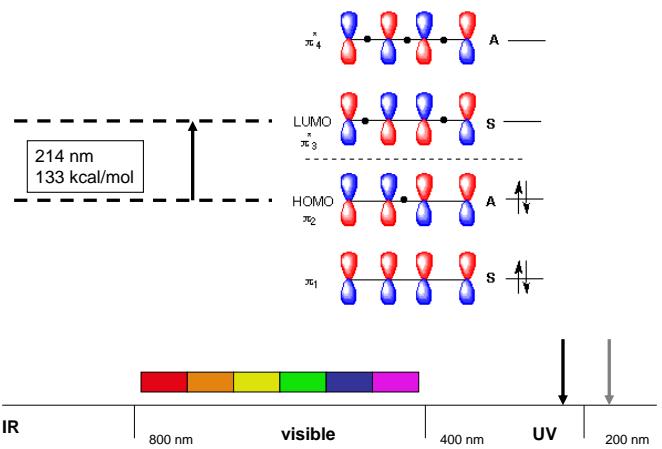
Ethylene π -Molecular Orbitals



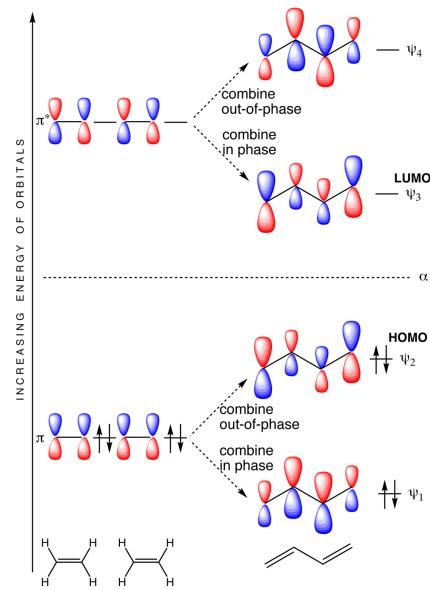
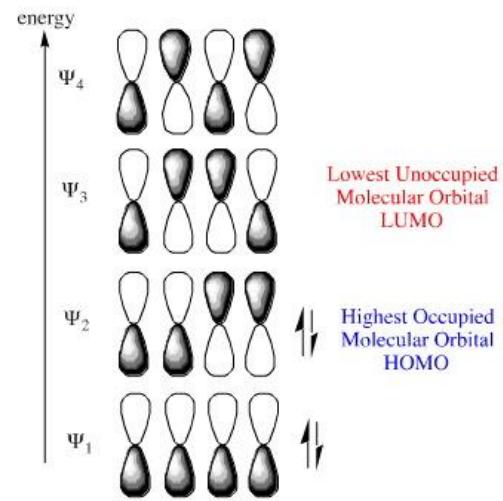
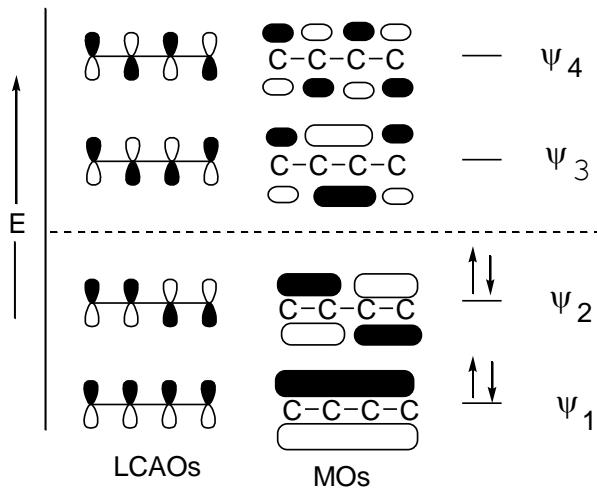
1,3-Butadiene from Ethylene



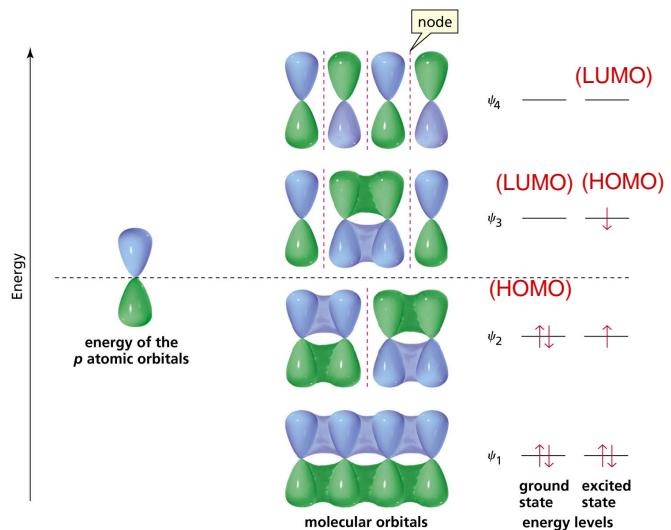
1,3-Butadiene π -Molecular Orbitals



1,3-butadiene



Four p atomic orbitals interact to give the four p MOs of 1,3-butadiene



Note

From the MO diagram of 1,3-butadiene ...

Ψ_1 and Ψ_3 are symmetric MOs

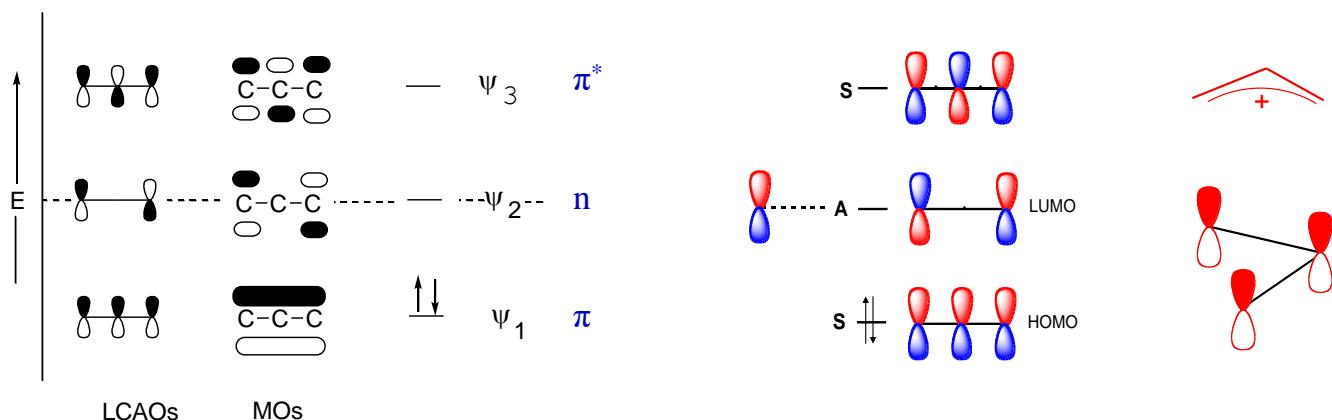
Ψ_2 and Ψ_4 are asymmetric MOs

The ground state HOMO and the excited HOMO have opposite symmetry

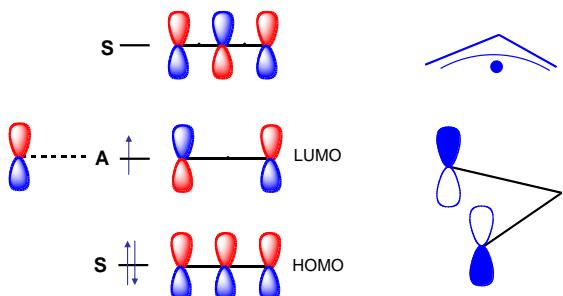
- A MO is bonding if the number of bonding interactions is greater than the number of nodes
- A MO is antibonding if the number of bonding interactions is fewer than the number of nodes
- The normal electronic state of a molecule is known as its ground state
- The ground state electron can be promoted 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

The Allylic System: Allyl Cation

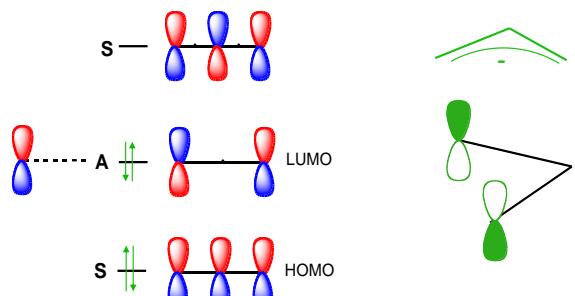
Allyl cation $\text{CH}_2=\text{CH}-\text{CH}_2^+$ 3 AO's \rightarrow 3 MO's 2 π e⁻



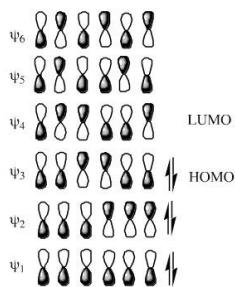
The Allylic System: Allyl Radical



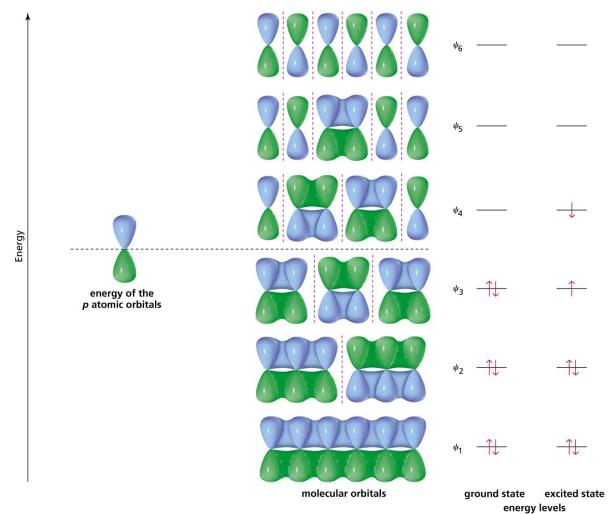
The Allylic System: Allyl Anion



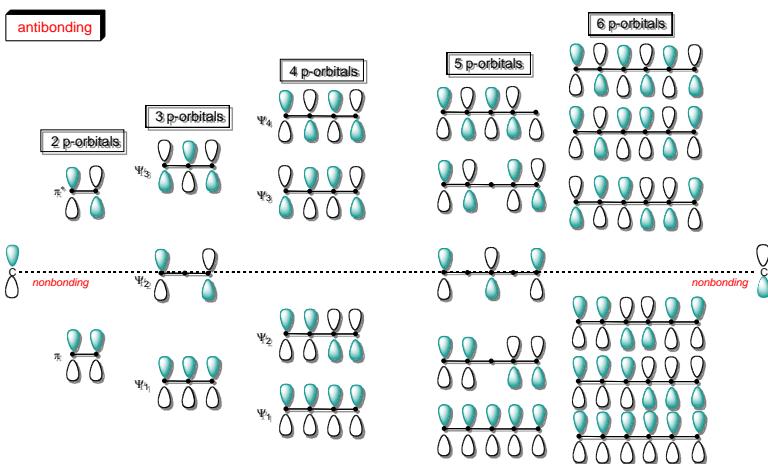
1,3,5-hexatriene



A Molecular Orbital Description of 1,3,5-hexatriene



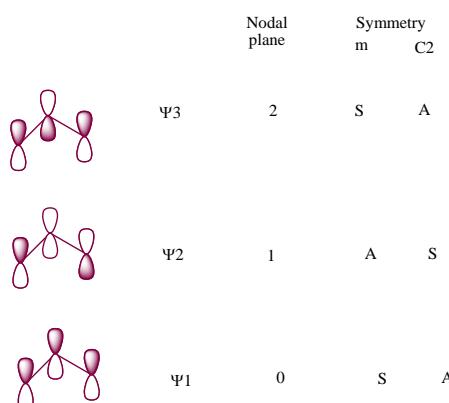
Molecular Orbitals in Conjugated Systems



Molecular Orbital, nodal plane and symmetry of Ethylene

Molecular Orbital	Nodal plane	Symmetry
m	C ₂	
$\pi^* \text{ MO}$	1	A S
$\pi \text{ MO}$	0	S A

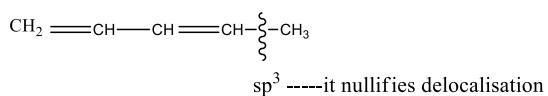
Molecular Orbital, nodal plane and symmetry of allyl system



Molecular Orbital of Butadiene

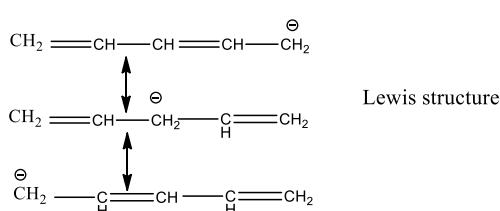
Molecular Orbital	Nodal plane	Symmetry
m	C ₂	
π_4^*	3	A S
π_3^*	2	S A
π_2	1	A S
π_1	0	S A

Pentadiene



Pentadiene is a localised system

Pentadienyl anion



Molecular Orbital of Pentadienyl anion

Molecular Orbital	Nodal plane	Symmetry
m	C ₂	
Ψ_5	4	S A
Ψ_4	3	A S
Ψ_3	2	S A
Ψ_2	1	A S
Ψ_1	0	S A

Molecular Orbital of 1,3,5-hexatriene

Molecular Orbital	Nodal plane m	Symmetry C ₂
Ψ_6	5	A S
Ψ_5	4	S A
Ψ_4	3	A S
Ψ_3	2	S A
Ψ_2	1	A S
Ψ_1	0	S A

Major Categories of Pericyclic Reactions

(1) ELECTROCYCLIC RING CLOSURE/RING OPENING:

An electrocyclic ring closure is the creation of a new σ -bond at the expense of the terminal π -orbitals of a conjugated π -system. There is a corresponding reorganization of the conjugated π -system. We usually classify the reaction according to the number of electrons involved.

Examples:

A 4 e⁻ electrocyclic reaction

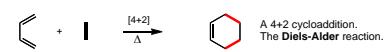
A 6 e⁻ electrocyclic reaction



(2) CYCLOADDITION REACTIONS/CYCLOREVERSION REACTIONS:

A cycloaddition reaction is the union of two smaller, independent π systems. Sigma bonds are created at the expense of π -bonds. A cycloaddition can occur in an intramolecular sense, but it must be between two independent π systems. Cycloaddition reactions are referred to as [m + n] additions when a system of m conjugated atoms combines with a system of n conjugated atoms. A cycloreversion is simply the reverse of a cycloaddition.

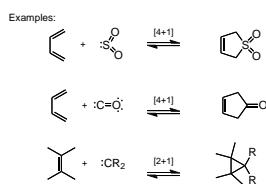
Examples:



Major Categories of Pericyclic Reactions

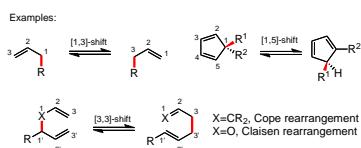
(3) CHELETROPIC REACTIONS:

Cheletropic reactions are a special group of cycloaddition/cycloreversion reactions. Two bonds are formed or broken at a single atom. The nomenclature for cheletropic reactions is the same as for cycloadditions.



(4) SIGMATROPIC REARRANGEMENTS:

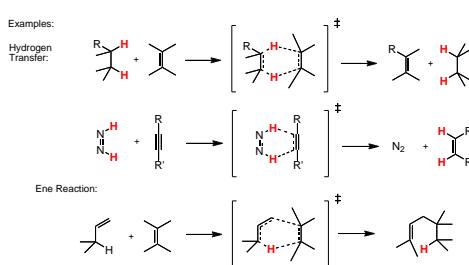
A sigmatropic rearrangement is the migration of a σ -bond from one position in a conjugated system to another position in the system, accompanied by reorganization of the connecting π -bonds. The number of π and σ bonds remains constant. The rearrangement is an [m,n] shift when the σ -bond migrates across m atoms of one system and n atoms of the second system.



Major Categories of Pericyclic Reactions

(5) GROUP TRANSFER REACTIONS:

In a group transfer reaction one or more groups get transferred to a second reaction partner.



WOODWARD-HOFFMANN RULES

To predict whether a pericyclic reaction is allowed or not under given condition, Woodward and Hoffmann proposed following set of rules based on conservation of orbital symmetry concept.

A thermal pericyclic reaction is allowed in the ground state, when the total number of (4q + 2), and (4r)s components is odd.

Otherwise, if the total of (4q + 2), and (4r)s components is even, the pericyclic reaction is allowed in the excited state i.e., under photochemical conditions.

Number of (4q + 2)s and (4r)s components	The condition under which the reaction is allowed
odd	Thermal
even	Photochemical

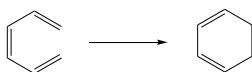
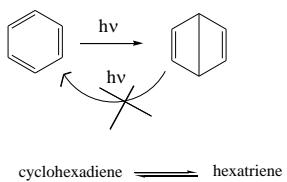
- Component: A bond(s) or an orbital(s) taking part in the pericyclic reaction as a single unit can be considered as a component. It can have any number of electrons but may not have mixtures of σ and π electrons.
- e.g. A double bond is considered as a π component, since there are two π electrons.
- A conjugated diene can be considered as π component, since there are four π electrons.
- 's' represents suprafacial. A suprafacial component forms new bonds on the same face at its both ends. In some cases suprafacial is equivalent to "dis-rotation".
- 'a' represents antarafacial. An antarafacial component forms new bonds on the opposite faces of both ends. In some cases antarafacial is equivalent to "con-rotation".
- e.g. π s represents a component containing two π electrons and forming new bonds in suprafacial manner.
- π 4a represents a component containing four π electrons and is going to form new bonds in antarafacial manner.
- q & r: These are integers.
- (4q + 2)s component: The suprafacial component, which may have either 2 or 6 or 10 or ... electrons of same type. These numbers are obtained by substituting 'q' by 0 or 1 or 2 or ...
- (4r)a component: The antarafacial component, which may have either 4 or 8 or 12 or ... electrons of same type. These numbers are obtained by substituting 'r' by 1 or 2 or 3 or ...
- Likewise the meanings of (4q + 2)a & (4r)s can be understood.

• To be continued.....

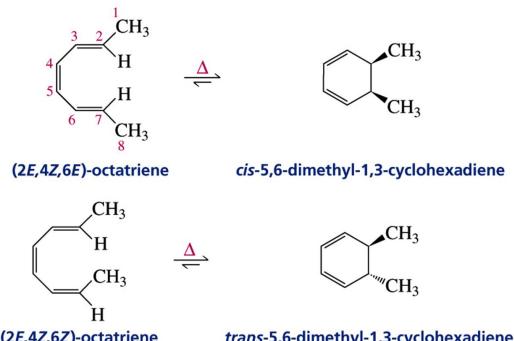
- Some illustrative examples follow:
- The Diels-Alder reaction (a (4+2)-cycloaddition) is $[+4\pi, +2\pi]$.
- The 1,3-dipolar cycloaddition of ozone and an olefin in the first step of ozonolysis (a (3+2)-cycloaddition) is $[+3\pi, +2\pi]$.
- The chelotropic addition of sulfur dioxide to 1,3-butadiene (a (4+1)-chelotropic addition) is $[+4\pi, +4\pi] + [+2\pi, +4\pi]$.
- The Cope rearrangement (a [3,3]-sigmatropic shift) is $[+2\pi, +2\pi, +2\pi]$ or $[+2\pi, +2\pi, +2\pi]$.
- The [1,3]-alkyl migration with inversion at carbon discovered by Berson (a [1,3]-sigmatropic shift) is $[+2\pi, +2\pi]$.
- The conrotatory electrocyclic ring closing of 1,3-butadiene (a 4π -electrocyclization) is $[+4\pi]$.
- The conrotatory electrocyclic ring opening of cyclobutene (a reverse 4π -electrocyclization) is $[+2\pi, +2\pi]$ or $[+2\pi, +2\pi]$.
- The disrotatory electrocyclic ring closing of 1,3-cyclooctadien-5-ide anion (a 6π -electrocyclization) is $[+6\pi]$.
- A Wagner-Meerwein shift of a carbocation (a [1,2]-sigmatropic shift) is $[+0\pi, +2\pi]$.

ECR EXAMPLES 2

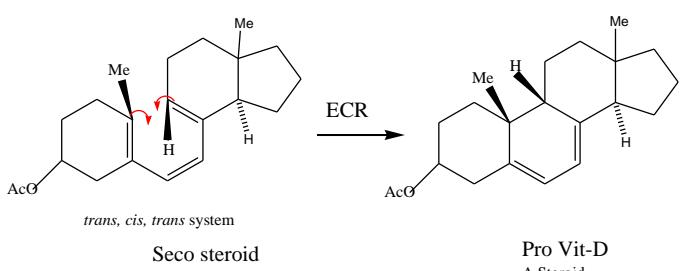
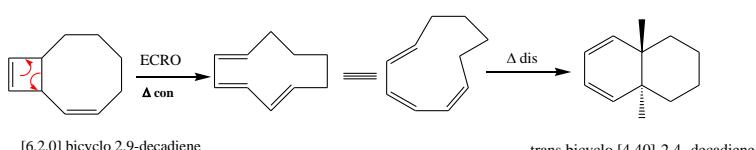
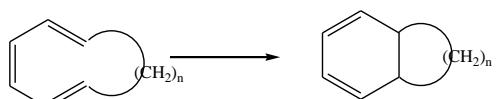
Thermal reactions of 6π system



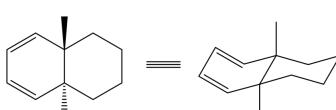
6π e thermal reactions are disrotatory



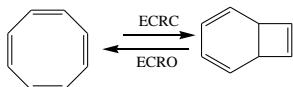
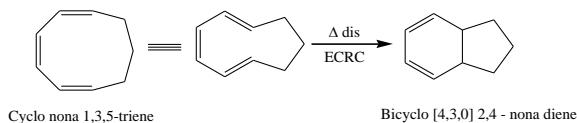
General reaction



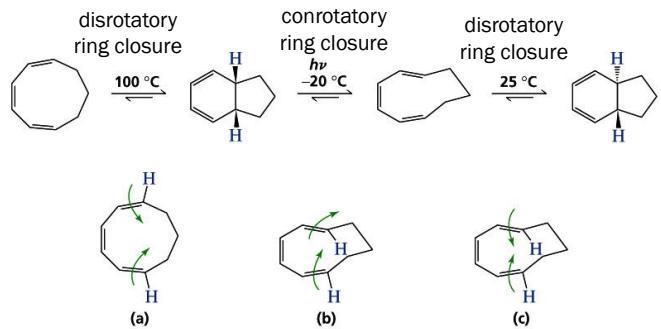
There is a sequence of two ECR; one is ring cleavage in con rotatory mode and then ring closure by dis mode



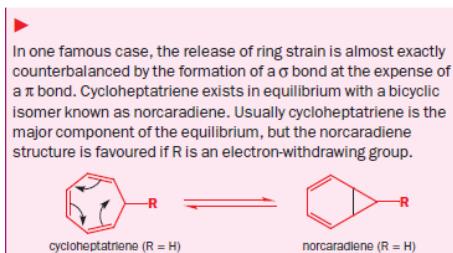
Isomerisation of cyclo nonadiene to bicyclo nonadiene



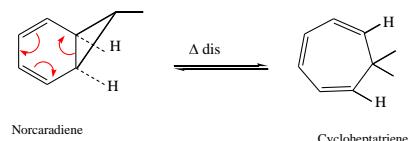
Determining the stereochemistry of the product of an electrocyclic reaction



Norcaradiene - cycloheptatriene interconversion

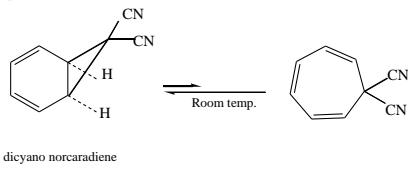


- Norcaradienes are converted to cycloheptatriene by electrocyclic ring opening.



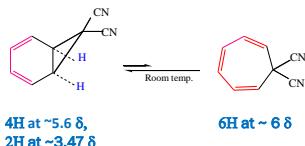
- The linear conjugated partner i.e. cycloheptatriene has 6π e system ($4n+2, n=1$). Hence according to Woodward Hoffmann selection rule it is dis rotatory under thermal condition.
- The valence tautomers exist in equilibrium at room temperature with cycloheptatriene in excess (relief of ring strain of small membered ring plays an important role here). At lower temperature its abundance increases .

- However , if $-CN$ groups are present at position 7, it stabilises the bridge head making norcaradiene more stable.

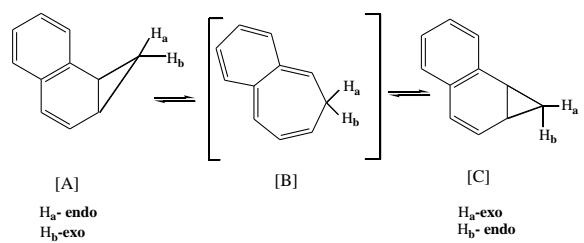


7,7-dicyano bicyclo [4.1.0] 2,4-heptadiene

- Since the compounds exist in equilibrium, their structures cannot be distinguished by chemical means e.g. both of them give cycloheptane on catalytic reduction. They are distinguished only by high resolution NMR technique.

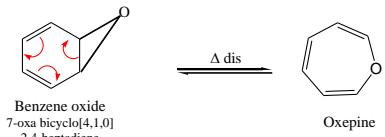


- If a benzene ring is fused with norcaradiene it becomes stabler than its cycloheptatriene partner. As the latter is not aromatic it is of higher energy. However it can give another isomer of norcaradiene.



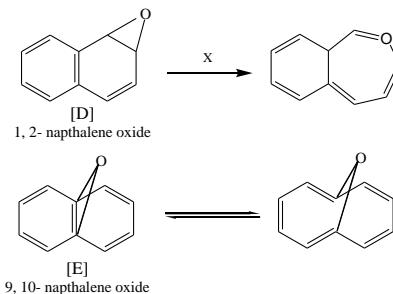
- In the above sequence [B] has not been isolated but [A] and [C] exist in equilibrium. For, the identical peaks of one of them at 0.34δ (for endo) and 1.3δ (for exo) gradually come closer on heating and finally get fixed at 0.46δ .

Interconversion of benzene oxide and oxepine



- Here an oxygen atom replaces bridge head CH₂ (or C<) group as lone pair of electrons of oxygen brings more bond character in oxepine making it much more stable. The two isomers can be distinguished by NMR at about -113°C.
- At room temperature, the automers are in equilibrium with appreciable amount of both isomers in the equilibrium mixture (the exact proportion depends on solvent and temperature).
- The activation energy barrier to the interconversion is much too low for the individual tautomers to be isolated at room temperature. As the temperature is lowered, the proportion of benzene oxide in the equilibrium mixture increases since the unfavourable entropy term TΔS becomes less significant.

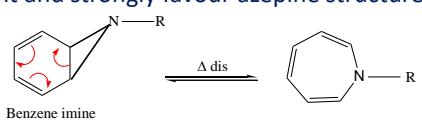
- Now, as before let us consider the system fused with benzene ring i.e. naphthalene oxide



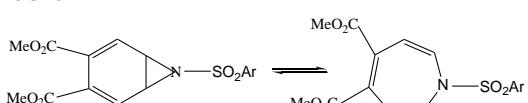
- Out of above two, [D] exists exclusively and doesn't isomerise to corresponding oxepine as aromaticity is lost. But [E] isomerises. For, oxepine of [E] is [10] annulene derivative and is aromatic (4n+2, n=2). Simple [10] annulene can't exist due to steric repulsion of inner H atoms but here oxide bond is out of plane, making the molecule stable.

Interconversion of benzene imine and azepine

- Another example of similar kind is interconversion of benzene imine and azepine, where the equilibrium is not temperature dependent and strongly favour azepine structure.



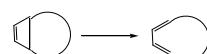
- However the following isomers are found to be temperature dependent.



- In this case the electron withdrawing substituents probably stabilize the benzene imine structure.

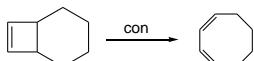
Metal catalysed ECR

- Transition metals (e.g. Fe, Rh, Mn, Co etc.) catalyse many ECR e.g. the following conversion takes place at about 230°C and takes 3-4 hrs.

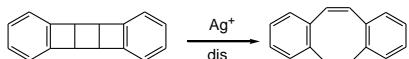
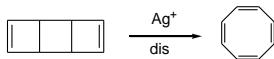


- But when Ag⁺ is used as catalyst the reaction takes place quickly at 0°C to room temperature.
- Catalysis also give the product resulting from a formerly disallowed thermal reaction.
- Silver ions and also some other metal catalysts have dramatic effect on the ring opening of strained cyclobutene derivatives. These reactions are disrotatory and as such are thermally disallowed as concerted process.

- The slow thermal conversion of bicyclo [4.2.0] octane to cis,cis 1,3 cyclooctadiene is enormously speeded up in the presence of silver ions.



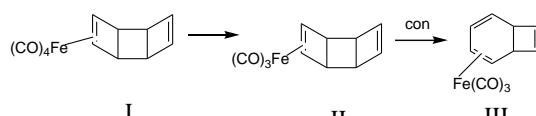
- Similarly the dis rotatory ring opening of the following fused cyclobutenes are catalysed by Ag⁺.



- The second reaction is almost instantaneous at room temperature.

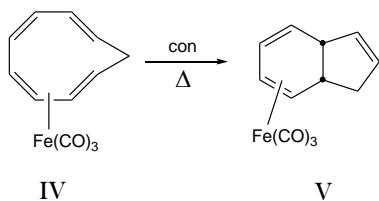
- The metal cation absorbs an electron and make the mode of rotation reverse (as configuration of HOMO and LUMO is opposite).

- However, mode of stereochemistry can be retained by making metal impregnated molecule instead of using catalyst.



- The preformed tetra carbonyl complex undergoes ring opening in bonding hexane to give cyclohexadiene-iron tetracarbonyl complex (III). The reaction proceeds via intermediate (II) and conversion of II to III is a true ECRO.

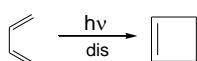
Photochemical ECR



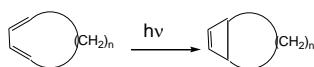
- Conversion of IV to V follows the same mode as thermally allowed cyclisation.

- Electrocyclic reactions brought about by irradiation with UV light are stereospecific but its mode is just opposite to the thermal process. This is synthetically important since by choosing the appropriate condition, the stereochemistry of the product can be selected.
- The LUMO of a linear conjugated polyene have opposite symmetry to the HOMO. So when a polyene is irradiated with UV an electron is excited to LUMO and reverse the direction of ring closure or opening compared with the ground state (thermal) system.
- For $4n$ system photochemical ring closure is dis rotatory while for $4n+2$ system it is con rotatory.

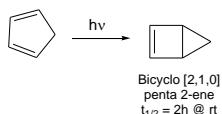
- Thus a butadiene is photochemically converted to cyclobutene:



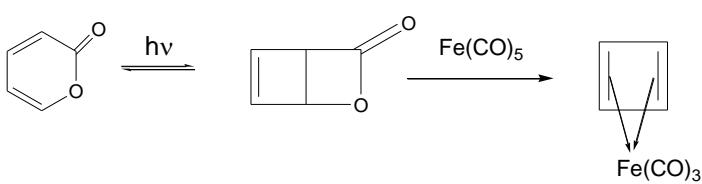
- Though the product is very strained, the reverse process doesn't occur, because conjugated systems are good absorber of UV light but single or isolated olefines are not. If a diene is part of a ring, fused cyclobutene system occurs.



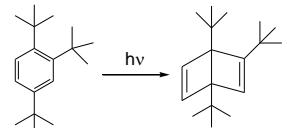
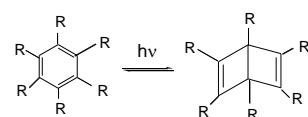
- As the reverse reaction is thermally disallowed the product is unexpectedly stable.



- 2 pyrone undergoes a similar reaction and in presence of iron-pentacarbonyl, the bicyclic product decarboxylate to cyclobutadiene iron tricarbonyl system.



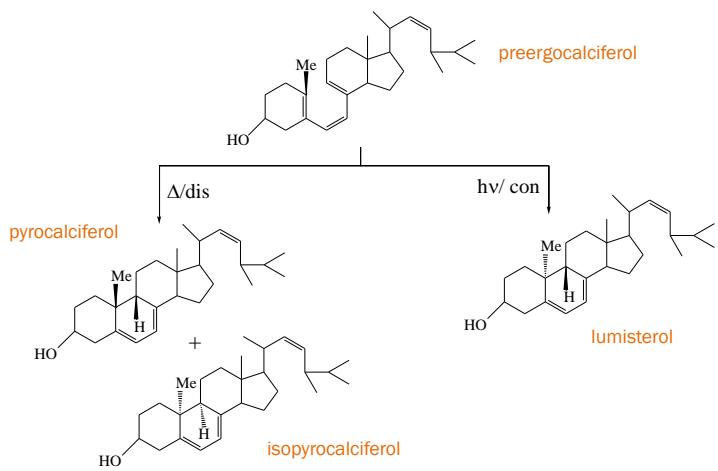
- Isomerisation of benzene to Dewar benzene can also be brought about photochemically:



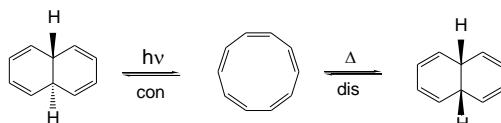
- The surprising thermal stability of Dewar benzene can be explained by the fact that thermal ring opening would occur in con rotatory mode which would give a trans arrangement. But planar benzene cannot have trans arrangement about any double bond.
- Further, as Dewar benzene does not contain any conjugated system reverse reaction is also forbidden photochemically.
- So it occurs due to orbital symmetry control only.

- The orbital symmetry control in organic reaction were first put forward to explain the difference in the thermal and photochemical cyclisation of hexatriene.

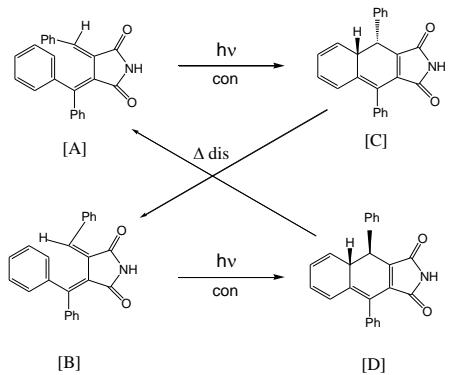
- Thus **preergocalciferol** thermally cyclises in a disrotatory mode to give two *cis* fused product viz. **pyrocalciferol** and **isopyrocalciferol**
- While photochemical cyclisation occur in con rotatory mode to give *trans* fused **lumisterol**



- Another such example is that all *cis* cyclodeca pentene equilibrates photochemically with *trans* 9,10-dihydronaphthalene by con rotatory 6π ECRC; but thermally it is converted to *cis* 9,10-dihydronaphthalene in dis rotatory closure

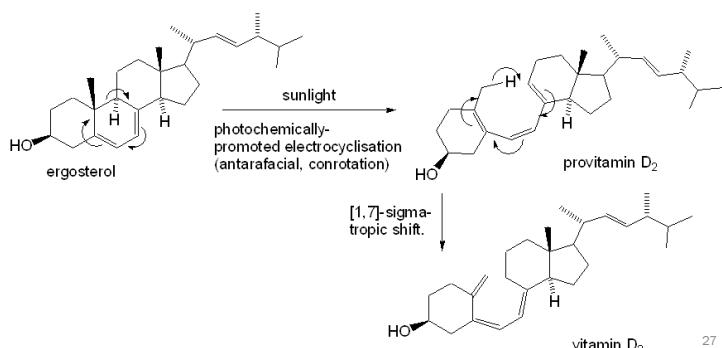


- Yellow imides A and B are photochemically converted to red isomers C and D
- But thermal dis rotatory ring opening of them give the yellow isomers of opposite stereochemistry



Synthetic applications of electrocyclic reactions:

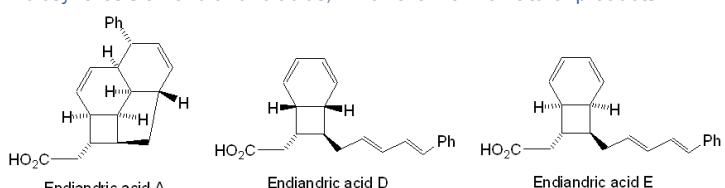
The conversion of ergosterol to vitamin D₂ proceeds through a ring-opening (reverse) electrocyclopentenation to give provitamin D₂, which then undergoes a second rearrangement (a [1,7]-sigmatropic shift). Stereochemical control in the sigmatropic shift process will be described in a later section of this course.



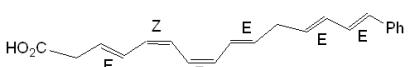
27

Synthetic applications of electrocyclic reactions:

A spectacular example of the power of electrocyclic reactions is in the biosynthesis of endiandric acids, which are marine natural products.



All of these are derived from the linear polyene shown below:

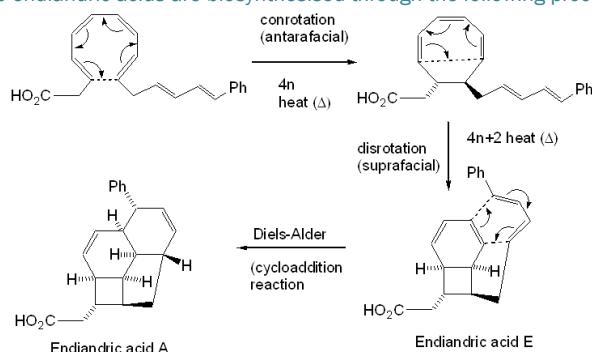


Although the compound has no chiral centres, the double-bond stereochemistry is critical.

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Synthetic applications of electrocyclic reactions:

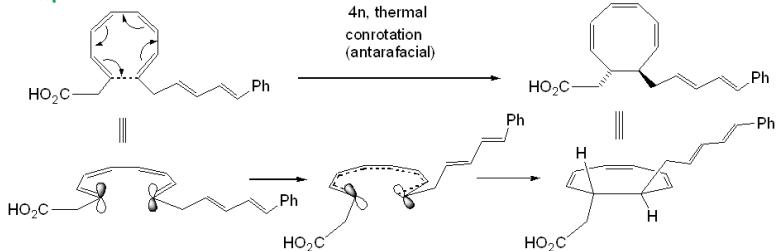
The endiandric acids are biosynthesised through the following process:



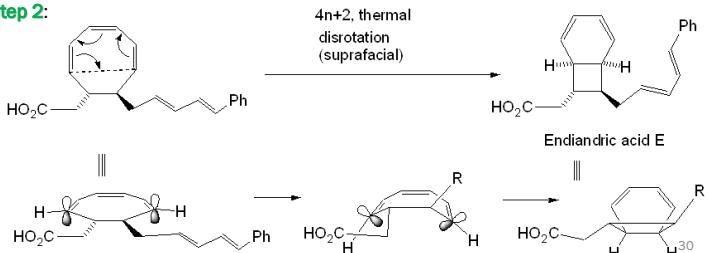
The first two steps are electrocyclics, whilst the final step, to make acid A, is a cyclo-addition (Diels-Alder reaction). There will be more discussion of cycloadditions later in this course. The stereochemical control in the first two steps is addressed in the next slide.

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Step 1:

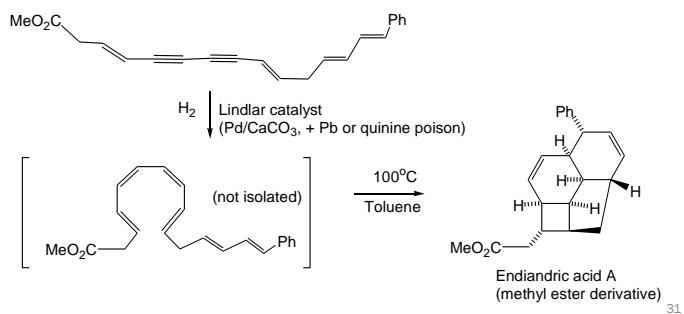


Step 2:



You might want to consider how Endiandric acid D is formed....

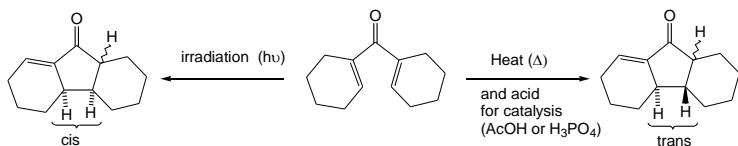
In 1982, K. C. Nicolaou's research group achieved a direct synthesis of endiandric acid A in the laboratory. This was achieved by the reduction of the two alkyne groups in the molecule below by Lindlar catalyst (*cis*-alkenes are formed selectively) which then formed the product upon heating in toluene. A pretty impressive 'one-pot' cyclisation.



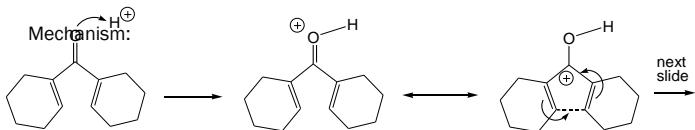
31

Electrocyclisation reactions of cations and anions also follow the Woodward-Hoffmann rules.

All you need to know is the number of electrons involved (i.e. 4n or 4n+2) and whether the reaction is photochemical or thermal:

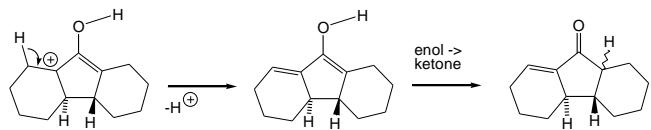


The reaction above is the Nazarov cyclisation (usually carried out under acidic/thermal conditions). Note that the position adjacent to the ketone is a mixture of isomers in each case. Only the relative stereochemistry between the lower hydrogens is controlled.

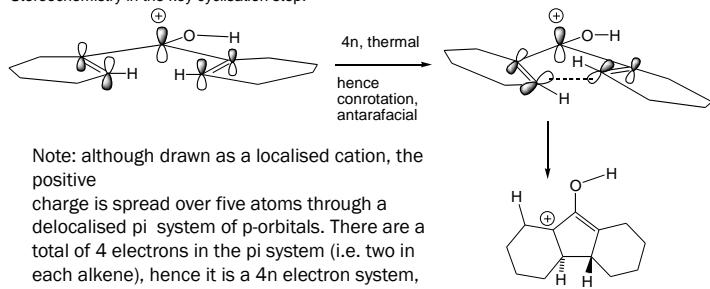


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Nazarov cyclisation, cont....



Stereochemistry in the key cyclisation step:



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1.3 dipolar cycloaddition

Introduction to 1,3-Dipolar Cycloaddition

- 1,3-Dipolar cycloaddition reactions:

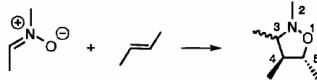


- History of 1,3dipoles and 1,3 -dipolar cycloaddition reactions:

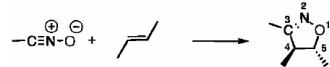
- Curtius discovered diazoacetic ester (1883)
- Buchner studied the reaction of diazoacetic ester with α,β -unsaturated esters and described the first 1,3-DC reaction. (1888)
- Huisgen established general application of 1,3-dipoles in organic synthesis (1960s)
- Woodward and Hoffmann developed conservation of orbital symmetry
- Newest challenge: Control of Stereochemistry

Examples of Typical 1,3-Dipolar Cycloadditions

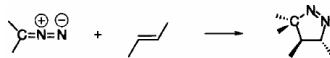
- 1,3-Dipolar Cycloaddition of Nitrones – Preparation of isoxazolidines



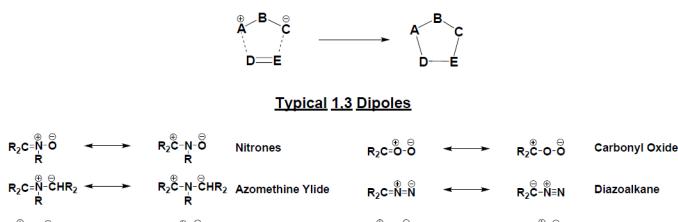
- 1,3-Dipolar Cycloaddition of Nitrile Oxides – Preparation of 2-isoxazolines



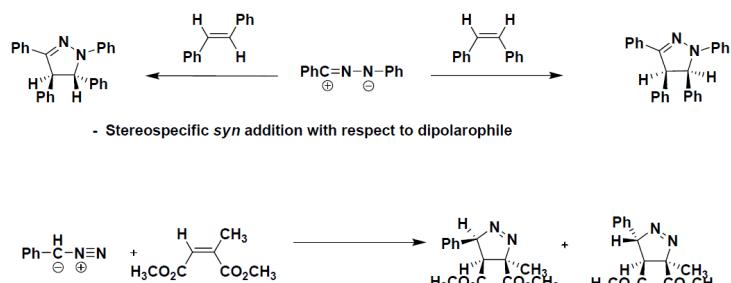
- 1,3-Dipolar Cycloaddition of Diazoalkanes – Preparation of 1-pyrazoline



1, 3 Dipolar Cycloadditions



Stereospecificity



Regioselectivity

- Dominated by Frontier Molecular Orbital (FMO) interactions
- Sterics can also play a role



1,3 Dipolar Cycloadditions of Azides and Alkynes

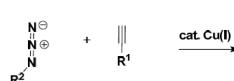


Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*. Wiley, New York, 1976, 154-157.



- HOMO and LUMO lowered by 0.5 eV

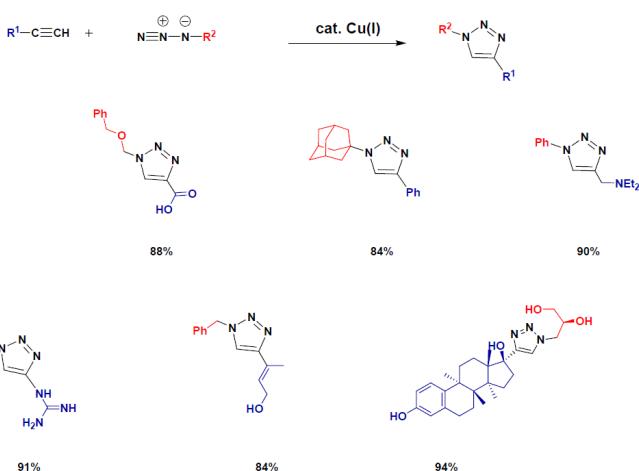
Clarke, D.; Mares, R.; McNab. *J. Chem. Soc., Perkin Trans. 1*. 1997, 1, 1799.



1, 4 regioisomer obtained exclusively

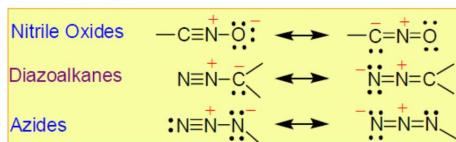
If the energies of the two interactions are similar, both reactions can occur.

The Cu(I) Catalyzed 1,3 Dipolar Cycloadditions of Azides and Alkynes

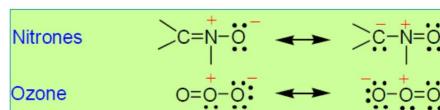


1,3-Dipoles

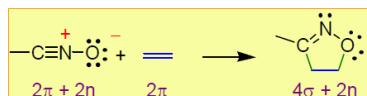
Propargyl–Allenyl Type



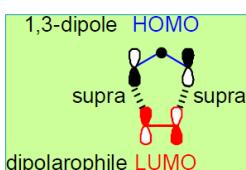
Allyl Type



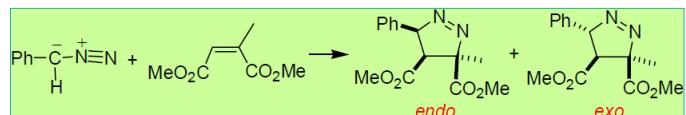
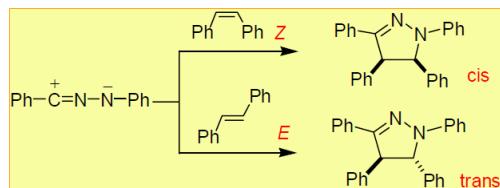
1,3-Dipole + Alkene (Dipolarophile)



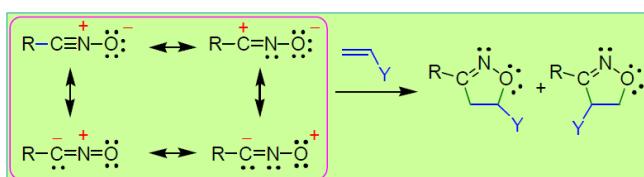
Concerted cycloaddition: Predictable stereochemistry



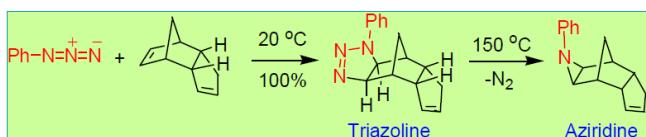
Stereochemistry



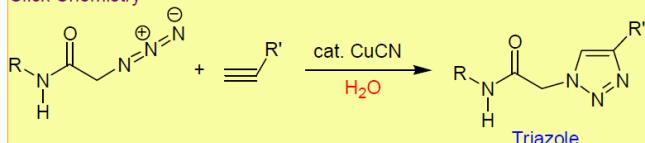
Regiochemistry: Less Predictable



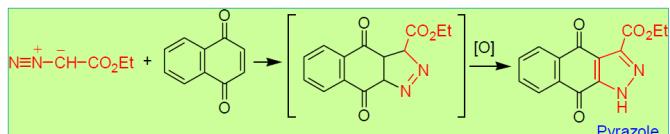
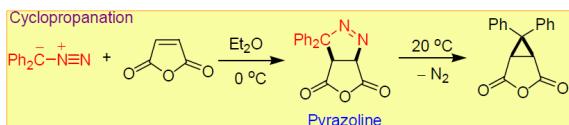
Azides



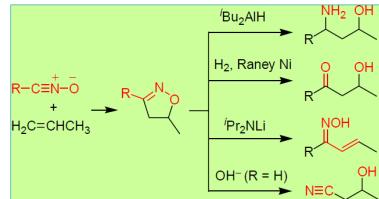
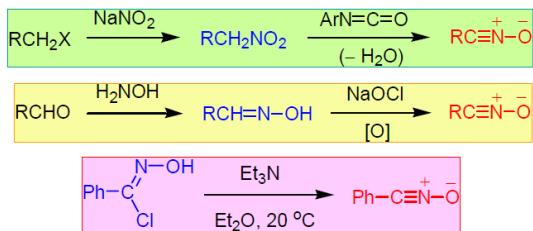
Click Chemistry



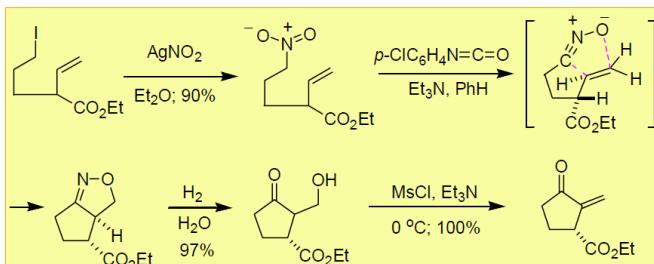
Diazoalkanes



Nitrile Oxides

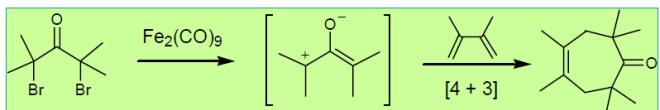
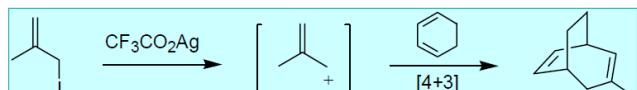


Nitrile Oxides: Intramolecular Cycloaddition



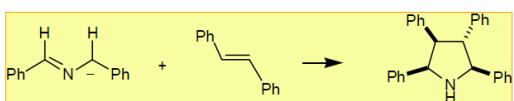
Cycloaddition Reactions with Allyl Cations

[4 + 3] Cycloaddition



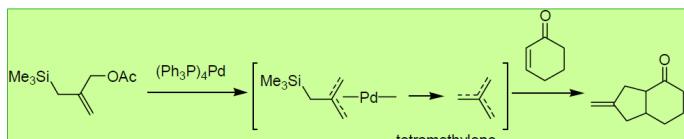
Cycloaddition Reactions with Allyl Anions

[3 + 2] Cycloaddition



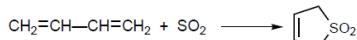
Cycloaddition Reactions with Tetramethylene

[3 + 2] Cycloaddition



Cheletropic reaction

- A form of *cycloaddition* across the terminal atoms of a fully *conjugated system* with formation of two new s-bonds to a single atom of the ('monocentric') reagent. There is formal loss of one p-bond in the substrate and an increase in *coordination number* of the relevant atom of the reagent. An example is the *addition* of sulfur dioxide to butadiene:

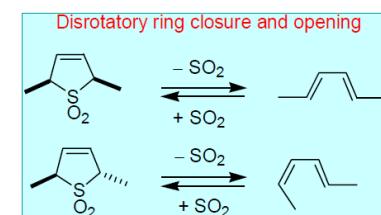


- The reverse of this type of reaction is designated 'cheletropic elimination'.

IUPAC Compendium of Chemical Terminology 2nd Edition (1997)

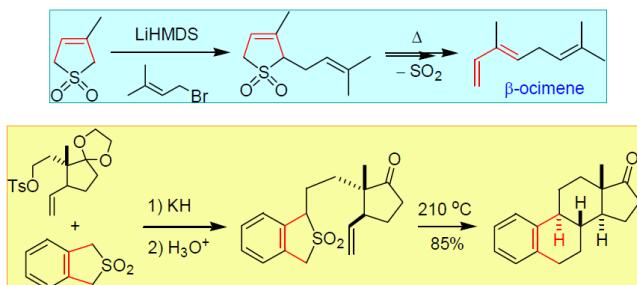
Cheletropic Reactions

Sulfolenes



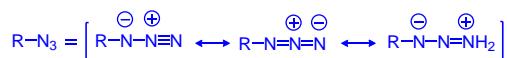
Cheletropic Reactions

Sulfolenes

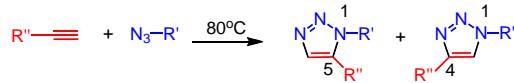


Historical Perspective of Azide/Akynne Cycloadditions

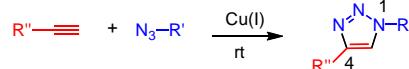
1933- Dipolar nature of azide first recognized by Linus Pauling



1960- Mechanism of 1,3-dipolar cycloaddition of azides and alkynes pioneered by Rolf Huisgen



2001- Copper catalyzed 1,3-Dipolar cycloaddition by Sharpless/Meldal



L. Pauling. Proc. Natl. Acad. Sci. USA 1933, 19, 860-867; Huisgen, R. Angew. Chem. Int. Ed. 1963, 2, 633-696
Sharpless, K.B. et al. Angew. Chem. Int. Ed 2002, 41, 2596-2599; Meldal,M.J. et al. J. Org. Chem. 2002, 67, 3057-3064

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Syllabus

- General information, Photo-chemical energy, effect of light intensity on the rate of photochemical reactions. Jablonski-diagram, photo-sensitisation and quenching. Norrish type-I, type-II processes, Paterno-Buchi reaction, photochemistry of unsaturated compounds.
- Types of photochemical reactions: Photo-dissociation, gas phase photolysis. Photochemistry of alkenes: Intramolecular reactions of the olefinic bond-geometrical isomerism, cyclisation reactions, rearrangement of 1,4- and 1,5-dienes.
- Photochemistry of Carbonyl compounds: Intramolecular reactions of carbonyl compounds saturated, cyclic and acyclic, β,γ -unsaturated and α,β -unsaturated compounds. Cyclohexadienones, Intermolecular cycloaddition reactions, dimerisation and oxetane formation.
- Aromatic compounds: Isomerisations, additions and substitutions. Miscellaneous photochemical reactions: Photo-Fries reactions of anilides, photofries rearrangement, Barton reaction, Singlet molecular oxygen reactions.
- Photochemical formation of smog.
- Photodegradation of polymers, photosubstitution, photoreduction of ketones, photooxidation, di- π methane rearrangement, photochemistry of areanes.
- Organometallic photochemistry, photochemistry of vision.

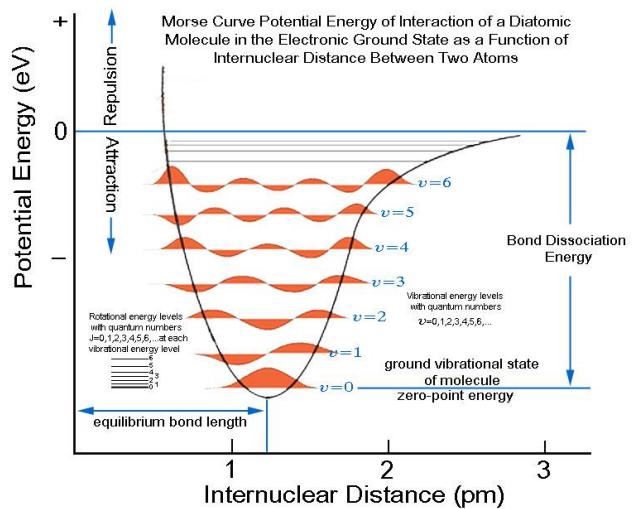
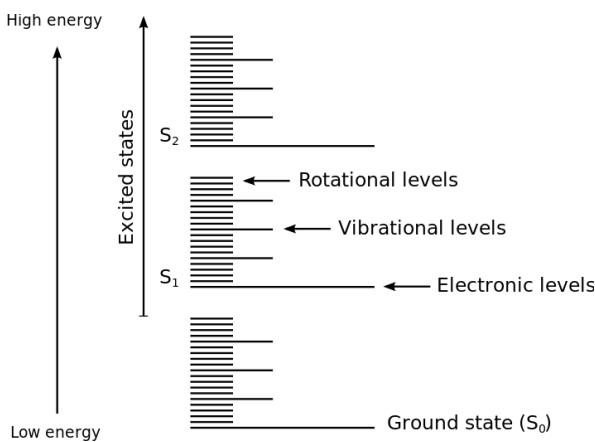
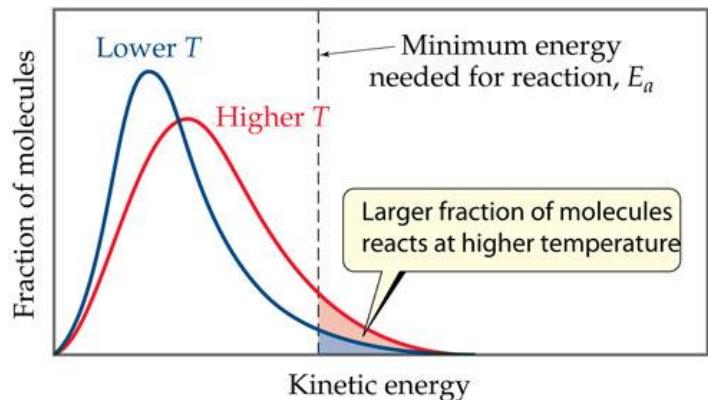
Photochemistry

Introduction

- The study of chemical reactions, isomerization and physical behaviour that may occur under the influence of visible and/or ultraviolet light is called **Photochemistry**.

- $E_{\text{Total}} = E_{\text{elec}} + E_{\text{vib}} + E_{\text{rot}} + E_{\text{trans}}$
- $E_{\text{elec}} \gg E_{\text{vib}} \gg E_{\text{rot}} \gg E_{\text{trans}}$
- $E = h\nu = hC/\lambda$

- There are two different means by which energy can be supplied to the molecules:
- Changing in temperature provides a continuous increase in energy – thermal chemistry
- A quantum of energy may be absorbed by a molecule from electromagnetic radiation photochemistry



Photochemical energy

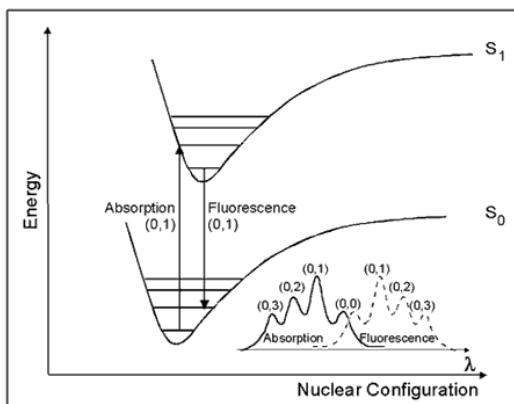
- From $E = hC/\lambda$, $E = \frac{(2.62 \times 10^4)}{\lambda}$
- Thus if $\lambda = 254 \text{ nm}$, $E = 113 \text{ kcal/mole}$,
sufficient to rupture most chemical bond

Energy of some covalent bonds and the corresponding approx. wavelengths

Bond	Energy in kcal/mole	λ in nm
C-H	95	300
C-O	88	325
C-C	83	345
Cl-Cl	58	495
O-O	35	820

Electronically Excited States

- The absorption of a UV or visible photon by a molecule produces an electronically excited state.
- The distribution of the electrons surrounding the nuclei change, as well as the forces between the atomic nuclei of a molecule.
- As a result, molecules in electronically excited states often have very different chemical and physical properties than their electronic ground states.
- For example, α -hydroxy naphthalene becomes a strong acid in its excited state. The ground state of α - hydroxy naphthalene has a pKa of 9.2, but this is reduced to 0.4 in the excited singlet state.
- Such molecules are known as photoacids.



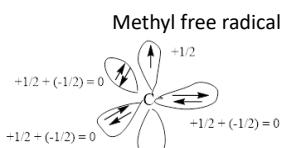
Franck-Condon Energy Level Diagram

Energy Level Diagram

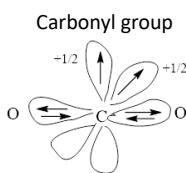
- One way to view the properties of molecular excited states is shown by the potential energy diagram in the previous slide.
- This diagram, known as a **Franck-Condon** energy level diagram, shows potential energy curves for the ground state (S_0), and first excited singlet state (S_1) of an organic molecule as a function of nuclear configuration.
- These curves are sometimes referred to as potential energy wells, because of their shape.
- The horizontal lines within each curve represent the vibrational levels of each electronic state.
- The lowest vibrational state for each energy level is designated as 0, and the levels above it are successively 1, 2, etc.
- The band assignments in brackets (e.g., (0, 1)) indicate respectively, the vibrational level of the initial state, and of the final state involved in a transition

Spin multiplicity

- Spin multiplicity of any species = $2S+1$, where S = sum of spins of the electrons
- Case 1:** All electrons are paired, $S=0$, Spin multiplicity = $2 \times 0 + 1 = 1$
- If Spin multiplicity is one, the state of the species is known as **singlet state**. e.g. methyl carbocation (all six electrons in its outermost orbit are paired)

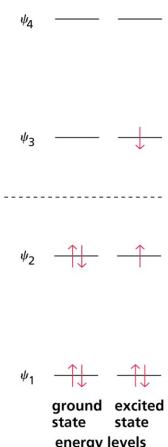


Spin state = $2S + 1 = 2 \times 1/2 + 1 = 2$
Spin state of methyl free radical is **doublet**



Sum of spin = $1/2 + 1/2$
Spin state = $2S + 1 = 2 \times 1 + 1 = 3$
Spin is **triplet**

- There are even number of electrons in typical organic molecules and these electrons are paired in ground state, as per Pauli principle. Molecular states with all paired electron are thus called singlet state, S_n , where $n = 0, 1, 2, 3, 4$.

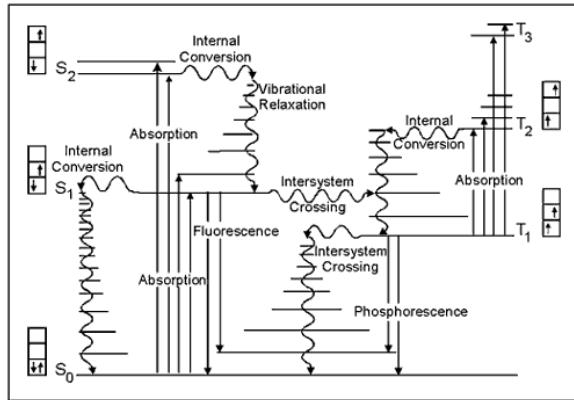


- Singlet excited state may undergo spin inversion giving a new excited state with two electrons of same spin (i.e. $S = (+\frac{1}{2}) + (+\frac{1}{2}) = 1$).
- Molecular state of such species having $S = 1$ is called triplet state ($2S+1 = 2 \times 1 + 1 = 3$), T_n , where $n = 0, 1, 2, 3$.

- T_0 = lowest energy state
- T_1 = higher energy state than T_0
- T_2 = higher energy state than T_0 and T_1
- The term singlet and triplet originate from the fact that singlet state does not split in a magnetic field while triplet state does as it has a magnetic moment and has three possible distinguishable energy states.

- Electronic transitions between states of same multiplicity i.e. singlet-singlet and triplet-triplet are spin allowed but transitions between states of different multiplicity i.e. singlet-triplet or triplet-singlet are spin forbidden.
- The most important difference between the lowest excited singlet state and the lowest excited triplet state is that the latter is much lower in energy.
- Triplet states are not readily obtained directly by absorption of photon as such absorption is strongly forbidden. Thus most observable spectra are singlet-singlet absorption spectra. Some triplet state can be generated **indirectly** by absorption of light as a result of a photophysical process referred as **intersystem crossing (ISC)** from the initially generated singlet state.
- Fluorescence almost invariably occurs from the S_1 state and phosphorescence from the T_1 state.

The Jablonski Diagram



- Photochemistry is the underlying mechanism for all of photobiology.
- When a molecule absorbs a photon of light, its electronic structure changes, and it reacts differently with other molecules.
- The energy that is absorbed from light can result in photochemical changes in the absorbing molecule, or in an adjacent molecule (e.g., photosensitization).
- The energy can also be given off as heat, or as lower energy light, i.e., fluorescence or phosphorescence, in order to return the molecule to its ground state.
- Each type of molecule has a different preference for which of these different mechanisms it uses to get rid of absorbed photon energy, e.g., some prefer fluorescence over chemistry.

The Jablonski Diagram

- The energy gained by a molecule when it absorbs a photon causes an electron to be promoted to a higher electronic energy level.
- Figure in the previous slide illustrates the principal photophysical radiative and non-radiative processes displayed by organic molecules in solution. The symbols S_0 , S_1 , T_2 , etc., refer to the ground electronic state (S_0), first excited singlet state (S_1), second excited triplet state (T_2), and so on. The horizontal lines represent the vibrational levels of each electronic state. Straight arrows indicate radiative transitions, and curly arrows indicate non-radiative transitions. The boxes detail the electronic spins in each orbital, with electrons shown as up and down arrows, to distinguish their spin.
- Note that all transitions from one electronic state to another originate from the lowest vibrational level of the initial electronic state. For example, fluorescence occurs only from S_1 , because the higher singlet states (S_2 , etc.) decay so rapidly by internal conversion that fluorescence from these states cannot compete.

The Basic Laws of Photochemistry

- **The First Law of Photochemistry**, the Grotthuss-Draper law, states that light must be absorbed by a compound in order for a photochemical reaction to take place.
- This is a simple concept, but it is the basis for performing photochemical and photobiological experiments correctly.
- If light of a particular wavelength is not absorbed by a system, no photochemistry will occur, and no photobiological effects will be observed, no matter how long one irradiates with that wavelength of light.

The Second Law of Photochemistry

- **The second law of photochemistry**, the Stark-Einstein law, states that for each photon of light absorbed by a chemical system, only one molecule is activated for subsequent reaction.
- This "photoequivalence law" was derived by Albert Einstein during his development of the quantum (photon) theory of light.
- This law is true for ordinary light intensities, however, with high-powered lasers, two-photon reactions can occur, i.e., the molecule is raised to a higher energy state than produced by single-photon absorption.

The Bunsen-Roscoe Law of Reciprocity

- **The Bunsen-Roscoe Law of Reciprocity** states that a photochemical effect is directly proportional to the total energy dose, irrespective of the time required to deliver the dose.
- This law is true for chemicals in a test tube, but the response of cells to radiation usually involves a sequence of interacting biological reactions, making a linear "dose x time" relationship highly unlikely.
- There is no reciprocity when damage is produced, e.g., DNA damage, but there can be reciprocity over a narrow range of doses for photoreceptors that trigger a response, such as phytochrome.

Quantum Yield (Φ) or Quantum efficiency

- The efficiency of photochemical process is often expressed in terms of quantum yield which is defined as the number of molecules reacting per quantum of light absorbed

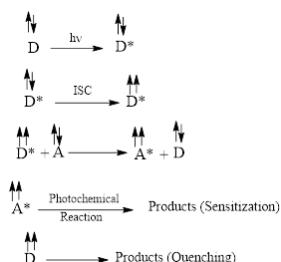
$$\Phi = \frac{\text{Number of molecules reacting in given time}}{\text{Number of quantum of radiation absorbed in the same time}}$$

- The energy E absorbed per mole of the reacting substance is called one Einstein

$$E = N_A h \nu = \text{one Einstein}$$

- Thus the quantum yield (ϕ) is also defined as the number of moles of product formed per Einstein of monochromatic light absorbed
- The quantum yield of the product formation
 - $\Phi = \frac{\text{Number of molecules of product formed}}{\text{Number of einstein of radiation absorbed}}$

- Although photons are absorbed by D, it is A which becomes excited. This phenomenon is known as **photosensitization** and D is referred as **photosensitizer**.
- The basic requirement for energy transfer is that the energy of donor molecule should have 5 kcal/mole more energy needed for excitation of acceptor molecule.

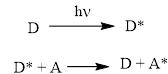


Some common sensitizers and their energy in triplet state

Sensitizer	Triplet Energy (kcal/mole)
Benzophenone	69
Benzyl	53
Acetophenone	74
Fluorenone	53
Benzene	85
Naphthalene	61
Biacetyl	56

Photosensitizer

- For many molecules, ISC ($S_1 \rightarrow T_1$) is not very efficient.
- Fortunately, triplet state can be populated by the use of donor molecule.
- Donor molecule is a substance with high ISC efficiency.
- Donor molecule produces in high yield by ISC and then this molecule transfers its excitation energy to the second molecule (acceptor).
- Excited state (S_1 or T_1) of donor molecule transfers its large amount of energy to the acceptor molecule and in this process acceptor (A) species promoted to excited state and the donor (D) species returns to its ground state.



The criteria of sensitizer

- It must be excited by the irradiation to be used
- It must be present in sufficient concentration and absorb more strongly than the other reactants under the conditions of the experiment so that it be the major light absorber
- The energy of triplet state of sensitizer (D^* or ${}^3D^*$ or ${}^3Sens^*$) must be greater than that of reactant. Otherwise, the energy transfer becomes endothermic
- It must be able to transfer energy to the desired product
- The sensitizer should possess high ISC, absorb at lower wavelength and does not interfere with any analytical procedure.

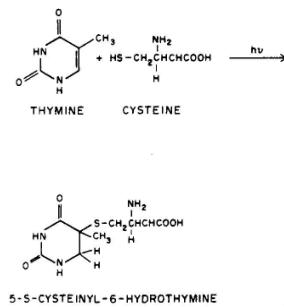
Quenching

- Intermolecular interaction between a molecule in its excited state and a molecule in its ground state can lead to deactivation of the electronically excited state and the generation of the excited state of other molecule. This phenomenon is known as quenching. Thus bimolecular deactivation is known as quenching.
- $M^* + Q \rightarrow M + Q^*$
- Quenching process is reverse to sensitization process.
- In sensitization process a molecule in its ground state is raised to its excited state by energy transfer from other excited molecule (sensitizer).
- $M + Sens^* \rightarrow M^* + Sens$
- The component that accelerates quenching is known as **quencher** and represented by Q.

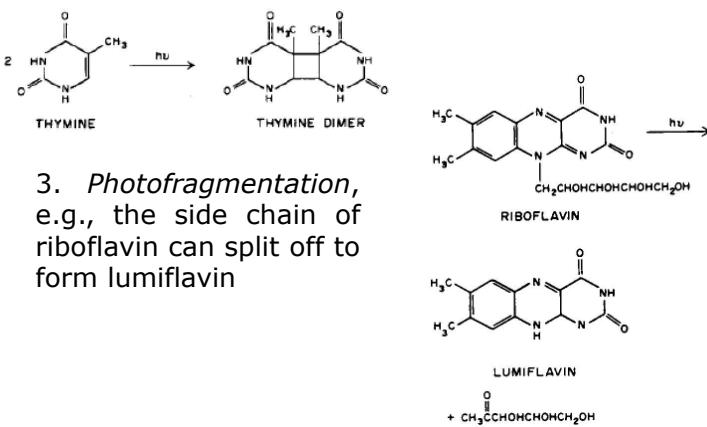
- There are two major routes of quenching:
 - (i) Photochemical quenching
 - (ii) Photophysical quenching
- In photochemical quenching the quencher transforms the excitation energy into chemical energy and a product is formed.
- Photophysical quenching can be divided into
 - Self-quenching or concentration quenching
 - Impurity quenching

Types of Photochemical Reactions

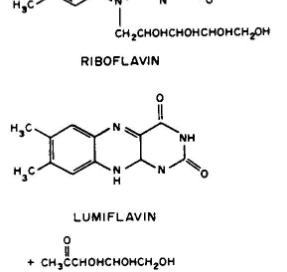
- 1. *Linear addition to an unsaturated molecule*, e.g., the pyrimidine base, thymine, in DNA can combine with the amino acid residue, cysteine, in proteins. This is a model for the photochemical crosslinking of DNA and proteins by UV radiation.



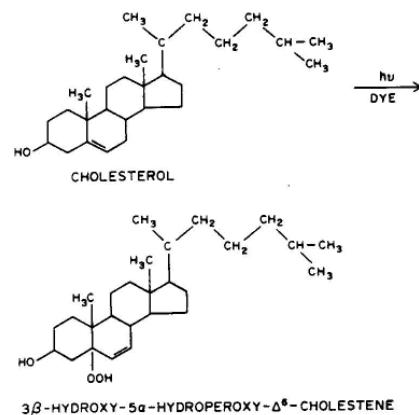
- 2. *Cycloaddition of unsaturated molecules*, e.g., two thymines can react to form a ring product, the thymine dimer, an important class of products formed in DNA by UV radiation



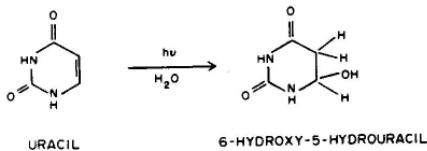
- 3. *Photofragmentation*, e.g., the side chain of riboflavin can split off to form lumiflavin



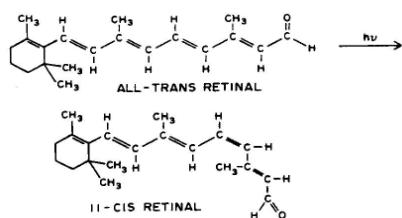
- 4. *Photooxidation*, e.g., the ring structure of cholesterol can add a peroxy group



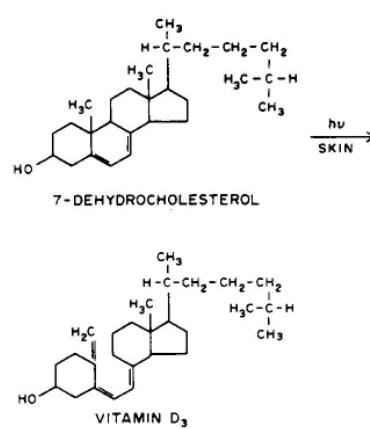
- 5. *Photohydration*, e.g., uracil can add a molecule of water to its 5-6 double bond when UV irradiated.



- 6. *Cis-Trans Isomerization*, e.g., all-trans retinal can be converted to 11-cis retinal

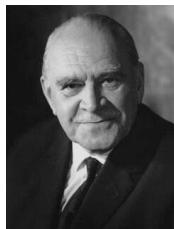


- 7. *Photorearrangement*, e.g., 7-dehydrocholesterol can be converted to vitamin D₃



Norrish reaction

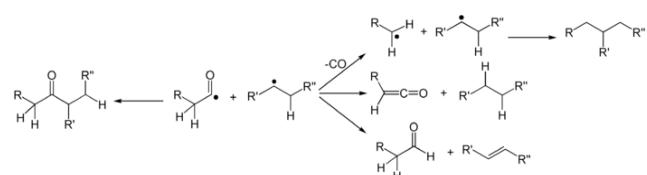
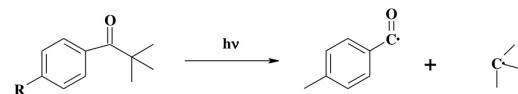
- The **Norrish reaction** in organic chemistry describes the photochemical reactions taking place with ketones and aldehydes. This type of reaction is subdivided in **Norrish type I reactions** and **Norrish type II reactions**. The reaction is named after Ronald George Wreyford Norrish.



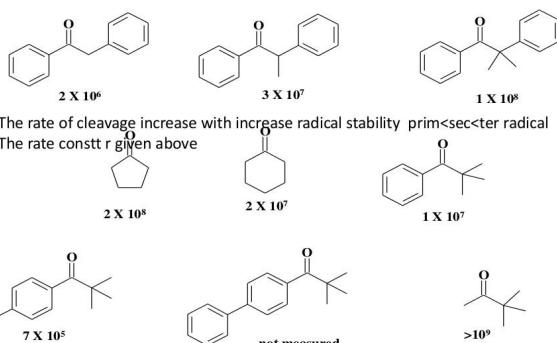
- Several secondary reaction modes are open to these fragments depending on the exact molecular structure.
- The fragments can simply recombine to the original carbonyl compound, with racemisation at the α -carbon.
- The acyl radical can lose a molecule of carbon monoxide, forming a new carbon radical at the other α -carbon, followed by formation of a new carbon–carbon bond between the radicals. The ultimate effect is simple extraction of the carbonyl unit from the carbon chain. The rate and yield of this product depends upon the bond-dissociation energy of the ketone's α substituents. Typically the more α substituted a ketone is, the more likely the reaction will yield products in this way.
- The abstraction of an α -proton from the carbonyl fragment may form a ketene and an alkane.
- The abstraction of a β -proton from the alkyl fragment may form an aldehyde and an alkene.

Type I

- The Norrish type I reaction is the photochemical cleavage or homolysis of aldehydes and ketones into two free radical intermediates.
- The carbonyl group accepts a photon and is excited to a photochemical singlet state.
- Through intersystem crossing the triplet state can be obtained.
- On cleavage of the α -carbon bond from either state, two radical fragments are obtained.
- The size and nature of these fragments depends upon the stability of the generated radicals; for instance, the cleavage of 2-butanone largely yields ethyl radicals in favor of less stable methyl radicals.



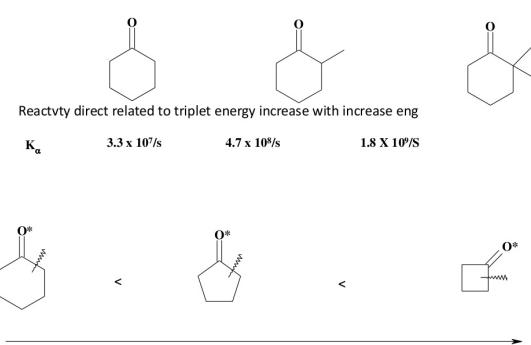
The synthetic utility of this reaction type is limited, for instance it often is a side reaction in the Paternò–Büchi reaction. One organic synthesis based on this reaction is that of bicyclohexylidene



Norrish type I reaction is much faster for $n-\pi^*$ compared to $\pi-\pi^*$ excited states

$n-\pi^*$ reactivity is due to the weakening of the α -bond by overlap of this bond with the half vacant n -orbital of oxygen.

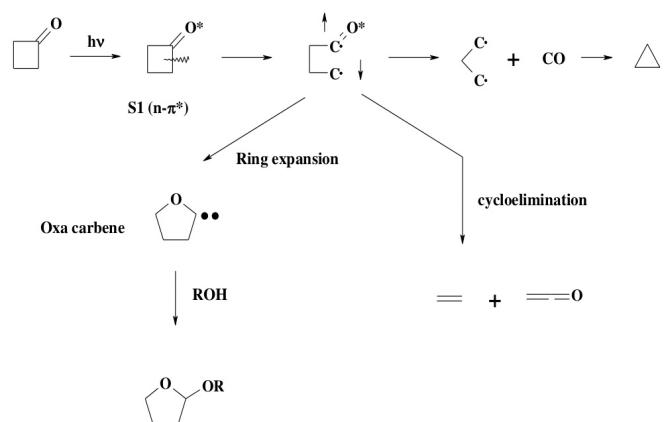
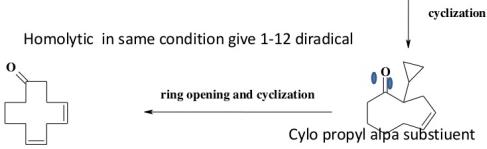
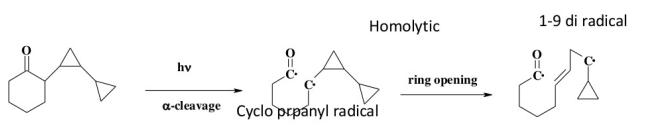
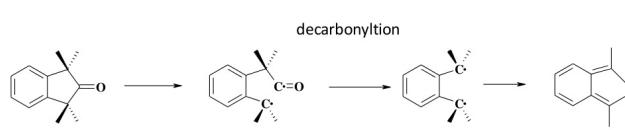
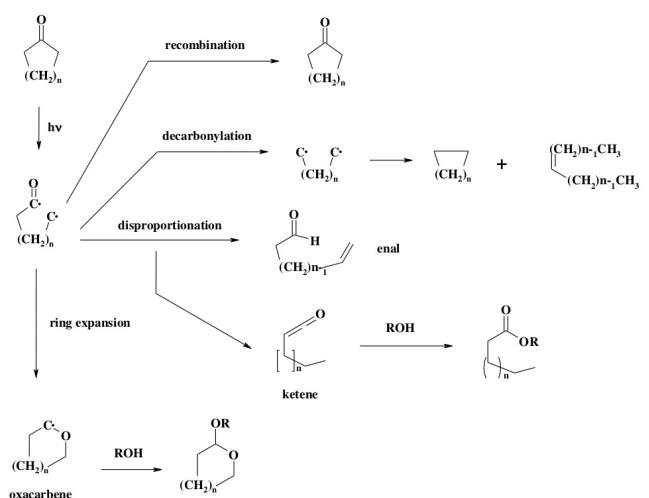
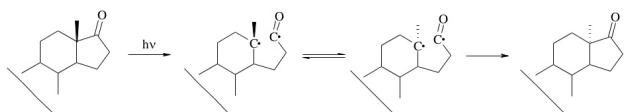
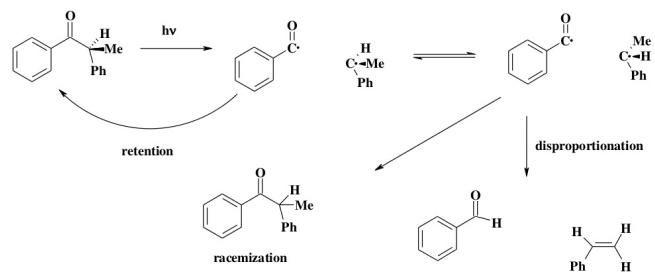
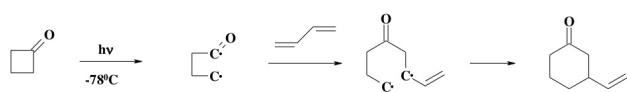
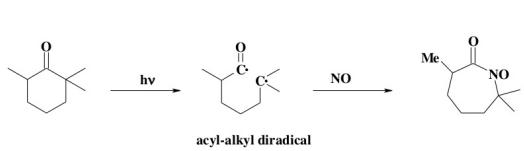
This overlap is not possible for $\pi-\pi^*$ excited states



Rate of α cleavage increasing ring strain

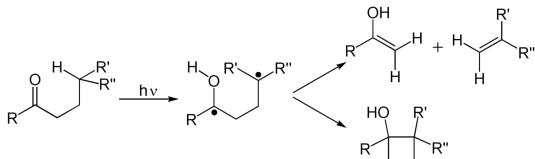
Increase with increase ring strain
cycl-pentone has less butanone has more

Intermediate trapping experiment

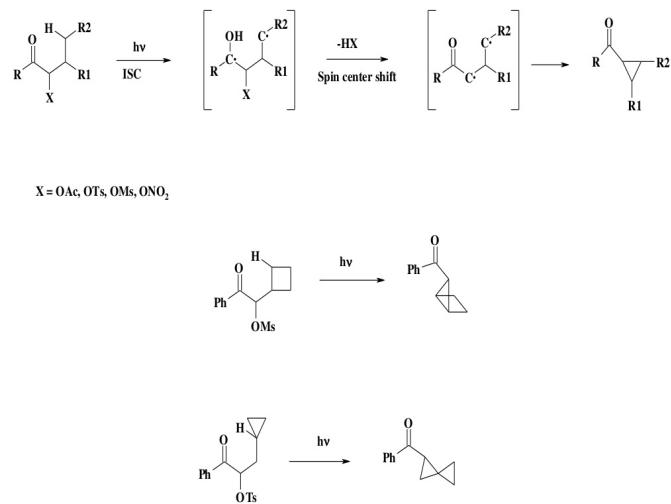
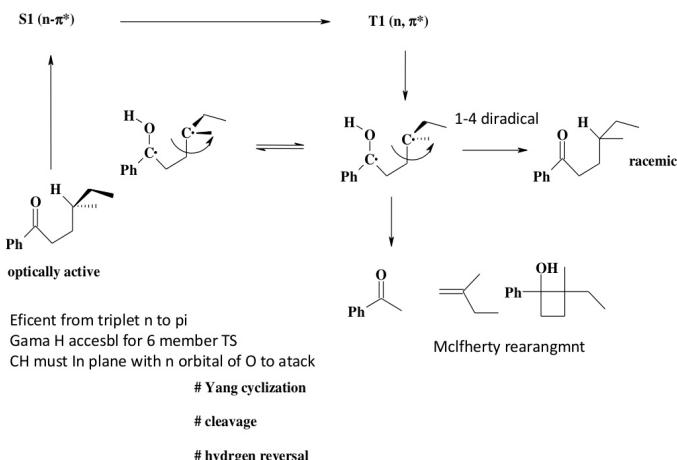
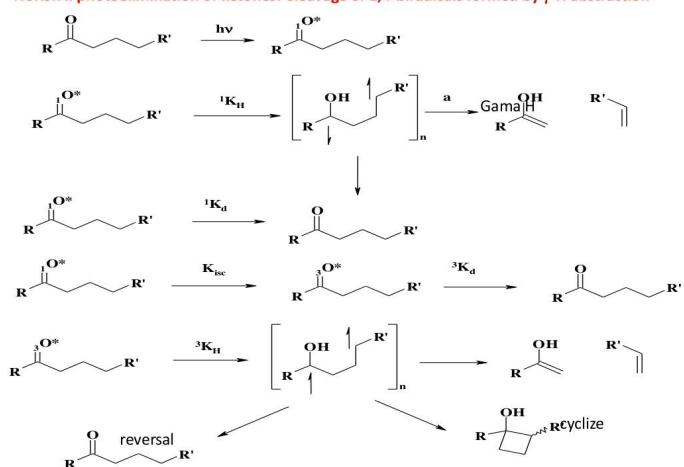


Type II

- A Norrish type II reaction is the photochemical intramolecular abstraction of a γ -hydrogen (a hydrogen atom three carbon positions removed from the carbonyl group) by the excited carbonyl compound to produce a 1,4-biradical as a primary photoproduct. Norrish first reported the reaction in 1937.

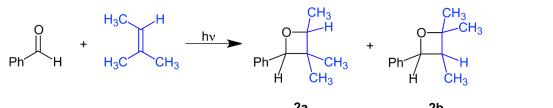


Norrish II photoelimination of ketones: Cleavage of 1,4-biradicals formed by γ -H abstraction



Paterno–Büchi reaction

- The **Paterno–Büchi reaction**, named after Emanuele Paternò and George Büchi who established its basic utility and form, is a photochemical reaction that forms four-membered oxetane rings from a carbonyl and an alkene. With substrates benzaldehyde and 2-methyl-2-butene the reaction product is a mixture of structural isomers



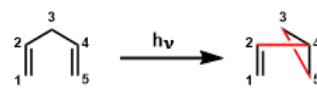
Here an electronically excited carbonyl group is added to a ground state olefin yielding an oxetane

Another substrate set is benzaldehyde and furan



di- π -methane rearrangement

- Photochemical reaction of a molecular entity comprising two π -systems, separated by a saturated carbon atom (a 1,4-diene or an allyl-substituted aromatic analogue), to form an ene- (or aryl-) substituted cyclopropane.

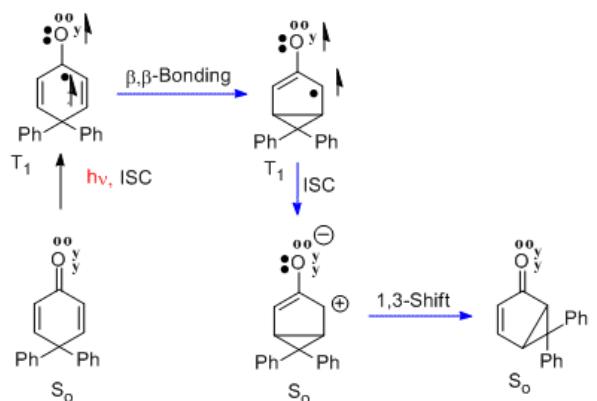
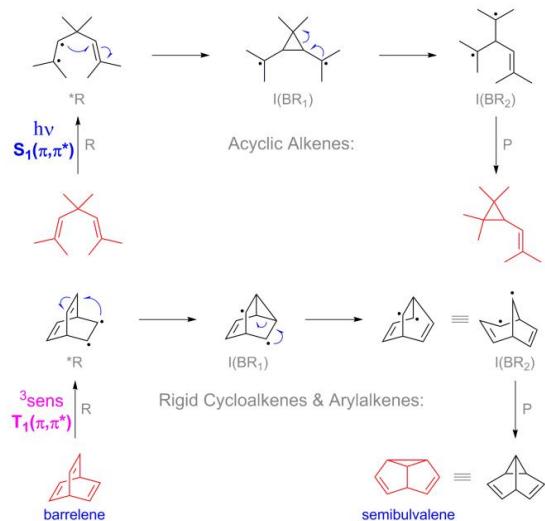
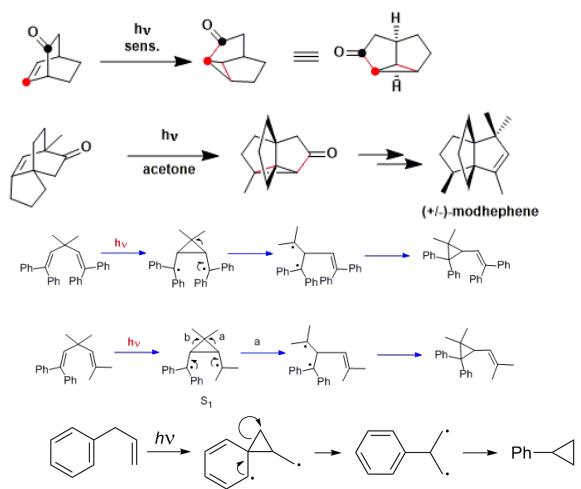
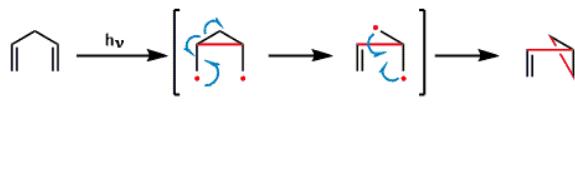


- The rearrangement formally amounts to a 1,2 shift of one ene group (in the diene) or the aryl group (in the allyl-aromatic analogue) and 'bond formation' between the lateral carbons of the non-migrating moiety

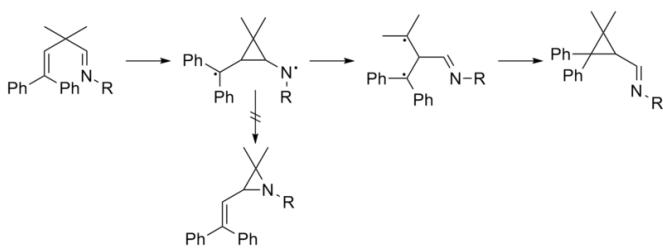
Examples

- 1,4-Dienes undergo light-promoted rearrangement to give vinylcyclopropanes. The scope of this reaction includes dienes containing heteroatoms such as oxygen and nitrogen and even certain benzene ring skeletons.

Reaction Mechanism



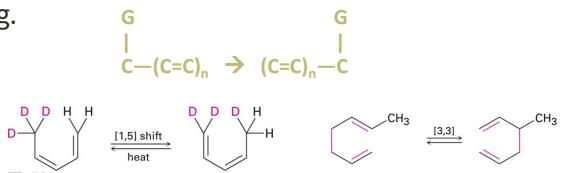
Aza-di-pi-methane rearrangement



Sigmatropic Reactions

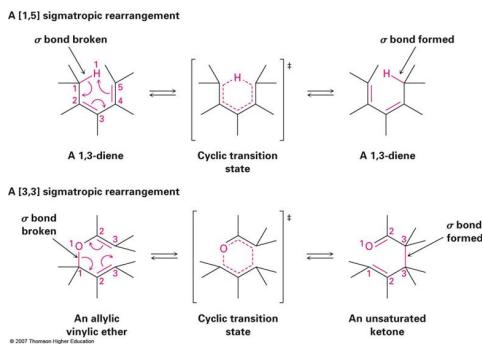
- **Sigmatropic rearrangements** are pericyclic reactions in which a σ bonded atom or group migrates from one end to another in an unanalyzed intramolecular process. They are generally thermal and very rarely photochemical.

e.g.

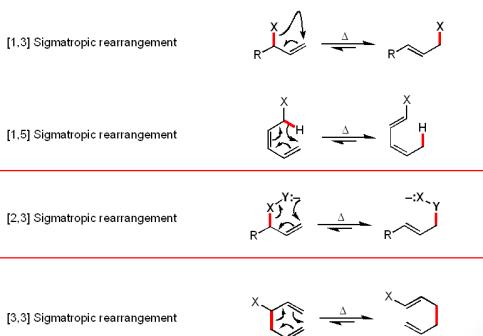


- Since here the sigma bond migrates, hence the name sigmatropic

- 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



- The sigmatropic reactions are in general described as $[i, j]$. The numbers in the bracket $[i, j]$ indicate the number of atoms i, j across which the bond migrates.
- The termini of the original σ bond are labeled 1,1 followed by numbering the chain sequentially. After the reaction the new bond defines the order.



The selection rule

- The migration of the σ bond may take place either *suprafacially* or *antarafacially*
- If the transition state consists of Mobius ($4n$) number of electrons (including those of σ bond) then it is *antarafacial* thermally
- But in Huckel type transition state transformation occurs *suprafacially* under thermal condition
- It should be pointed out that total number of electrons involved in the transition is equal to $(i+j)$ in case of neutral species.
- But for charged system we have to add or deduct electron(s) according to the charge.

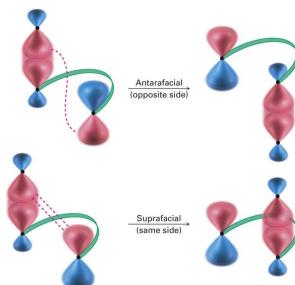
The selection rule

No. of electrons	Polyene $[i, j]$ shift			Thermally allowed migration
	Neutral	Cation	Anion	
2		$[1, 2]$		Suprafacial with retention
4 or 4n	$[1, 3] / [1, 7]$	$[1, 4]$	$[1, 2]$	Antarafacial with retention
	$[1, (4n-1)]$	$[1, 4n]$	$[1, (4n-2)]$	Suprafacial with inversion
6 or $[4n+2]$	$[1, 5] / [3, 3]$	$[1, 6]$	$[1, 4]$	Suprafacial with retention Antarafacial with inversion

Photochemically the stereochemistry is just reverse.
But photochemical sigmatropic reactions are very rare

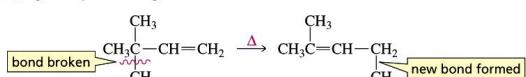
Sigmatropic Stereospecificity: Suprafacial and Antarafacial

- Migration of a group across the same face of the π system is a *suprafacial* rearrangement
- Migration of a group from one face of the π system to the other face is called an *antarafacial* rearrangement

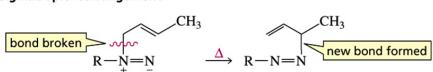


Some Examples of Sigmatropic Rearrangements

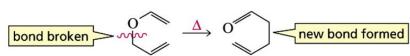
a [1,3] sigmatropic rearrangement



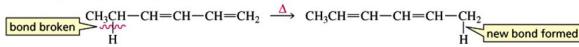
a [2,3] sigmatropic rearrangement



a [3,3] sigmatropic rearrangement

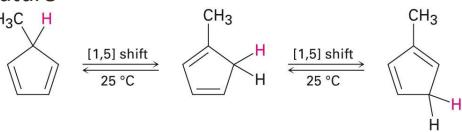


a [1,5] sigmatropic rearrangement

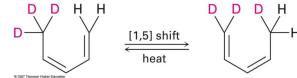


Some Examples of Sigmatropic Rearrangements

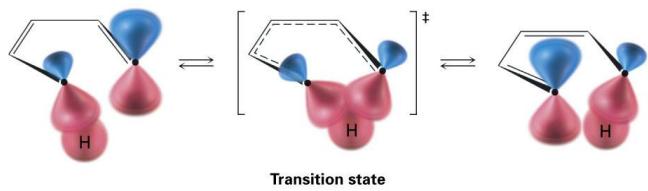
- A [1,5] sigmatropic rearrangement involves three electron pairs (two π bonds and one σ bond)
- Orbital-symmetry rules predict a suprafacial reaction
- 5-methylcyclopentadiene rapidly rearranges at room temperature



- Heating 5,5,5-trideutero-(1,3Z)-pentadiene causes scrambling of deuterium between positions 1 and 5

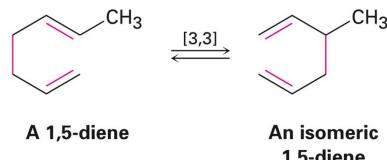


Orbital Picture of a Suprafacial [1,5]-H Shift



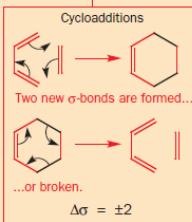
Cope Rearrangements

- It is a case of thermal [3,3] sigmatropic rearrangement; e.g. isomerisation of 1,5 diene system on heating.
- The reaction is generally reversible and gives a equilibrium mixture of reactant and product. The temperature required to bring about the reaction depends on substitution on it

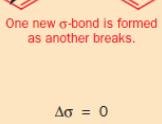


- The types of pericyclic reactions are distinguished by the number of σ bonds made or broken

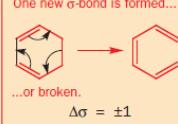
Types of pericyclic reactions



Sigmatropic rearrangements

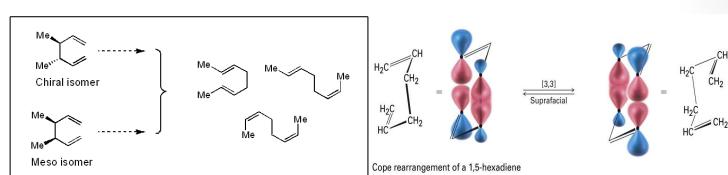


Electrocyclic reactions

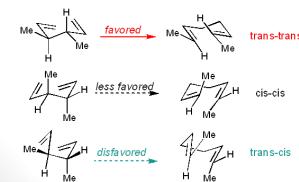


[12]

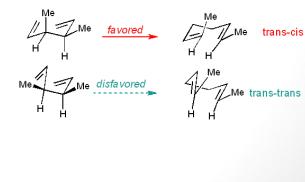
- The reaction is highly stereospecific
- The T.S. for 1,5 diene prefers a chair to a boat conformation



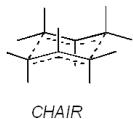
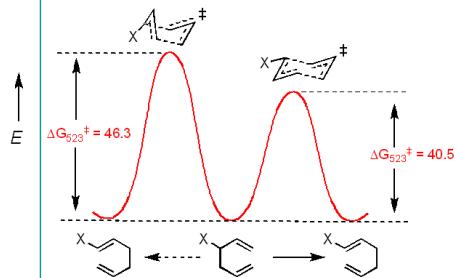
Predictions: Chiral isomer:



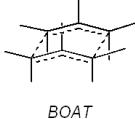
Predictions: Meso isomer:



[12]



CHAIR

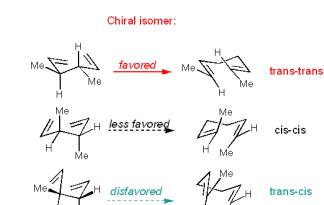


BOAT

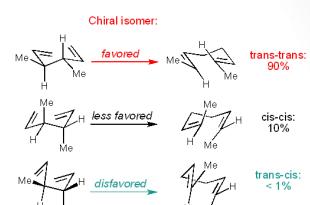
Relative Energy $\Delta\Delta G^\ddagger$: 0

+ 5.8 kcal/mol

Predictions:



Results:



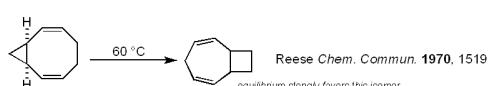
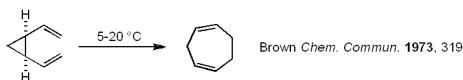
Meso isomer:



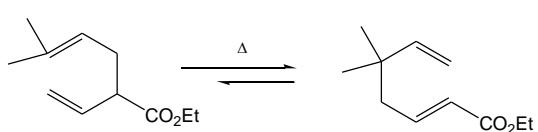
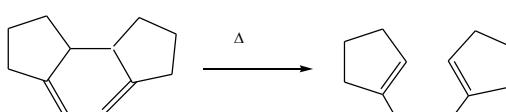
Meso isomer:



- Many important compounds may be synthesized using Cope reaction

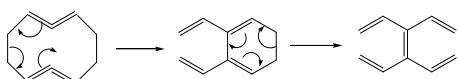


- Here relief of small ring strain is the driving force.



α,β,ϵ unsaturated heptadiene carboxylate

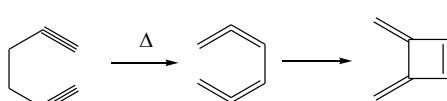
- The 1,5 diene system may be inside a ring or part of allene system



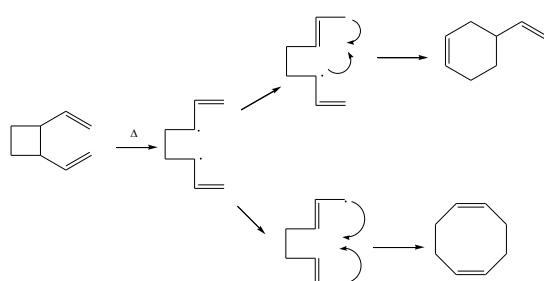
- but reaction doesn't take place if one of the bond is part of an aromatic system



- When heated 1,5 diynes are converted to 3,4 dimethylene cyclo butene

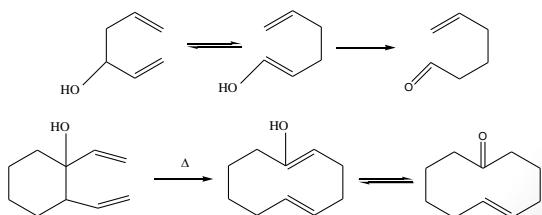


- All Cope rearrangements do not occur in pericyclic mechanism. Thus *cis* 1,2 divinyl cyclobutane gives 1,5 cyclooctadiene smoothly. The *trans* isomer also gives the product, but here main product is 4-vinyl cyclohexene

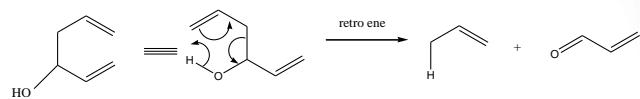


Oxycope rearrangement

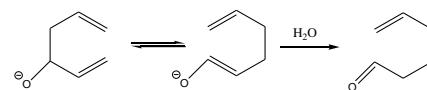
- If the 1,5 diene has a 3-hydroxy substituent, the reaction is called oxycope rearrangement.
- It is different from ordinary Cope rearrangement in two respects
 - In ordinary Cope rearrangement both reactant and product exist in equilibrium after the reaction as it is reversible. But here the product is enol which can't be isolated as it tautomerises to keto form and hence reverse reaction does not occur.



- The [3,3] shift competes with a retro ene reaction, so the products of both reactions are normally isolated

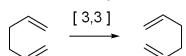


- The oxycope reaction is accelerated ($10^{10} - 10^{17}$ times) if alkoxide is used instead of alcohol. In this case the direct product is the enolate ion, which is hydrolysed to ketone.

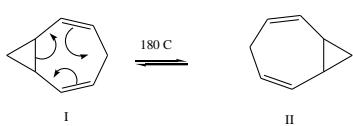


Degenerate Cope Rearrangements

- The simplest example of Cope rearrangement is rearrangement of 1,5 hexadiene to 1,5 hexadiene.

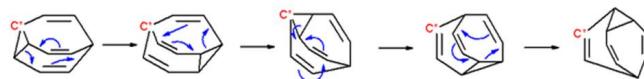


- Here the reactant and product are indistinguishable. Such reactions are called degenerate Cope rearrangement.
- Another such example is bicyclo [5,1,0] octadiene.



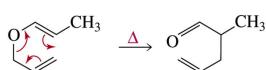
- At room temperature the NMR spectrum indicate only existence of str. I but at 180°C the NMR shows I & II exist in equilibrium mixture. At this temperature the molecule rapidly ($>10^3$ times sec^{-1}) changes back & forth between two structures. This is called valence tautomerism and is distinct from resonance even though only electrons shift.

- Molecules which exhibit valence tautomerism are said to have fluxional structure.
- The number of possible valence tautomers for bullvalene is 1,209,600, five of which are shown.

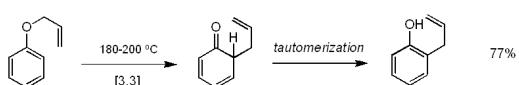


Claisen Rearrangements

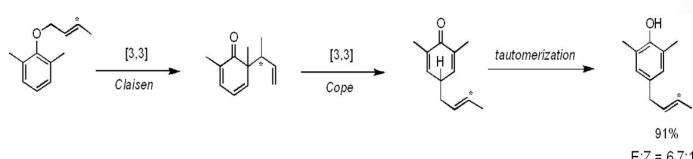
- This rearrangement is basically a thermal [3,3] sigmatropic rearrangement of an allyl and vinyl ether. The product is β,γ unsaturated aldehyde or ketone



- The rearrangement is better known for allyl aryl ether.
- The product *ortho* dienone tautomerises to o – allyl phenols



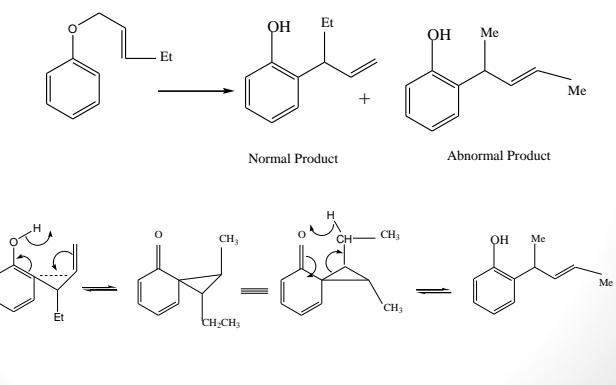
- If one or both *ortho* positions are blocked, the reactant gives *para* substituted product via two consecutive [3,3] shift.
- The reaction is intramolecular and mechanism gets support from labeling experiment



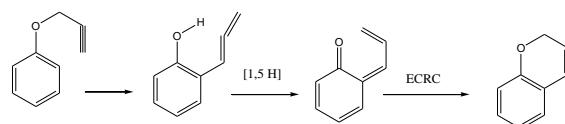
- If *ortho* position is not substituted, keto-enol tautomerism takes place faster than second Claisen shift. But often *para* substituted product occur along with *ortho* one even when *ortho* positions are open.

[25]

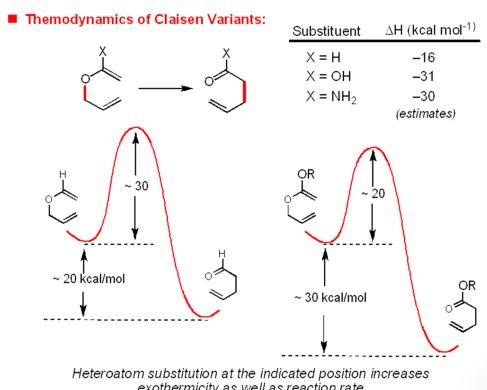
- Ethers with an alkyl substitution in γ position often gives abnormal product along with normal products. The abnormal product is actually derived from normal o-allyl phenol by two [1,5] homodienyl shift.



- Another reaction closely related to abnormal Claisen reaction is heating of phenyl propargyl ether. The normal product o-allenyl phenol undergoes a [1,5] H shift and an electrocyclic ring closure.



- The reaction is not ionic and hence should not be greatly dependent on presence or absence of substitution in ring. Electron donating group increases rate of reaction and electron withdrawing group decreases the rate but effect is small. However, effect of solvent is greater.



Sigmatropic Rearrangements

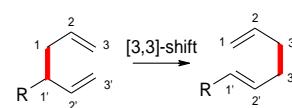
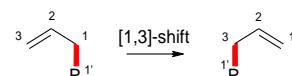
Neil Stevenson
12/01/05

Pericyclic Reactions

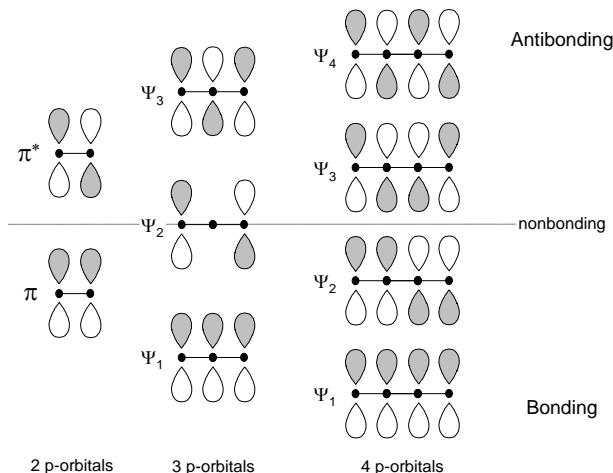
- Continuous concerted reorganisation of electrons
- 5 major categories:
 - Electrocyclic ring opening/closure
 - Cycloaddition/cycloreversion reactions
 - Cheletropic reactions (e.g. carbene addition)
 - Group transfer reactions (e.g. H₂ transfer)
 - Sigmatropic rearrangements

Sigmatropic Rearrangements

- Migration of a σ -bond across a conjugated π -system
- [m,n] shift when the σ -bond migrates across m atoms of one system and n of another

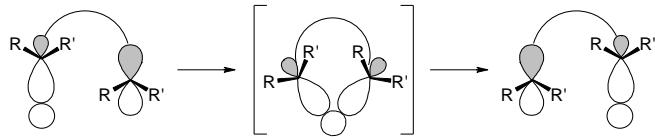


Conjugated π Systems

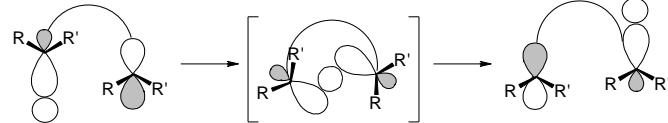


Suprafacial/Antarafacial

- Suprafacial migration: Group moves across same face

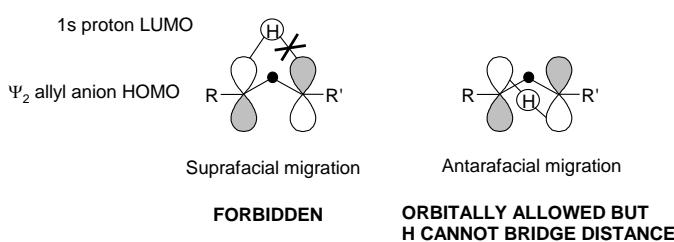
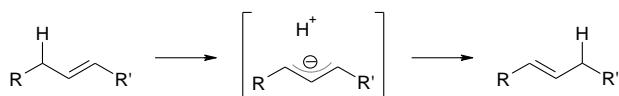


- Antarafacial migration: Group moves from one face to the other



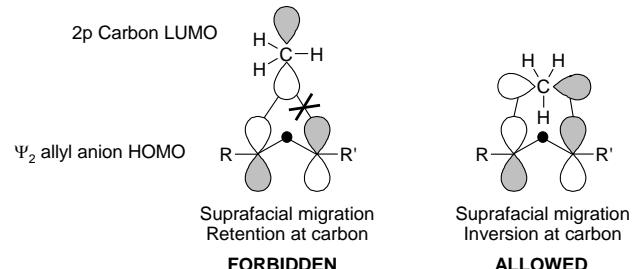
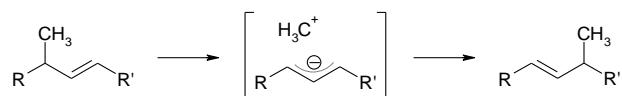
FMO Analysis

- [1,3] Sigmatropic Rearrangements: H migration



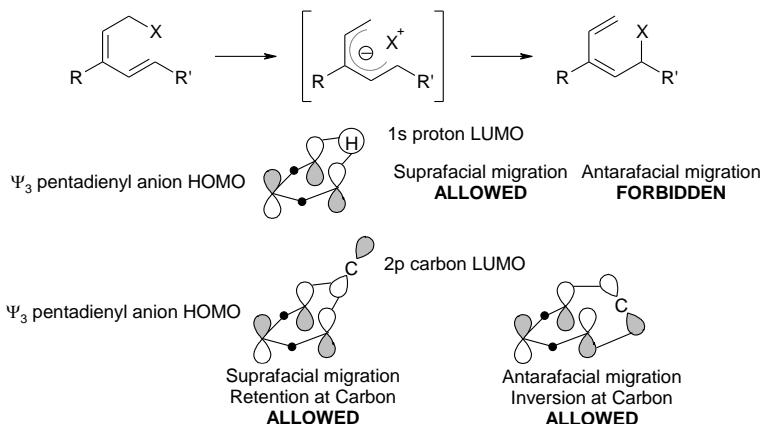
FMO Analysis

- [1,3] Sigmatropic Rearrangements: C migration



FMO Analysis

- [1,5] Sigmatropic Rearrangements



Dewar-Zimmerman

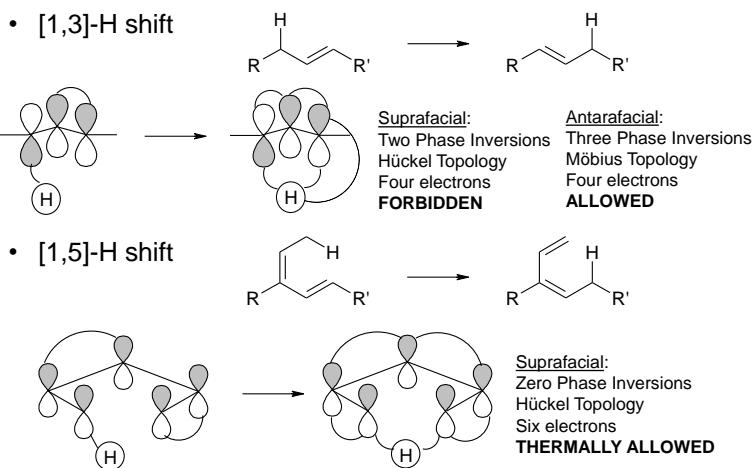
- Dewar-Zimmerman model:

- Choose a set of 2p atomic orbitals and arbitrarily assign phase
- Connect the orbitals in the starting material
- Allow reaction to proceed according to postulated geometry and connect reacting lobes.
- Count number of phase inversions: Odd = Möbius, Even = Hückel
- Assign transition state as aromatic or antiaromatic based on number of electrons:

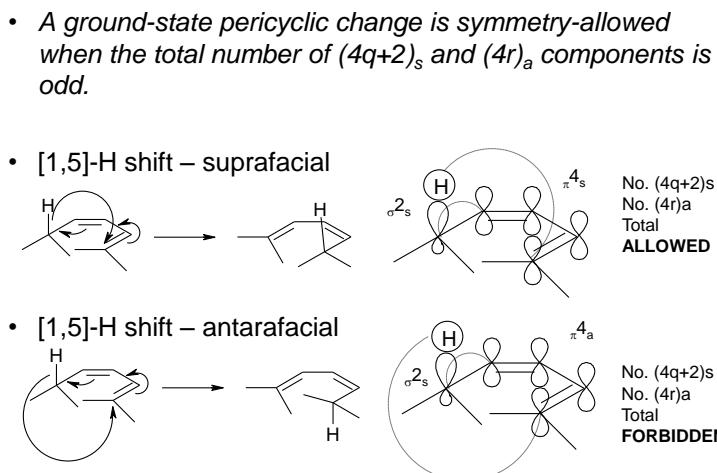
System	Aromatic	Antiaromatic
Hückel	$4n + 2$	$4n$
Möbius	$4n$	$4n + 2$

- Aromatic = Thermally allowed (Photochemically forbidden)
- Antiaromatic = Thermally forbidden (Photochemically allowed)

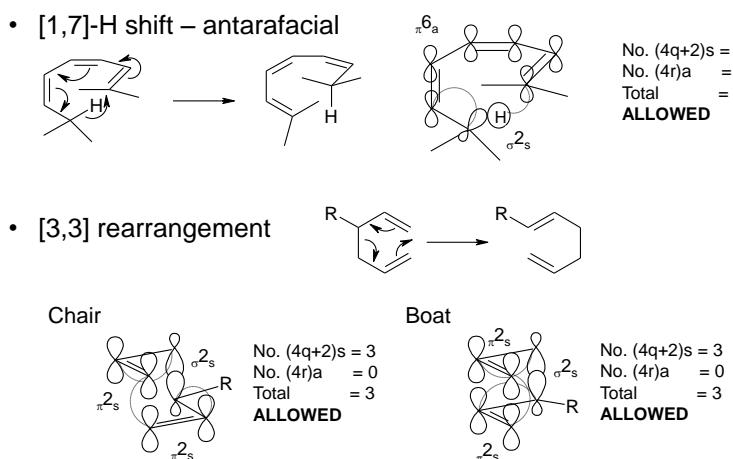
Dewar-Zimmerman



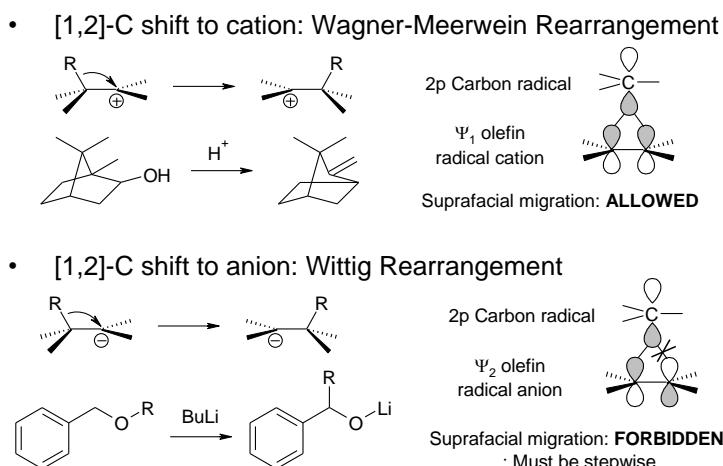
Woodward-Hoffman



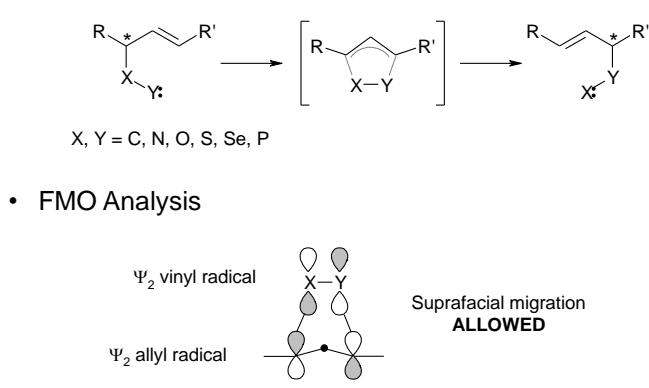
Woodward-Hoffman



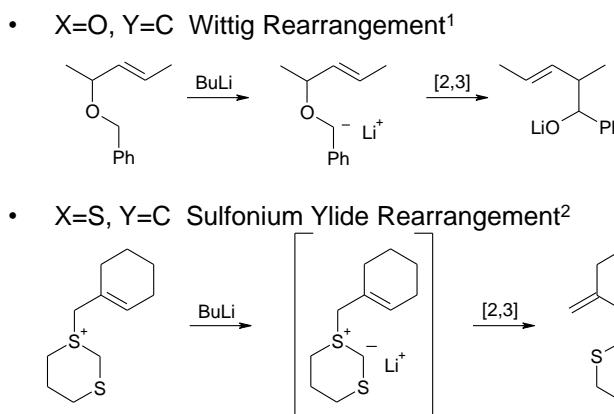
[1,2] Sigmatropic Rearrangements



[2,3] Sigmatropic Rearrangements



[2,3] Sigmatropic Rearrangements

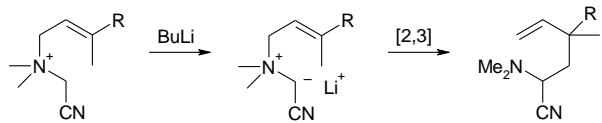


1. Baldwin, JACS 1971, 93, 3556

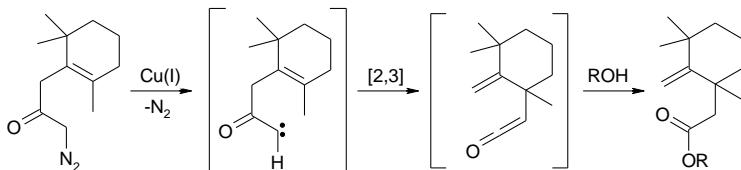
2. Lythgoe, Chem. Comm. 1972, 757

[2,3] Sigmatropic Rearrangements

- X=N, Y=C Ammonium Ylide Rearrangement³ (Stevens)



- X=C, Y=C All-carbon Rearrangement⁴

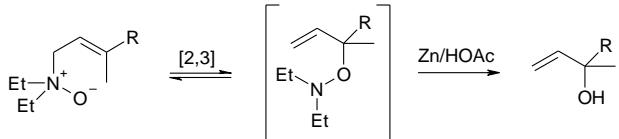


3. Buchi, *J. Am. Chem. Soc.* **1974**, *96*, 7573

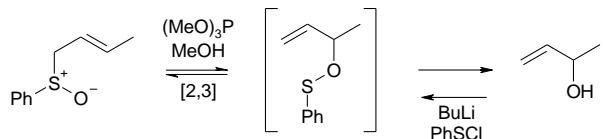
4. Smith, *J. Org. Chem.* **1977**, *42*, 3165

[2,3] Sigmatropic Rearrangements

- X=N, Y=O Meisenheimer Rearrangement⁵



- X=S, Y=O Sulfoxide Rearrangement⁶

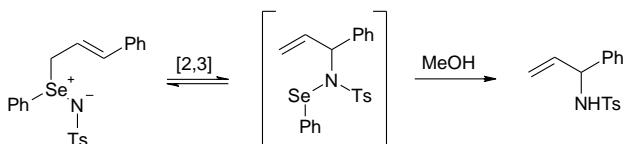


5. Tanabe, *Tet. Lett.* **1975**, 3005

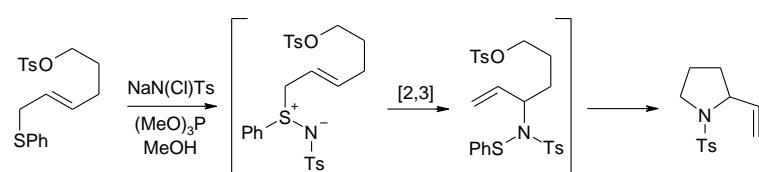
6. Evans, *Acccts. Chem. Res.* **1974**, *7*, 147

[2,3] Sigmatropic Rearrangements

- X=Se, Y=N Related Rearrangement⁷



- X=S, Y=N Related Rearrangement⁸



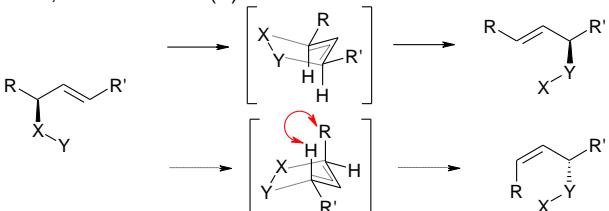
7. Hopkins, *Tet. Lett.* **1984**, *25*, 15

8. Dolle, *Tet. Lett.* **1989**, *30*, 4723

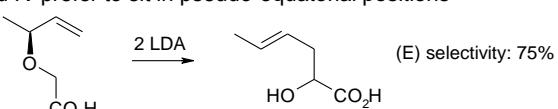
[2,3] Sigmatropic Rearrangements

- Olefin Selectivity from starting olefin

- 1,2-Disubstitution(E)



- R and R' prefer to sit in pseudo-equatorial positions⁹

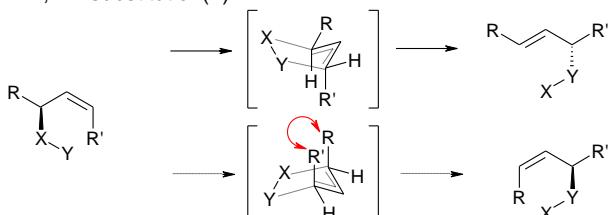


9. Nakai, *Tet. Lett.* **1981**, *22*, 69

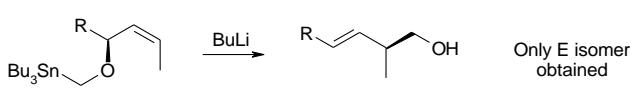
[2,3] Sigmatropic Rearrangements

- Olefin Selectivity from starting olefin

- 1,2-Disubstitution(Z)



- Generally, higher levels of 1,3 induction seen with Z olefins¹⁰

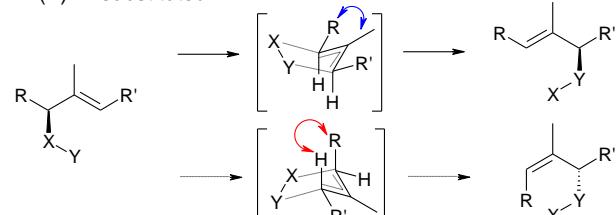


10. Still, *J. Am. Chem. Soc.* **1978**, *100*, 1927

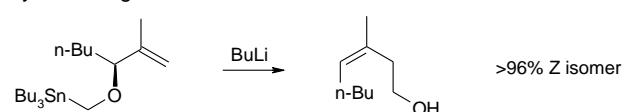
[2,3] Sigmatropic Rearrangements

- Olefin Selectivity from starting olefin

- (E)-Trisubstituted

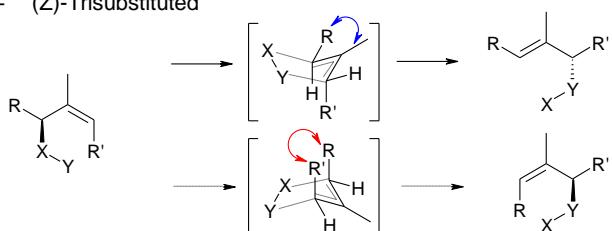


- E transition state still generally preferred but R-Me interaction may cause significant destabilisation¹⁰



[2,3] Sigmatropic Rearrangements

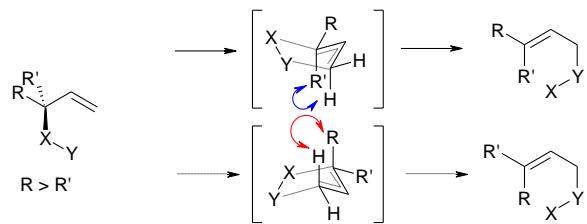
- Olefin Selectivity from starting olefin
 - (Z)-Trisubstituted



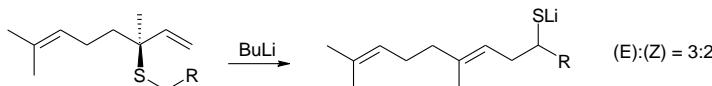
- Again, generally higher levels of 1,3 induction seen with Z olefins due to highly destabilising R-R' interaction

[2,3] Sigmatropic Rearrangements

- Olefin Selectivity from allylic position



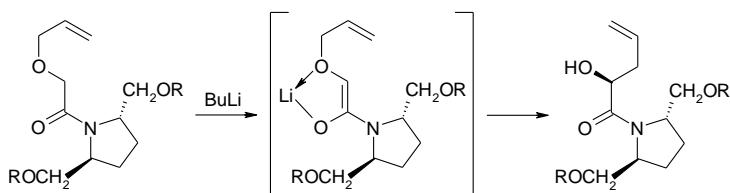
- May expect selectivity dependent on size difference of R vs. R'¹¹



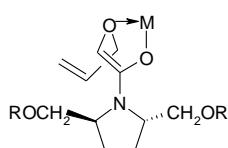
11. Rautenstrauch, *Helv. Chim. Acta* **1971**, *54*, 739

[2,3] Sigmatropic Rearrangements

- Chiral Auxiliaries¹²



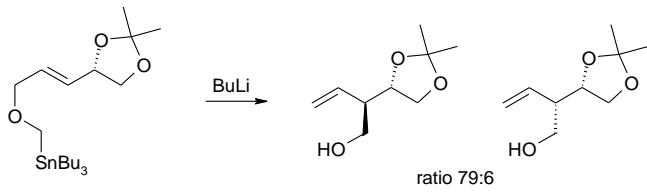
- Via:



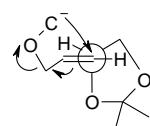
12. Katsuki, *Tet. Lett.* **1986**, *27*, 4577

[2,3] Sigmatropic Rearrangements

- Internal Relay of Stereochemistry¹³



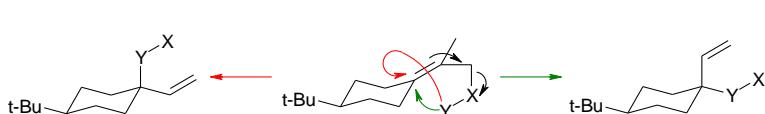
- Via: (Felkin-Ahn)



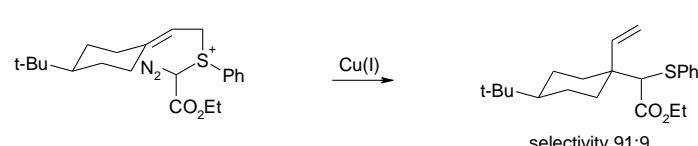
13. Bruckner, *Angew. Chem. Int. Ed.* **1988**, *27*, 278

[2,3] Sigmatropic Rearrangements

- Steric Effects



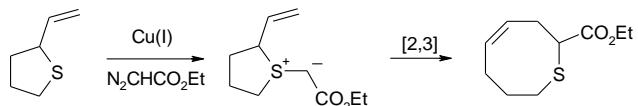
- Pseudo-equatorial attack generally favoured¹⁴



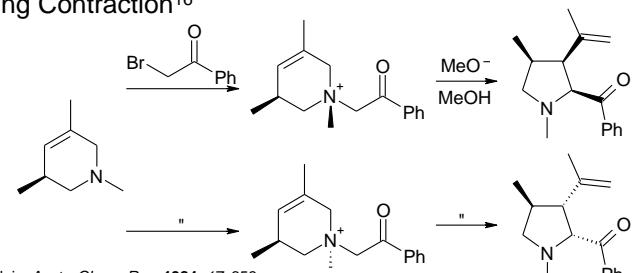
14. Evans, *J. Am. Chem. Soc.* **1972**, *94*, 3672

[2,3] Sigmatropic Rearrangements

- Ring Expansion¹⁵



- Ring Contraction¹⁶

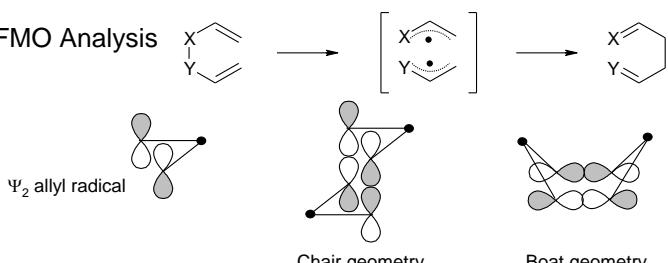


15. Vedejs, *Accts. Chem. Res.* **1984**, *17*, 358

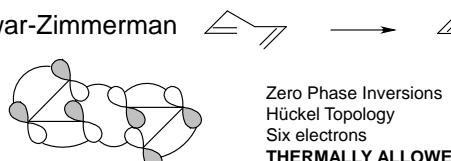
16. Stevenson, *Tet. Lett.* **1990**, *31*, 4351

[3,3] Sigmatropic Rearrangements

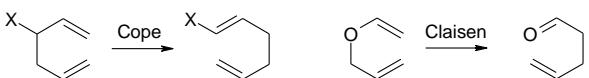
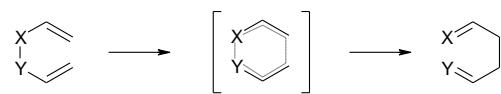
- FMO Analysis



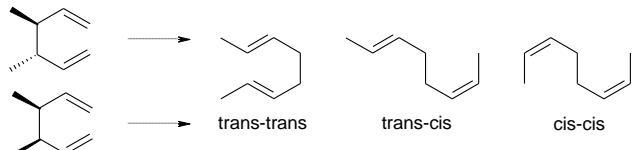
- Dewar-Zimmerman



[3,3] Sigmatropic Rearrangements



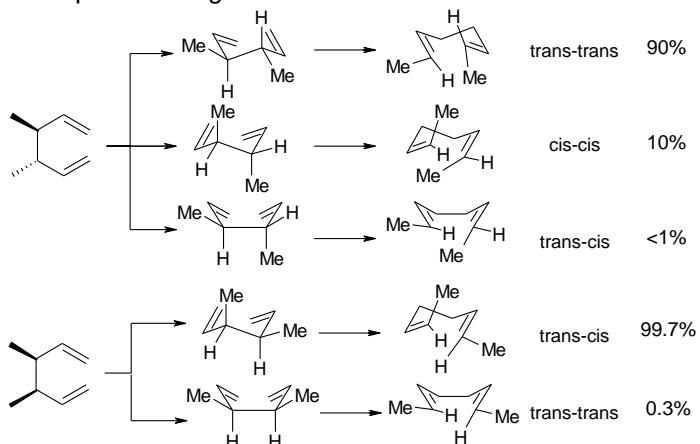
- Cope Rearrangement: Boat vs. Chair Transition State¹⁷



17. Doering, Roth, *Tetrahedron* **1962**, *18*, 67

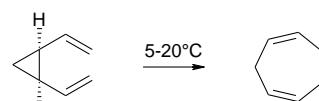
[3,3] Sigmatropic Rearrangements

- Cope Rearrangement: Boat vs. Chair Transition State



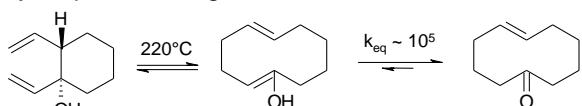
[3,3] Sigmatropic Rearrangements

- Cope Rearrangement: Use of ring strain¹⁸



- Relief of ring strain upon rearrangement

- Oxy-Cope Rearrangement¹⁹



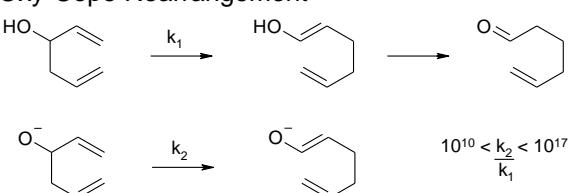
- Tautomerism shifts equilibrium to right

18. Brown, *Chem. Comm.* **1973**, 319

19. Marvell, *Tet. Lett.* **1970**, 509

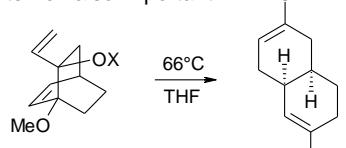
[3,3] Sigmatropic Rearrangements

- Oxy-Cope Rearrangement



- Significant rate acceleration for anionic Oxy-Cope.²⁰

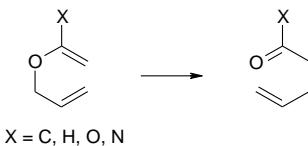
- Counter-ion also important



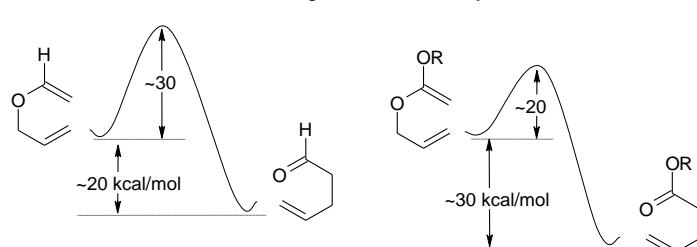
20. Golob, *J. Am. Chem. Soc.* **1975**, *97*, 4765

[3,3] Sigmatropic Rearrangements

- Claisen Rearrangement

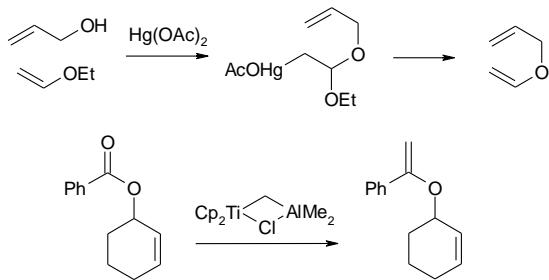


- Thermodynamic driving force: (C-O) π -bond and (C-C) σ -bond formation
- X=Heteroatom leads to higher exothermicity and reaction rate



[3,3] Sigmatropic Rearrangements

- Synthesis of allyl vinyl ethers^{21,22}

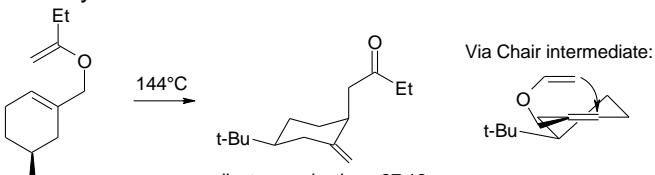


21. Watanabe, Conlon, *J. Am. Chem. Soc.* **1957**, 79, 2828

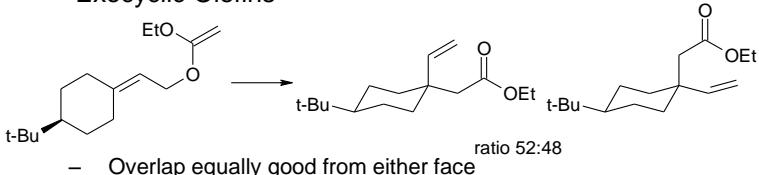
22. Evans, Grubbs, *J. Am. Chem. Soc.* **1980**, 102, 3272

[3,3] Sigmatropic Rearrangements

- Endocyclic Olefins²³



- Exocyclic Olefins²⁴



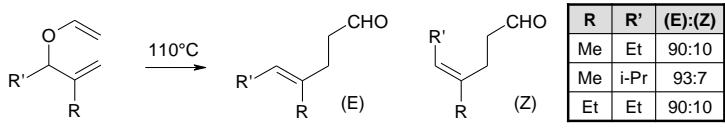
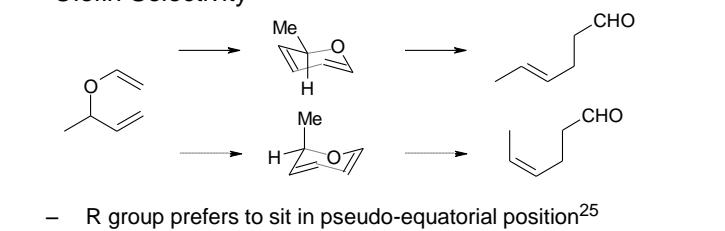
– Overlap equally good from either face

23. Ireland, *J. Org. Chem.* **1983**, 48, 1829

24. House, *J. Org. Chem.* **1975**, 40, 86

[3,3] Sigmatropic Rearrangements

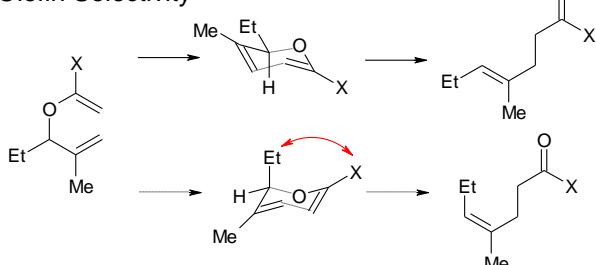
- Olefin Selectivity



25. Faulkner, *J. Am. Chem. Soc.* **1973**, 95, 553

[3,3] Sigmatropic Rearrangements

- Olefin Selectivity

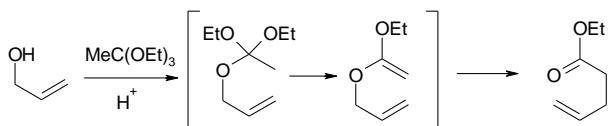


- Extra substituents lead to enhanced diastereoselection²⁵
Larger X => better selectivity

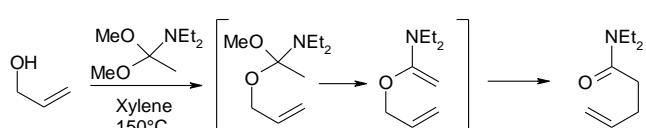
X	(E):(Z)
H	90:10
Me	>99:1
MeO	>99:1
Me ₂ N	>98:2

[3,3] Sigmatropic Rearrangements

- Claisen Variants: Johnson Orthoester Claisen²⁶



- Claisen Variants: Eschenmoser Claisen²⁷

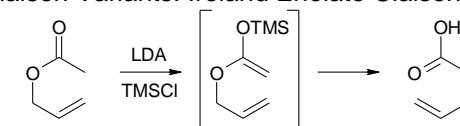


26. Johnson, Faulkner, Peterson, *J. Am. Chem. Soc.* **1970**, 92, 741

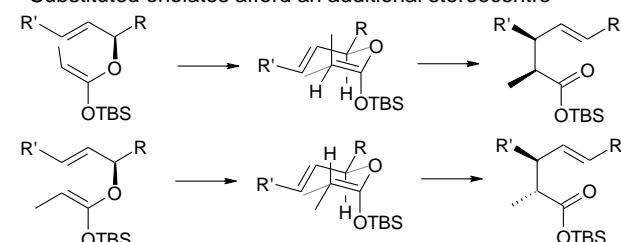
27. Eschenmoser, *Helv. Chim. Acta* **1964**, 47, 2425

[3,3] Sigmatropic Rearrangements

- Claisen Variants: Ireland Enolate Claisen²⁸



- Substituted enolates afford an additional stereocentre²⁹

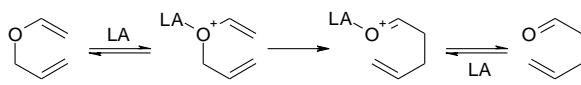


28. Ireland, *J. Am. Chem. Soc.* **1976**, 98, 2868

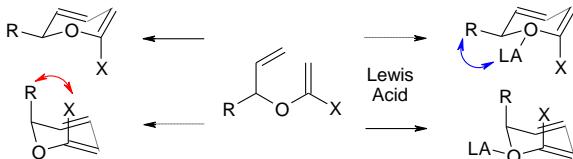
29. Ireland, *J. Org. Chem.* **1991**, 56, 650

[3,3] Sigmatropic Rearrangements

- Lewis Acid catalysed Claisen rearrangement



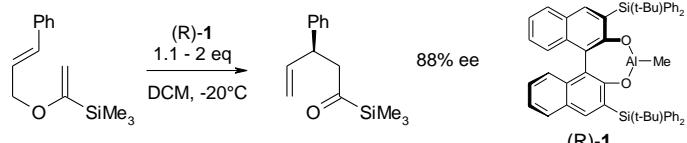
- Presence of Lewis Acid can influence rearrangement³⁰



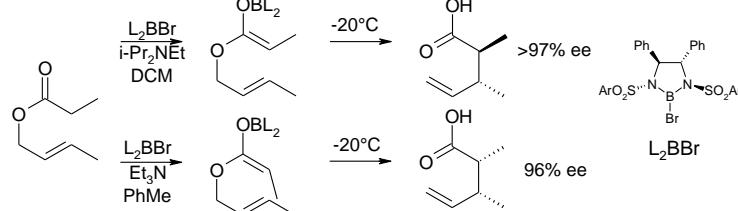
30. Yamamoto, J. Am. Chem. Soc. 1990, 112, 316

[3,3] Sigmatropic Rearrangements

- Chiral Lewis Acid promoted Claisen rearrangement³¹



- Enantioselective Claisen Rearrangements³²

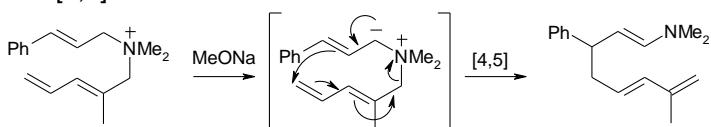


31. Yamamoto, J. Am. Chem. Soc. 1990, 112, 7791

32. Corey, J. Am. Chem. Soc. 1991, 113, 4026

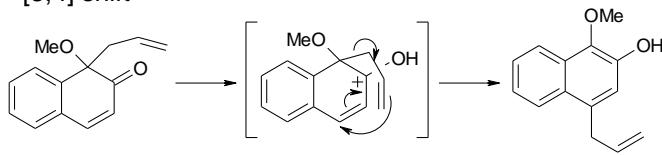
[m,n] Sigmatropic Rearrangements

- [4,5] shift



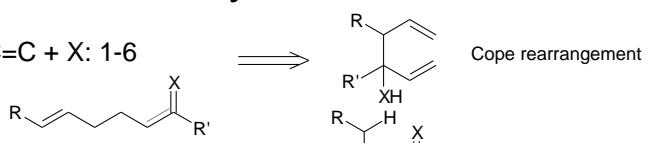
- [2,3] possible but [4,5] favoured. [2,5] and [3,4] forbidden

- [3,4] shift



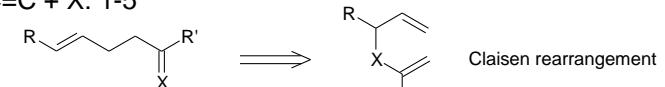
Key Retrons

- C=C + X: 1-6



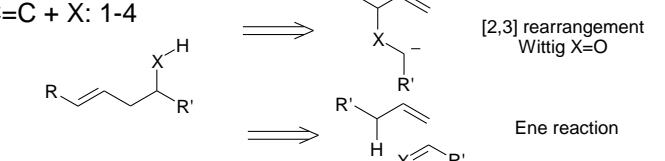
Cope rearrangement

- C=C + X: 1-5



Retro-ene reaction

- C=C + X: 1-4



Claisen rearrangement

[2,3] rearrangement Wittig X=O



Ene reaction

Definition

- Cycloaddition is the formation of two sigma bonds between the termini of two isolated pi systems to form a cyclic product without elimination of any fragment
- Cycloaddition is a process in which two or more reactants combine to form a stable cyclic molecule during which no small fragment is eliminated and σ bonds are formed but not broken.
- Such reactions are generally inter molecular but intramolecular cycloaddition is also known.

Cycloaddition

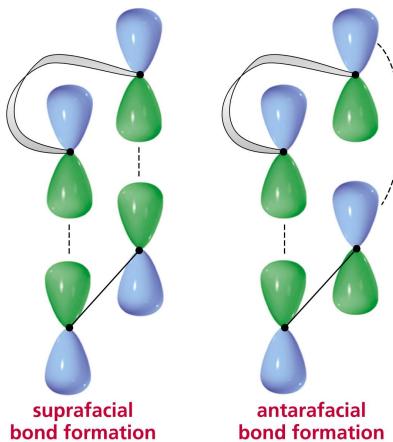


- The addition is generally cis addition or supra-supra addition (i.e. addition to the same side of the double bonds)
- However there are other processes where trans addition or supra-antarafacial addition occurs to maintain orbital symmetry
- Cycloaddition reactions are also highly stereospecific. Stereospecificity is controlled by mode of attack (s,s or s,a)
- Selection rule for cycloaddition correlates mode of attack under thermal and photochemical conditions for different systems.

$m + n$	No. of π bonds	Δ	$h\nu$
$4q$ $q = 1, 2, 3, \dots$	even	(s,a) or (a,s)	s,s
$4q+2$ $q = 0, 1, 2, 3, \dots$	odd	s,s	(s,a) or (a,s)

m and n are number π of electrons in the two π systems

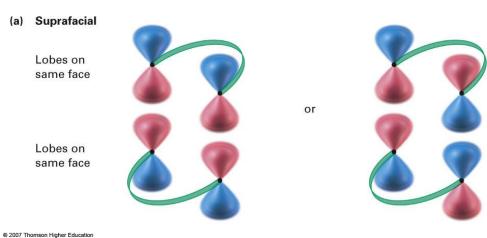
The frontier molecular orbitals of both reactants must be considered: the HOMO and LUMO



Rules for Cycloadditions - Suprafacial Cycloadditions

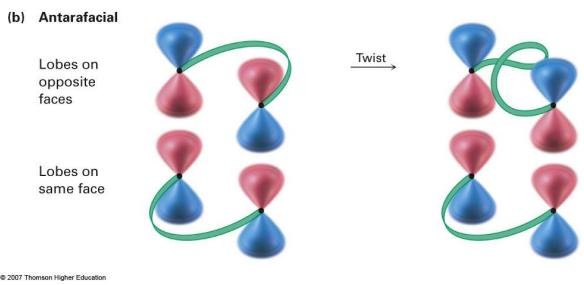
The terminal π lobes of the two reactants must have the correct symmetry for bonding to occur

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



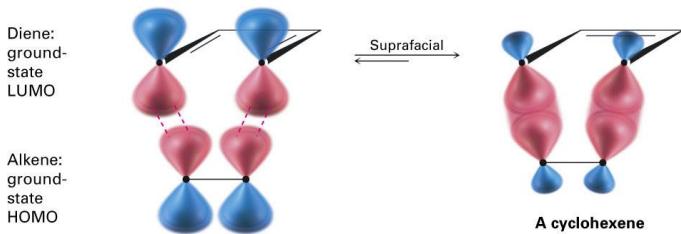
Rules for Cycloadditions - Antarafacial Cycloadditions

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)



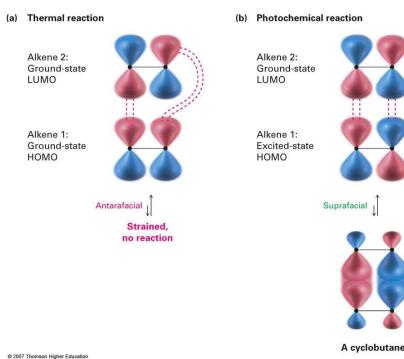
Stereochemistry of Cycloadditions

HOMO of one reactant combines with LUMO of other
Possible in thermal [4 + 2] cycloaddition



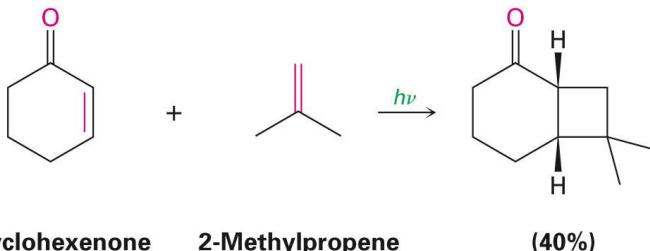
[2+2] Cycloadditions

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



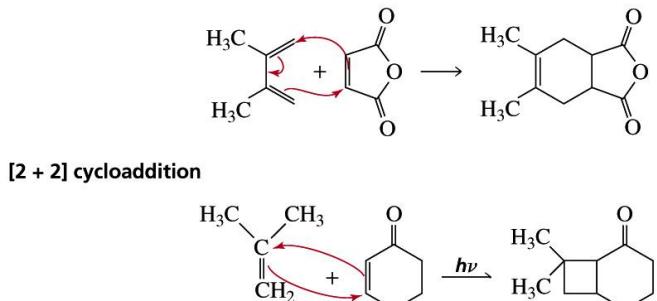
Formation of Four-Membered Rings

Photochemical [2 + 2] cycloaddition reaction occurs smoothly



Cycloadditions are classified according to the number of π electrons that interact in the reaction

[4 + 2] cycloaddition (a Diels–Alder reaction)



Diels–Alder Reaction



Otto Diels

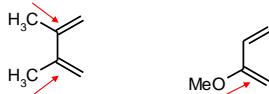


Kurt Alder

- Method for synthesis of 6-membered ring
- One-step, concerted reaction
- Termed [4+2] cycloaddition reaction where 4π and 2π electrons react.

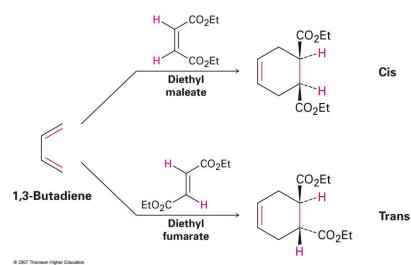


Diene – electron-rich nucleophile
electron-donating groups make it more reactive.



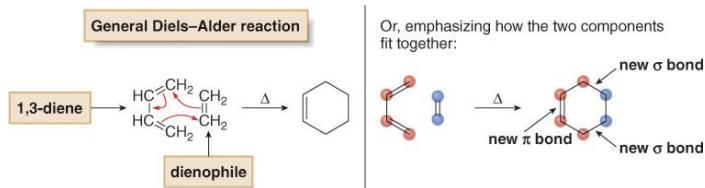
Diels–Alder Reactions

The Diels–Alder cycloaddition reaction is a pericyclic process that takes place between a diene (four π electrons) and a dienophile (two π electrons) to yield a cyclohexene product. Stereospecific with respect to substituents

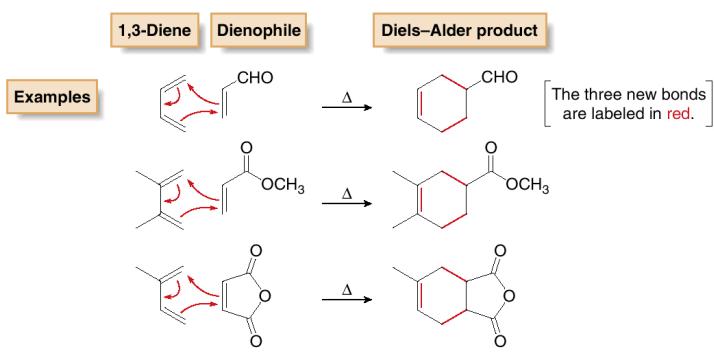


The Diels–Alder Reaction

The Diels–Alder reaction is an addition reaction between a 1,3-diene and an alkene (called a dienophile), to form a new six-membered ring.



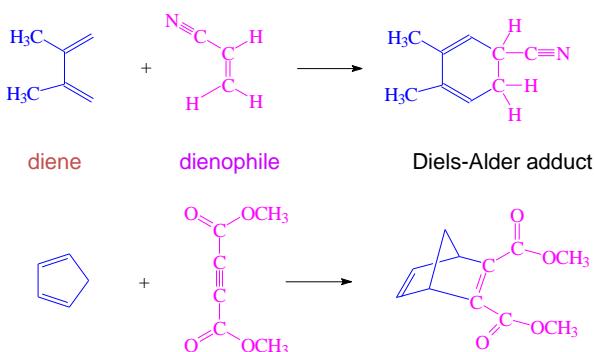
Some examples of Diels–Alder reactions are shown below:



Three curved arrows are needed to show the cyclic movement of electron pairs because three π bonds break and two σ bonds and one π bond form.

Because each new σ bond is ~20 kcal/mol stronger than a π bond that is broken, a typical Diels–Alder reaction releases ~40 kcal/mol of energy.

Examples of Diels-Alder Reactions

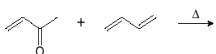


All Diels-Alder reactions have the following features in common:

- They are initiated by heat; that is, the Diels-Alder reaction is a thermal reaction.
- They form new six-membered rings.
- Three π bonds break, and two new C—C σ bonds and one new C—C π bond forms.
- They are concerted; that is, all old bonds are broken and all new bonds are formed in a single step.

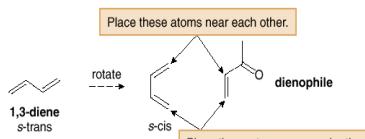
How To Draw the Product of a Diels–Alder Reaction

Example Draw the product of the following Diels–Alder reaction:

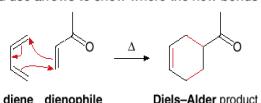


Step [1] Arrange the 1,3-diene and the dienophile next to each other, with the diene drawn in the s-cis conformation.

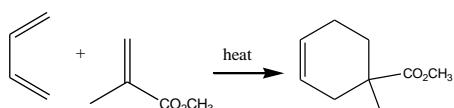
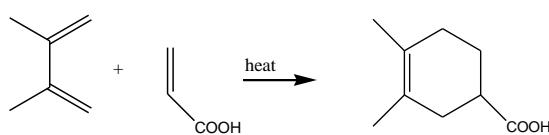
- This step is key: Rotate the diene so that it is drawn in the s-cis conformation, and place the end C's of the diene close to the double bond of the dienophile.



Step [2] Cleave the three π bonds and use arrows to show where the new bonds will be formed.

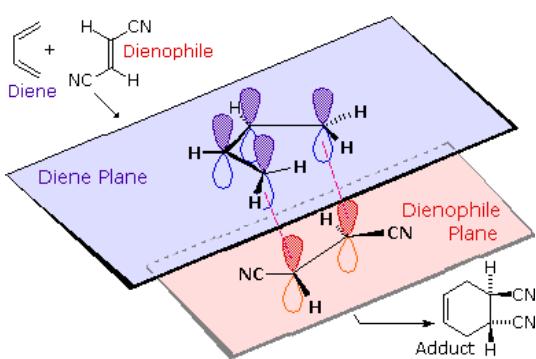


Predict the products.



Mechanism of Diels-Alder:

one-step, simultaneous (concerted) bond-making and bond-breaking involving 6 π electrons

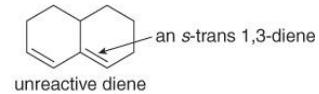
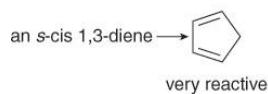


Several rules govern the course of the Diels-Alder reaction.

- The diene can react only when it adopts the s-cis conformation.

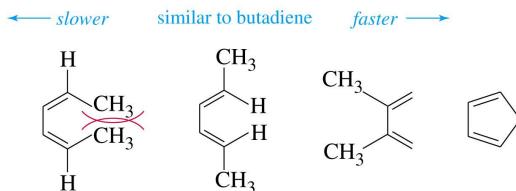


This rotation is prevented in cyclic alkenes. When the two double bonds are constrained to an s-cis conformation, the diene is unusually reactive. When the two double bonds are constrained in the s-trans conformation, the diene is unreactive.



s-cis conformation

Diels–Alder rate compared with that of 1,3-butadiene

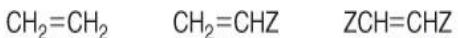


2. Electron-withdrawing substituents in the dienophile increase the reaction rate.

In a Diels–Alder reaction, the conjugated diene acts as a nucleophile and the dienophile acts as an electrophile.

Electron-withdrawing groups make the dienophile more electrophilic (and thus more reactive) by withdrawing electron density from the carbon–carbon double bond.

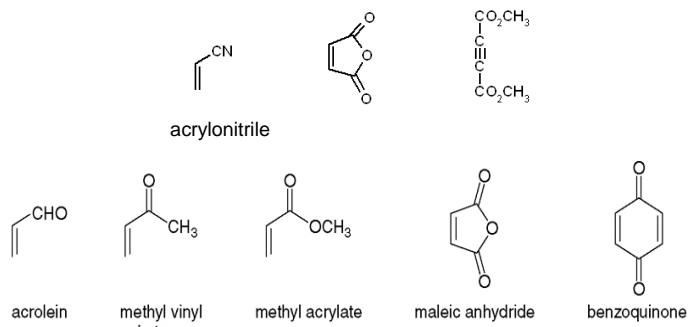
If Z is an electron-withdrawing group, then the reactivity of the dienophile increases as follows:



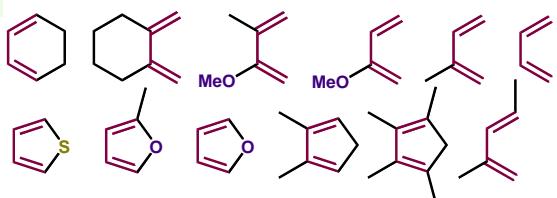
Increasing reactivity

A carbonyl group is an effective electron-withdrawing group because it bears a partial positive charge ($\delta+$), which withdraws electron density from the carbon–carbon double bond of the dienophile.

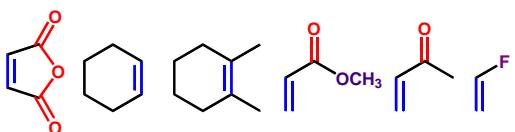
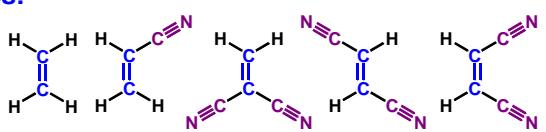
Some common dienophiles are shown below:



Dienes:

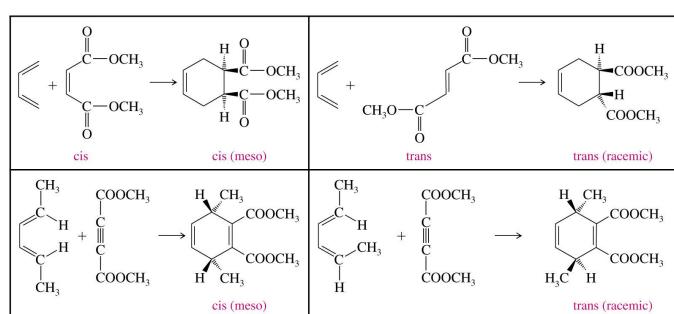
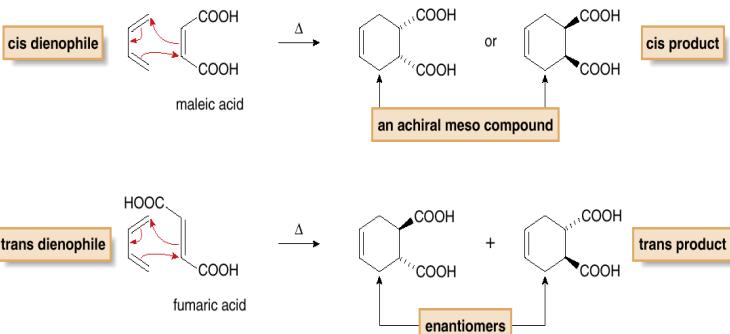


Dienophiles:

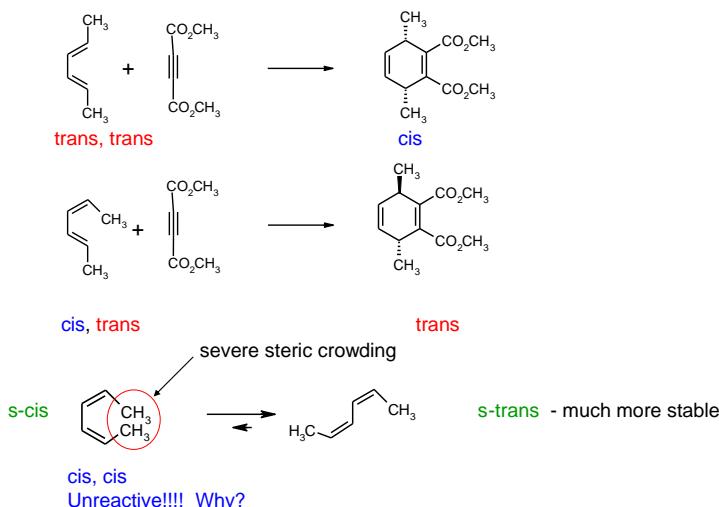


3. The stereochemistry of the dienophile is retained.

syn stereochemistry



What about the diene?

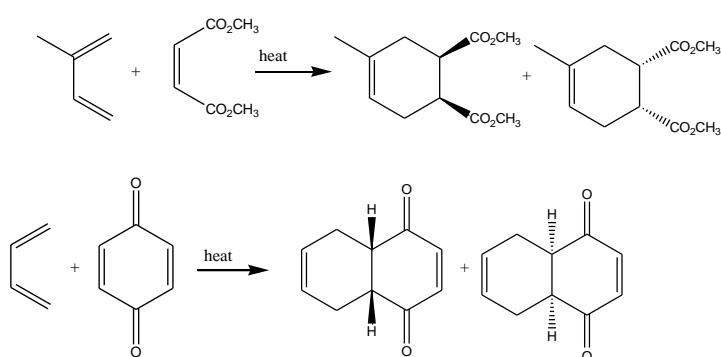


Conclusion:

Diels-Alder is stereospecific with respect to the diene.

- trans, trans → cis product
- trans, cis → trans product
- cis, trans → trans product
- cis, cis → unreactive

Predict the products.

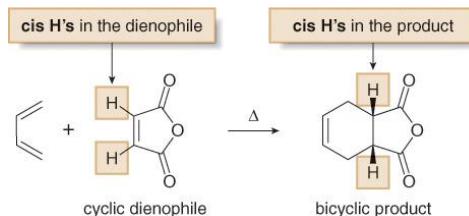


These two cis products are identical.

• A cyclic dienophile forms a bicyclic product.

• A bicyclic system in which two rings share a common C—C bond is called a fused ring system. The two H atoms of the ring fusion must be cis, because they were cis in the starting dienophile

• A bicyclic system of this sort is said to be cis-fused.

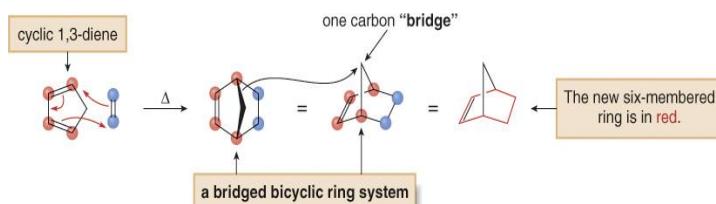


4. When endo and exo products are possible, the endo product is preferred.

• Consider the reaction of 1,3-cyclopentadiene with ethylene. A new six-membered ring forms and above the ring there is a one atom “bridge.”

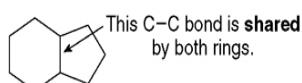
• Thus, the product is bicyclic, but the carbon atoms shared by both rings are non-adjacent.

• A bicyclic ring system in which the two rings share non-adjacent carbon atoms is called a bridged ring system.



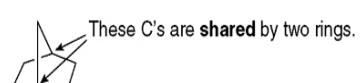
Fused and bridged bicyclic ring systems compared

A fused bicyclic system



- One bond is shared by two rings.
- The shared C's are adjacent.

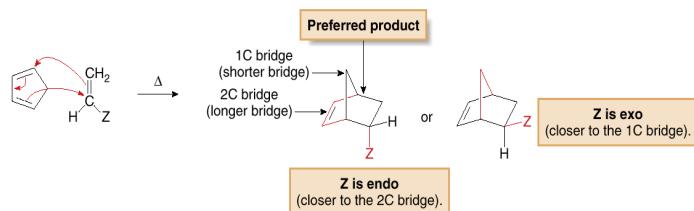
A bridged bicyclic system



- Two non-adjacent atoms are shared by both rings.

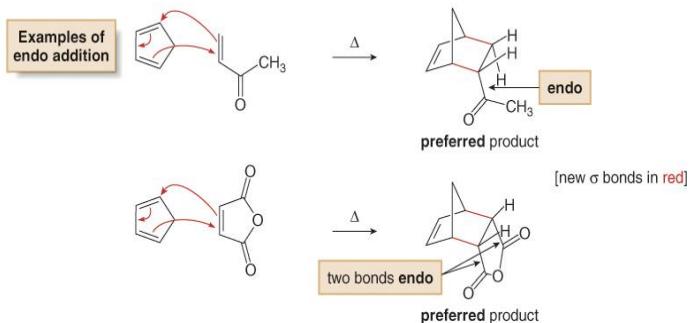
When cyclopentadiene reacts with a substituted alkene as the dienophile ($\text{CH}_2=\text{CHZ}$), the substituent Z can be oriented in one of two ways in the product.

The terms **endo** and **exo** are used to indicate the position of Z.

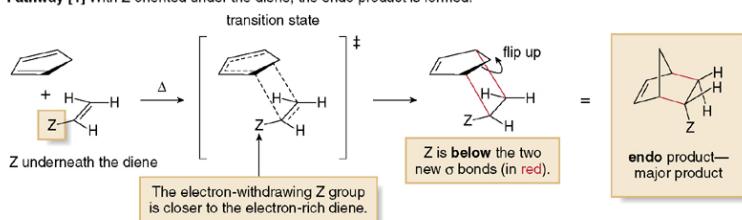


- A substituent on one bridge is **endo** if it is closer to the **longer** bridge that joins the two carbons common to both rings.
- A substituent is **exo** if it is closer to the **shorter** bridge that joins the carbons together.

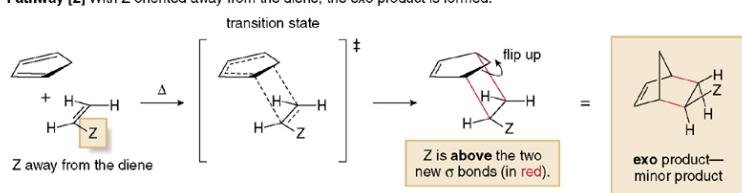
In a Diels-Alder reaction, the **endo** product is preferred, as shown in the two examples below. The transition state leading to the **endo** product allows more interaction between the electron rich diene and the electron-withdrawing substituent Z on the dienophile, an energetically favorable arrangement.



Pathway [1] With Z oriented under the diene, the endo product is formed.

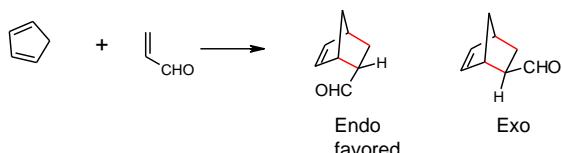


Pathway [2] With Z oriented away from the diene, the exo product is formed.



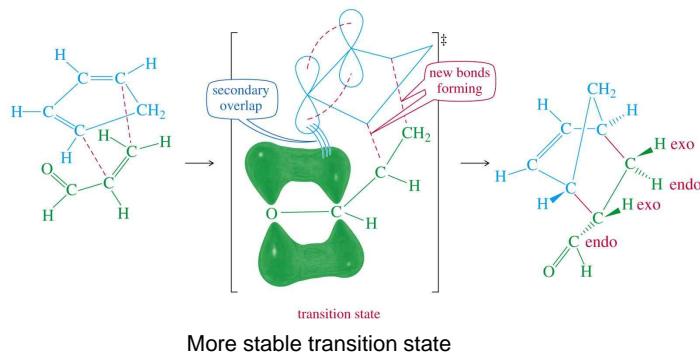
Endo Rule

when substituted bicyclic structures form ,the endo product is favored over the exo product.

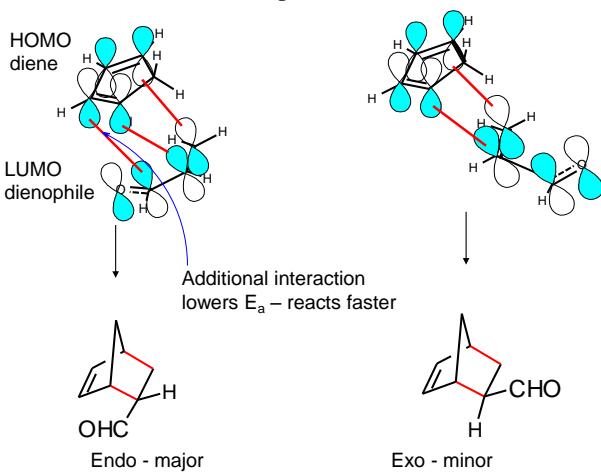


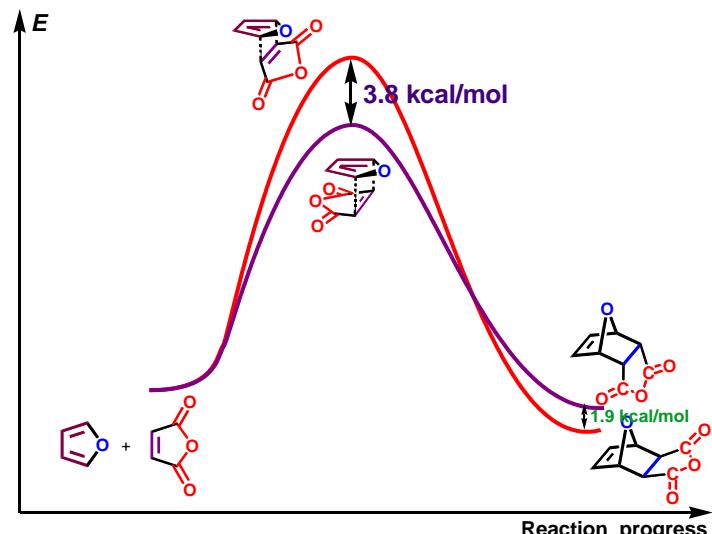
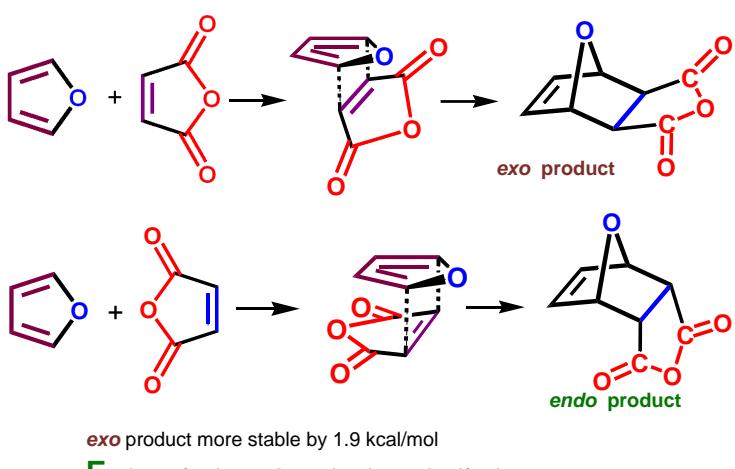
Endo Rule

If the electron-withdrawing group(s) on the dienophile have a pi bond, there is secondary overlap with the p orbitals of C2 and C3 in the diene.

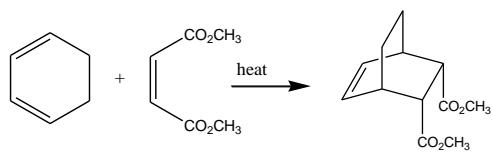
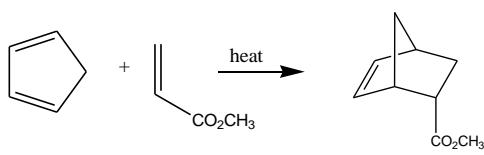


Explanation of Endo Rule: There are two possible approaches between the diene and dienophile in this reaction.





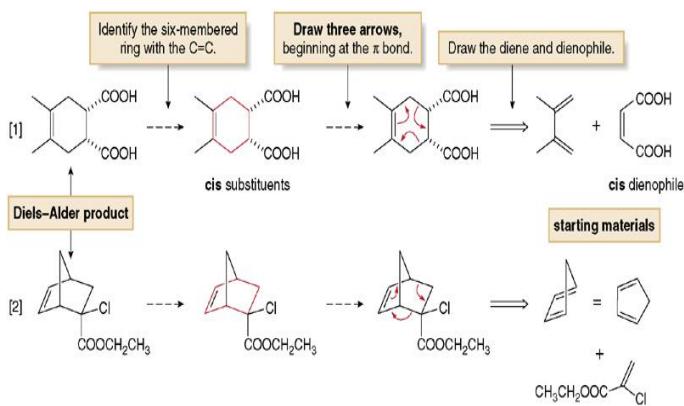
Predict the products.



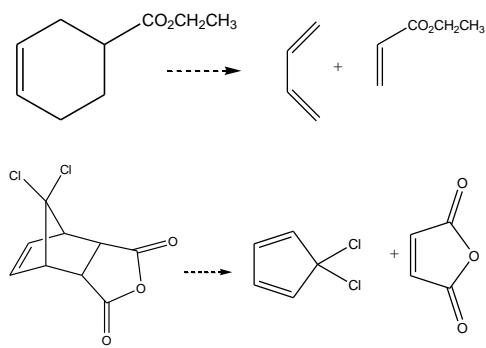
The Diels-Alder Reaction—Retrosynthetic Analysis

To draw the starting materials from a given Diels-Alder adduct:

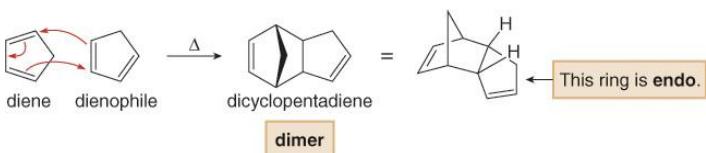
- Locate the six-membered ring that contains the C=C.
- Draw three arrows around the cyclohexane ring, beginning with the π bond and two σ bonds, and forming three π bonds.
- Retain the stereochemistry of substituents on the C=C of the dienophile; cis substituents on the six-membered ring give a cis dienophile.



Predict the starting materials.



The Retro Diels-Alder Reaction

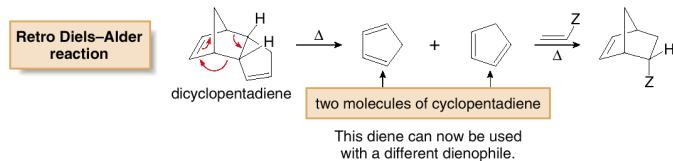


• When heated, dicyclopentadiene undergoes a **retro Diels-Alder reaction**, and two molecules of cyclopentadiene are re-formed.

• If the newly produced cyclopentadiene is immediately treated with a different dienophile, it reacts to form a new Diels-Alder adduct with this dienophile.

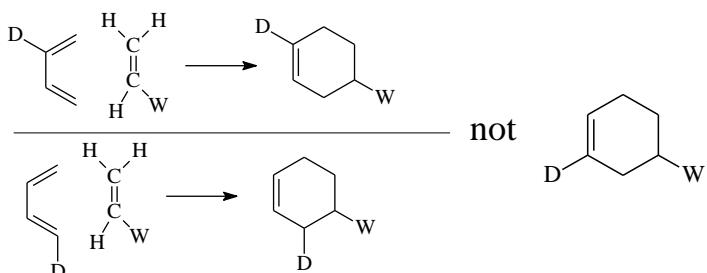
• This is how cyclopentadiene used in Diels-Alder reactions is produced.

• The formation of dicyclopentadiene is so rapid that it takes only a few hours at room temperature for cyclopentadiene to completely dimerize.

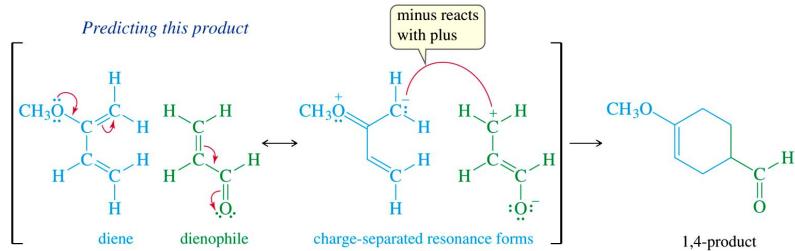
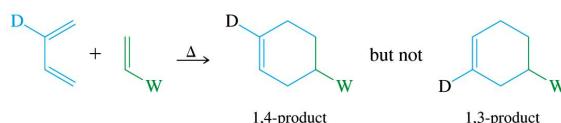


Regiospecificity

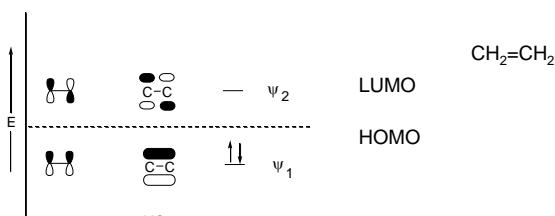
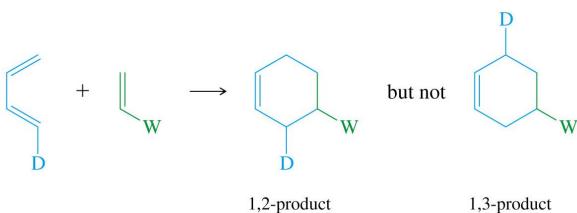
The 6-membered ring product of the Diels-Alder reaction will have electron-donating and electron-withdrawing groups 1,2 or 1,4 but not 1,3.



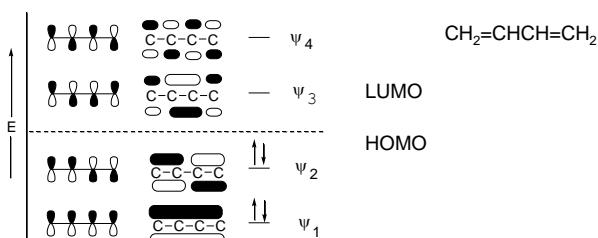
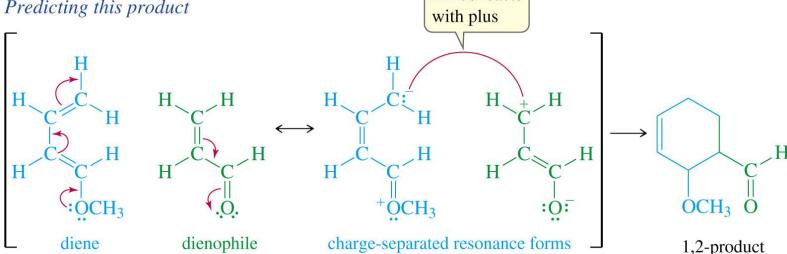
Formation of 1,4-product



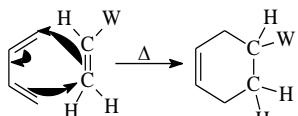
Formation of 1,2-product



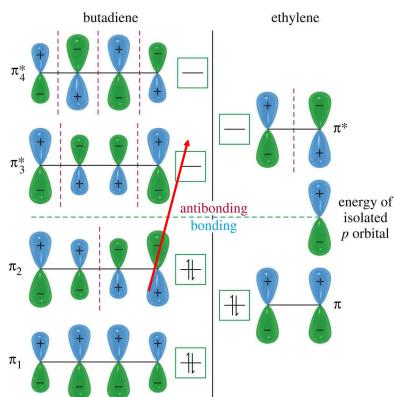
Predicting this product



MO's must overlap smoothly



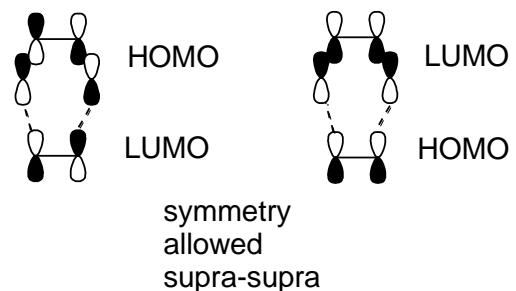
Conservation of Orbital Symmetry



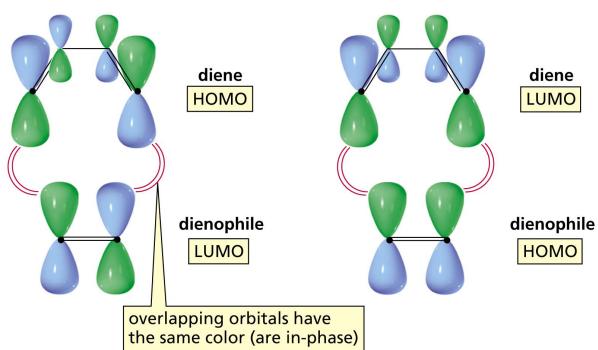
Which orbitals? thermal = HOMO + LUMO

HOMO = highest occupied molecular orbital

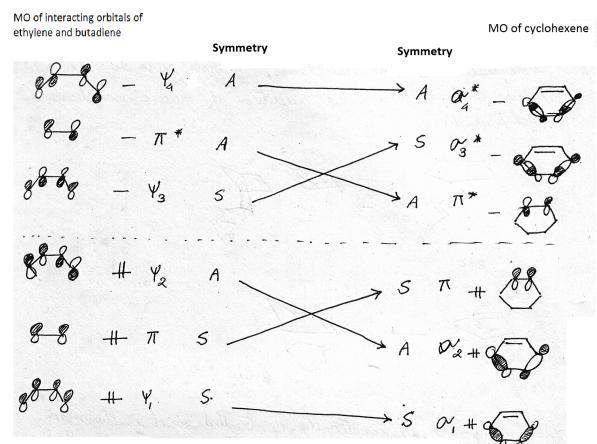
LUMO = lowest unoccupied molecular orbital



Frontier Orbital Analysis of a [4 + 2] Cycloaddition Reaction



Correlation Diagram of Diels-Alder reaction

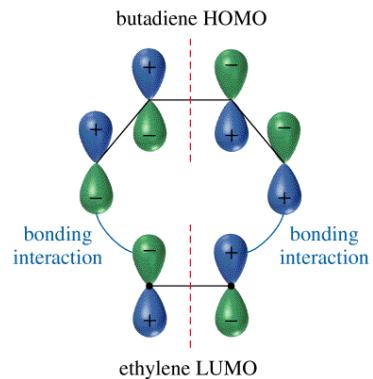


Correlation Diagram of Diels Alder reaction

- In the correlation diagram symmetries associates with the MOs of reactants in the bonding and antibonding state as well as MOs of products in the bonding and antibonding state are considered.
- There is a perfect correlation and conservation of symmetries of MOs of the reactants and products. Also there is no crossover of any kind between bonding and antibonding state.
- Hence it is a symmetry allowed reaction and takes place thermally

Symmetry-Allowed Reaction

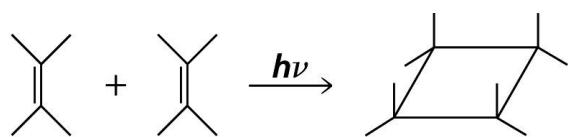
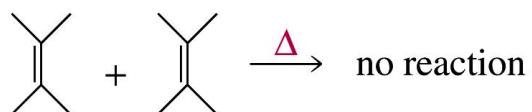
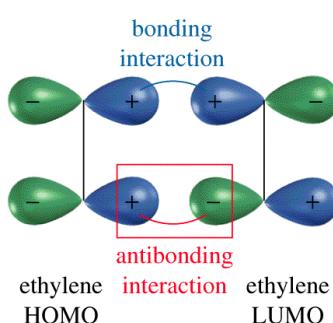
- Diene contributes electrons from its highest energy occupied orbital (HOMO).
- Dienophile receives electrons in its lowest energy unoccupied orbital (LUMO).



A [2 + 2] Cycloaddition Reaction

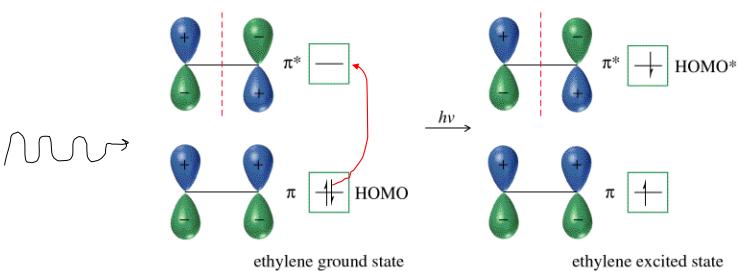
"Symmetry Forbidden" Cycloaddition

[2 + 2] cycloaddition of two ethylenes to form cyclobutene has anti-bonding overlap of HOMO and LUMO



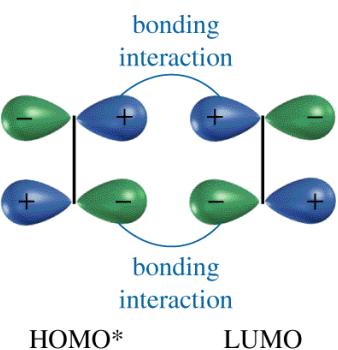
Photochemical Induction

Absorption of correct energy photon will promote an electron to an energy level that was previously unoccupied.

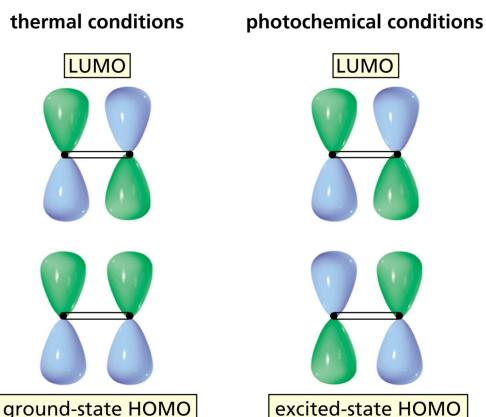


[2 + 2] Cycloaddition

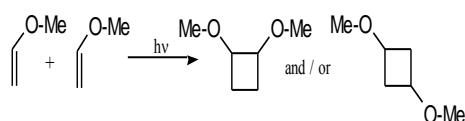
Photochemically allowed, but thermally forbidden.



Frontier MO Analysis of the [2 + 2] Cycloaddition Reaction



Regiochemical Predictions



Woodward – Hofmann Rules for Cycloadditions:

Table 29.3 Woodward–Hoffmann Rules for Cycloaddition Reactions

Sum of the number of π bonds in the reacting systems of both reagents	Reaction conditions	Allowed mode of ring closure
Even number	Thermal	Antarafacial ^a
	Photochemical	Suprafacial
Odd number	Thermal	Suprafacial
	Photochemical	Antarafacial ^a

^a Although antarafacial ring closure is symmetry-allowed, it can occur only with large rings.

[i + j]	Thermal	Photochemical
4n	supra-supra forbidden	supra-supra allowed
	supra-supra allowed	supra-supra forbidden

