Pericyclic Reactions
6 Lectures, Year 3, Michaelmas 2016

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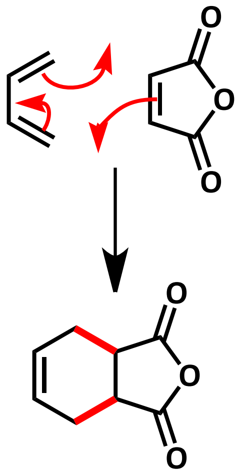
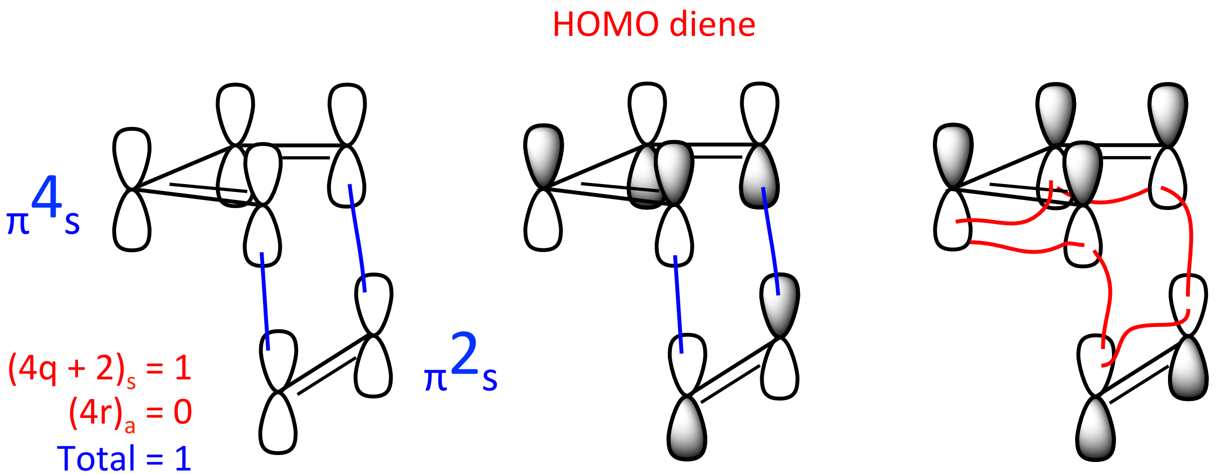




$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

LUMO dienophile
constructive overlap ✓

6 electrons
no nodes
Hückel
allowed ✓

http://burton.chem.ox.ac.uk/teaching.html

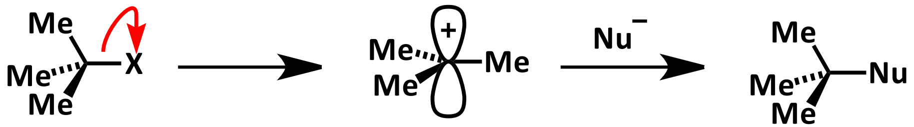
- *Pericyclic Reactions*, Oxford Chemistry Primer no. 67; Ian Fleming
- *Organic Chemistry* Jonathan Clayden, Nick Greeves, Stuart Warren, Peter Wothers
- *Advanced Organic Chemistry: Reactions, Mechanisms and Structures*; Jerry March
- *Frontier Orbitals and Organic Chemical Reactions*; Ian Fleming
- *Molecular Orbitals & Organic Chemical Reactions*; Ian Fleming
- *Modern Physical Organic Chemistry*; Eric Anslyn and Dennis Docherty

Synopsis

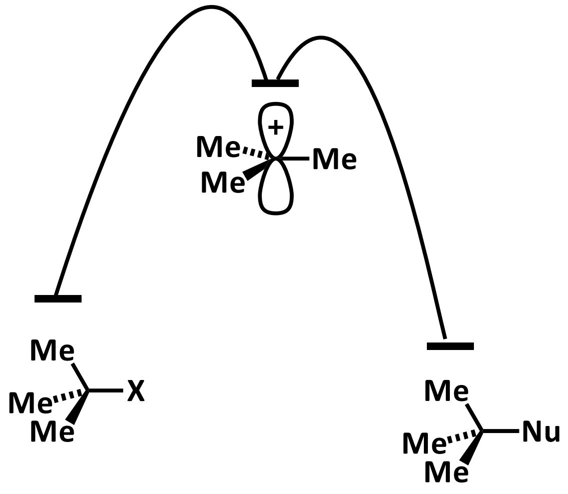
- The nature of pericyclic reactions
- Examples of pericyclic reactions
- Drawing molecular orbitals
- Correlation diagrams
- The Woodward-Hoffmann rule
- Frontier Molecular Orbitals
- Möbius-Hückel Method
- Cycloadditions
- Electrocyclic reactions
- Sigmatropic rearrangements
- Group transfer reactions

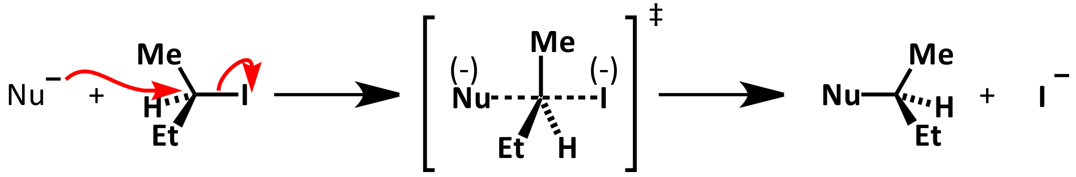
The nature of pericyclic reactions

- Ionic reactions – may or may not have an intermediate

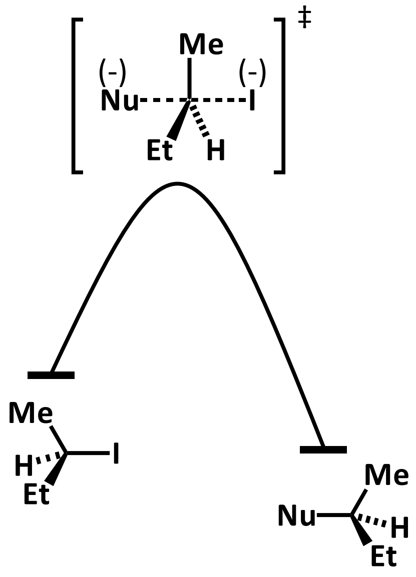


- S_N1 reactions are stepwise and have a defined intermediate



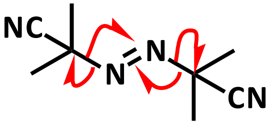


- S_N2 reactions are *concerted* and have no intermediate

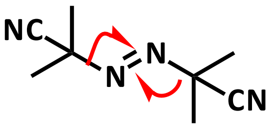


- In ionic reactions the curly arrows identify where the electrons have come from and where they are going and which bonds have been made and which broken.

- Radical reactions involve the correlated movement of single electrons



frequently shortened to



Pericyclic Reactions

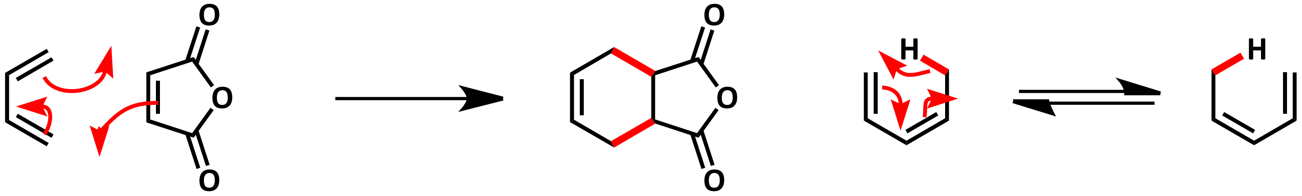
- Third distinct class of reactions

Pericyclic reactions – Reactions in which all first-order changes in bonding relationships take place in concert on a closed curve. *R. B. Woodward and R. Hoffmann 1969*.

i.e. the reactions have cyclic transition states in which all bond-forming and bond-breaking take place in a concerted manner without the formation of an intermediate.

- Pericyclic reactions involve a transition state with a cyclic array of interacting orbitals; a reorganisation of σ and π-bonds occurs within this cyclic array.

- Originally termed ‘ no mechanism reactions’ – they could not be explained by standard nucleophile/electrophile mechanisms.

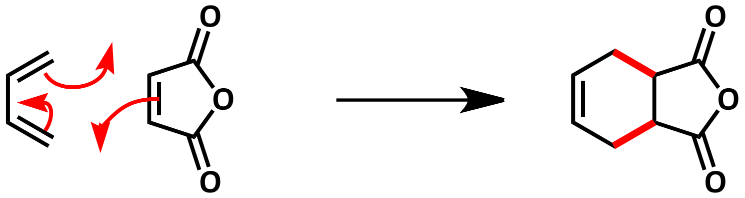


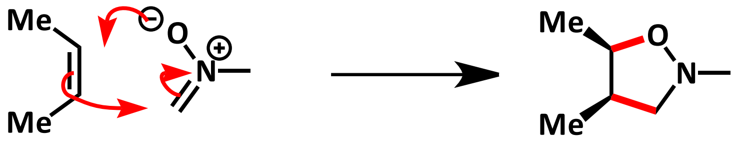
- No absolute sense in which the electrons flow from one component to another; however, sometimes it is more sensible to push the arrows in only one direction.

- Here curly arrows are used to show which bonds are being made/broken rather than the direction of flow of electrons.

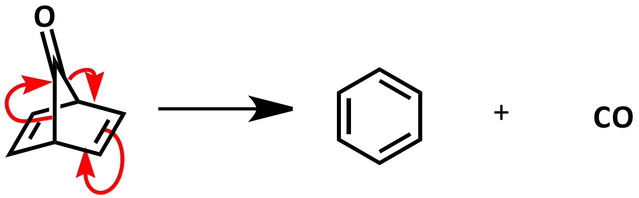
Pericyclic Reactions – four classes.

- Cycloadditions - **Two components** come together to form two new σ-bonds at the ends of both components and joining them together to form a **ring**.

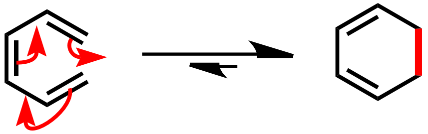


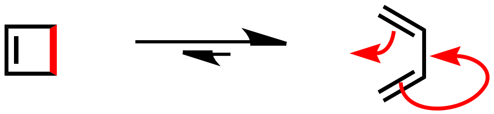


- Cheletropic reactions are a sub-class of cycloaddition reactions in which the **two σ – bonds** are made or broken to the **same atom**.

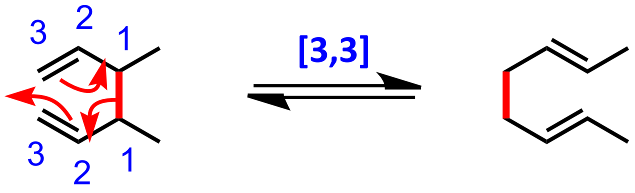


- Electrocyclic Reactions – **Unimolecular** reactions characterised by the **formation of a ring** from an open chain conjugated system with a σ-bond forming across the ends of the conjugated system.

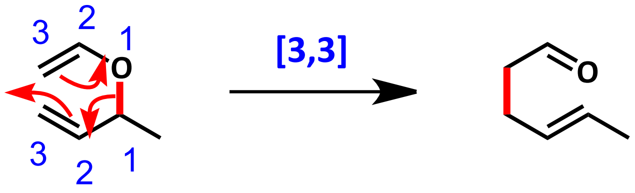




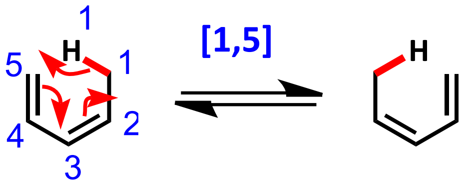
- Sigmatropic rearrangements – **Unimolecular isomerisations** which formally involve the overall movement of a σ-bond from one position to another.



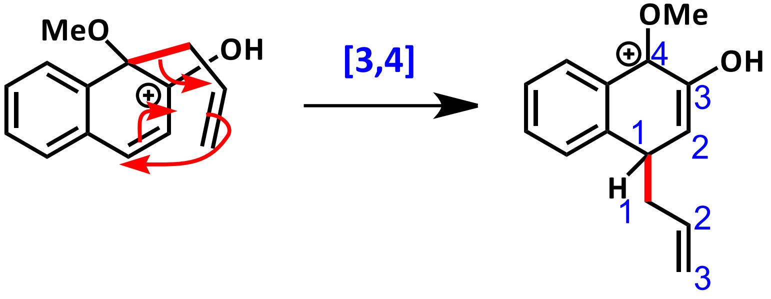
Cope rearrangement



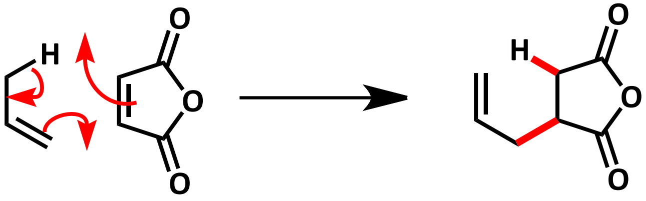
Claisen rearrangement



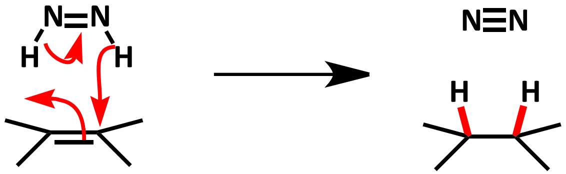
[1,5]-hydride shift



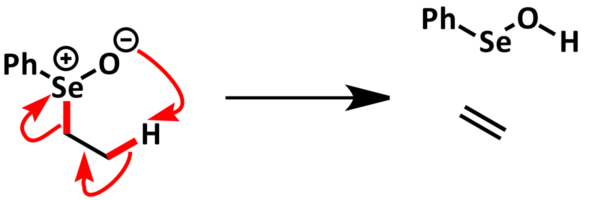
- Group transfer – appear to be a mix of a sigmatropic rearrangement and a cycloaddition. They are **bimolecular** and so are not sigmatropic rearrangements, and **no ring is formed** so they are not cycloadditions.



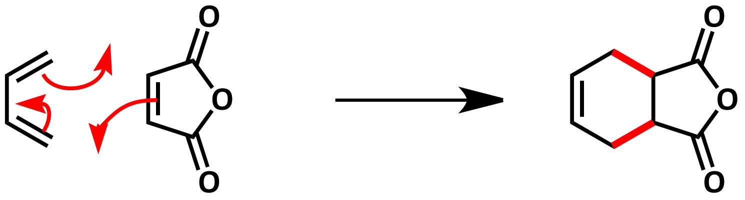
Alder-ene - reactions

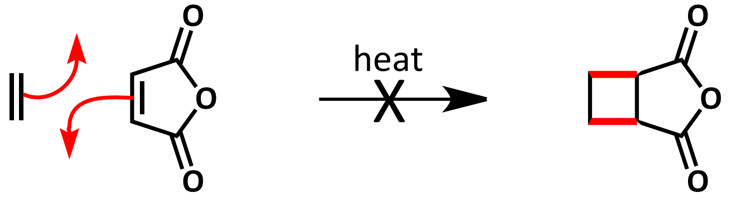


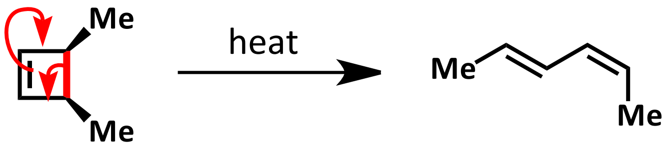
diimide reduction

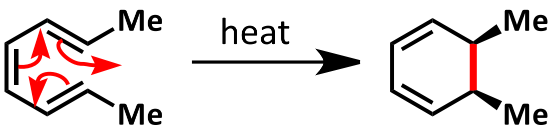


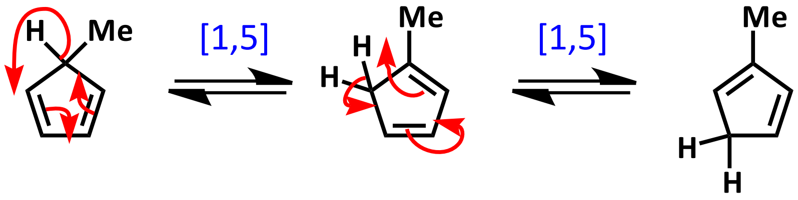
- Require a theory/theories to explain these results

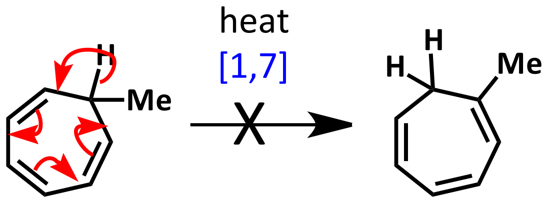


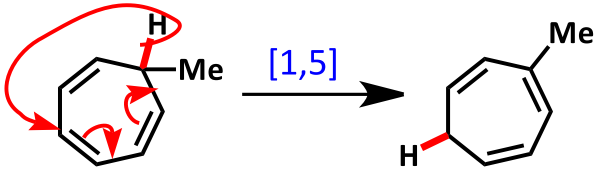


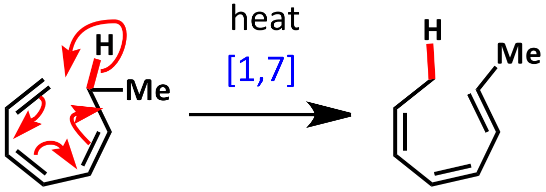




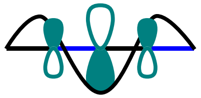






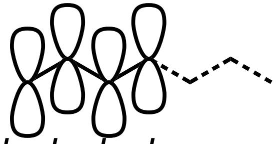


- Hückel Molecular Orbital Theory for Linear π-systems.
- Applicable to conjugated planar cyclic and acyclic systems.
- Only the π-system is included; the σ-framework is ignored (in reality σ-framework affects π-system).
- Used to calculate the wave functions (ψ_k) and hence *relative* energies by the LCAO method.

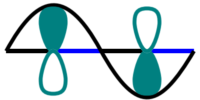


MO = ψ_k, AO = ϕ_i and $\psi = \sum_{i=1}^{n} c_{ki}\phi_i$ i.e. $\psi_k = c_1\phi_1 + c_2\phi_2 + c_3\phi_3 + c_4\phi_4 + c_5\phi_5$ .....

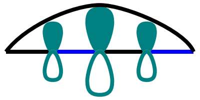
k = MO number (1→n); i = atom position in π system (1→n); n = number of p-orbitals



For n contributing p-orbitals there will be n molecular orbitals
$c_{ki} = (2/(n + 1))^{1/2} \bullet \sin(\pi ki/(n + 1))$



- For each MO ψ_k $\Sigma c_i^2 = 1$ (normalisation) i.e. the sum of the squares of the coefficients for any MO must be 1.



- For each AO ϕ_i $\Sigma c_k^2 = 1$ i.e. the sum of the squares of the coefficients for any AO over all MOs must be 1.
- Each MO must be symmetric or antisymmetric with respect to any symmetry operation of the molecule.
- Molecular Orbital Energies = $E_k = \alpha + m_j\beta$ $m_j = 2\cos[j\pi/(n+1)]$ j = 1, 2……n

- To draw a molecular orbital diagram:

i) count the number of p-orbitals – n

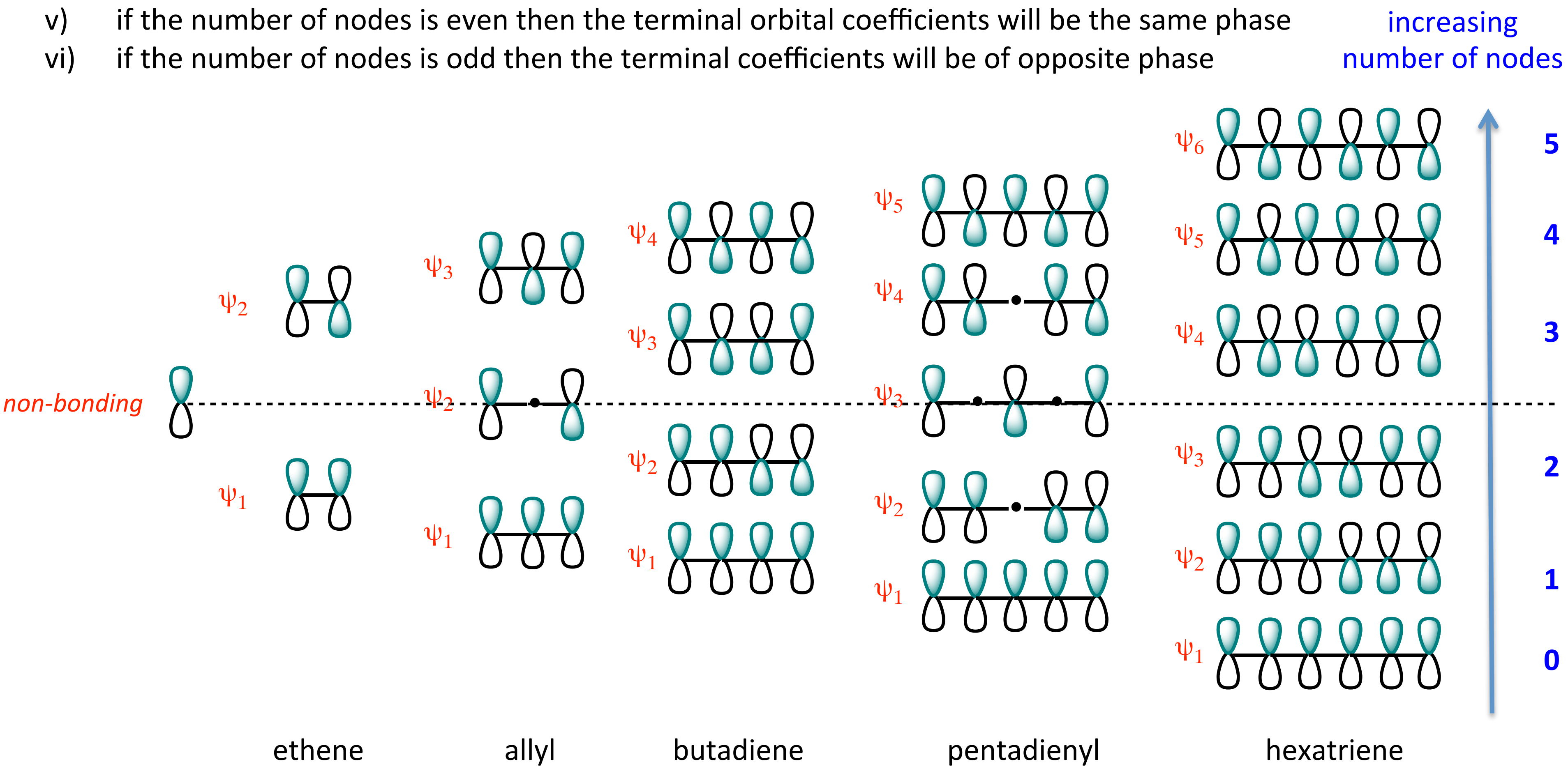
ii) count the number of electrons – π-bond = 2, unpaired electron = 1, carbanion = 2, carbocation = 0

iii) draw n horizontal lines stacked on top of one another to represent the MOs

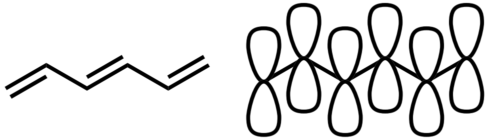
iv) draw the molecular orbitals as the combination of p-orbitals with an increasing number of nodes from 0 for ψ_1 to n-1 for ψ_n such that ***each MO is symmetric or antisymmetric with respect to any symmetry operation of the molecule.***

v) if the number of nodes is even then the terminal orbital coefficients will be the same phase

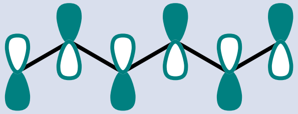
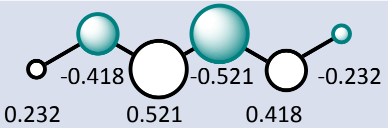
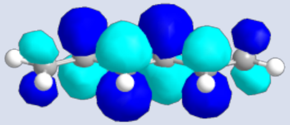
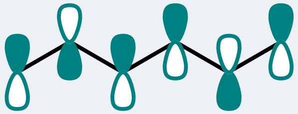
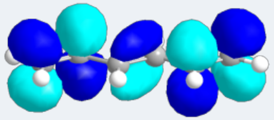
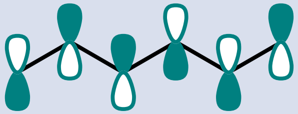
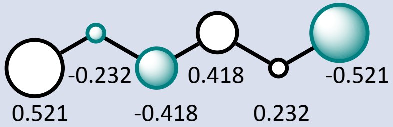
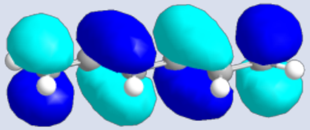
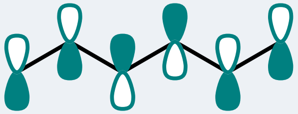
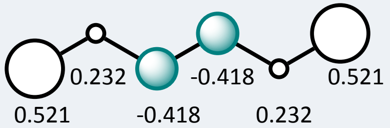
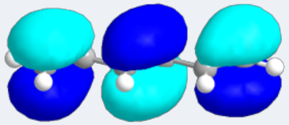
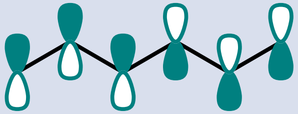
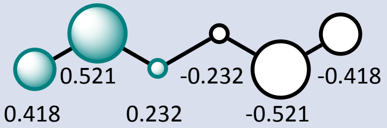
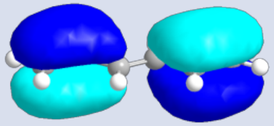
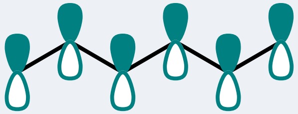
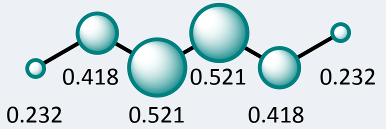
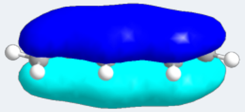
vi) if the number of nodes is odd then the terminal coefficients will be of opposite phase



- 1,3,5-Hexatriene
- six 2p atomic orbitals give 6π molecular orbitals; *n* = 6, j = 1, 2, 3, 4, 5, 6



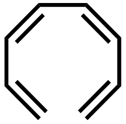
- $m_j = 2\cos(\pi/7) = 1.80$ $2\cos(2\pi/7) = 1.25$ $2\cos(3\pi/7) = 0.45$...... and the corresponding negative values
- energy $E = \alpha + 1.80\beta$ $\alpha + 1.25\beta$ $\alpha + 0.45\beta$ $\alpha - 0.45\beta$.....etc

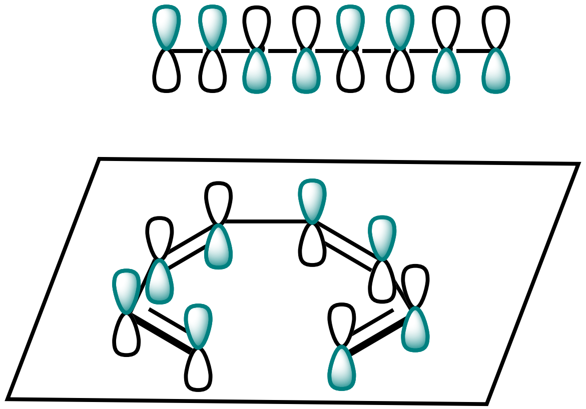
MO		no. nodes	energy		HMOT MO (calculated)	
ψ_6		5	$\alpha - 1.80\beta$			
ψ_5		4	$\alpha - 1.25\beta$			
ψ_4		3	$\alpha - 0.45\beta$			
ψ_3		2	$\alpha + 0.45\beta$			
ψ_2		1	$\alpha + 1.25\beta$			
ψ_1		0	$\alpha + 1.80\beta$			

- stabilisation energy = $E_{stab} = 2(3\alpha + 3.5\beta)$ **= 6α + 7β** remember $E_{stab\ (ethene)} = 2\alpha + 2\beta$

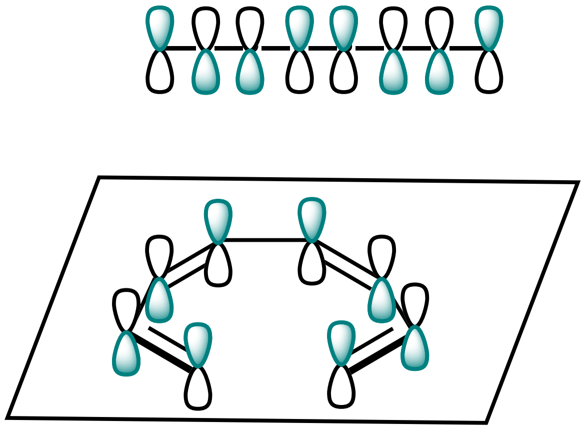
- The HOMO of (neutral) polyenes can be readily constructed by putting nodes on the single bonds; hence the HOMO appears to be alternating isolated π-bonding pairs.

- The LUMO of (neutral) polyenes can be constructed by beginning with an 'isolated' p-orbital and then alternating 'isolated' π-bonding pairs and ending with an 'isolated' p-orbital.
- The HOMO and LUMO are termed the Frontier Orbitals.





HOMO



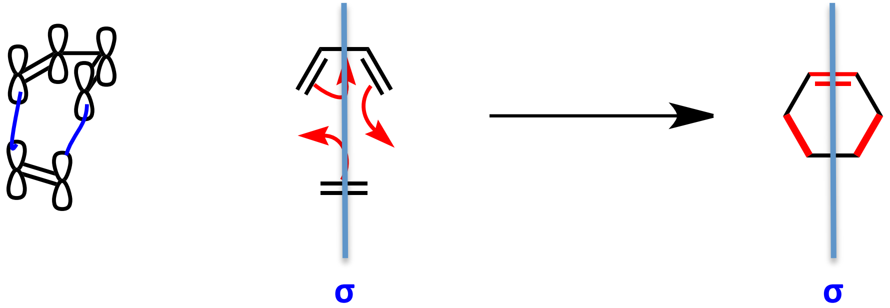
LUMO

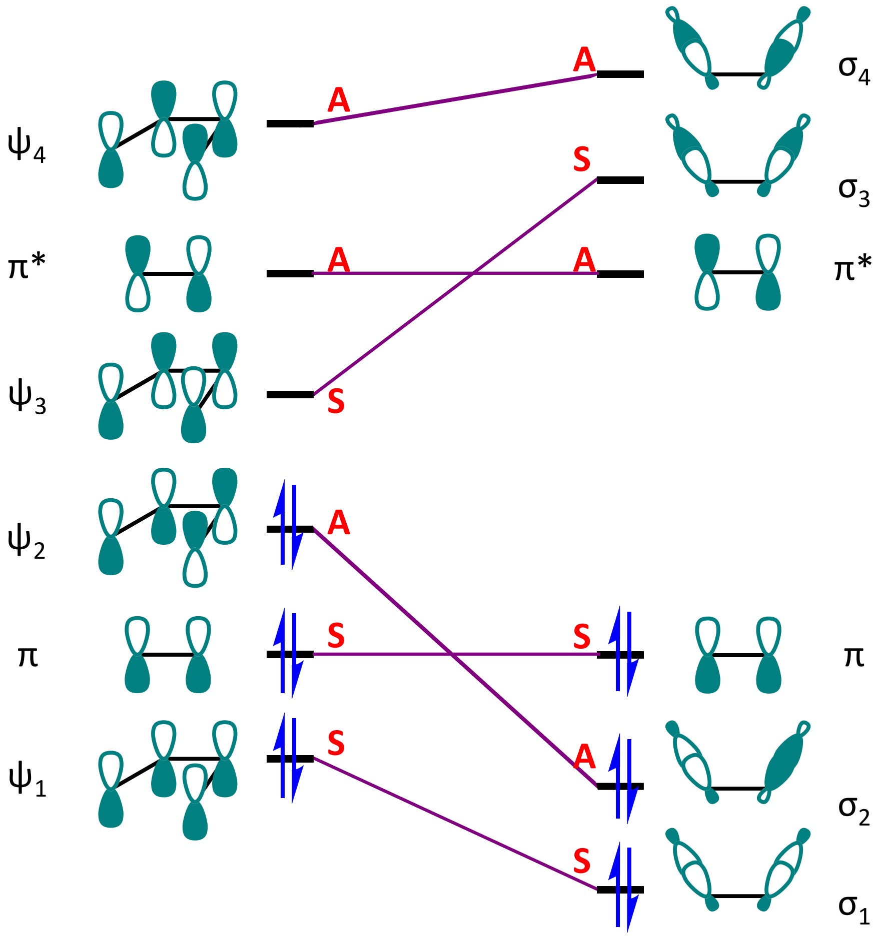
Correlation Diagrams

- During a pericyclic reaction the orbitals of the starting material are smoothly converted into the orbitals of the product.

- This means that the symmetry of the orbitals with respect to any symmetry operations of the molecule must be conserved in moving from the starting material(s) to product – this is the 'Conservation of Orbital Symmetry', which is readily depicted in an 'orbital correlation diagram'

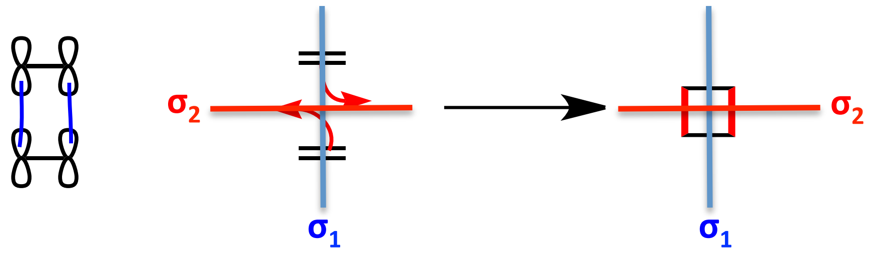
- Draw bare bones of reaction.
- Identify orbitals undergoing change.
- Draw sensible approach of substrates.
- Identify symmetry elements maintained during reaction.
- Rank orbitals approximately by energy.
- Classify each orbital with respect to the symmetry element(s) conserved during reaction.
- Construct orbital correlation diagram connecting orbitals of starting materials with those closest in energy and of the same symmetry in the product.
- In the Diels-Alder reaction a plane of symmetry, perpendicular to the molecular planes of both the diene and dienophile and passing through the double bond of the dienophile and the central single bond of the diene.
- In the orbital correlation diagram of the Diels- Alder reaction all interacting bonding orbitals in the diene/ dienophile are correlated with new *bonding* orbitals in the product. The reaction is *thermally allowed.*

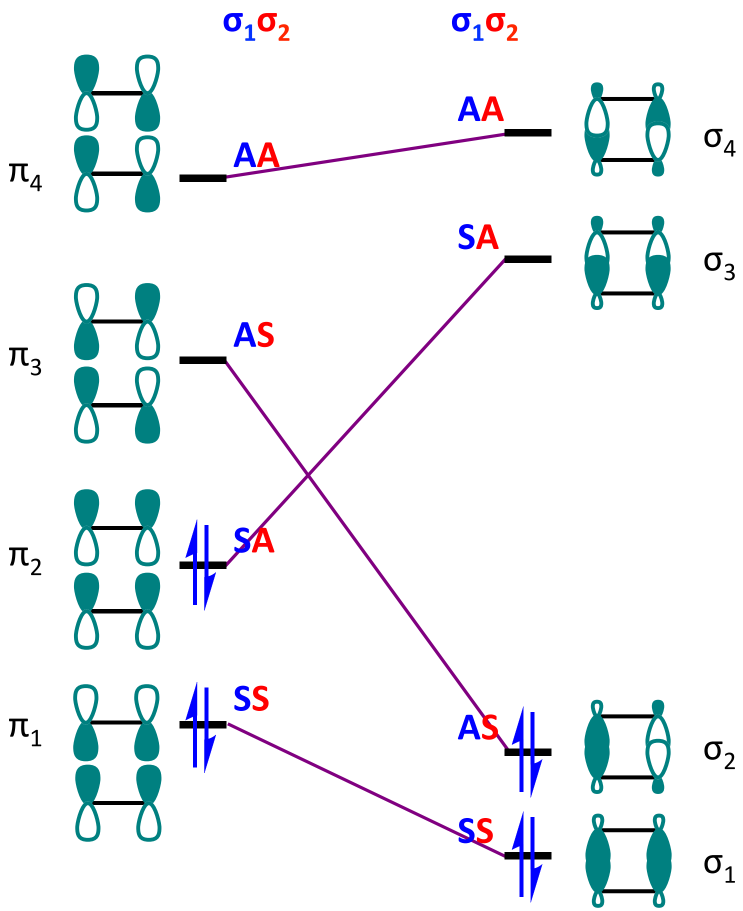




Correlation diagram for [2+2] cycloaddition of alkenes

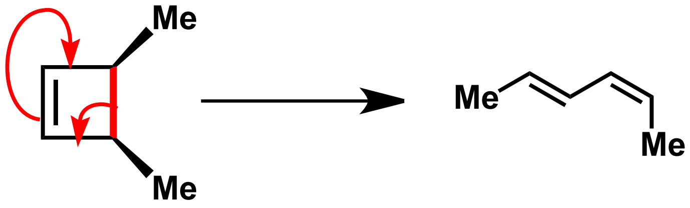
- Identify orbitals undergoing change (curly arrows tell us which orbitals these are) – π.
- Draw sensible approach of substrates – in this case face on approach of the two alkenes for maximum orbital overlap.
- Identify symmetry elements maintained during reaction – in this case two planes of symmetry, **σ_1** and **σ_2**.
- Rank orbitals approximately by energy.
- Classify each orbital with respect to symmetry element(s) conserved during reaction.
- Construct orbital correlation diagram connecting orbitals of starting materials with those closest in energy and of the same symmetry in the product.
- Here the ground state $\pi_1^2\pi_2^2$ does not correlate with the ground sate of the product ($\sigma_1^2\sigma_2^2$) but with a doubly excited state $\sigma_1^2\sigma_3^2$ – the thermal [2+2] cycloaddition of alkenes is thermally disallowed.





*For more on correlation diagrams see: R. B. Woodward, R. Hoffmann, Angew. Chem. Int. Ed. **1969**, 8, 781-932.*

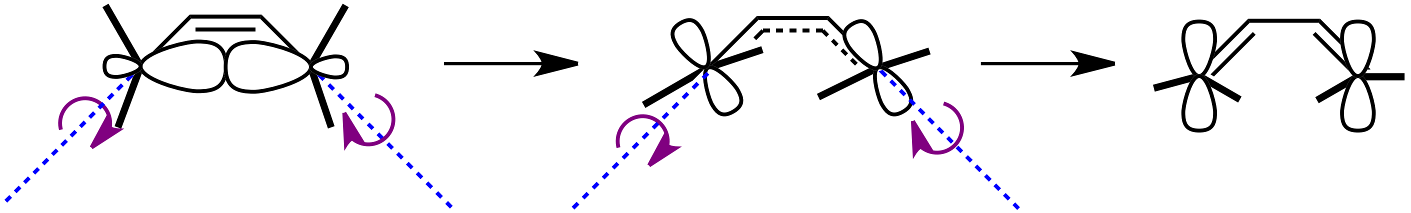
- Correlation diagram for electrocyclic reactions



Z,E : *E,E* 20,000:1

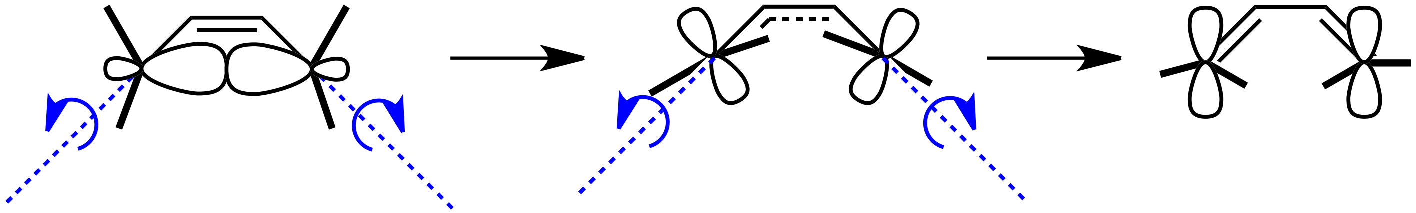
Longuet-Higgins & Abrahamson, *J. Am. Chem. Soc.*, **1965**, *87*, 2045.

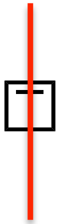
- There are two modes of opening – *conrotatory* or *disrotatory*
- *Conrotatory – rotation around the axes of the σ-bonds (dotted lines) occurs in the same direction -* throughout this process the molecule retains a C_2-axis which passes through the plane of the molecule and the breaking σ bond.



C_2
plan view

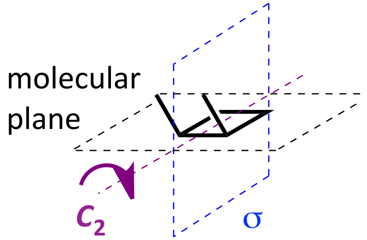
- *Disrotatory – rotation around the axes of the σ-bonds (dotted lines) occurs in opposite directions –* throughout this process the molecule retains a plane of symmetry which is perpendicular to the plane of the molecule and passes through the breaking σ-bond

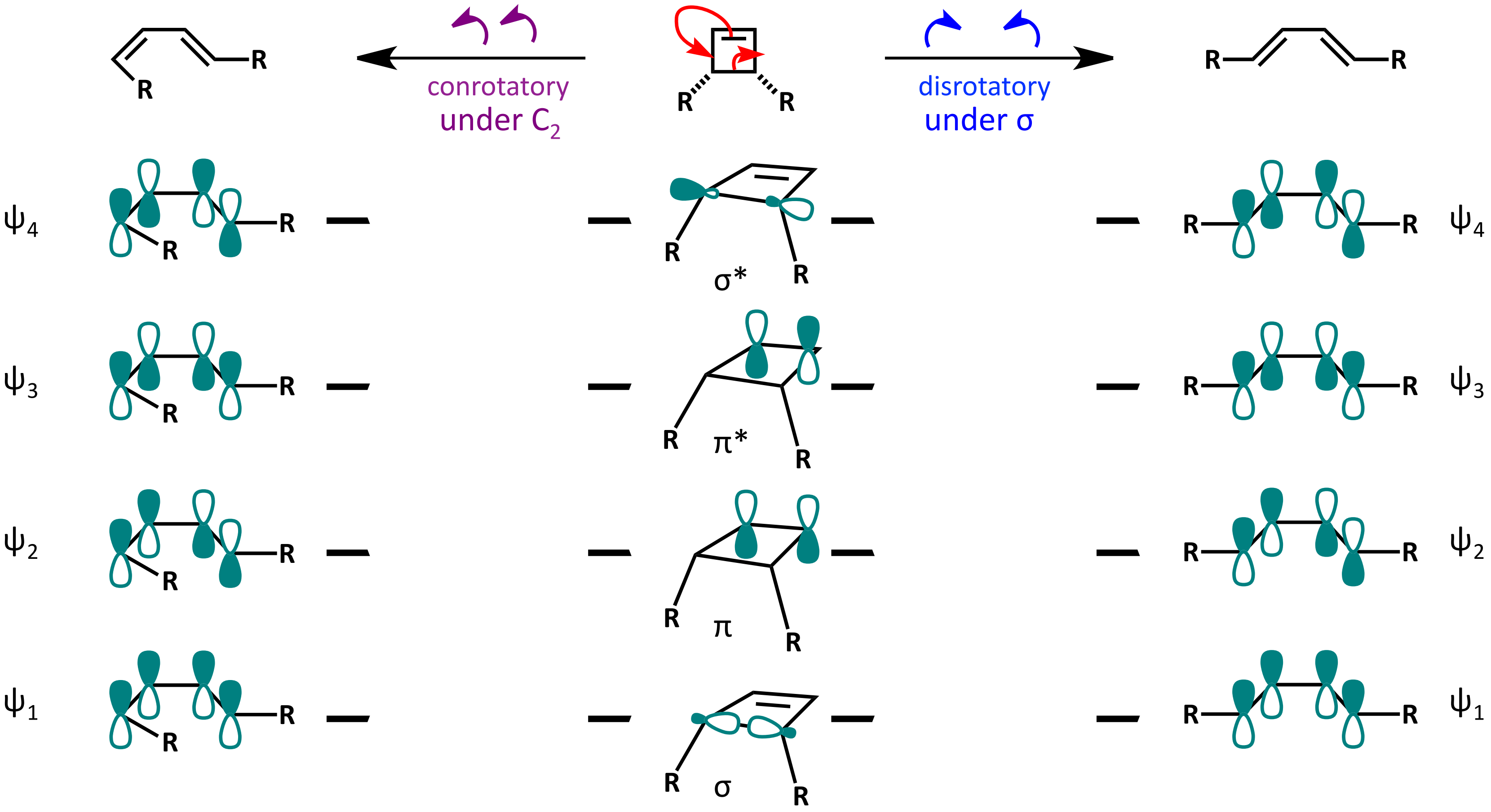


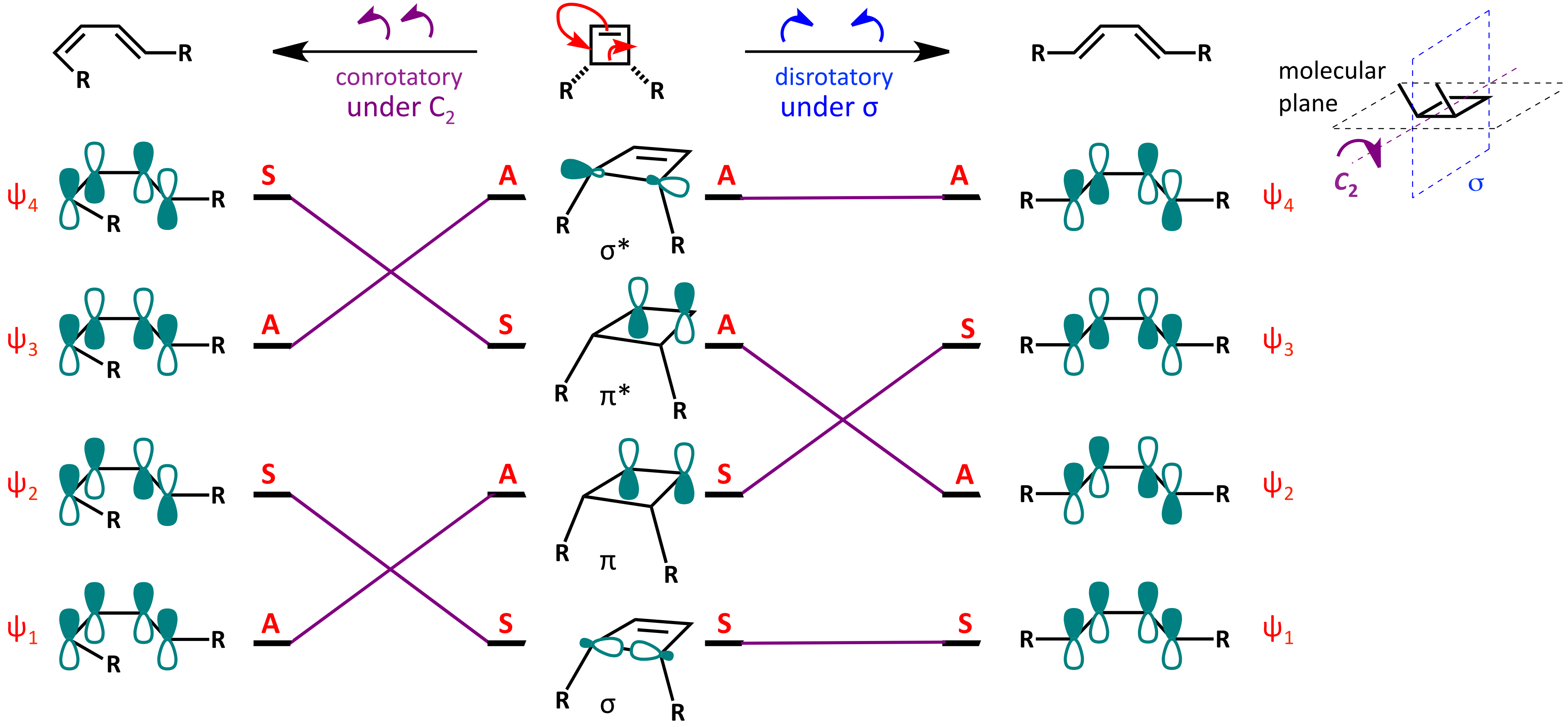


σ
plan view

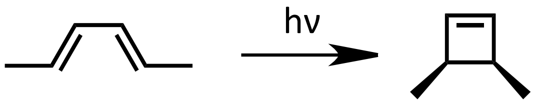
- Correlation diagram for electrocyclic reactions.
- Identify orbitals undergoing change (curly arrows) – σ and π.
- The orbitals undergoing change are either symmetric or antisymmetric with respect to the symmetry elements preserved during the reaction.
- Rank orbitals approximately by energy.
- Label orbitals as ‘S’ or ‘A’.
- Construct orbital correlation diagram connecting orbitals of starting materials with those closest in energy and of the same symmetry in the product.







- In the conrotatory mode, all ground state bonding orbitals in cyclobutene ($\sigma^2\pi^2$) correlate with ground state bonding orbitals in butadiene ($\psi_1^2\psi_2^2$) – the conrotatory opening of butadiene is **thermally** allowed (favoured).
- In the disrotatory mode, the ground state bonding orbitals in cyclobutene ($\sigma^2\pi^2$) correlate with a doubly excited state of butadiene ($\psi_1^2\psi_3^2$) – the disrotatory opening of butadiene is **thermally** forbidden (disfavoured).
- The **photochemical** ring closure of butadiene to give cyclobutene is disrotatory.
The 1st excited sate of butadiene is $\psi_1^2\psi_2^1\psi_3^1$ which correlates smoothly with the 1st excited sate of cyclobutene ($\sigma^2\pi^1\pi^{*1}$); under conrotatory ring closure $\psi_1^2\psi_2^1\psi_3^1$ correlates with a much high energy state in cyclobutene ($\sigma^1\pi^2\sigma^{*1}$).



- Correlation diagrams can be distilled into a simple rule for predicting which pericyclic reactions are "allowed".

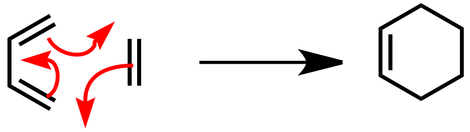
The Woodward-Hoffmann Rules:

A ground state pericyclic reaction is symmetry allowed when the total number of $(4q + 2)_s$ and $(4r)_a$ components is odd (q and r must be integers).

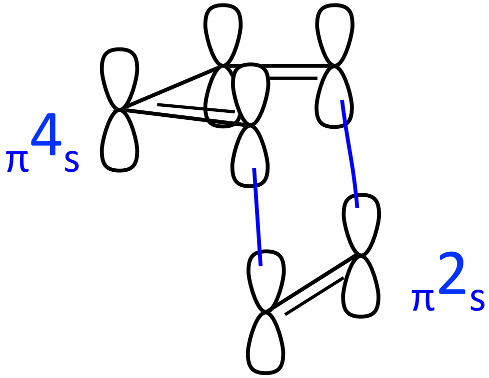
A pericyclic change in the first electronically excited state (i.e. a photochemical reaction) is symmetry-allowed when the total number of $(4q + 2)_s$ and $(4r)_a$ components is even.

- We will use the Diels-Alder reaction to exemplify the application of the Woodward-Hoffmann rules.
- Draw a 'curly arrow' mechanism to identify the components.
- For the Diels-Alder reaction these are 4π (diene) and 2π (dienophile).
- Draw a convincing 3-D orbital diagram to show the overlap of the components.
- Label the components as supra or antarafacial.
- Sum the components according to the Woodward-Hoffmann rule.

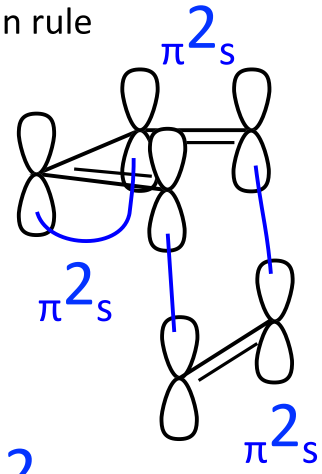
- Draw a 'curly arrow' mechanism – this generally allows identification of the components.
- For the Diels-Alder reaction these are 4π (diene) and 2π (dienophile),
- Draw a convincing 3-D orbital diagram to show the overlap of the components.



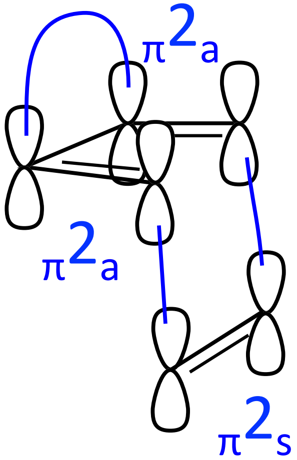
- Label the components as supra or antarafacial. Here the diene is being used in a suprafacial manner – the two new bonds are being formed on the same face of the diene.
The alkene is also being used in a suprafacial manner being used in a suprafacial manner
- Sum the components according to the Woodward-Hoffmann rule



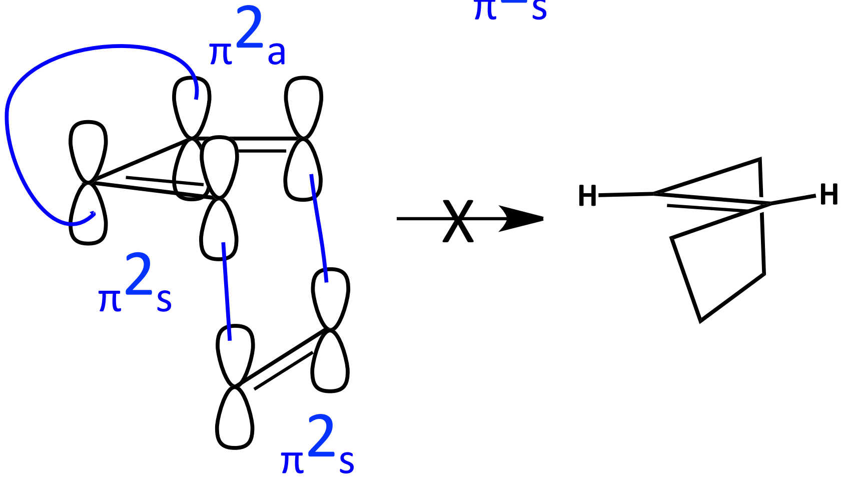
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed



$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed



$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

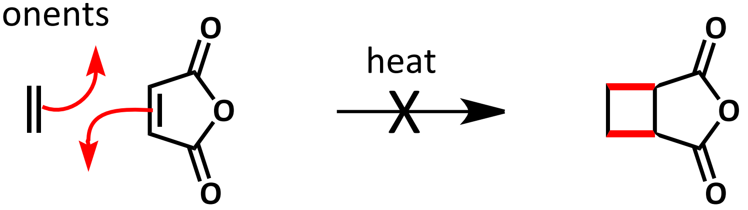


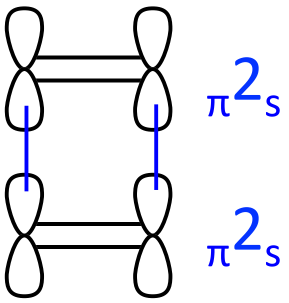
$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✗
forbidden

- Generally simplest to maximise suprafacial components and not subdivide conjugated systems.

[2 + 2] cycloadditions

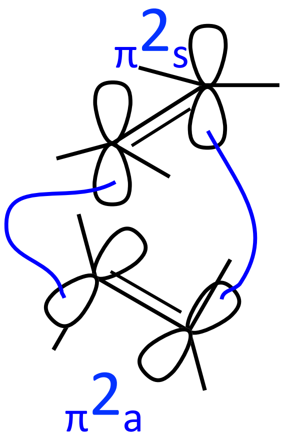
- Draw a ‘curly arrow’ mechanism to identify the components – 2π, 2π
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Label the components as supra or antarafacial.
- Sum the components according to the Woodward-Hoffmann rule

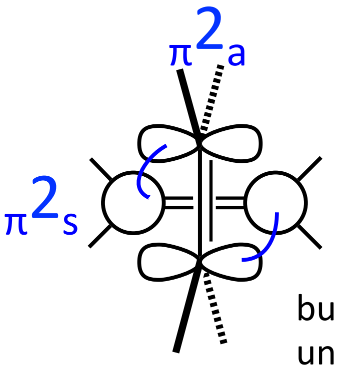




$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✗
forbidden
(thermally)

$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✓
allowed –
photochemically





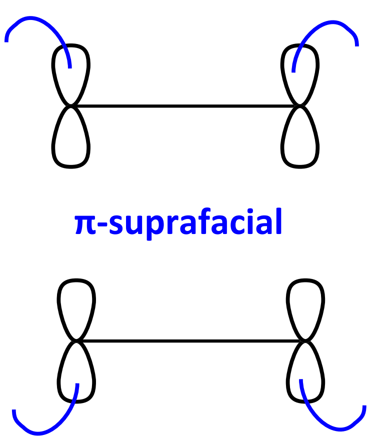
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed
(thermally)

but geometrically unreasonable, therefore does not occur

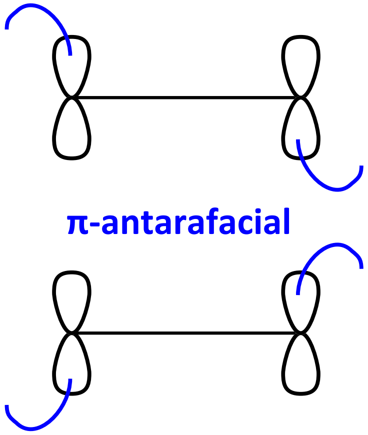
- Woodward-Hoffmann rule gives you the symmetry allowed orbital overlap but *you* have to decide whether the overlap *you* have drawn is geometrically reasonable.

Nomenclature for suprafacial and antarafacial components.

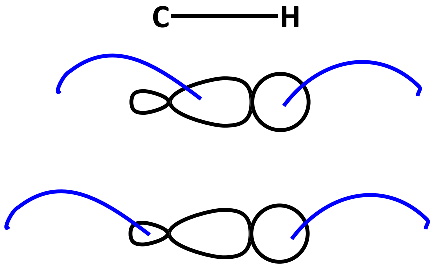
- Suprafacial and antarafacial refer to modes of bond formation that are respectively on the same face or on opposite faces of a molecular component.



π-suprafacial

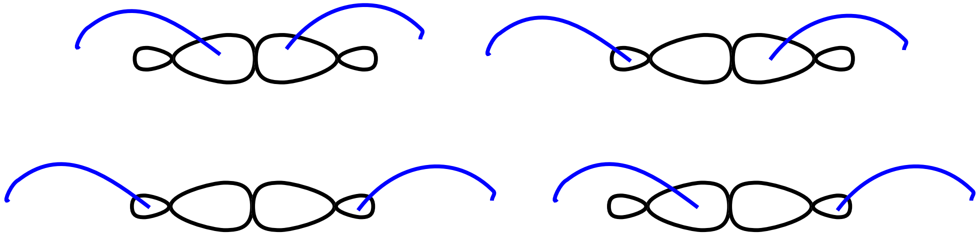


π-antarafacial

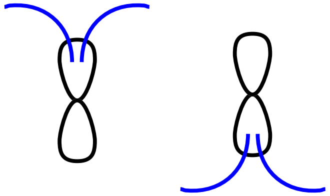


σ-suprafacial

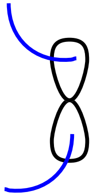
σ-antarafacial



σ-suprafacial **σ-antarafacial**

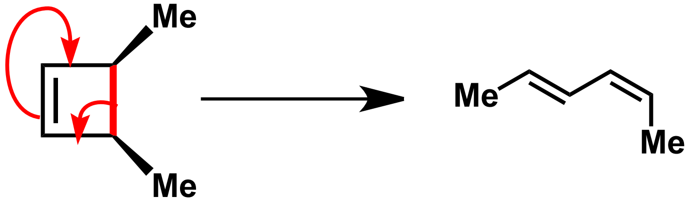


ω-suprafacial

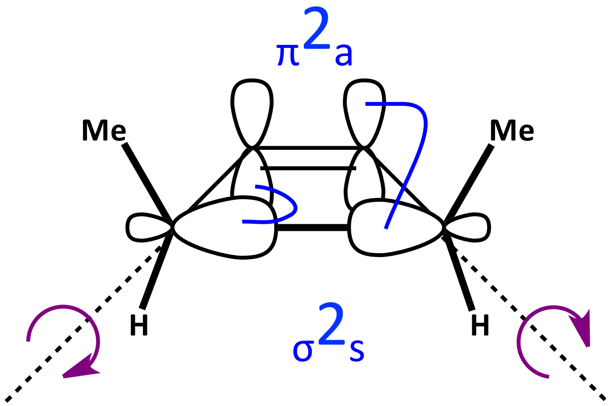


ω-antarafacial

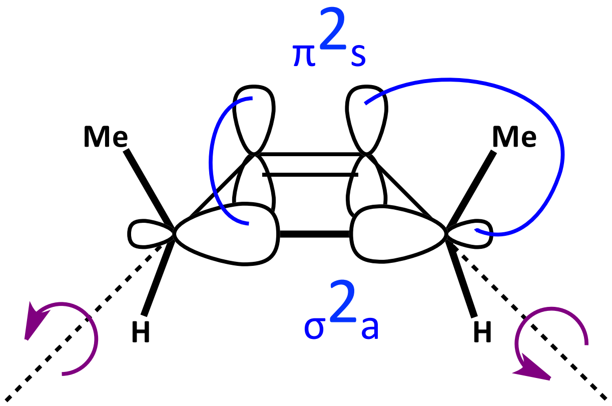
Woodward-Hoffmann approach for thermal electrocyclic reactions



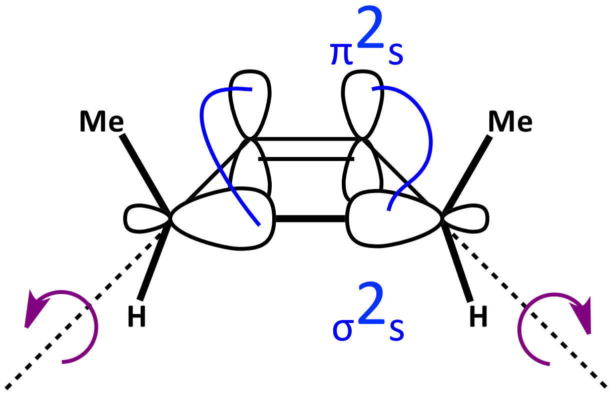
- Draw a ‘curly arrow’ mechanism to identify the components – these are 2π (alkene) and 2σ (single bond)
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Label the components as supra or antarafacial.
- Sum the components according to the Woodward-Hoffmann rule.



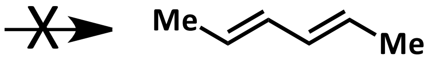
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed
(conrotatory)



$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed
(conrotatory)



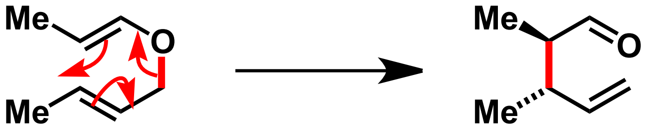
$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✗
forbidden
disrotatory

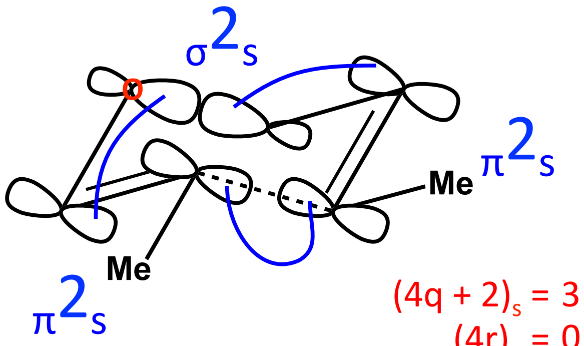


- Thermal ring opening of cyclobutene is *conrotatory.* Thermal *disrotatory* opening is symmetry forbidden.

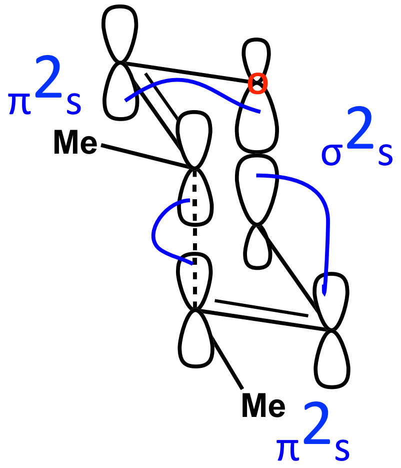
Woodward-Hoffmann approach for sigmatropic rearrangements

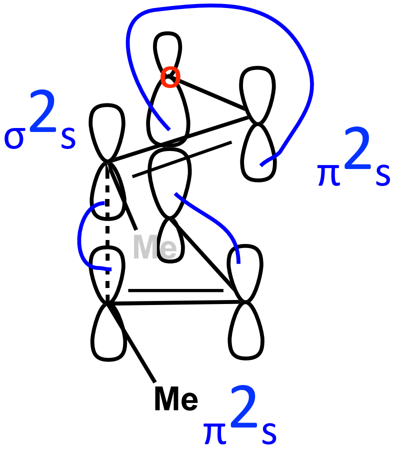
- Draw a 'curly arrow' mechanism to identify the components – 2π, 2σ, 2π
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Label the components as supra or antarafacial.
- Sum the components according to the Woodward-Hoffmann rule.





$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed





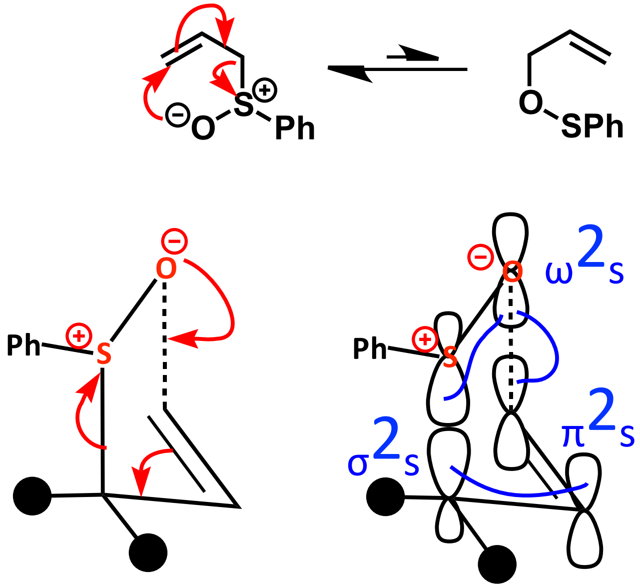
$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed

- Claisen rearrangement *via* chair TS is allowed.
- Claisen rearrangement *via* boat TS is allowed.

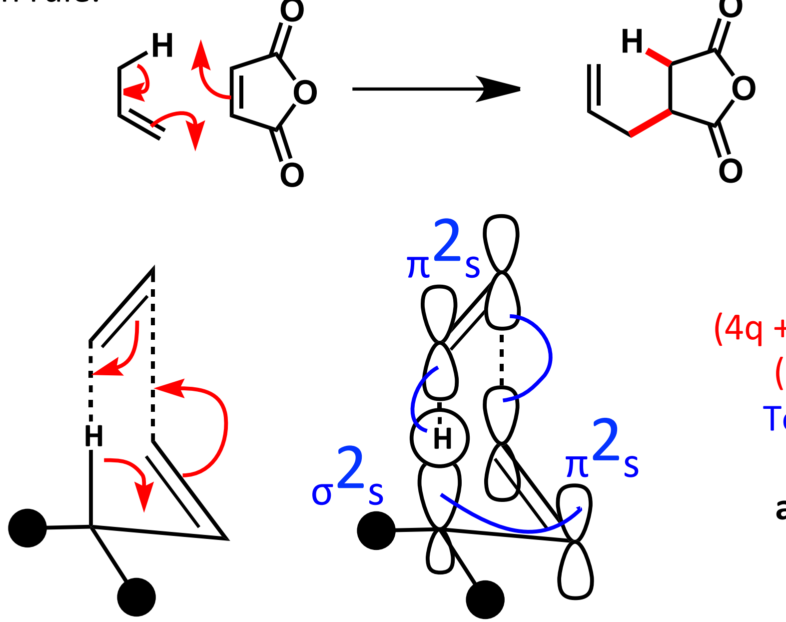
- Woodward-Hoffmann rule does not tell us that the chair TS is lower in energy than the boat TS. You need to use your chemical knowledge/intuition to decide that a chair is generally lower in energy than the corresponding boat and that it is generally more favourable to have equatorial substituents than axial substituents on a chair.

Woodward-Hoffmann approach for sigmatropic rearrangements and group transfer

- Draw a ‘curly arrow’ mechanism to identify the components
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Label the components as supra or antarafacial.
- Sum the components according to the Woodward-Hoffmann rule.



$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed



$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed

- [2,3]-sigmatropic rearrangement *via* envelope TS.
- ene-reaction (group transfer) *via* envelope TS.

For thermal cycloadditions and group transfers:
- If the total number of electrons is (4n + 2) both components can be used in a suprafacial manner.
- If the total number of electrons is (4n) one of the components is suprafacial and the other antarafacial.

For electrocyclic reactions:
- Thermal electrocyclic processes will be *conrotatory* if the total number of electrons is 4n and *disrotatory* if the total number of electrons is (4n +2).

Frontier Molecular Orbital approach – revision

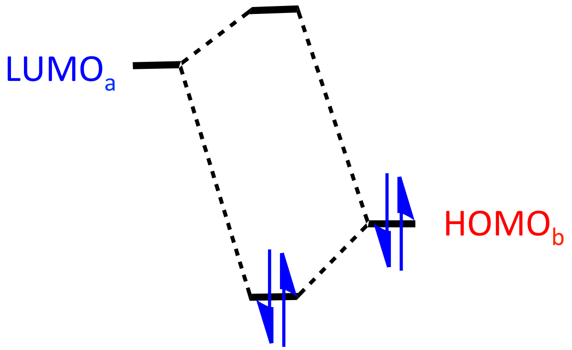
'As two molecules approach each other, three major forces operate:

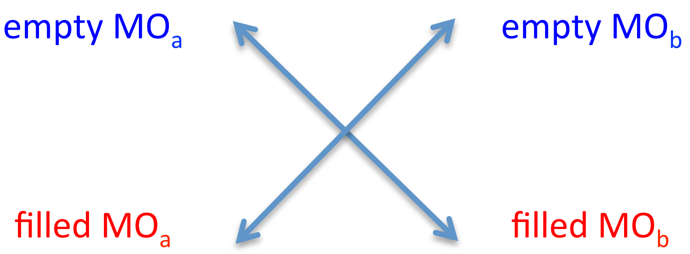
(i) The occupied orbitals of one repel the occupied orbitals of the other.

(ii) Any positive charge on one attracts any negative charge on the other (and repels any positive)

(iii) The occupied orbitals (especially the HOMOs) of each interact with the unoccupied orbitals (especially the LUMOs) of the other, causing an attraction between the molecules.' (from Fleming, Molecular Orbitals and Organic Chemical Reactions)

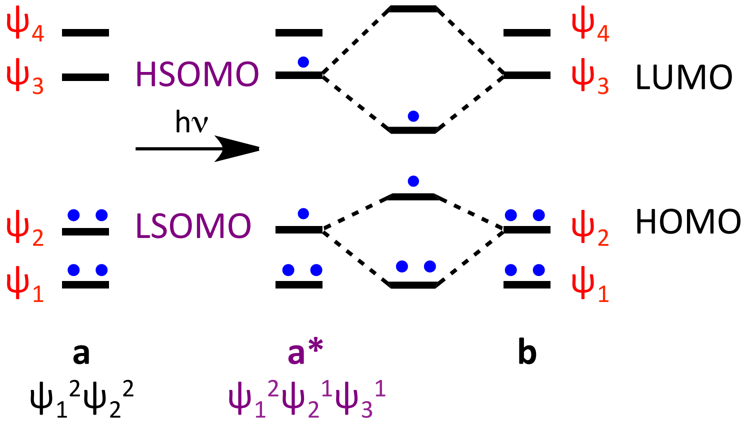
Frontier Molecular Orbital considers the interaction of the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO) to be of overriding importance.





thermal reaction

For *photochemical* reactions one molecule is in the excited state

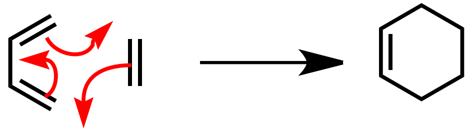


excited state **a**		ground state **b**
$HSOMO_a$	⟷	unoccupied MO ψ_3
$LSOMO_a$	⟷	occupied MO ψ_2

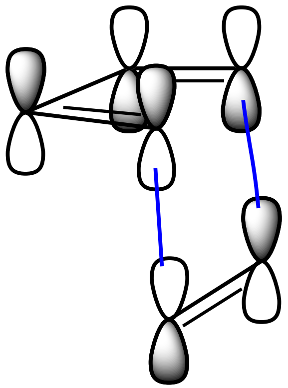
The FMO approach

- To apply the FMO method one has to assign a single HOMO and a single LUMO to the reaction components and see how they interact.

- The FMO approach is simple to apply to reactions with two components (e.g. cycloadditions, electrocyclic ring opening) but its application to sigmatropic rearrangements and group transfer reactions is somewhat contrived.
- Draw a 'curly arrow' mechanism to identify the components
- Assign a single HOMO and a single LUMO to the reaction
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Check to see if there is constructive overlap between the orbitals



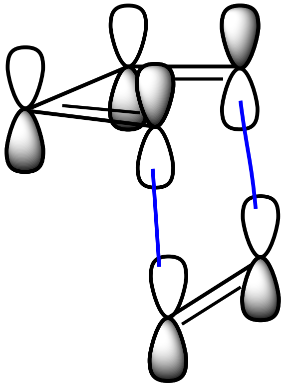
HOMO diene



LUMO dienophile

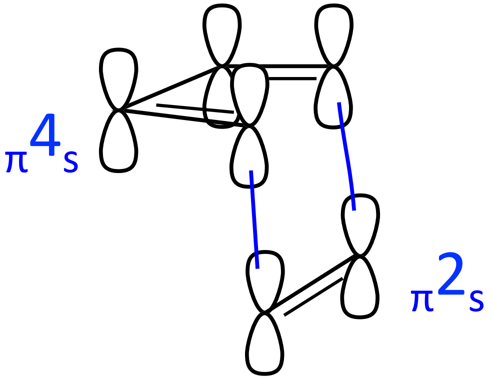
constructive overlap ✓

LUMO diene



HOMO dienophile

constructive overlap ✓



$(4q + 2)_s = 1$

$(4r)_a = 0$

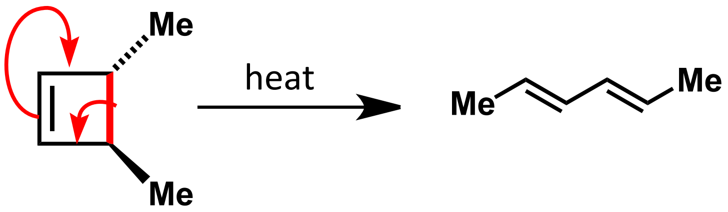
Total = 1

odd ✓

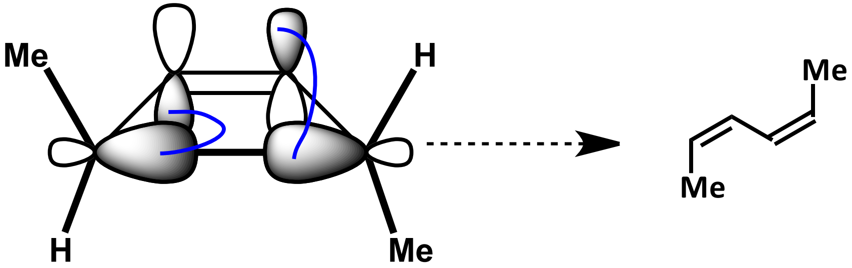
allowed

The FMO approach

- Draw a 'curly arrow' mechanism to identify the components
- Assign a single HOMO and a single LUMO to the reaction
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Check to see if there is constructive overlap between the orbitals



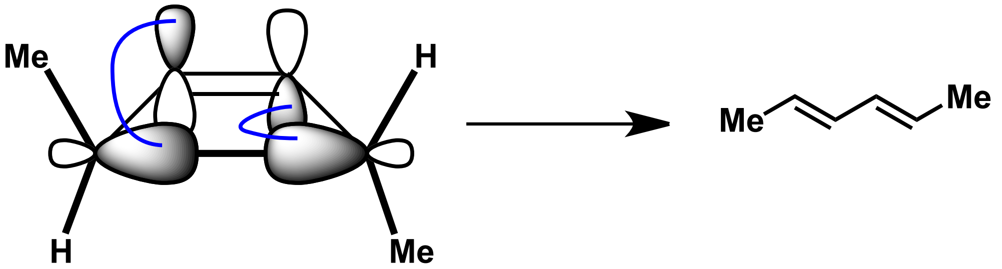
LUMO alkene



HOMO sigma

constructive overlap

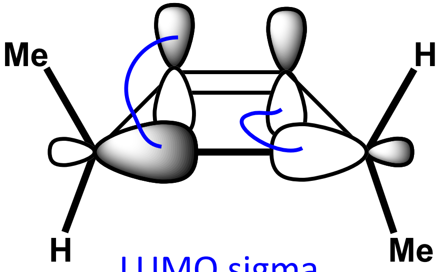
LUMO alkene



HOMO sigma

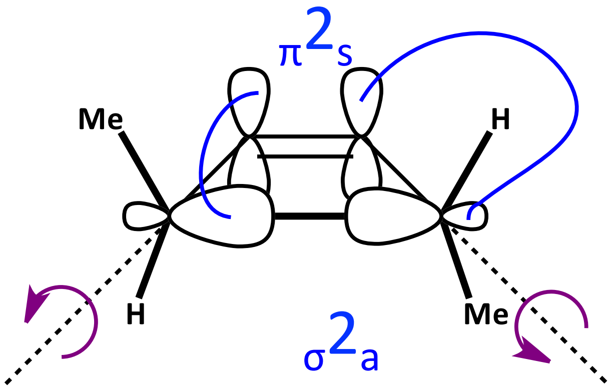
constructive overlap ✓

HOMO alkene



LUMO sigma

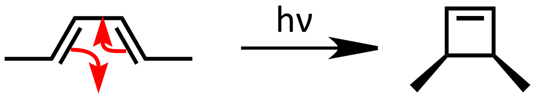
constructive overlap ✓



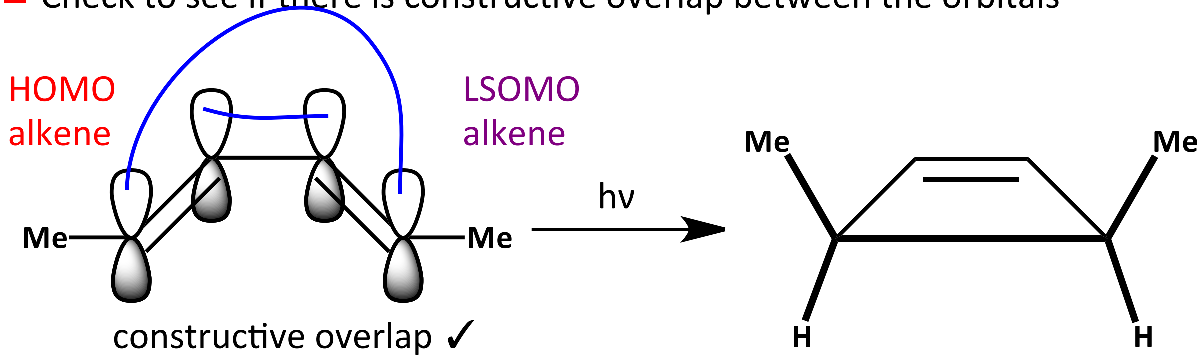
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 3
odd ✓
allowed
(conrotatory)

- The preference of one conrotatory (or disrotatory) mode is termed *torqueoselectivity* (more later).

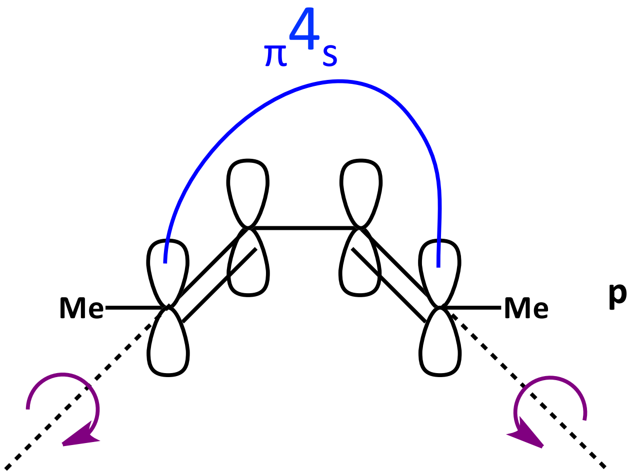
The FMO approach



- ■ Draw a 'curly arrow' mechanism to identify the components
- ■ Assign a single **HSOMO** and a single LUMO to the reaction, (or a single **LSOMO** and HOMO) – note a **HSOMO** has the same phases as the 'LUMO' and a **LSOMO** has the same phases as the HOMO)
- ■ Draw a convincing 3-D orbital diagram to show the overlap of the components
- ■ Check to see if there is constructive overlap between the orbitals



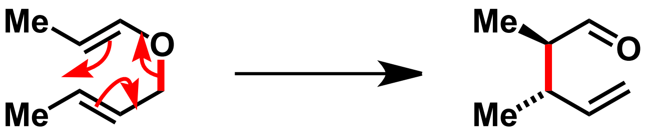
constructive overlap ✓
(disrotatory)

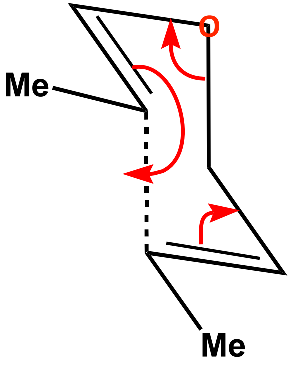


$(4q + 2)_s = 0$
$(4r)_a = 0$
Total = 0
even ✓
allowed
photochemically
(disrotatory)

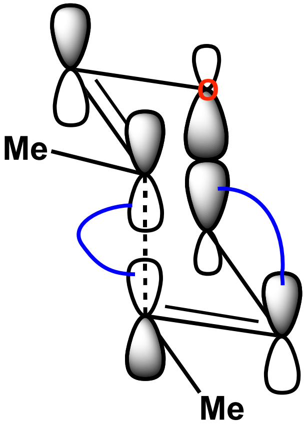
The FMO approach

- Draw a ‘curly arrow’ mechanism to identify the components
- Assign a single HOMO and a single LUMO to the reaction
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Check to see if there is constructive overlap between the orbitals



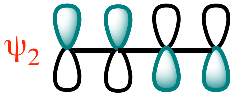


HOMO ‘π + σ’



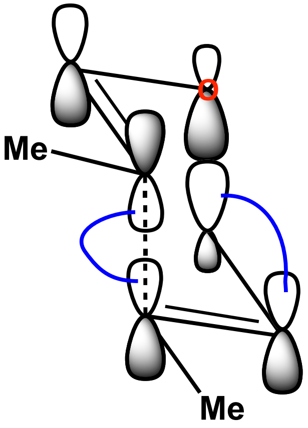
LUMO alkene

constructive overlap ✓



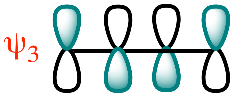
HOMO butadiene

LUMO ‘π + σ’

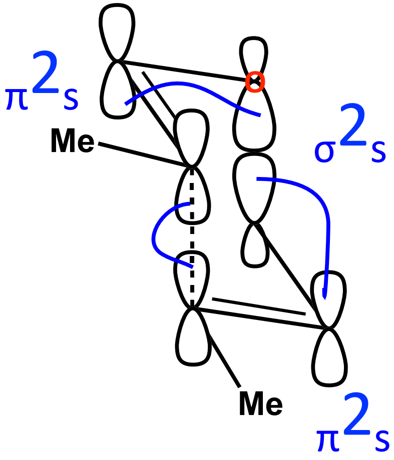


HOMO alkene

constructive overlap ✓



LUMO butadiene



$(4q + 2)_s = 1$

$(4r)_a = 0$

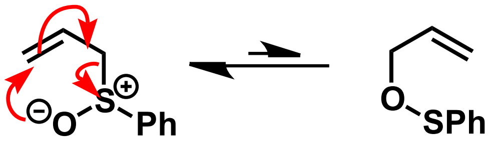
Total = 3

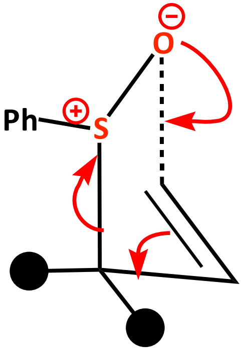
odd ✓

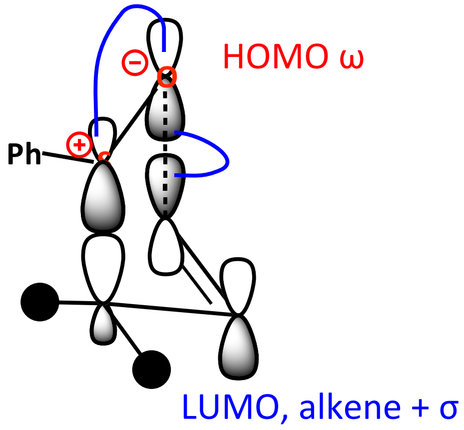
allowed

The FMO approach

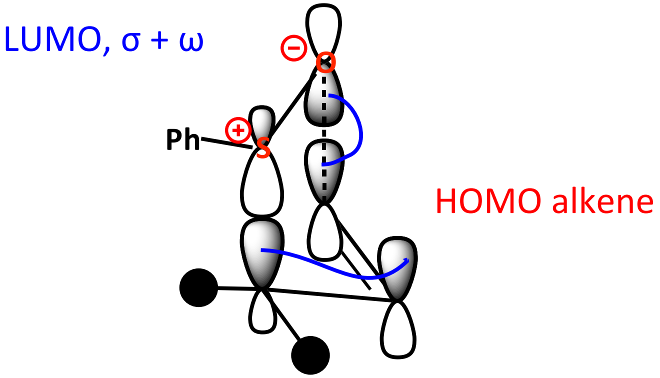
- Draw a ‘curly arrow’ mechanism to identify the components
- Assign a single HOMO and a single LUMO to the reaction
- Draw a convincing 3-D orbital diagram to show the overlap of the components
- Check to see if there is constructive overlap between the orbitals



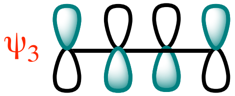




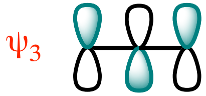
constructive overlap ✓



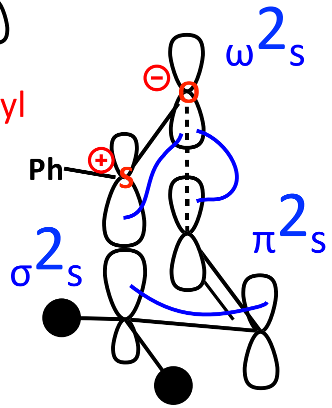
constructive overlap ✓



LUMO butadiene



LUMO 4e$^-$ allyl



$(4q + 2)_s = 3$

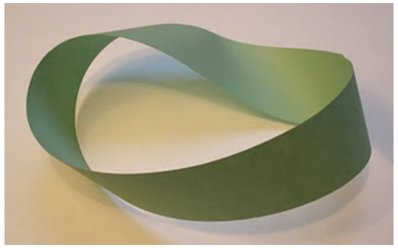
$(4r)_a = 0$

Total = 3

odd ✓

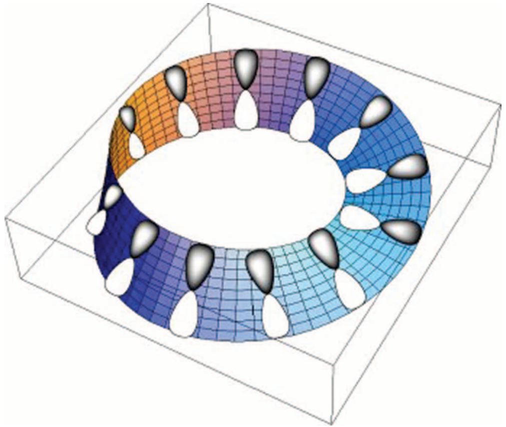
allowed

The Möbius-Hückel Method

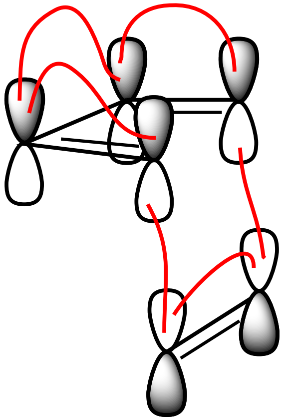


- Draw a curly arrow mechanism to assign components
- Draw a convincing 3-D orbital diagram to show the overlap of the components (easiest to draw ψ_1 for all components and minimise number of nodes).
- Count the number of phase inversions in the closed loop of interacting orbitals – as always, phase inversions within an (atomic) orbital are not counted.
- Even number of phase inversions: Hückel topology
- Odd number of phase inversions: Möbius topology
- A thermal pericyclic reaction involving a Hückel topology is allowed when the total number of electrons is (4n +2).

A thermal pericyclic reaction involving a Möbius topology is allowed when the total number of electrons is 4n.
(For photochemical reactions the rules are reversed.)

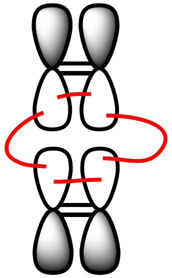


from H. S. Rzepa *J. Chem. Ed.*, **2007**, *84*, 1535



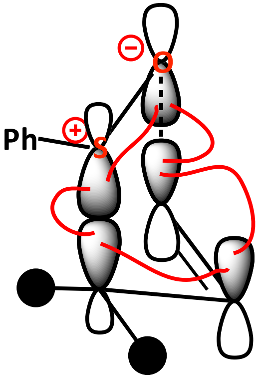
Diels-Alder reaction

no phase inversions,
Hückel system
6 electrons
allowed ✓



[2 + 2] cycloaddition

no phase inversions,
Hückel system
4 electrons
forbidden (thermally) ✗



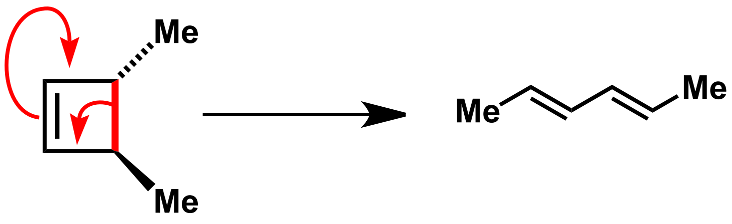
Sigmatropic rearrangement

no phase inversion
Hückel system
6 electrons
allowed ✓

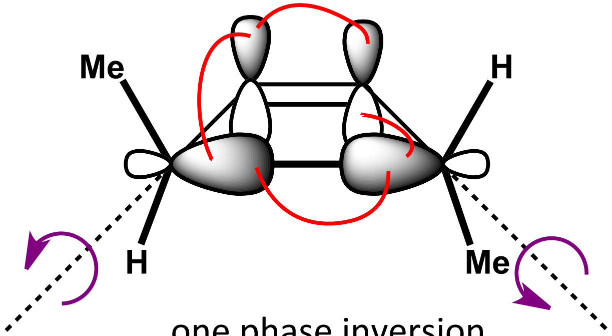
The Möbius-Hückel Method

- A thermal pericyclic reaction involving a Hückel topology is allowed when the total number of electrons is (4n +2).

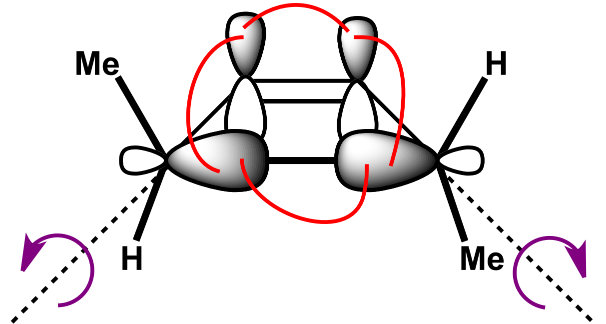
- A thermal pericyclic reaction involving a Möbius topology is allowed when the total number of electrons is 4n.
(For photochemical reactions the rules are reversed.)



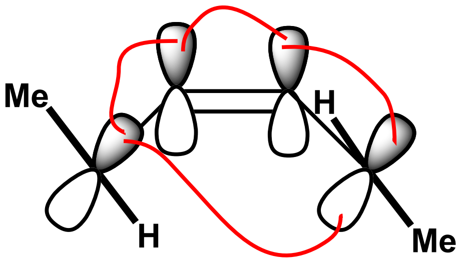
electrocyclic reactions

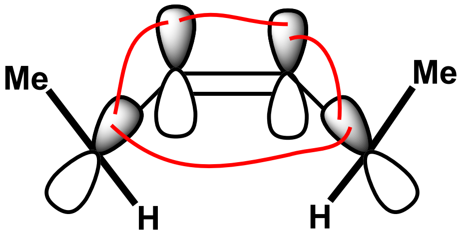


one phase inversion
Möbus system
4 electrons
allowed ✓
(conrotatory)



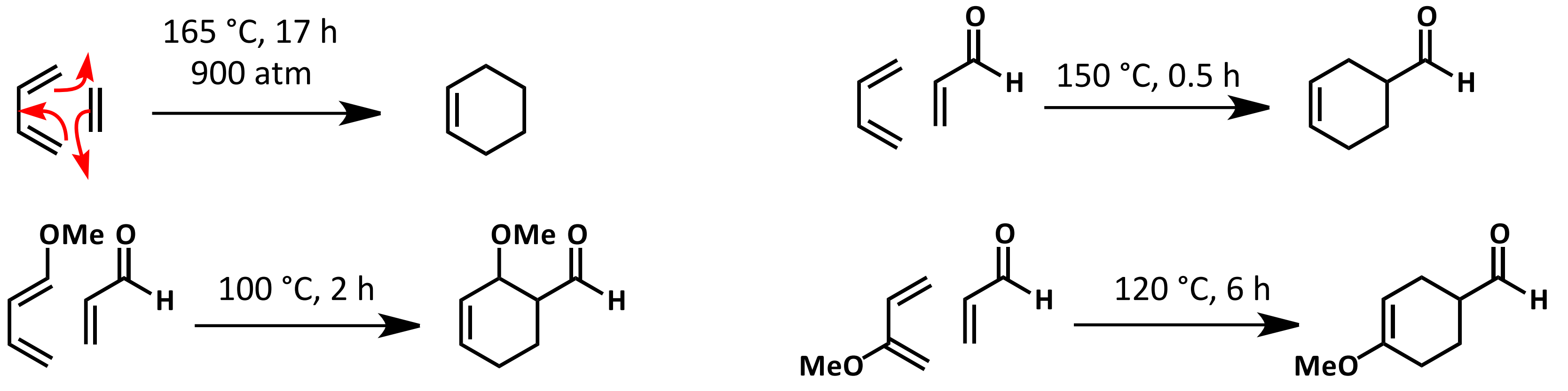
no phase inversions,
Hückel system
4 electrons
forbidden (thermally) ✗
(disrotatory)



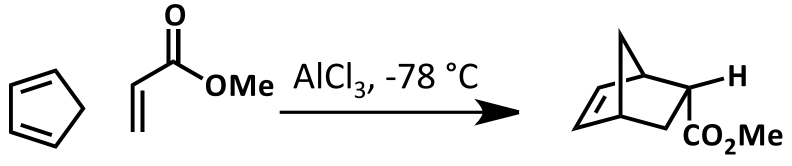


Cycloadditions

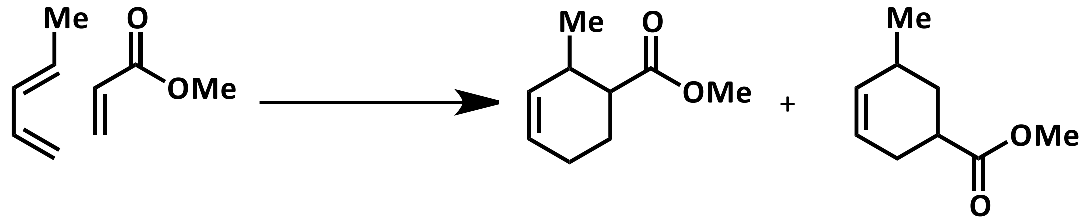
- The Diels-Alder reaction is greatly accelerated by having an EDG on the diene and an EWG on the dienophile.



- ‘ortho’ and ‘para’ products predominate.
- Lewis acids catalyse the reaction.
- ‘endo’ products predominate.



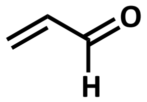
endo

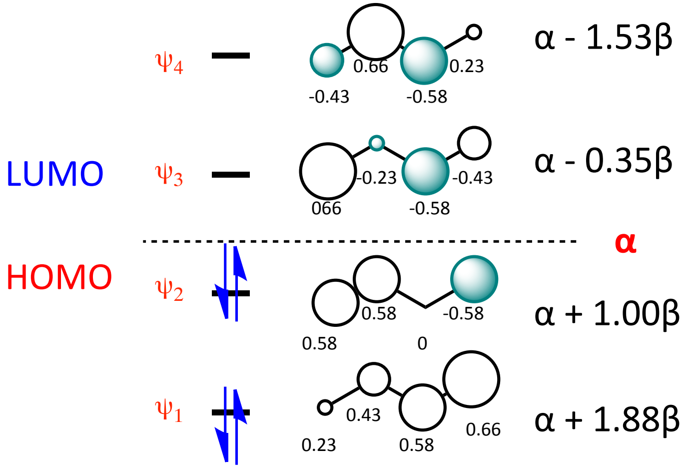


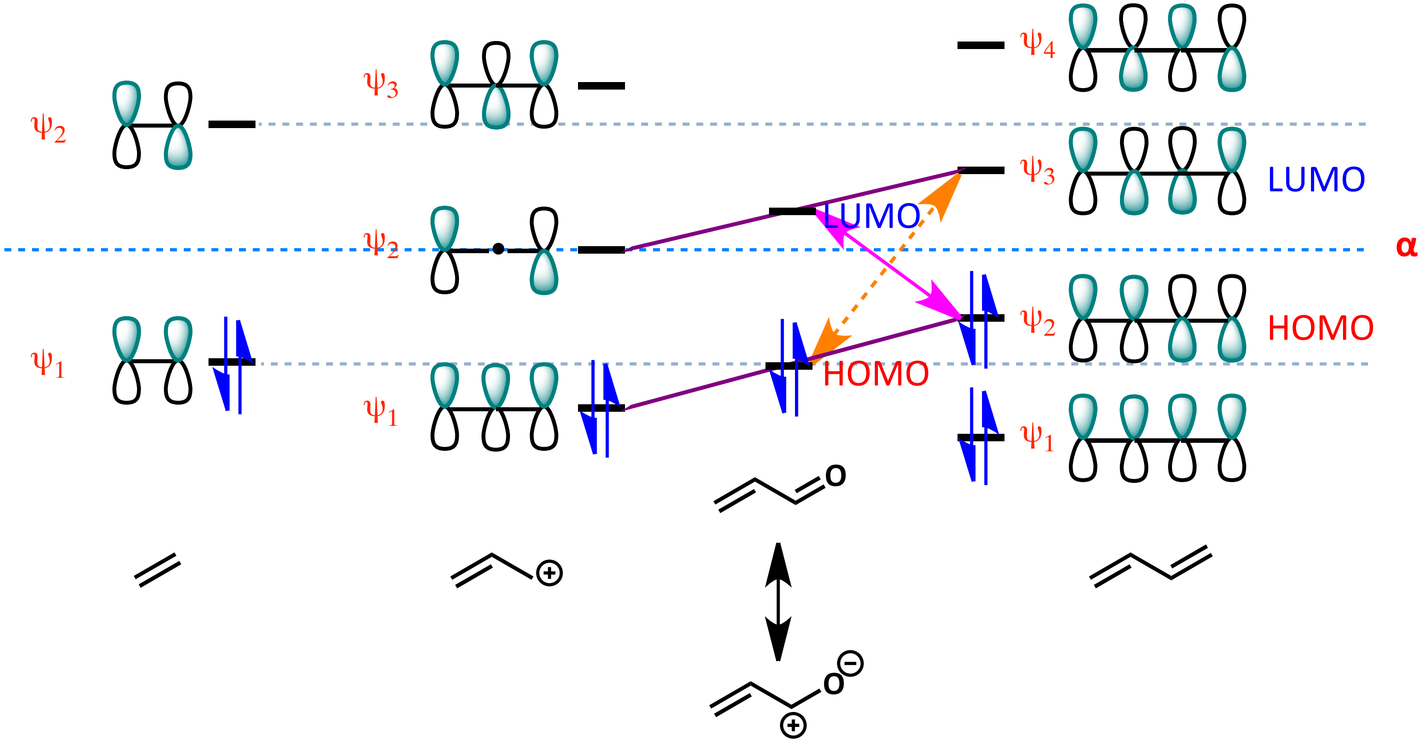
without catalysis	90%	10%
with AlCl$_3$	98%	2%

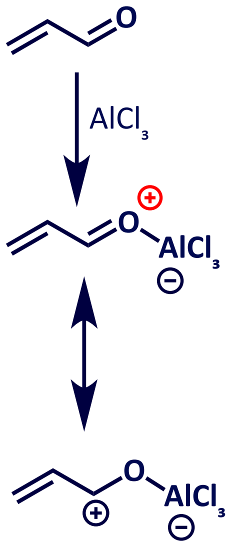
Cycloadditions

- Increase rate of reaction with EWG on dienophile.
- An EWG (‘Z’ substituent) on the dienophile lowers the energy of the LUMO (and of all orbitals). (HOMO ethene is α + β, LUMO is α – β).
- The best energy match is therefore the HOMO of the diene with the LUMO of the dienophile (full double-headed arrow) rather than the HOMO of the dienophile with with the LUMO of the diene (dashed double-headed arrow).
- Catalysis by Lewis acids arises from further lowering of the LUMO of the dienophile.



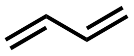


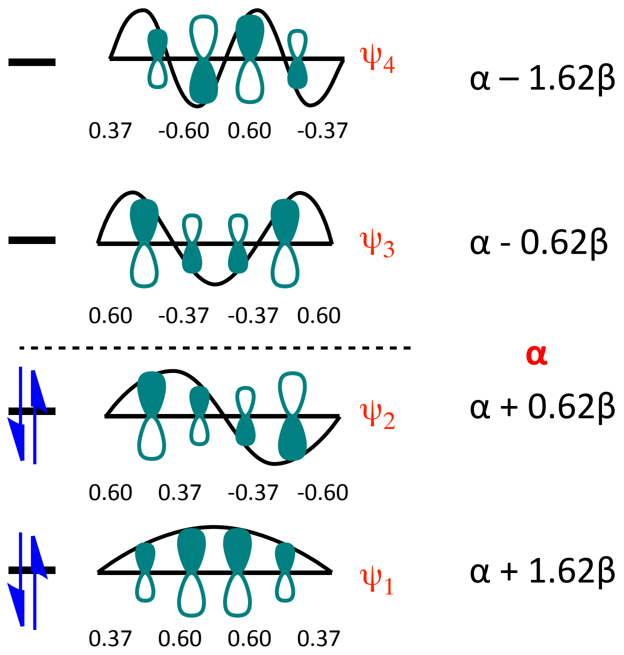


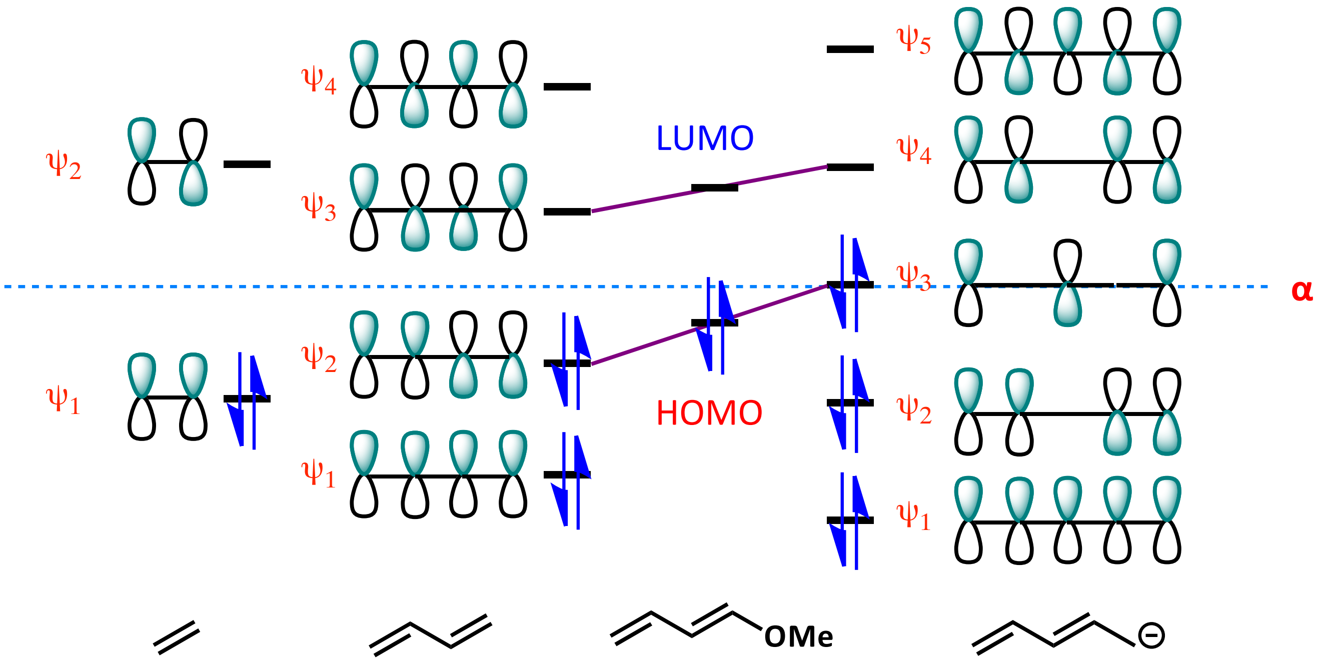


Cycloadditions

- In a similar manner placing an EDG on the diene raises the energy of the HOMO making it a better energy match for the **LUMO** of the dienophile.
- Having an EDG on the dienophile (higher energy HOMO) and an EWG on the diene (lower energy LUMO) is generally less effective at increasing the late of the Diels-Alder reaction. (Inverse electron demand)







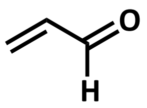
- In general:

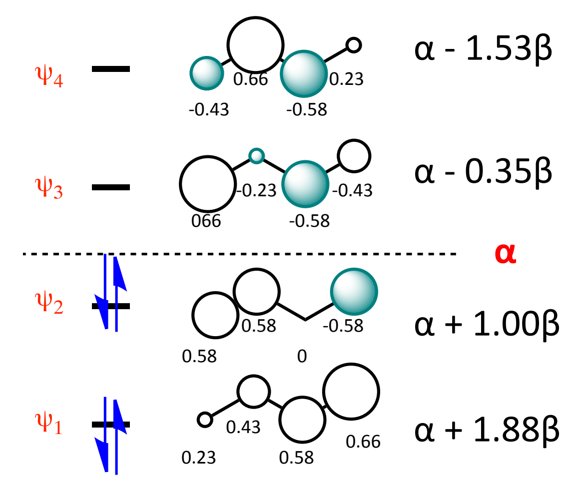
EWG (Z-substituents) lower HOMO & LUMO energies
EDG (X-substituents) raise HOMO & LUMO energies
carbon conjugating systems e.g. C=C, raise HOMO & lower LUMO

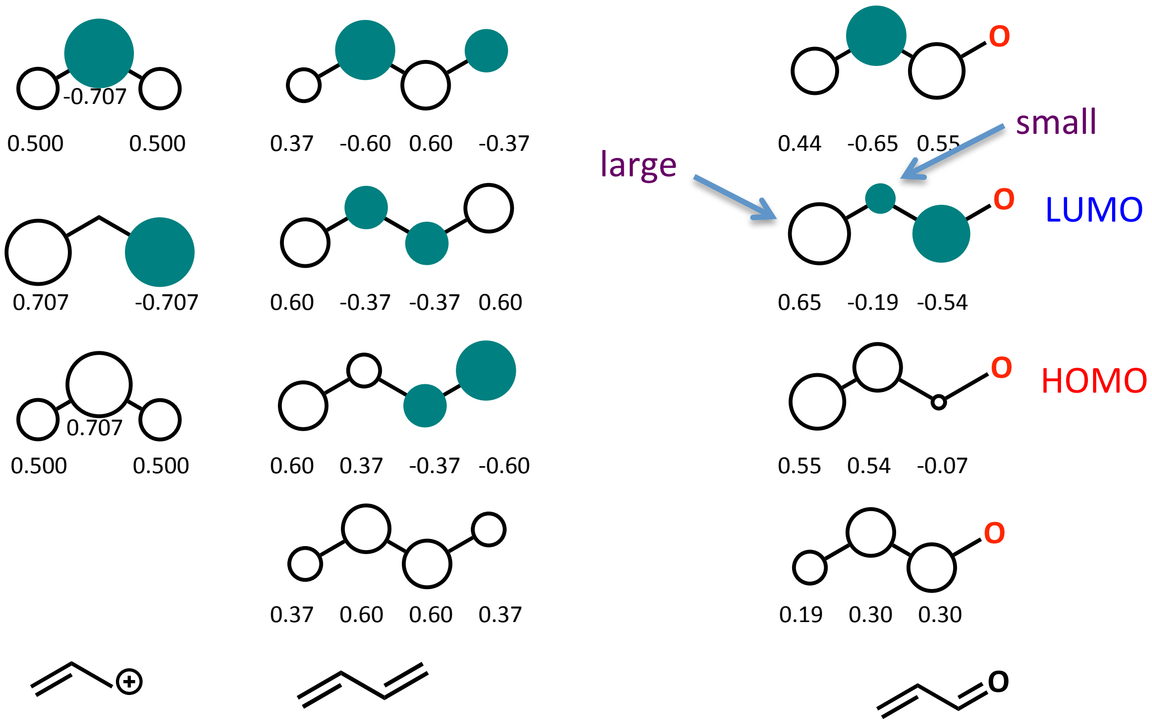
- These groups distort orbital coefficients.

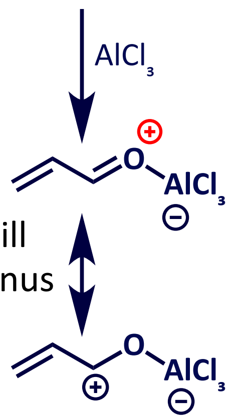
Cycloadditions

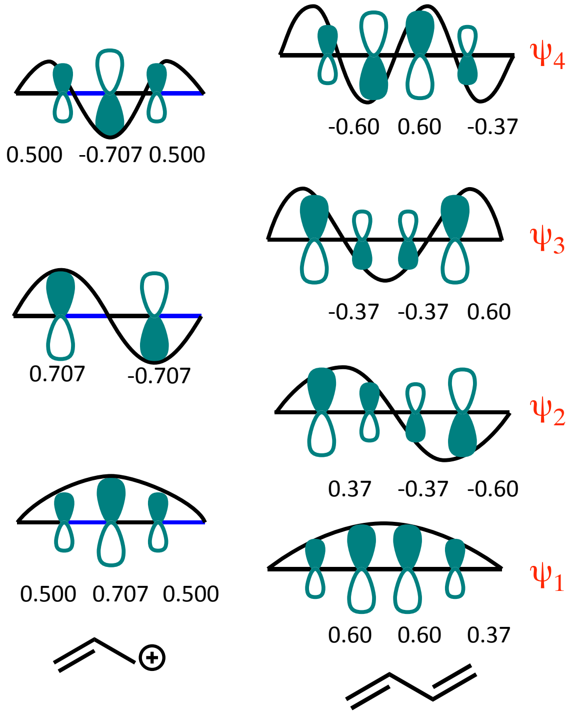
- Diels-Alder reaction regioselectivity









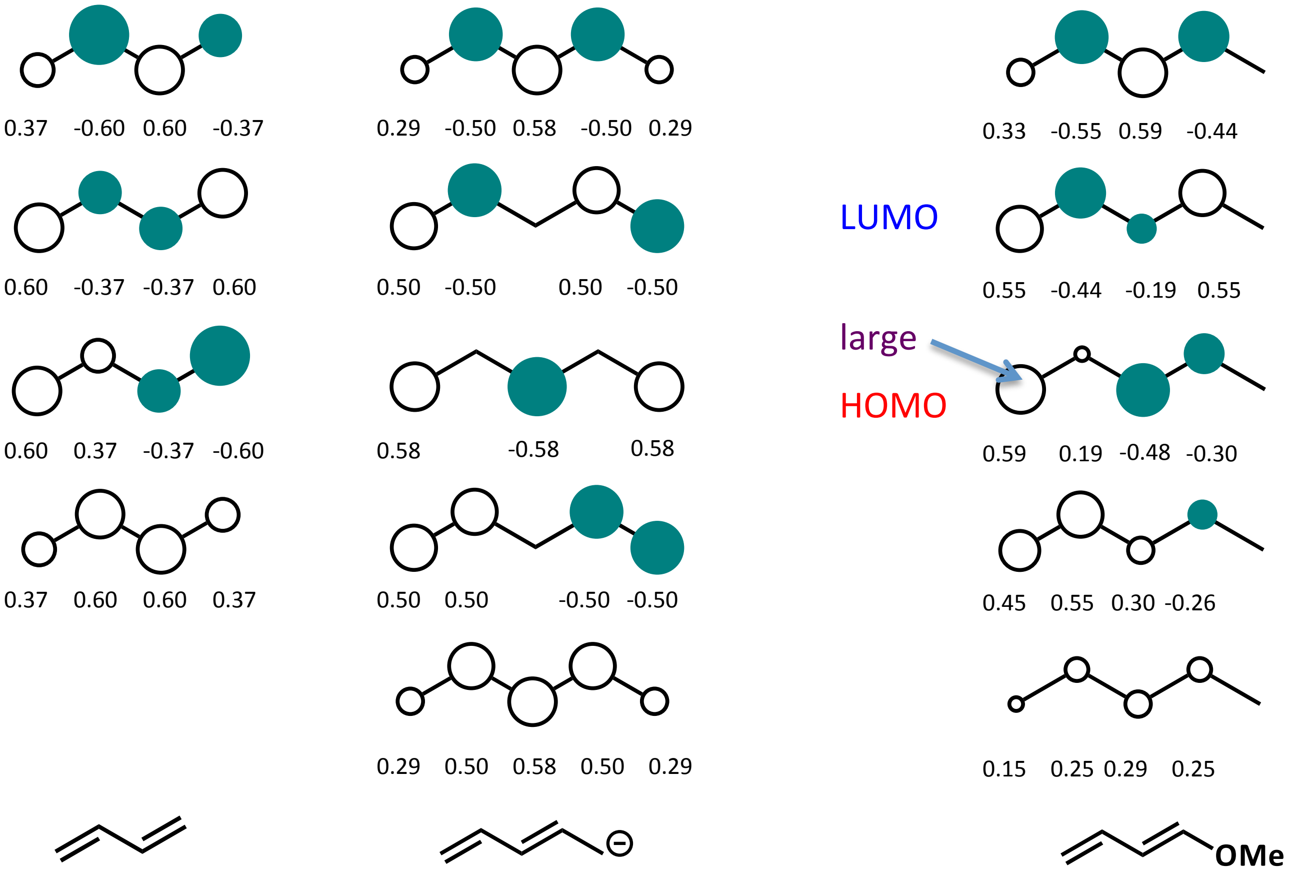


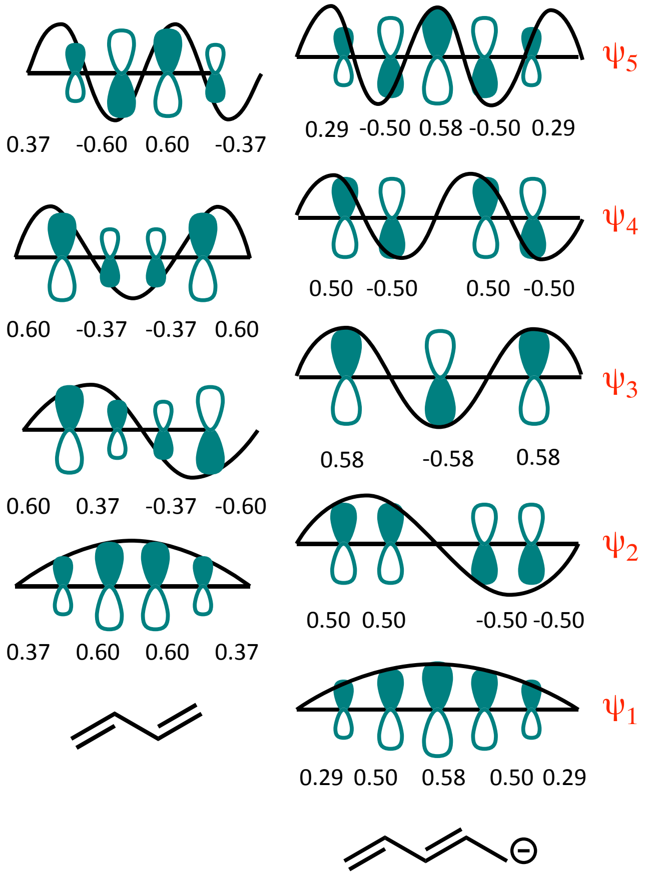
- Coefficients for acrolein just taken as average of allyl cation and butadiene coefficients – see Fleming.

- In the presence of a Lewis acid (e.g. $AlCl_3$) acrolein will have more allyl cation character and hence the C-terminus coefficient of the LUMO will be larger.

Cycloadditions

- Diels-Alder reaction regioselectivity





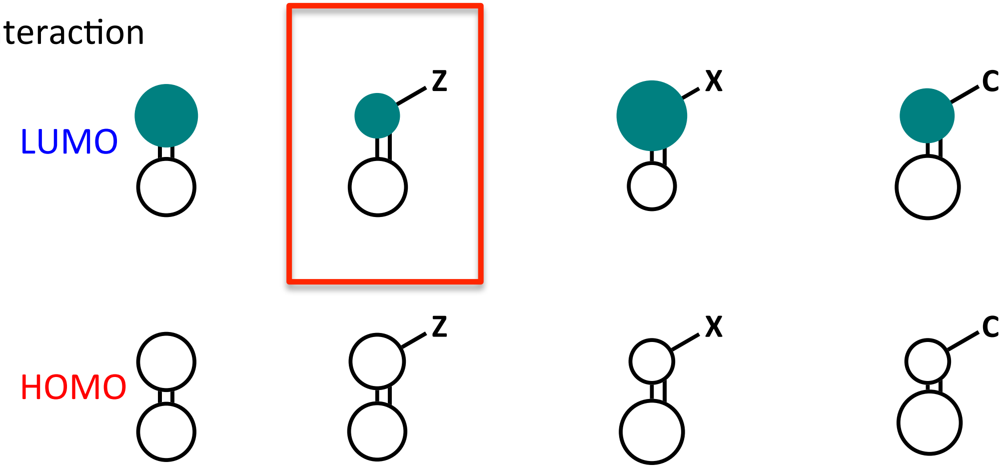
Cycloadditions

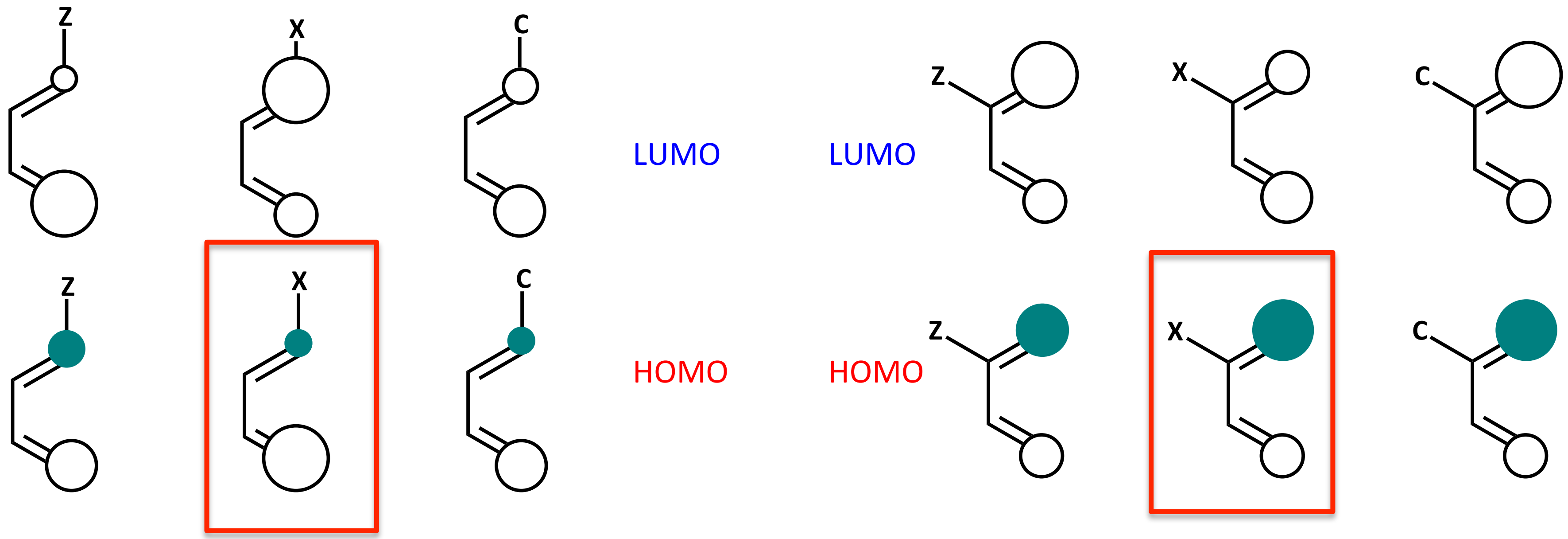
- Diels-Alder reaction regioselectivity (Z = EWG e.g. CO_2Me; X = EDG e.g. OMe.

- HOMO diene / LUMO dienophile is the predominant interaction

- Large-large and small-small overlap is best.

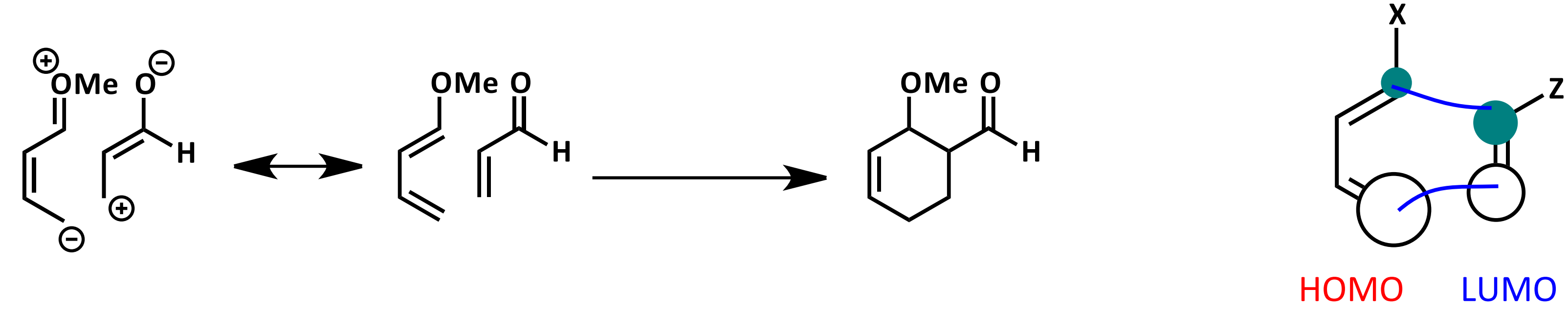
- As noted previously, in the presence of a Lewis acid (e.g. $AlCl_3$) C-terminus coefficient of the LUMO of a Z-substituted alkene will be larger leading to increased regioselecitivity in the Diels-Alder reaction.



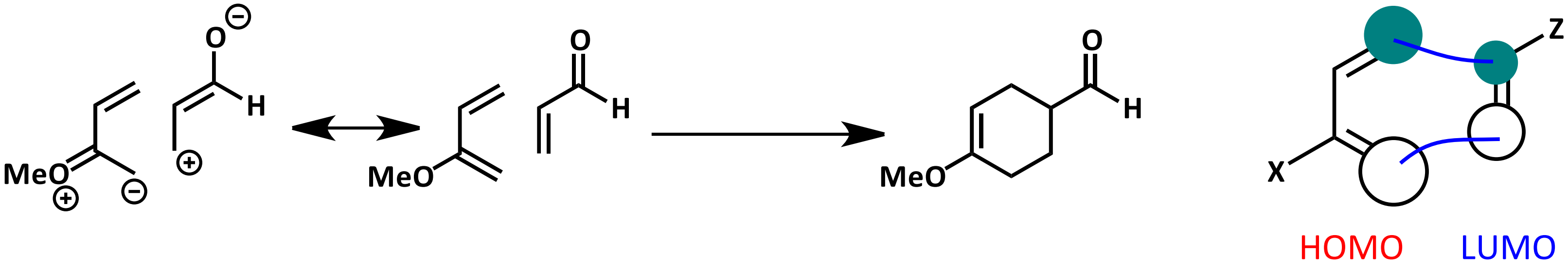


Cycloadditions

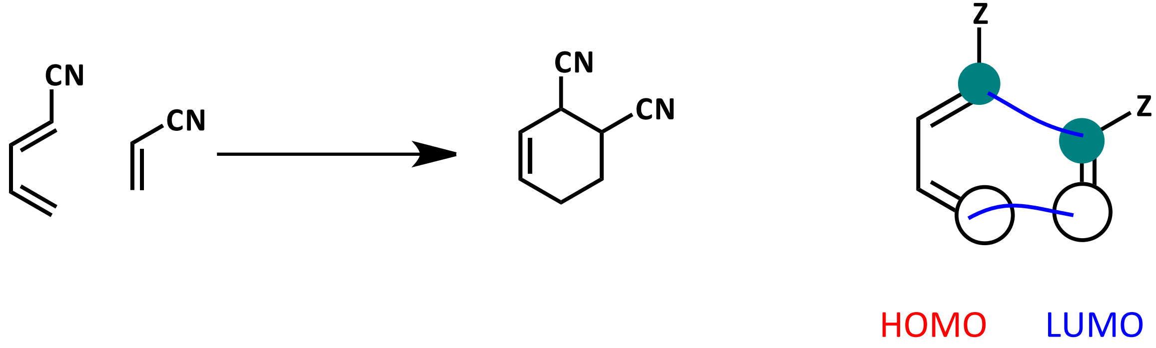
- Diels-Alder reaction regioselectivity (Z = EWG e.g. CO_2Me; X = EDG e.g. OMe.



‘ortho’ product



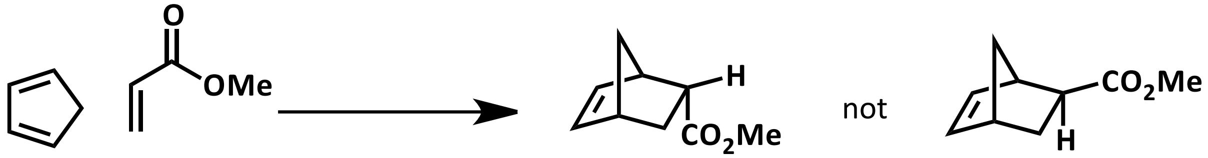
‘para’ product



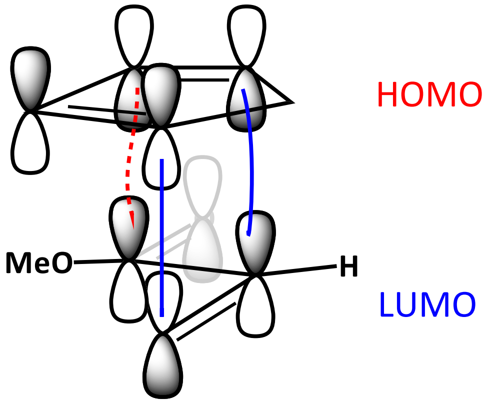
‘ortho’ product

Cycloadditions

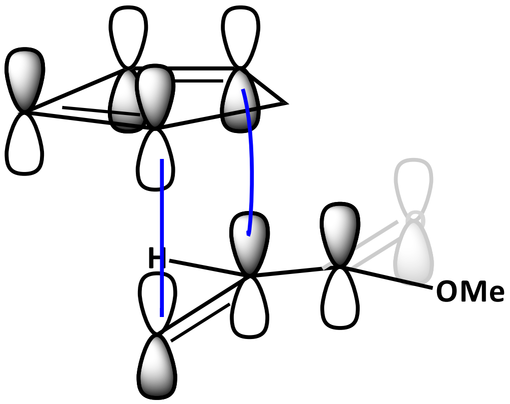
- Diels-Alder reaction the *endo* rule – *endo*-product is generally the major product with dienophiles containing π-conjugating substituents .



- Secondary orbital overlap is a simple explanation for the kinetic preference for the *endo*-adduct –

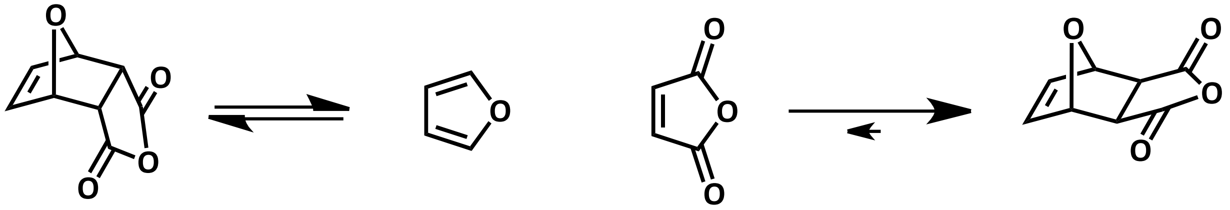


endo



exo

- In cases where the reaction readily reverses (e.g. Diels Alder reactions with furan) the thermodynamically preferred *exo*-adducts are usually obtained.

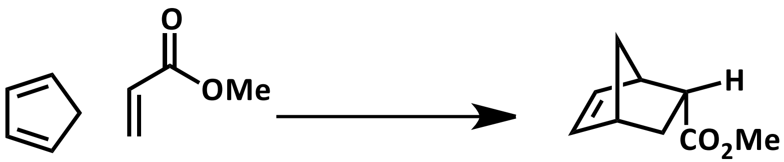


endo-kinetic

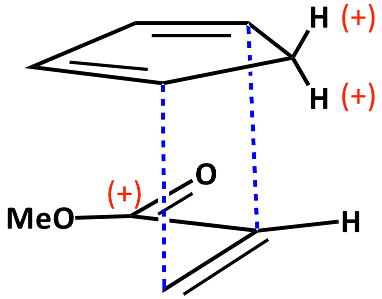
exo-thermodynamic

Cycloadditions

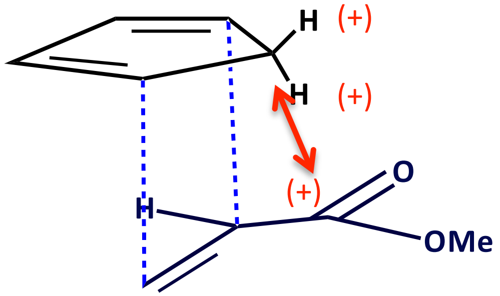
- Electrostatic arguments have also been proposed as a reasonable explanation for ‘*endo*’-selectivity



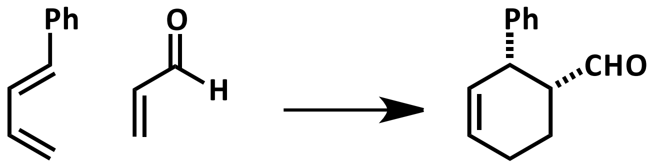
endo



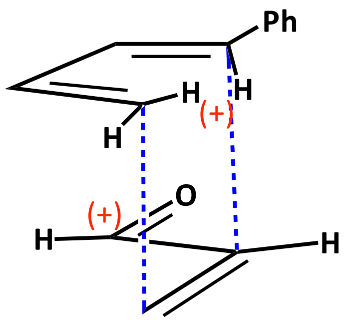
endo (favoured)



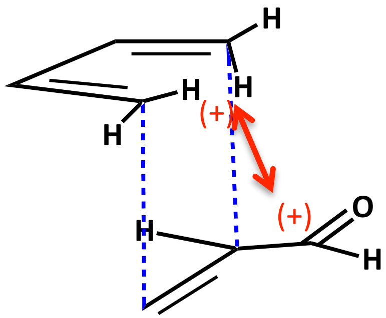
exo (disfavoured)



endo

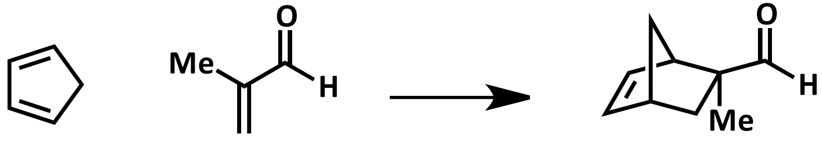


endo (favoured)

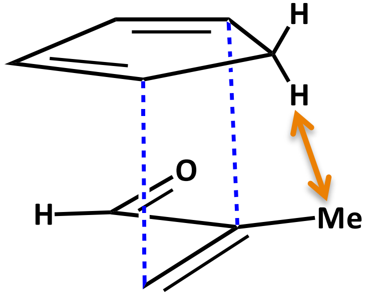


exo (disfavoured)

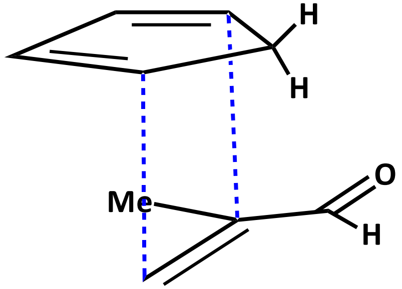
- Steric effects can favour the *exo* product.



exo

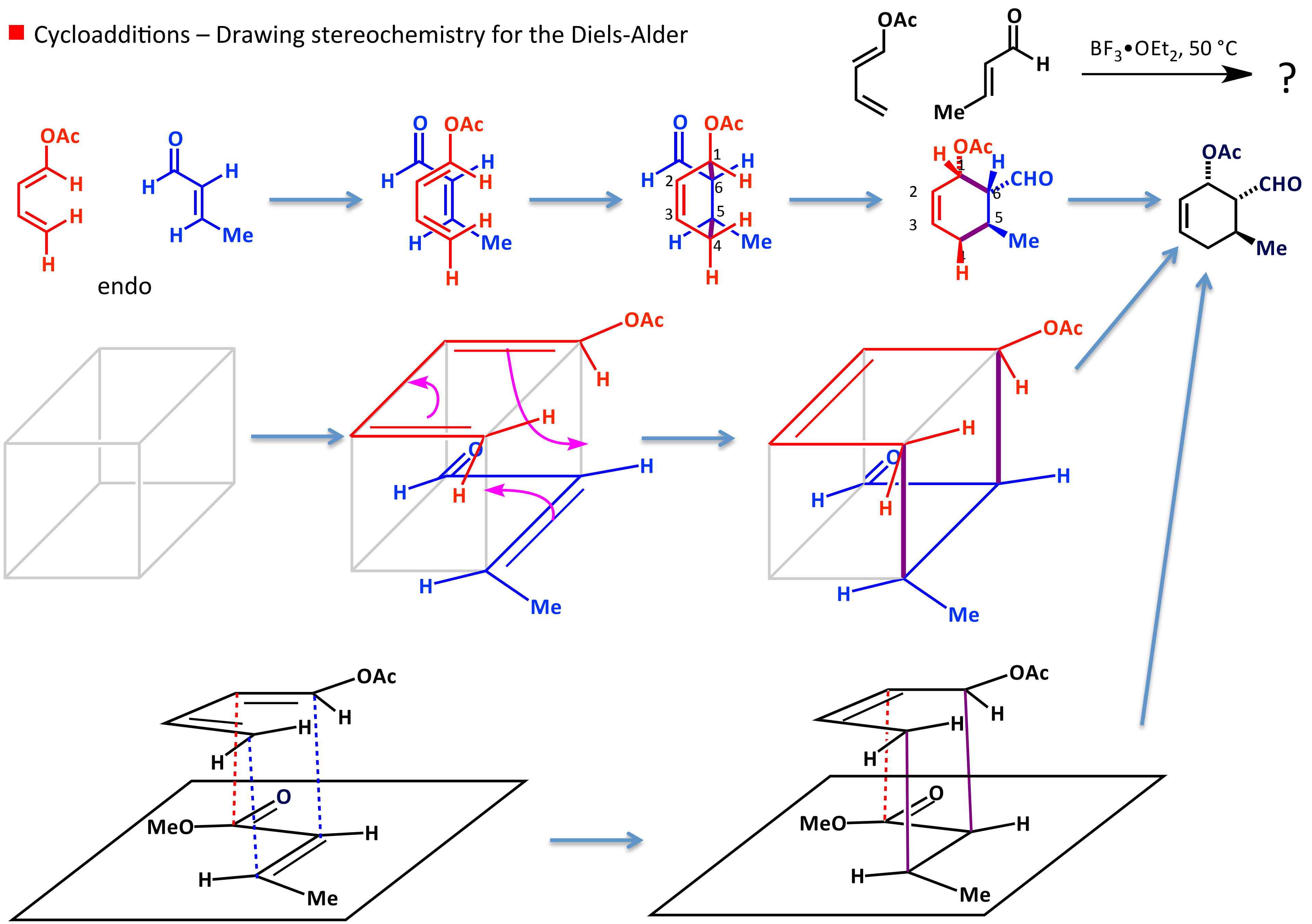


endo (disfavoured)



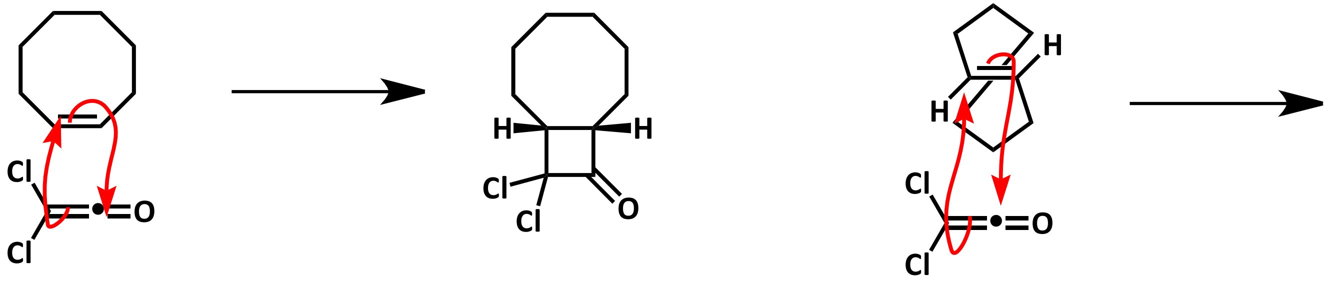
exo (favoured)

■ Cycloadditions – Drawing stereochemistry for the Diels-Alder

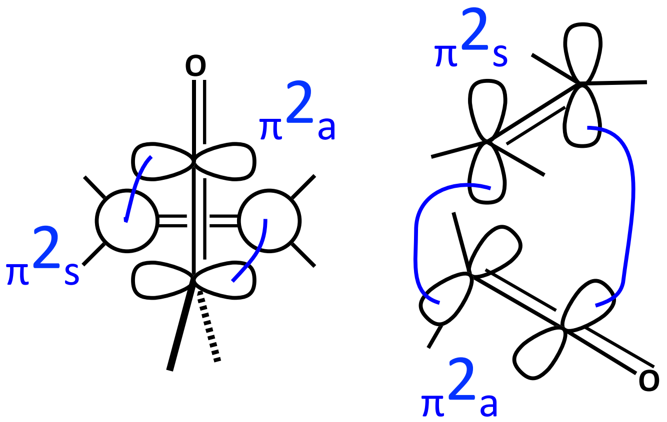


Cycloadditions

- Ketenes undergo (thermal) [2+2]-cycloadditions with alkenes providing an excellent method for cyclobutane synthesis.

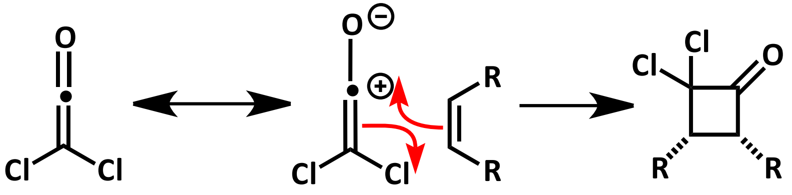


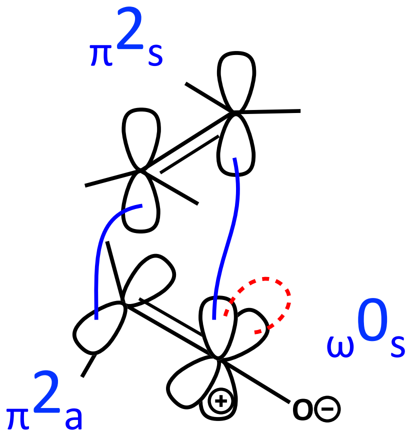
- The simplest explanation for this reaction is that the orbitals of the ketene are used as an antarafacial component.



$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

- Treating the ketene as a vinyl cation allows a geometrically more reasonable overlap to orthogonal orbitals

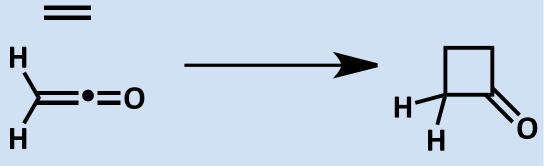


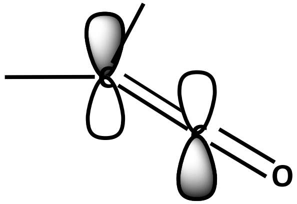


$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

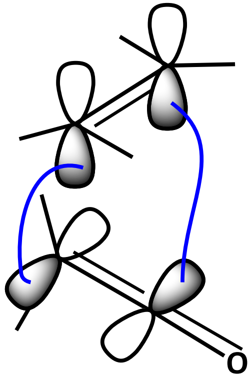
Cycloadditions

- Ketene Frontier Orbitals





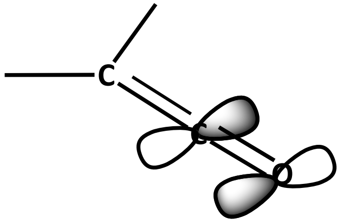
LUMO + 1
(C=C π^*)



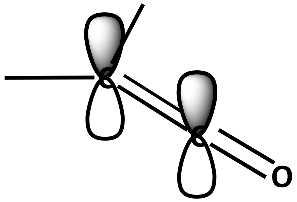
HOMO alkene

LUMO + 1 ketene

constructive overlap ✓

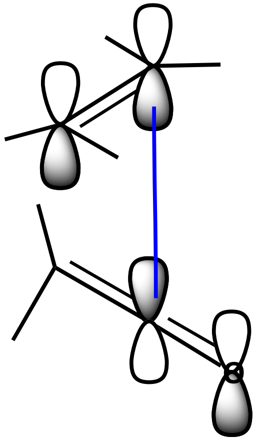


LUMO
(C=O π^*)



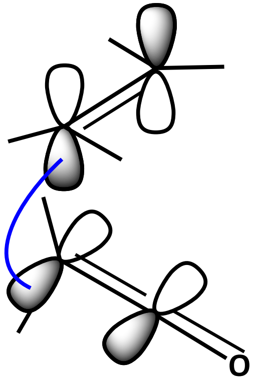
HOMO
(C=C π)

HOMO alkene



LUMO ketene

LUMO alkene

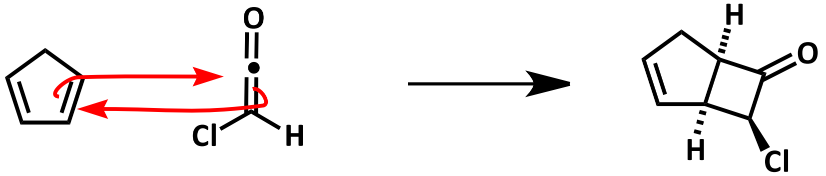


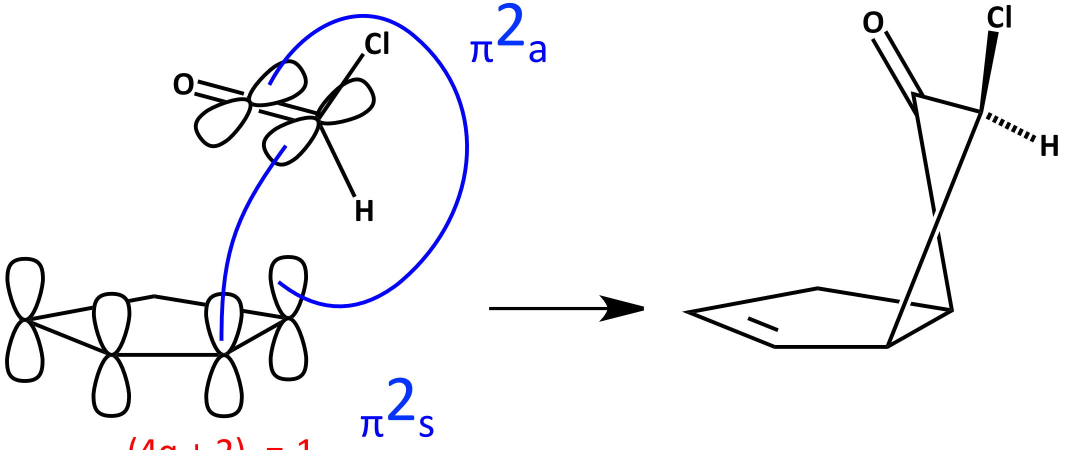
HOMO ketene

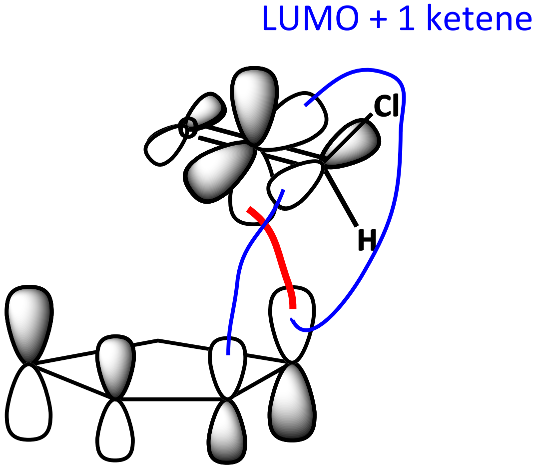
- With ketenes it is probable that the low lying C=O π^* orbital is involved in the reaction.
- Other cumulated π systems which contain a central sp-hybridised carbon atom (e.g. allenes, vinyl cations) also readily undergo [2+2] cycloaddition.

Cycloadditions

- Ketenes readily react with cyclopentadiene to give cyclobutanes.







$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

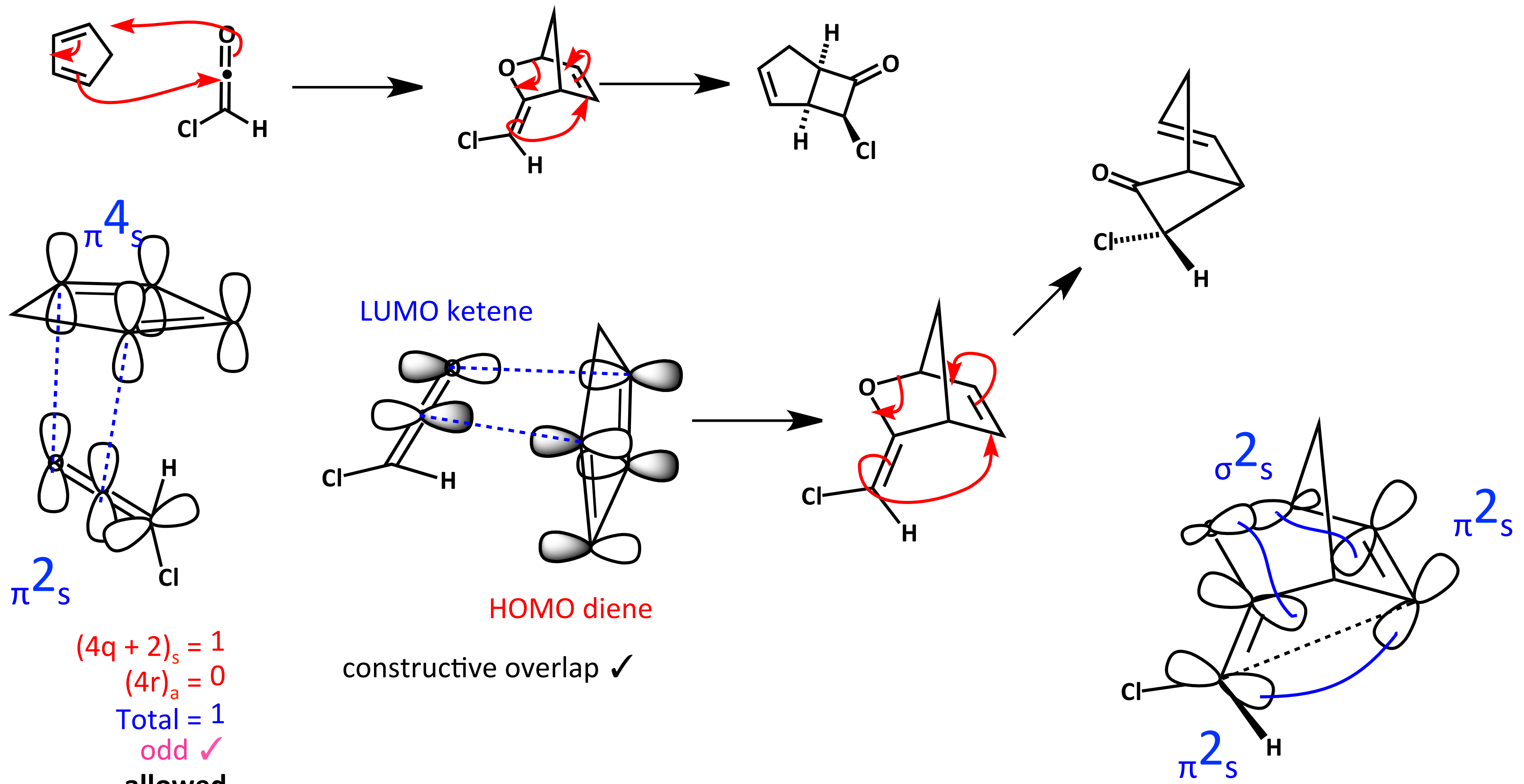
HOMO diene

constructive overlap ✓

- With an unsymmetrical ketene, the larger ketene substituent will point away from the plane of the alkene.
- Regioselectivity can be predicted from simple “arrow-pushing” arguments (the C=O carbon of ketenes is very electrophilic), or from looking at FMO coefficients.
- In reactions of unsymmetrical alkenes the less sterically demanding C=O part of the ketene will be oriented above the larger alkene substituents.

Cycloadditions

- Another possible mechanism is a hetero Diels-Alder reaction followed by a Claisen rearrangement.



$(4q + 2)_s = 1$

$(4r)_a = 0$

Total = 1

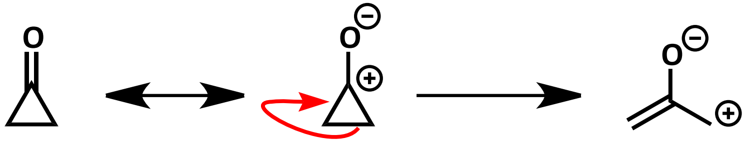
odd ✓

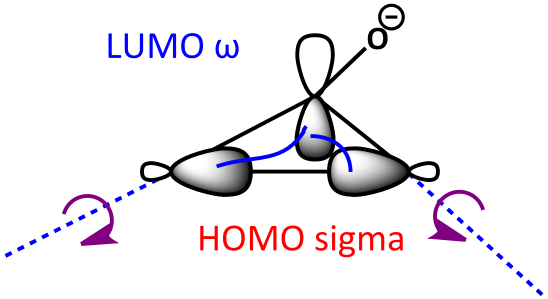
allowed

constructive overlap ✓

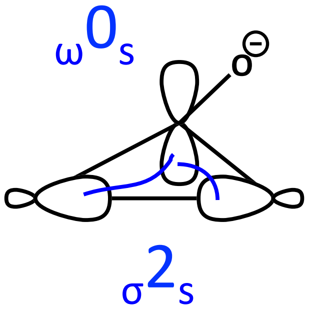
- Certain ketenes appear to react with cyclopentadiene *via* both a [2+2] cycloaddition, and a [4+2] cycloaddition followed by a Claisen rearrangement mechanism.

🟥 Oxyallyl-diene

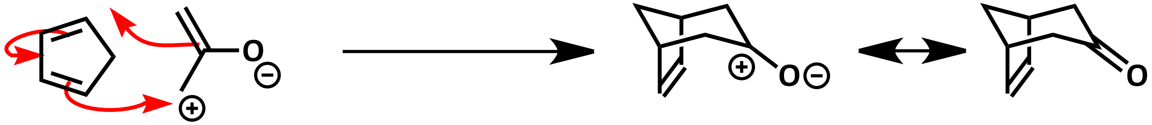




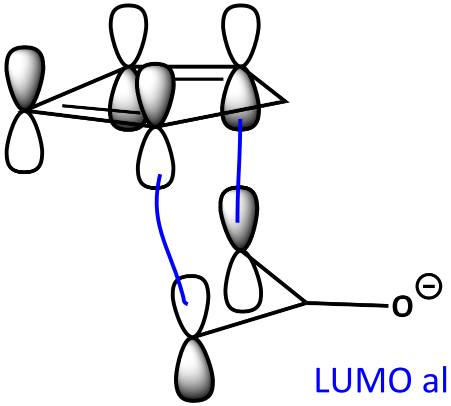
constructive overlap ✓
disrotatory



$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed
disrotatory

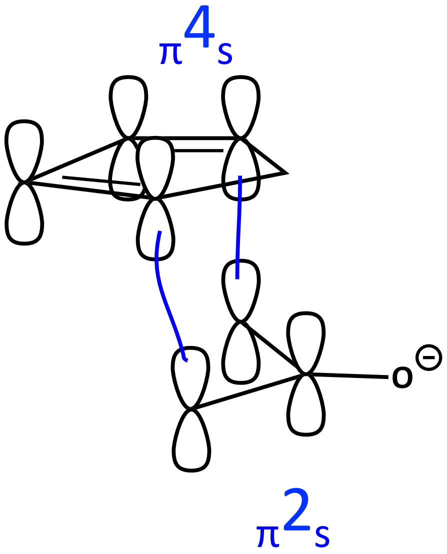


HOMO diene



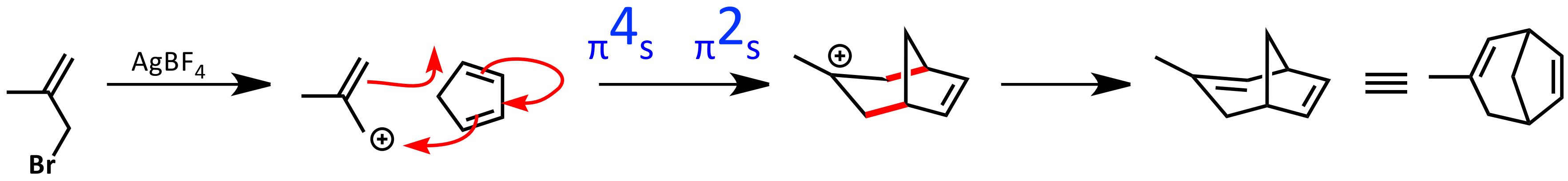
LUMO allyl cation

constructive overlap ✓

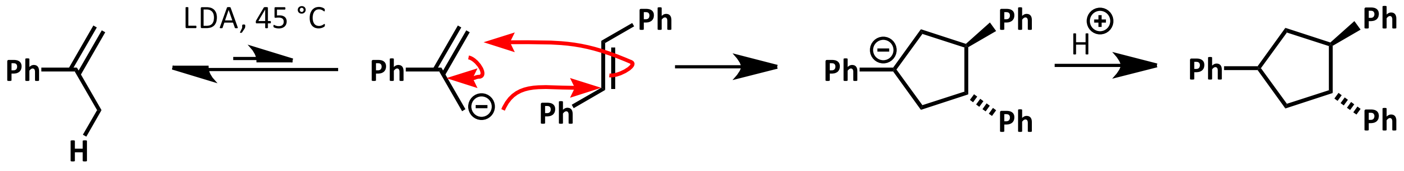


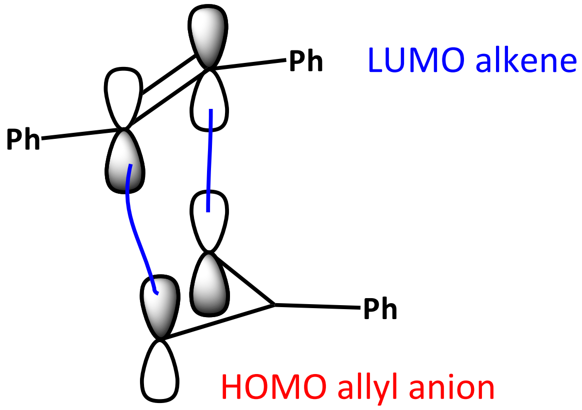
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

Allyl cation-diene

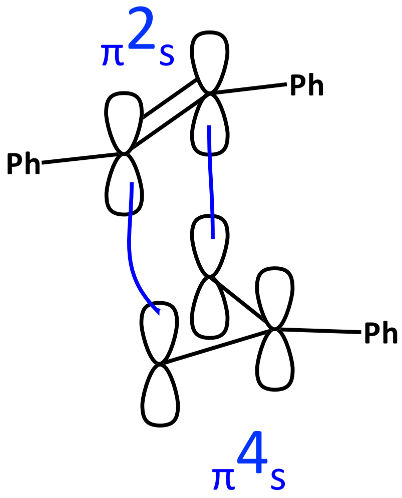


Allyl anion-alkene and reverse process



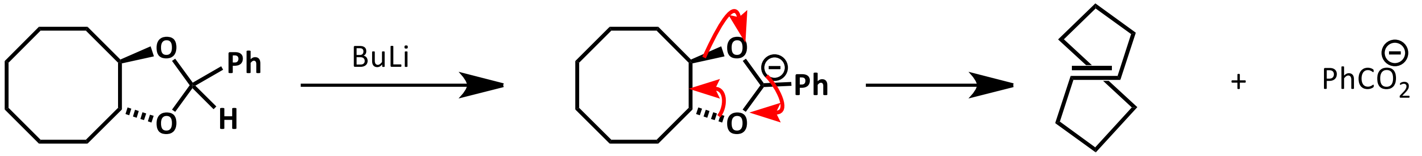


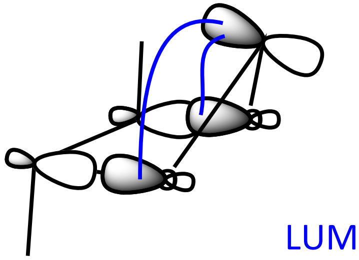
constructive overlap ✓



$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

- Allyl anion-alkene (reverse process)

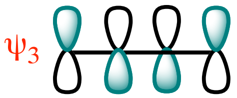




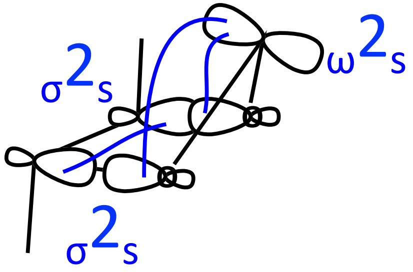
HOMO ω

LUMO σ +σ

constructive overlap ✓



LUMO butadiene



$(4q + 2)_s = 3$

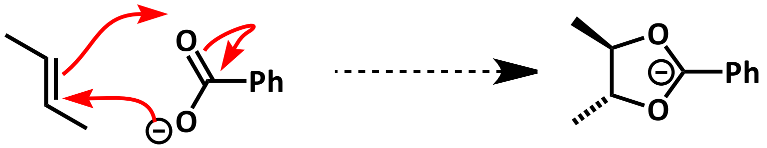
$(4r)_a = 0$

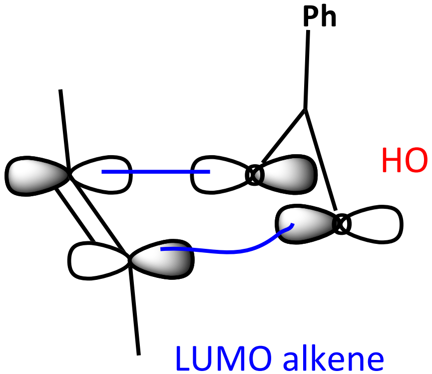
Total = 3

odd ✓

allowed

- It can be easier to analyse the reverse reaction.



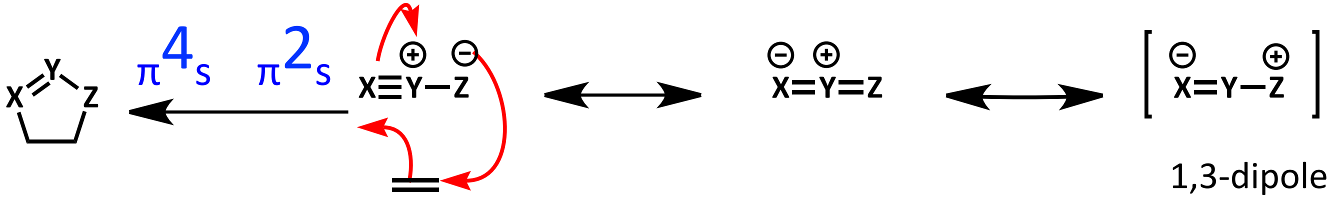


HOMO carboxylate

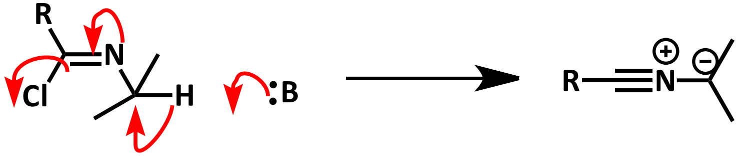
LUMO alkene

constructive overlap ✓

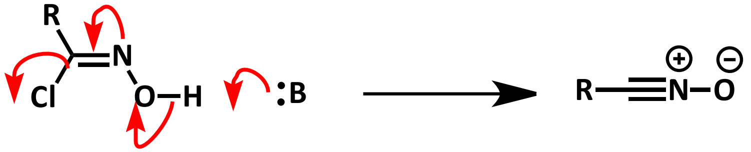
- 1,3-Dipolar cycloadditions.
- sp-hybridized central atom



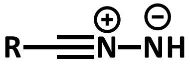
- nitrile ylids



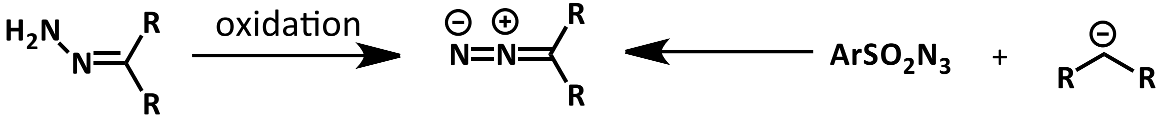
- nitrile oxides



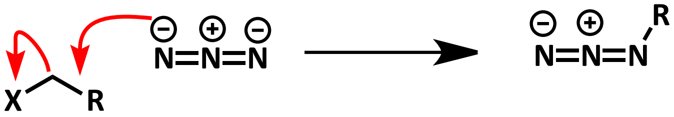
- nitrile imines



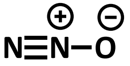
- diazoalkanes



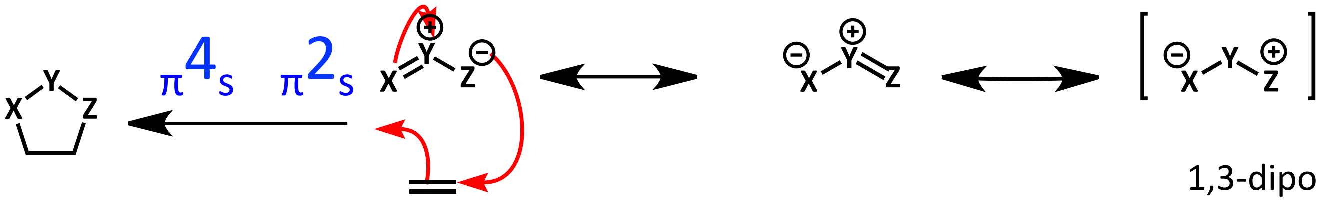
- alkyl azides



- nitrous oxide

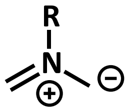


- 1,3-Dipolar cycloadditions.
- sp^2-hybridized central atom

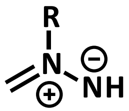


1,3-dipole

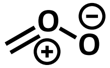
- azomethine ylids



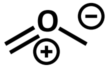
- azomethine imines



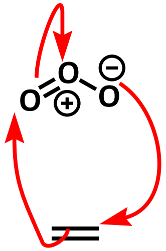
- carbonyl oxides



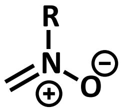
- carbonyl ylids



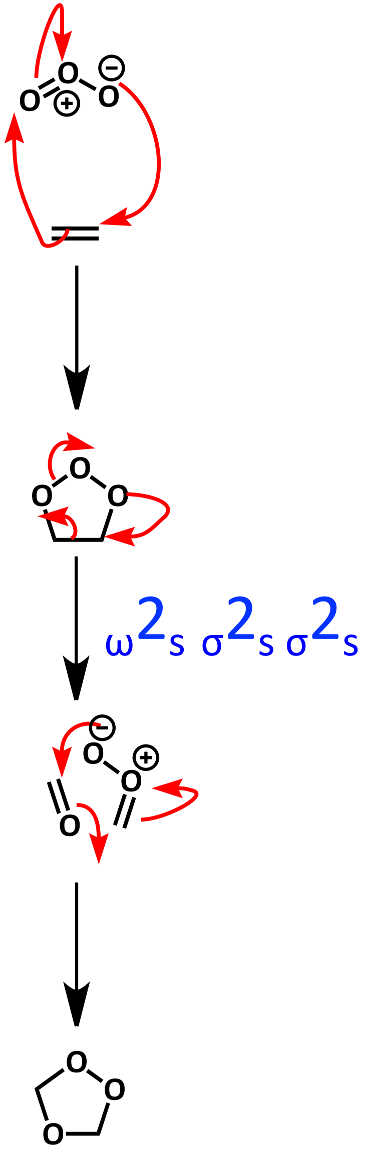
- ozone



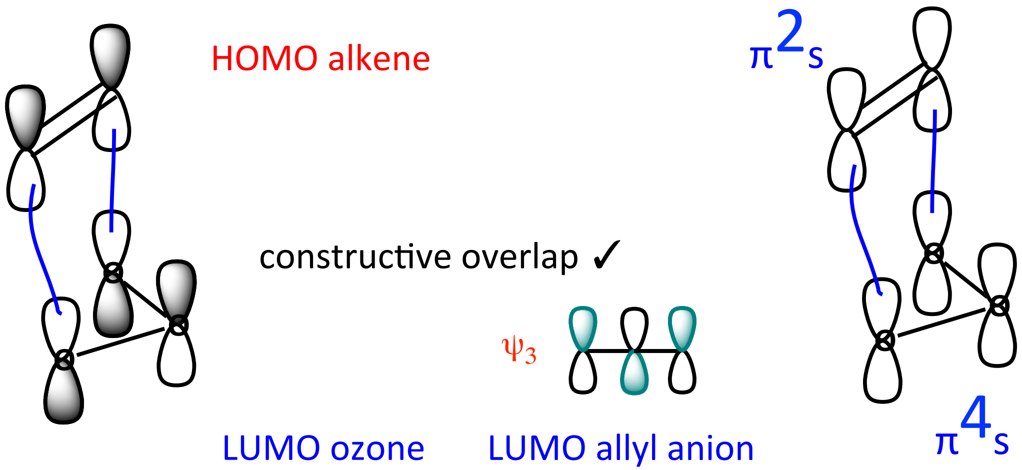
- nitrones



- Ozonolysis



$_{\omega}2_s\ _{\sigma}2_s\ _{\sigma}2_s$



HOMO alkene

constructive overlap ✓

ψ_3

LUMO ozone

LUMO allyl anion

$_{\pi}2_s$

$_{\pi}4_s$

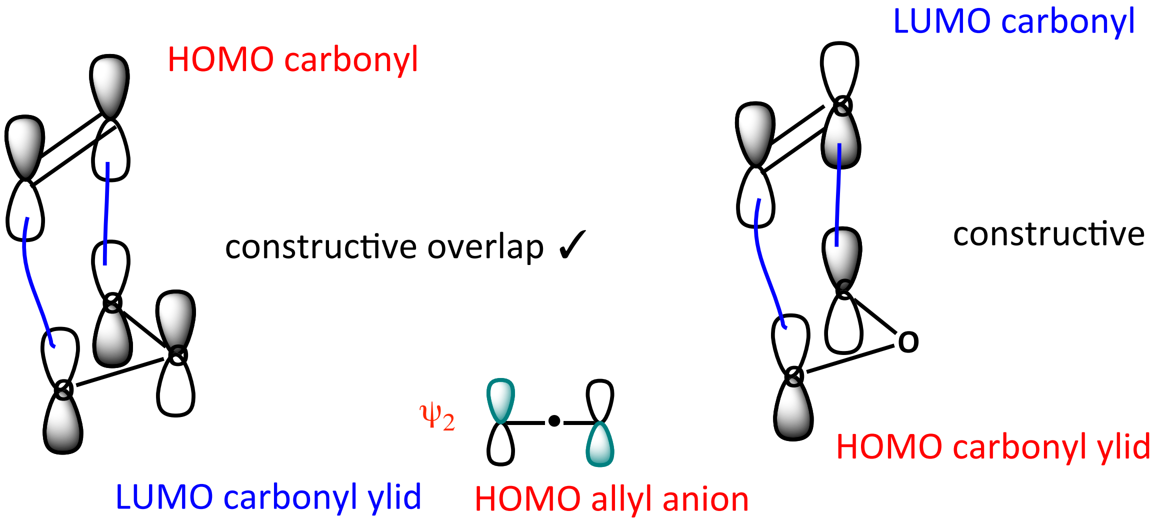
$(4q + 2)_s = 1$

$(4r)_a = 0$

Total = 1

odd ✓

allowed



LUMO carbonyl

HOMO carbonyl

constructive overlap ✓

constructive overlap ✓

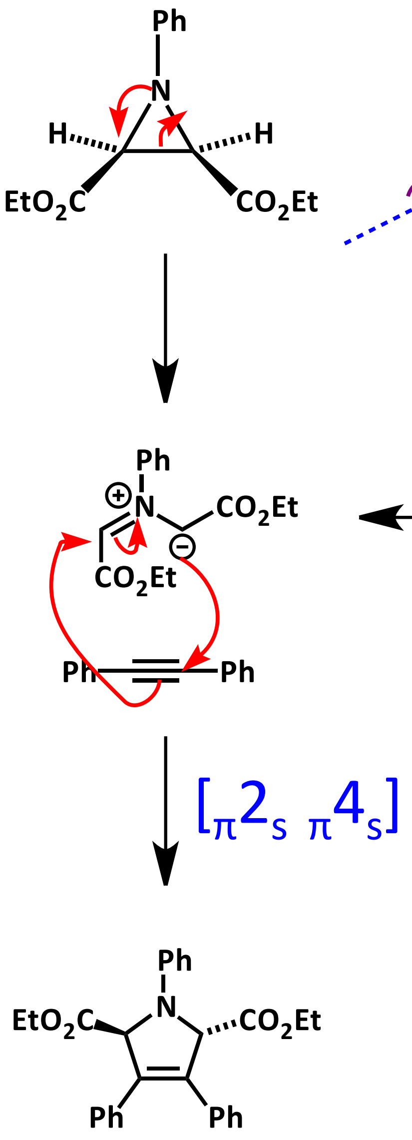
ψ_2

LUMO carbonyl ylid

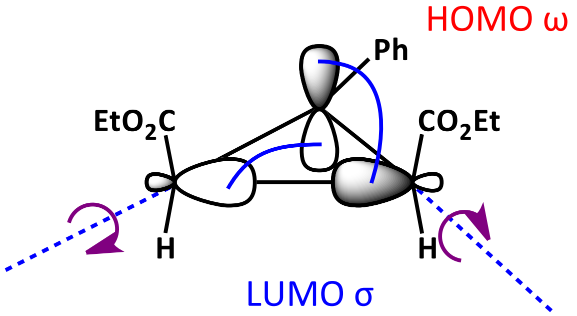
HOMO allyl anion

HOMO carbonyl ylid

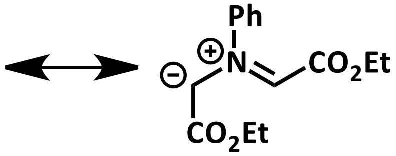
- Azomethine ylids.

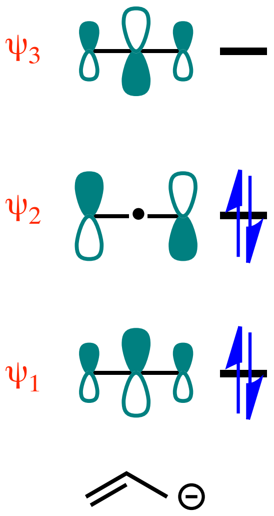


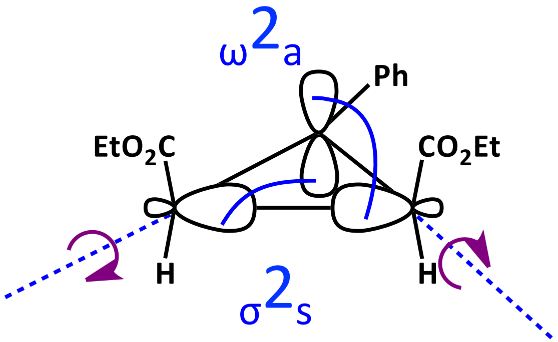
$[{}_{\pi}2_s\ {}_{\pi}4_s]$



constructive overlap ✓
conrotatory







$_{\omega}2_a$

$_{\sigma}2_s$

$(4q + 2)_s = 1$

$(4r)_a = 0$

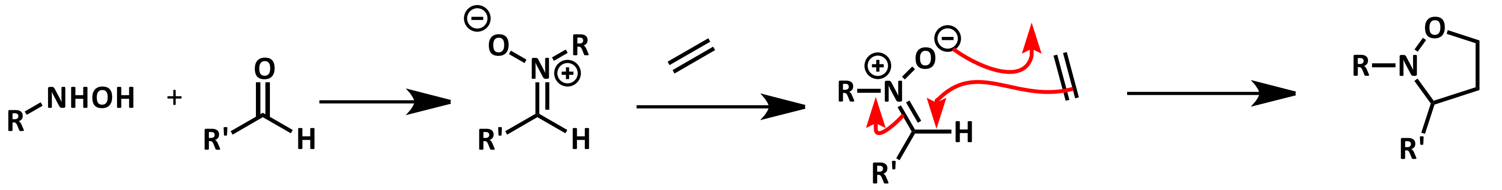
Total = 1

odd ✓

allowed

conrotatory

- Nitrone cycloadditions.
- Nitrones are readily formed between aldehydes and substituted hydroxylamines.
- The nitrone cycloaddition can predominantly HOMO$_{\text{nitrone}}$ LUMO$_{\text{dipolarophile}}$, or LUMO$_{\text{nitrone}}$ HOMO$_{\text{dipolarophile}}$ depending on the substituents on the dipolarophile.

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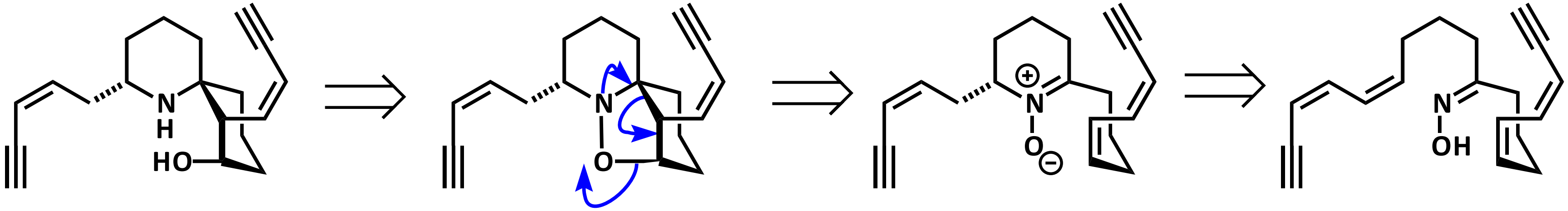
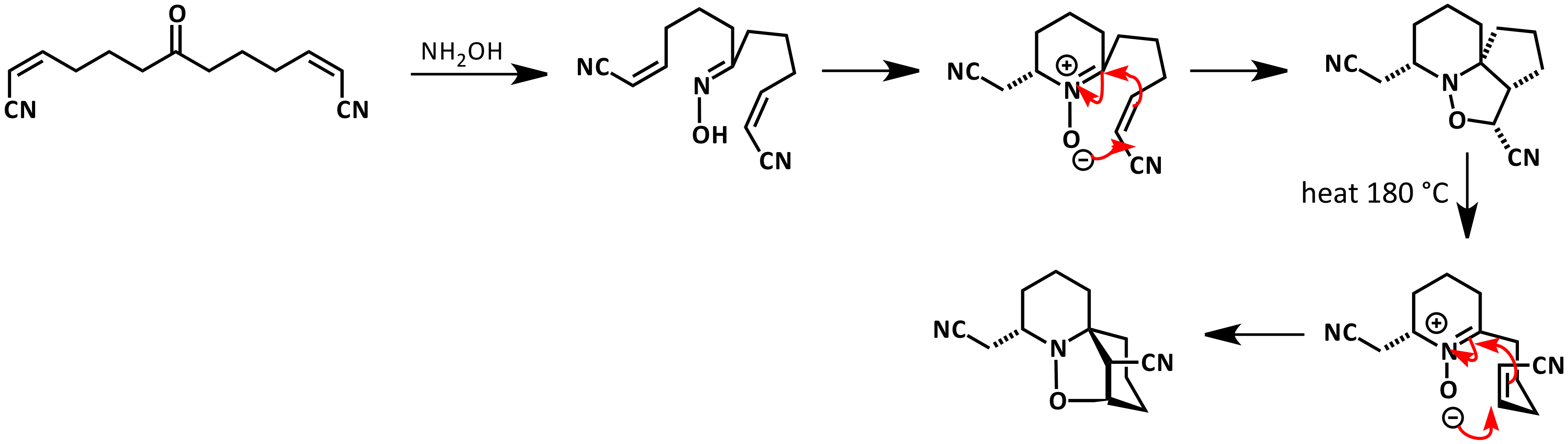
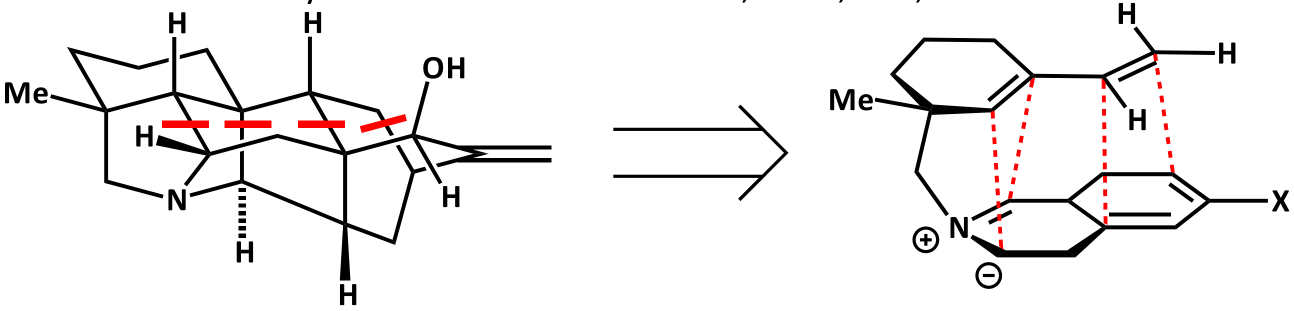
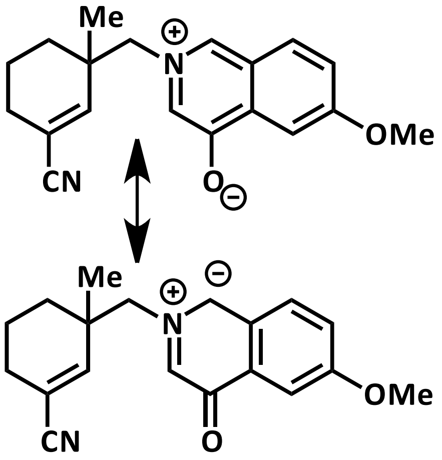
- Stockman synthesis of histrionicotoxin; *J. Am. Chem. Soc.*, **2006**, *128*, 12656.

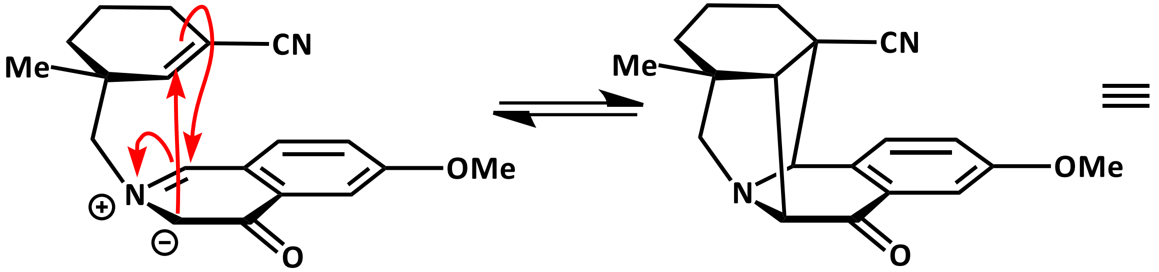


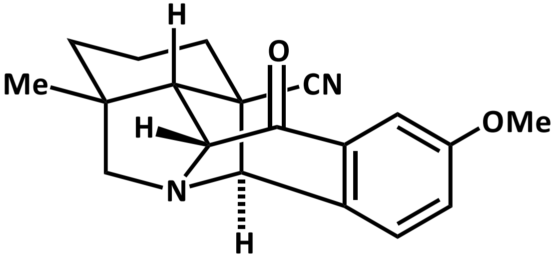


- Gin’s Nominine synthesis – *J. Am. Chem. Soc.*, **2006**, *128*, 8734.









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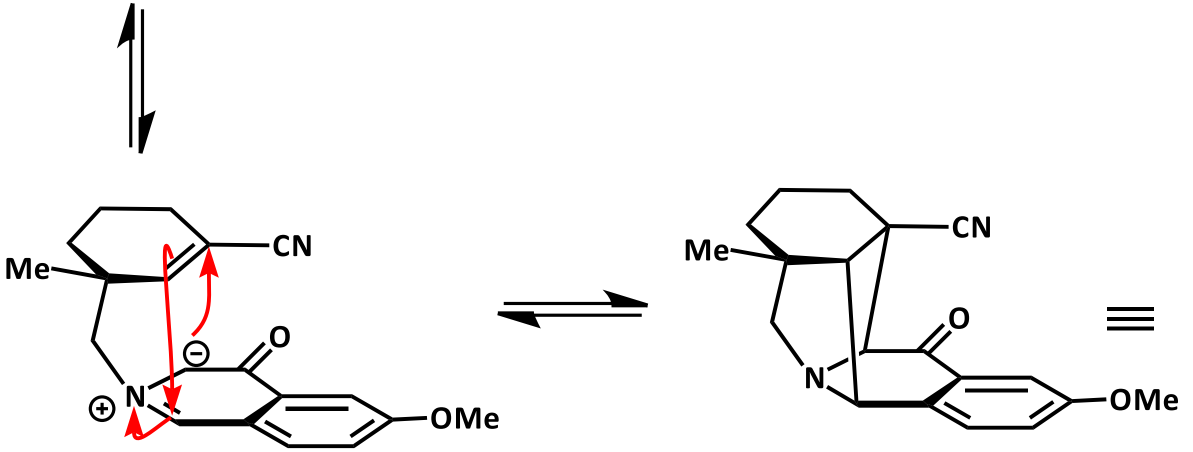
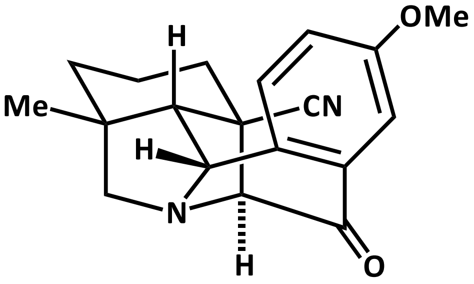
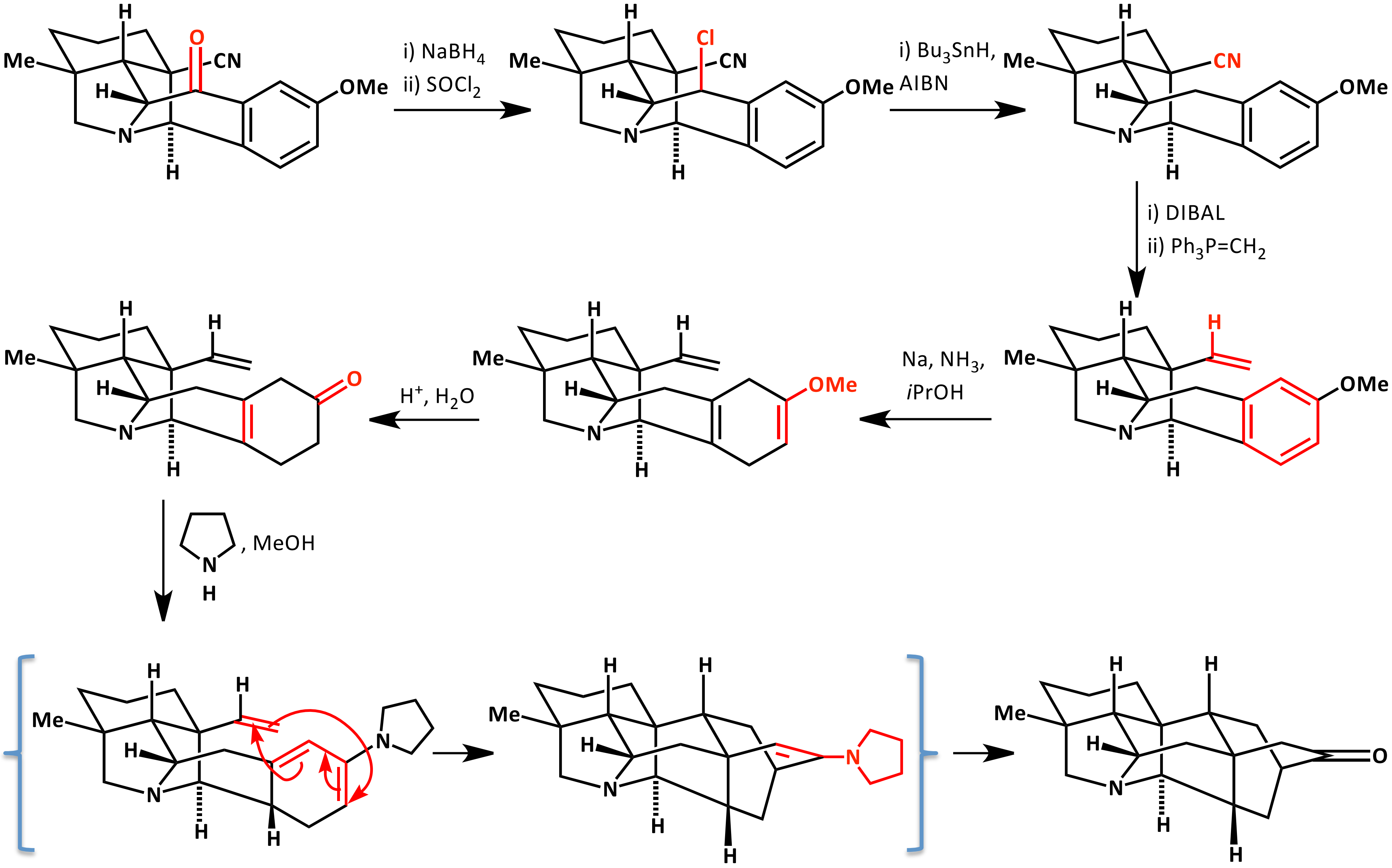


3.6

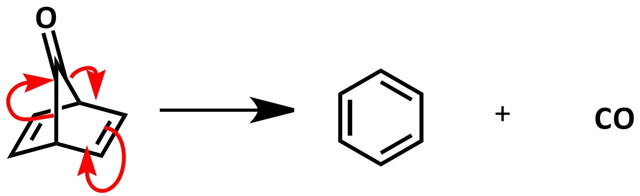


- Gin's Nominine synthesis – *J. Am. Chem. Soc.*, **2006**, *128*, 8734.

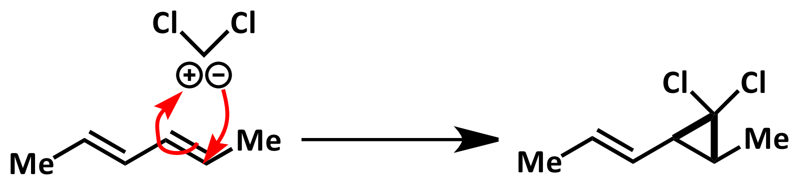


Cheletropic Reactions

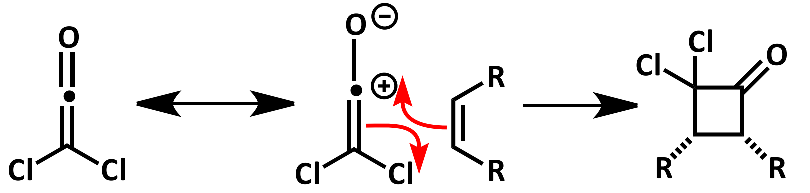
- A sub-class of cycloaddition/cycloreversion reactions in which the **two σ – bonds** are made or broken to the **same atom**.



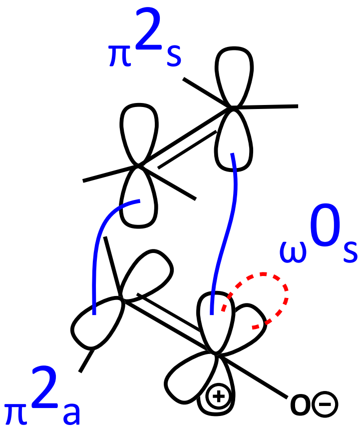
- More important are the reactions of singlet carbenes with alkenes which are stereospecific.
- Side on approach of the carbene is required for conservation of orbital symmetry.



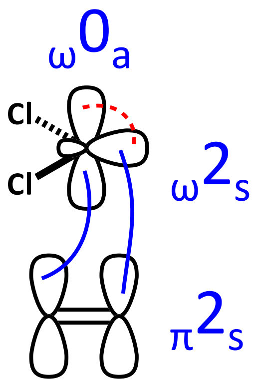
- c.f. ketenes as vinyl cations

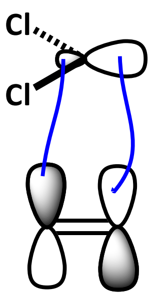


$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed



$(4q + 2)_s = 2$
$(4r)_a = 1$
Total = 3
odd ✓
allowed

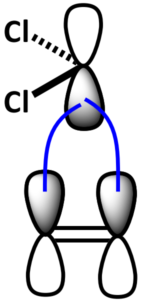




HOMO carbene

LUMO alkene

constructive overlap ✓

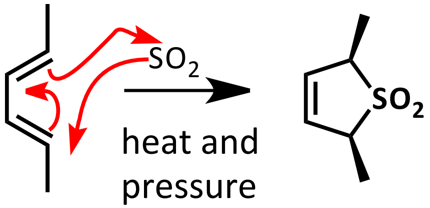


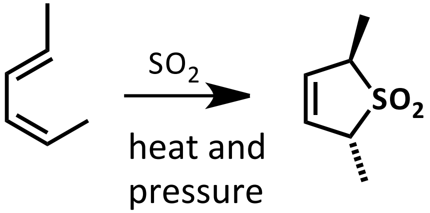
LUMO carbene

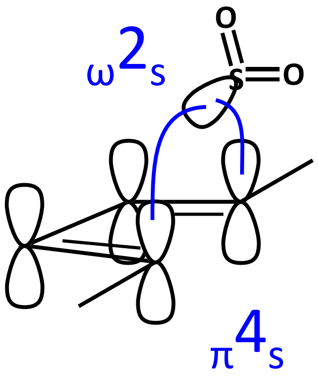
HOMO alkene

constructive overlap ✓

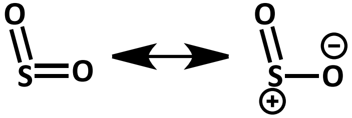
- Cheletropic Reactions
- The other important cheletropic reactions involve the reversible addition of sulfur dioxide to polyenes.

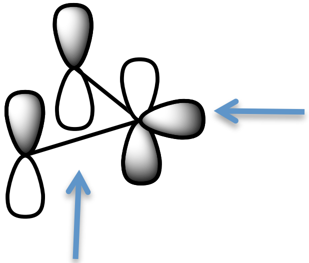




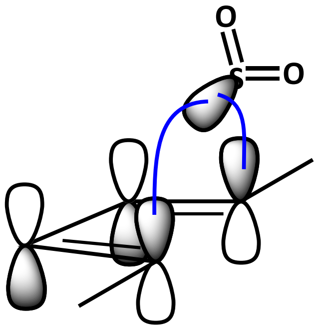


$(4q + 2)_s = 1$
$(4r)_a = 0$
$\text{Total} = 1$
odd ✓
allowed





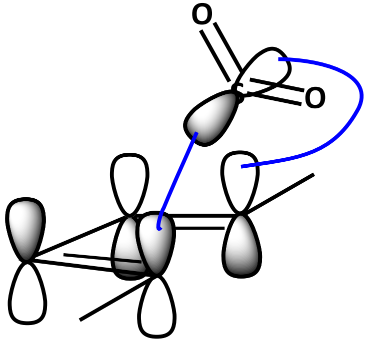
LUMO



HOMO SO_2

LUMO diene

constructive overlap ✓



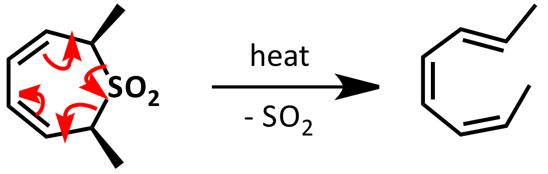
LUMO SO_2

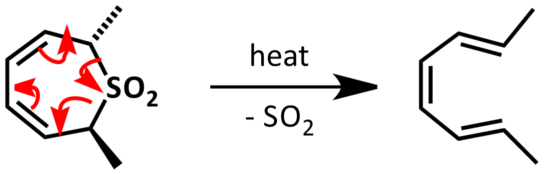
HOMO diene

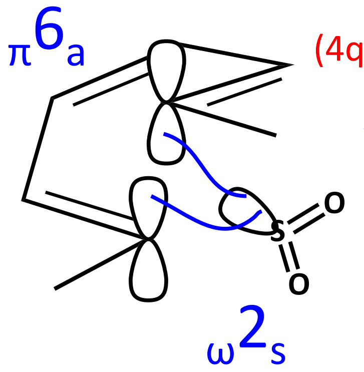
constructive overlap ✓

- Cheletropic Reactions

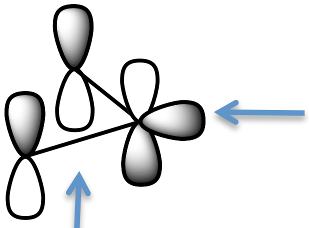
- With trienes the extrusion process dominates but considering the reverse process the reaction must be antarafacial with respect to the triene component.





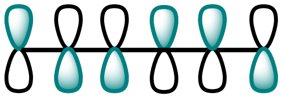


$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed



HOMO – lone pair

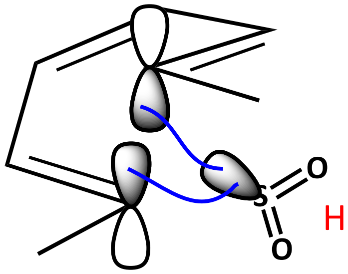
LUMO



LUMO hexatriene

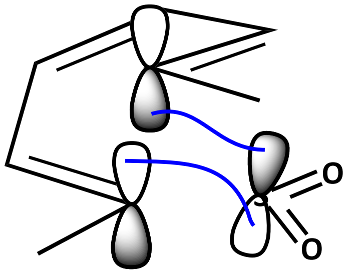
LUMO triene

HOMO triene



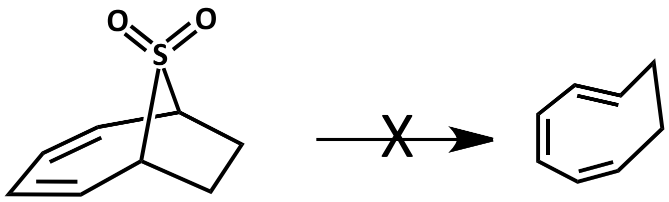
HOMO SO$_2$

constructive overlap ✓

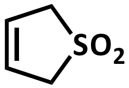


LUMO SO$_2$

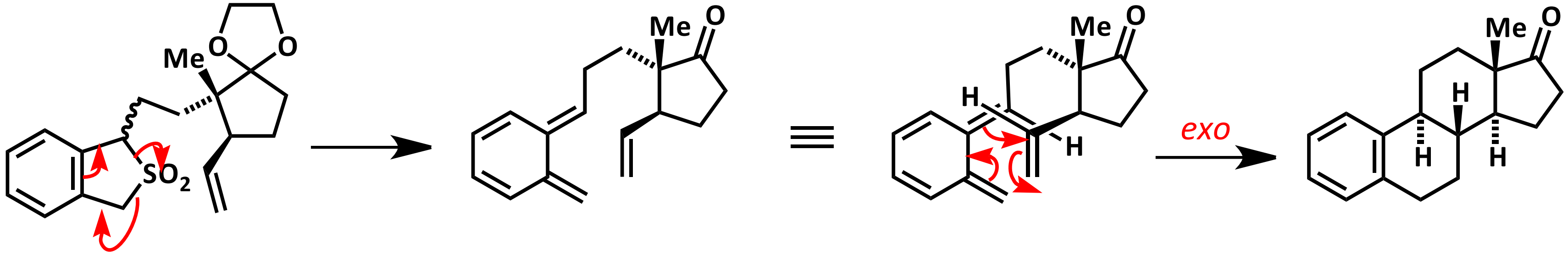
constructive overlap ✓



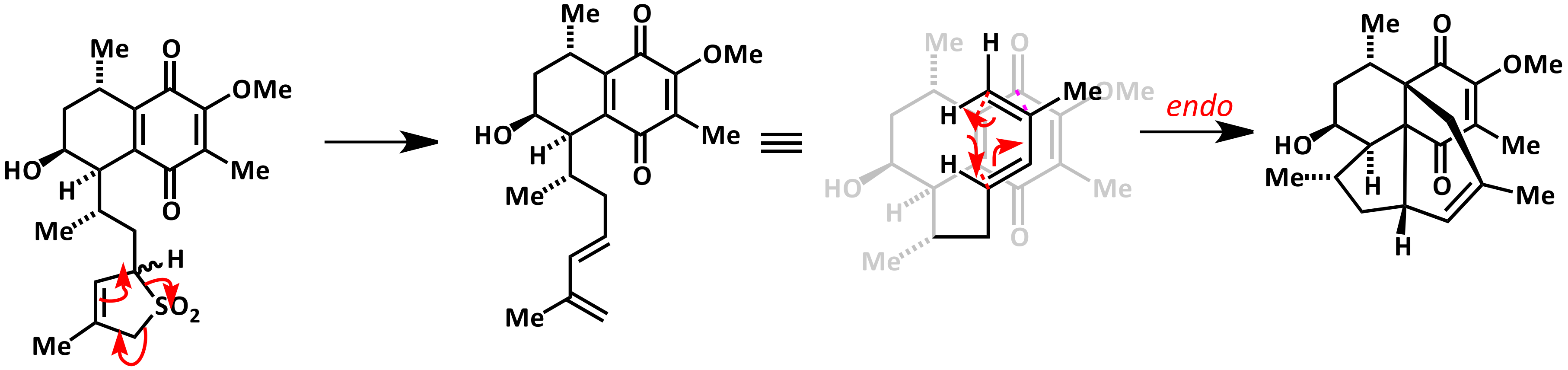
too strained; *ca*. 10^4 times less reactive than



- Cheletropic Reactions in Synthesis
- Steroid synthesis



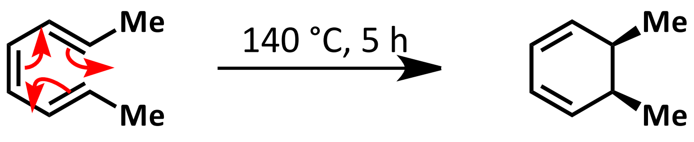
- Colombiasin

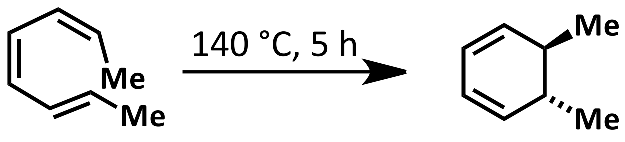


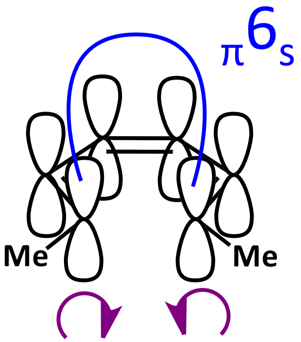
- Electrocyclic reactions

- Thermal electrocyclic processes will be *conrotatory* if the total number of electrons is 4n and *disrotatory* if the total number of electrons is (4n +2) – this is reversed for photochemical reactions.

- All electrocyclic reactions are allowed (provided they are are not constrained by the geometry of the product).







$(4q + 2)_s = 1$

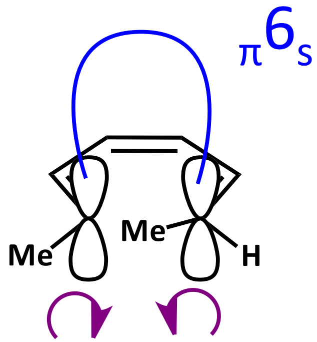
$(4r)_a = 0$

Total = 1

odd ✓

allowed

disrotatory



$(4q + 2)_s = 1$

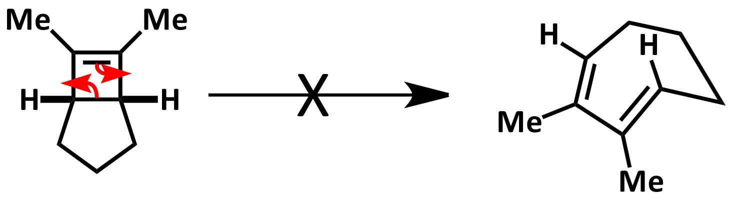
$(4r)_a = 0$

Total = 1

odd ✓

allowed

disrotatory



$(4q + 2)_s = 1$

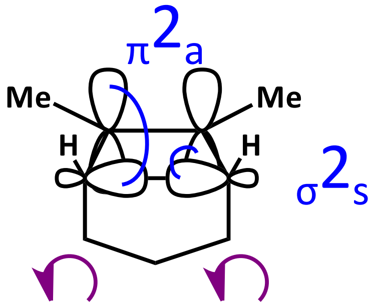
$(4r)_a = 0$

Total = 1

odd ✓

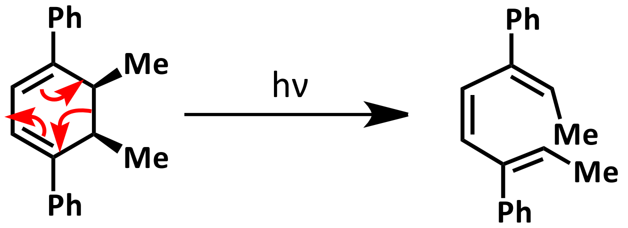
allowed

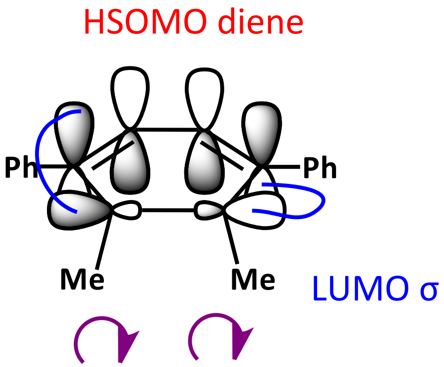
conrotatory



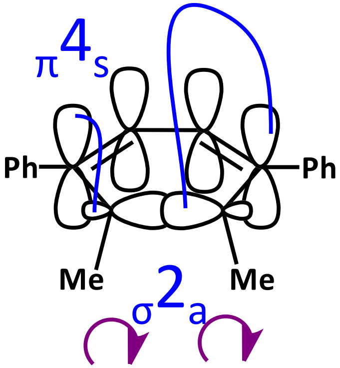
but geometrically constrained therefore does not occur.

Electrocyclic reactions



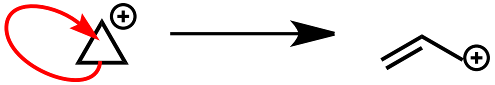


constructive overlap ✓
conrotatory

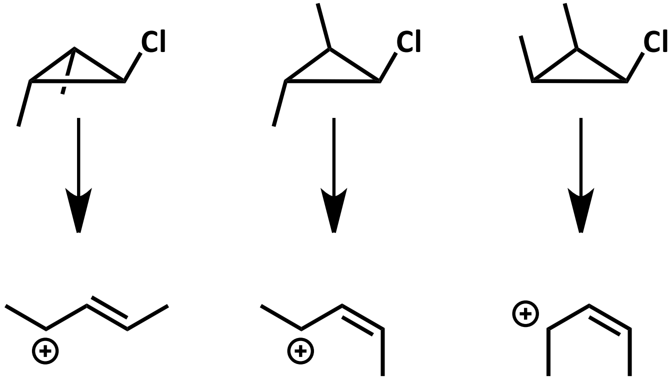


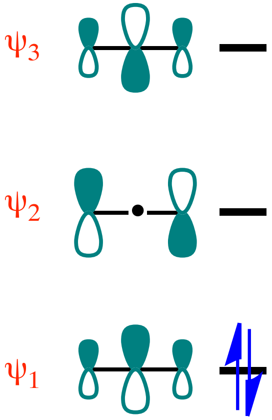
$(4q + 2)_s = 0$
$(4r)_a = 0$
Total = 0
even ✓
allowed
conrotatory

Cyclopropyl cation / allyl cation interconversion

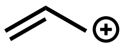


Lewis acid
low temperature



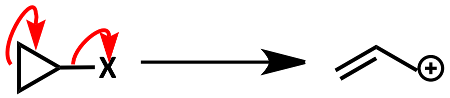


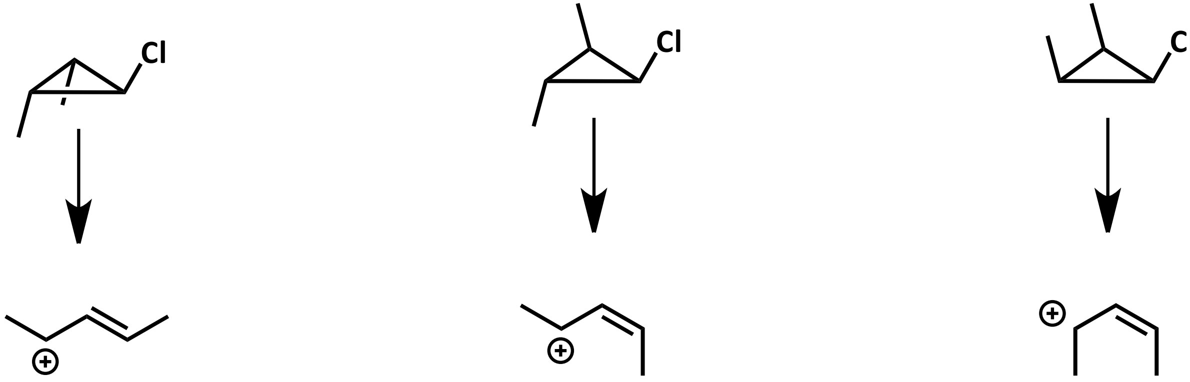
- The ionisation of cyclopropyl halides and tosylates is a concerted process to give allyl cations (i.e. discrete cyclopropyl cations are not formed).

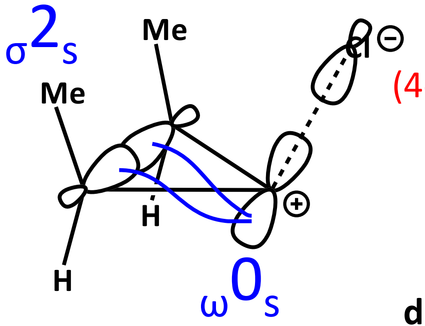


- The reaction can be viewed as an internal substitution in which the electrons in a σ-bond (HOMO) feed into the C-X σ* (LUMO).
- The reaction is disrotatory and the sense of rotation (torquoselectivity) is specified – this dictates the geometry of the allyl cation and can have a large influence on reaction rate.

Electrocyclic reactions







$(4q + 2)_s = 1$

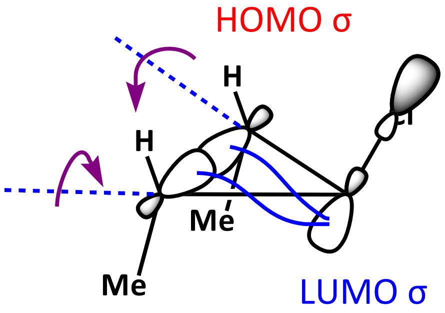
$(4r)_a = 0$

Total = 1

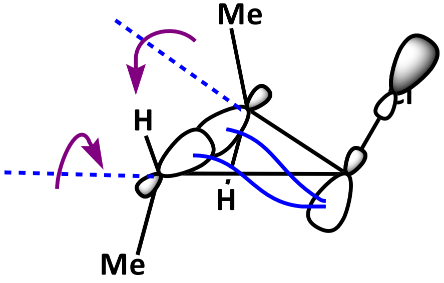
odd ✓

allowed

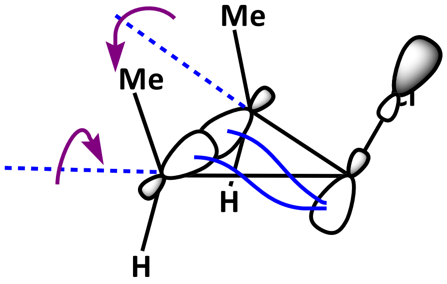
disrotatory



constructive overlap ✓
disrotatory

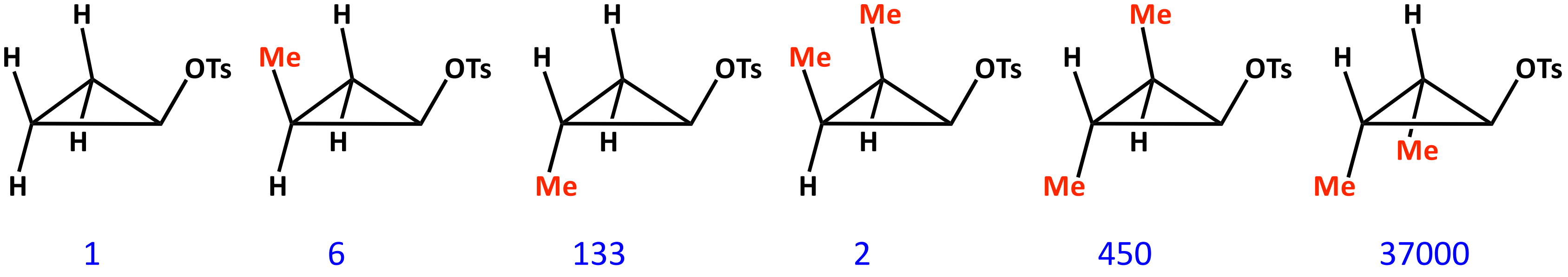


constructive overlap ✓
disrotatory

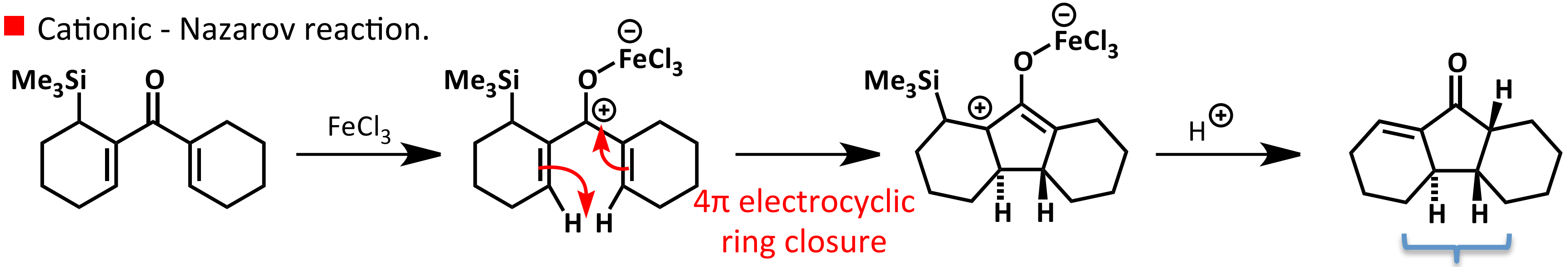


constructive overlap ✓
disrotatory

Influence on rates – solvolysis in acetic acid

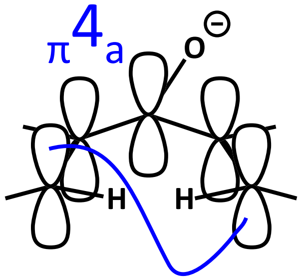


- Electrocyclic reactions - pentadienyl systems.
- Cationic - Nazarov reaction.



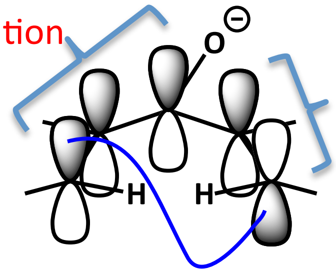
4π electrocyclic ring closure

relative configuration set by pericyclic reaction



$(4q + 2)_s = 0$
$(4r)_a = 1$
Total = 1
odd ✓
allowed
conrotatory

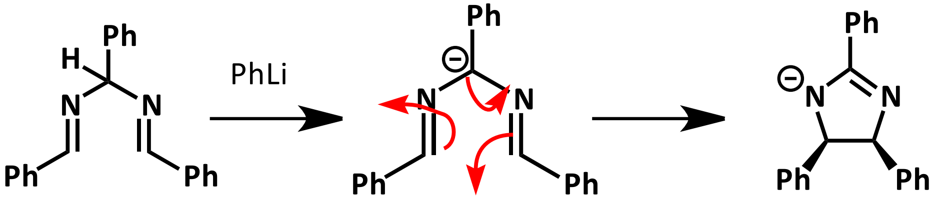
HOMO
allyl cation



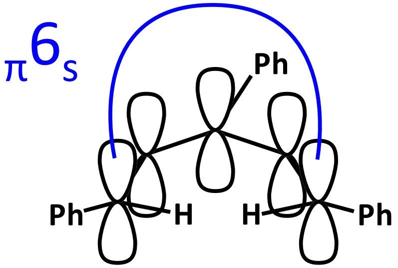
LUMO
alkene

constructive overlap ✓
conrotatory

- Thermal Nazarov cyclisation is conrotatory; photochemical Nazarov reaction is disrotatory.
- Anionic.

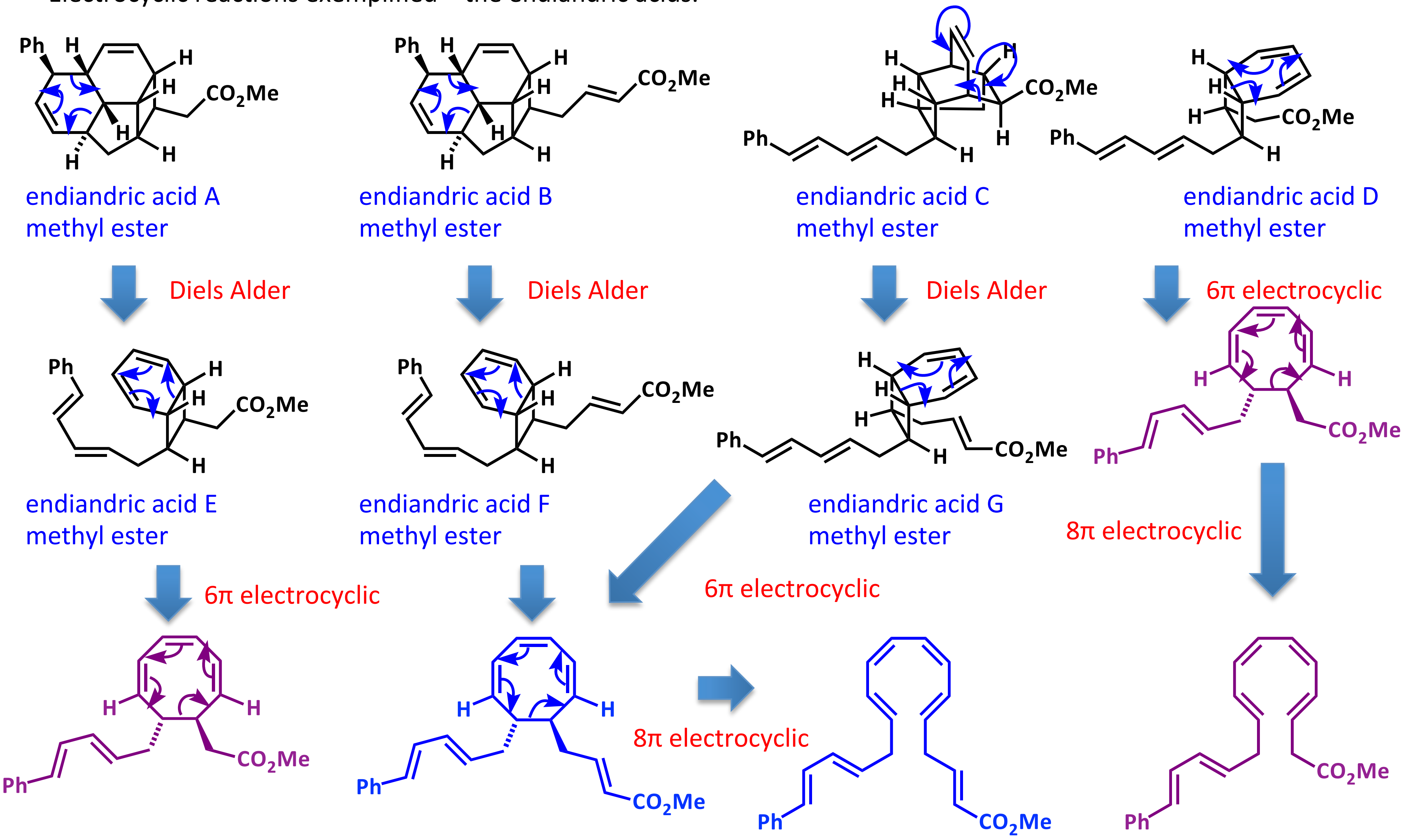


6π electrocyclic ring closure



$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed
disrotatory

- Electrocyclic reactions exemplified – the endiandric acids.



endiandric acid A methyl ester

endiandric acid B methyl ester

endiandric acid C methyl ester

endiandric acid D methyl ester

Diels Alder

Diels Alder

Diels Alder

6π electrocyclic

endiandric acid E methyl ester

endiandric acid F methyl ester

endiandric acid G methyl ester

8π electrocyclic

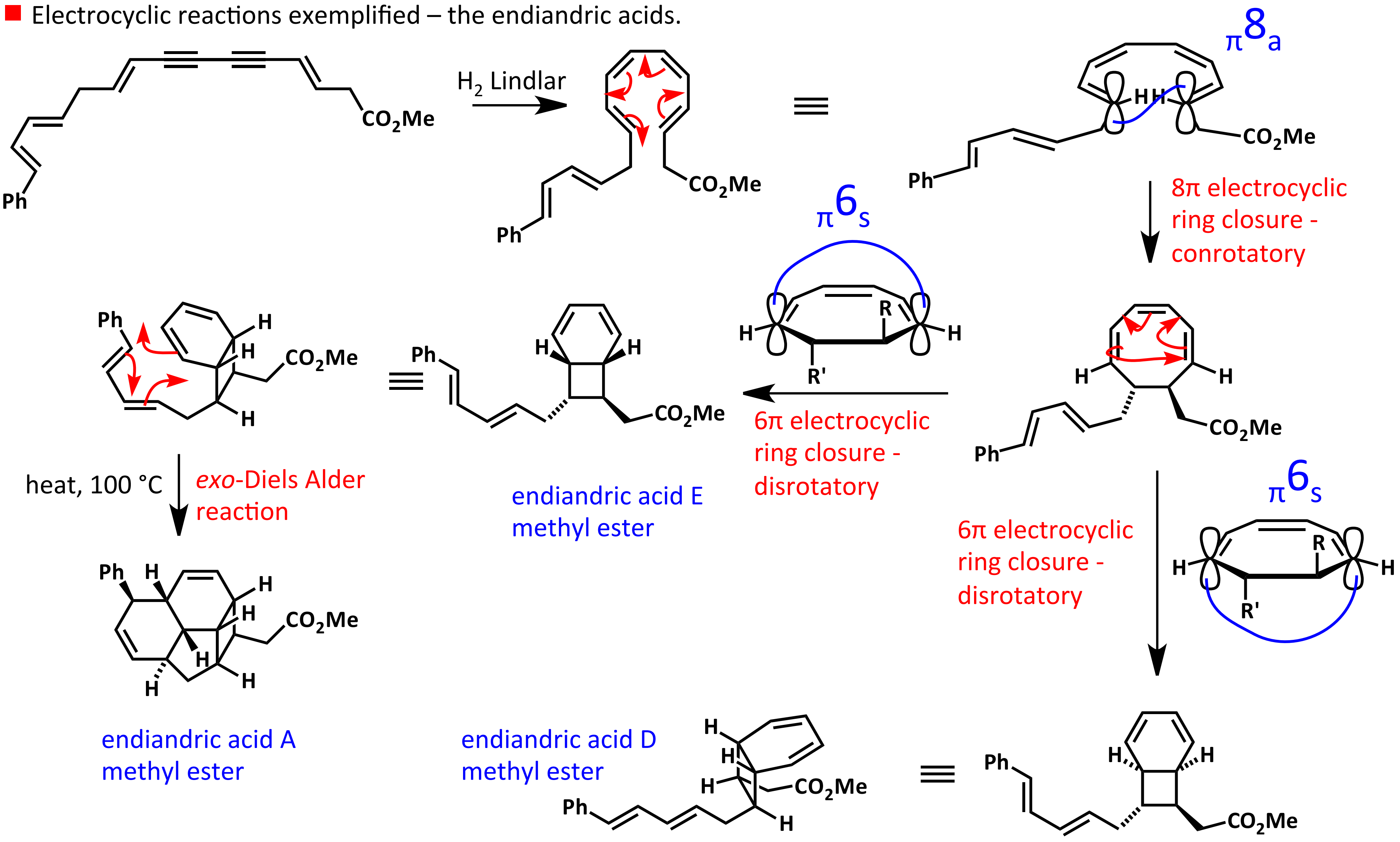
6π electrocyclic

6π electrocyclic

8π electrocyclic

- Biosynthesis proposed by Black *J. Chem. Soc., Chem. Commun.*, **1980**, 902.
- Biomimetic synthesis by K. C. Nicolaou, *J. Am. Chem. Soc.*, **1982**, *104*, 5558.

- Electrocyclic reactions exemplified – the endiandric acids.

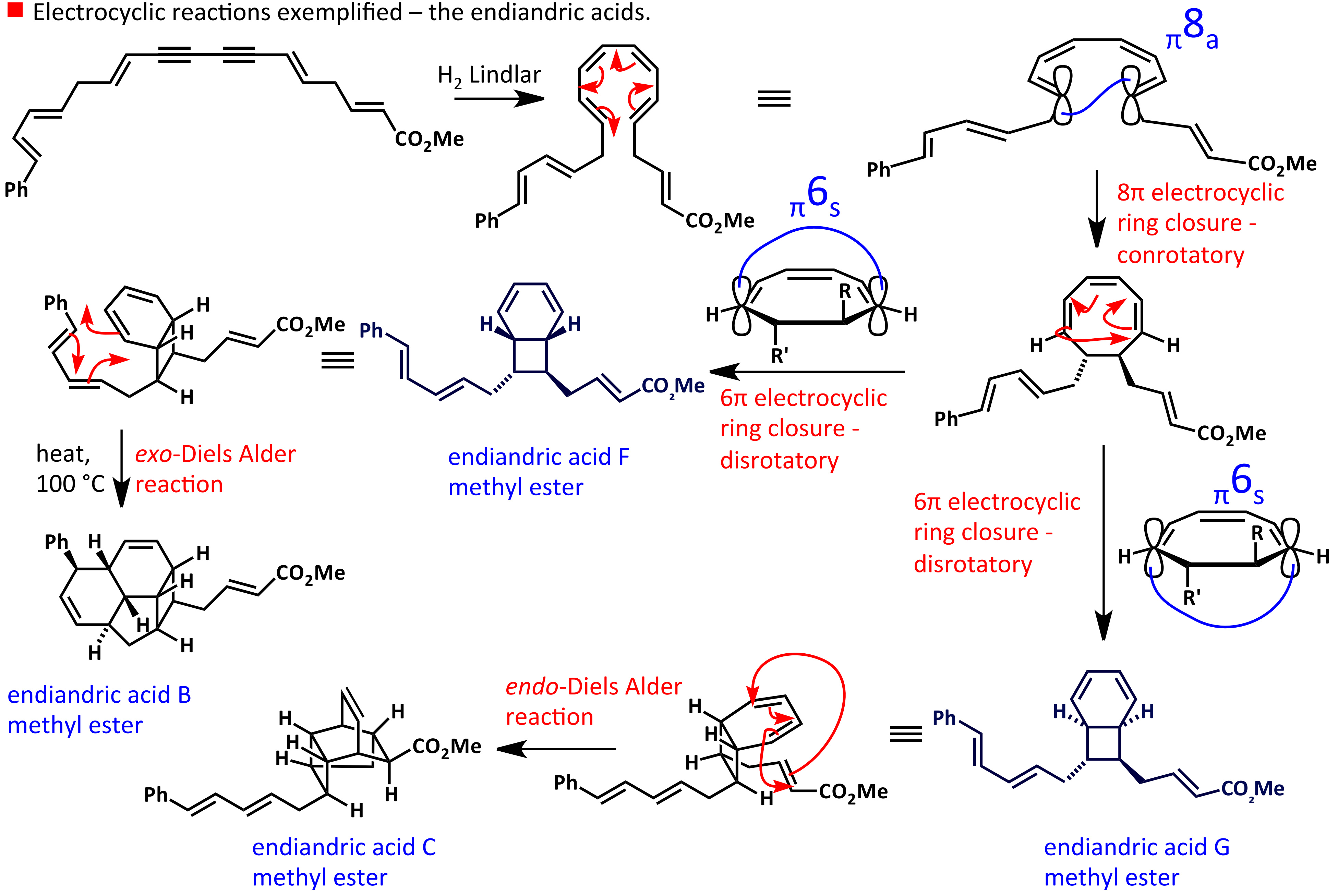


endiandric acid E methyl ester

endiandric acid A methyl ester

endiandric acid D methyl ester

- Electrocyclic reactions exemplified – the endiandric acids.



endiandric acid F methyl ester

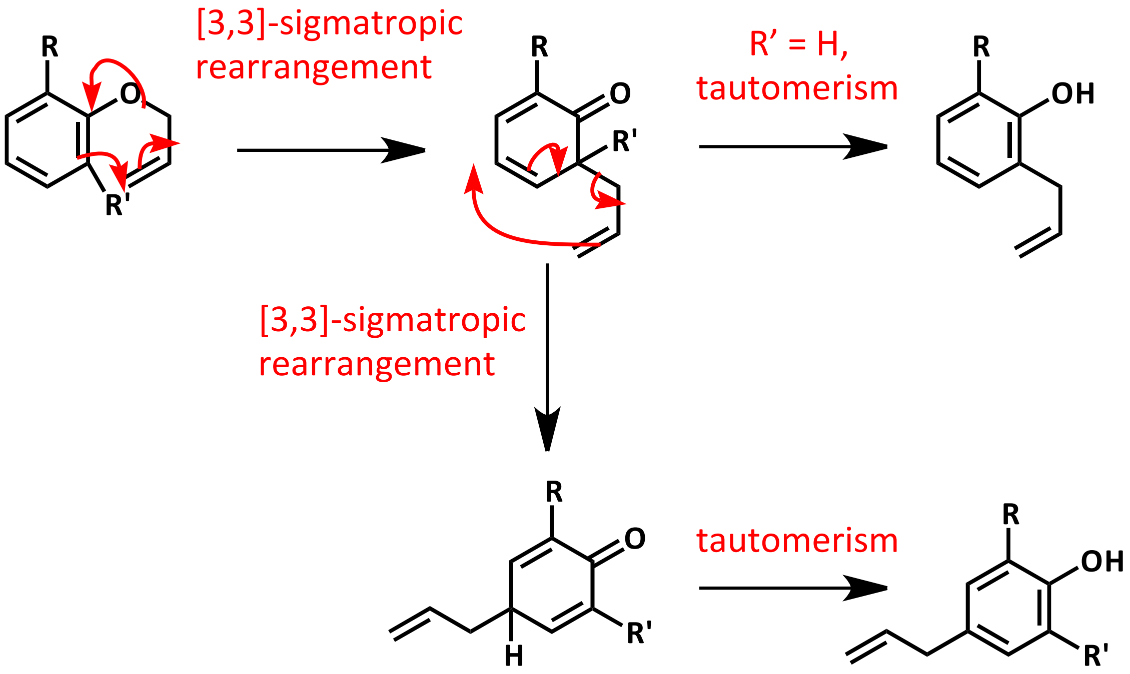
endiandric acid B methyl ester

endiandric acid C methyl ester

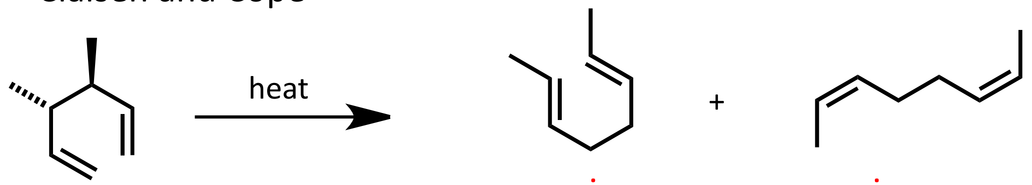
endiandric acid G methyl ester

- Sigmatropic rearrangements.
- Synthetically the most important sigmatropic rearrangements are the Cope and Claisen rearrangements and variants thereof.
- The Claisen/Cope rearrangements can proceed *via* chair-like or boat-like transition states – the chair-like transition state is strongly favoured unless there are steric constraints that force a boat-like transition state.
- Where possible, substituents generally adopt equatorial sites in the chair-like transition state.

- Classical Claisen rearrangement.



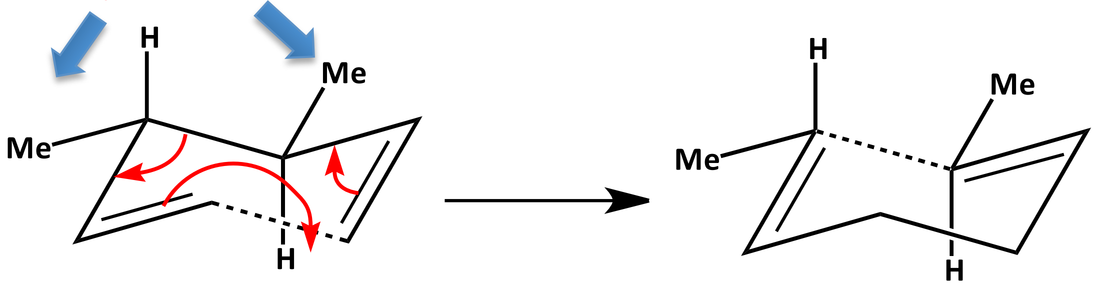
Claisen and Cope



major

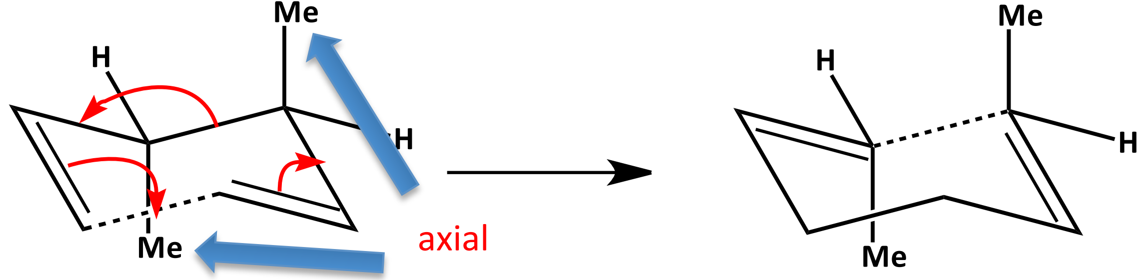
minor

equatorial

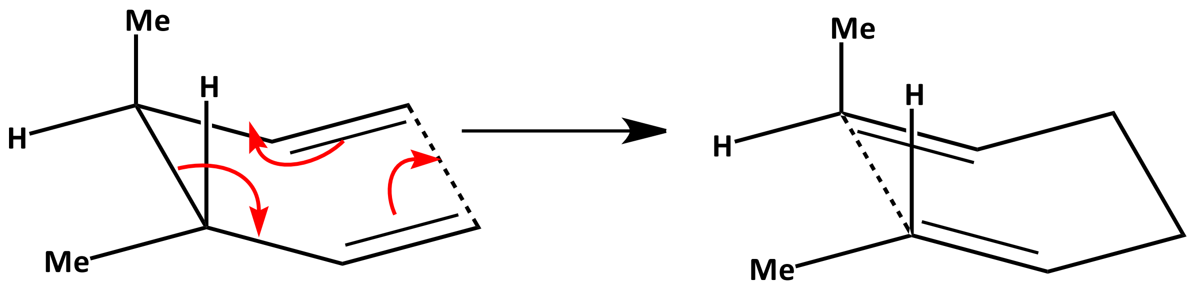


chair

trans, trans - major

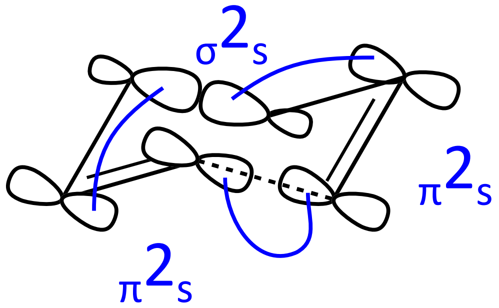


cis, cis - minor



boat

cis, trans - trace



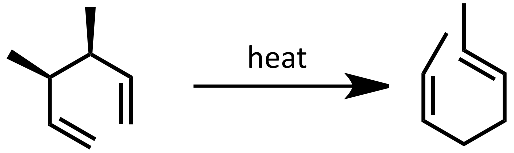
$(4q + 2)_s = 3$

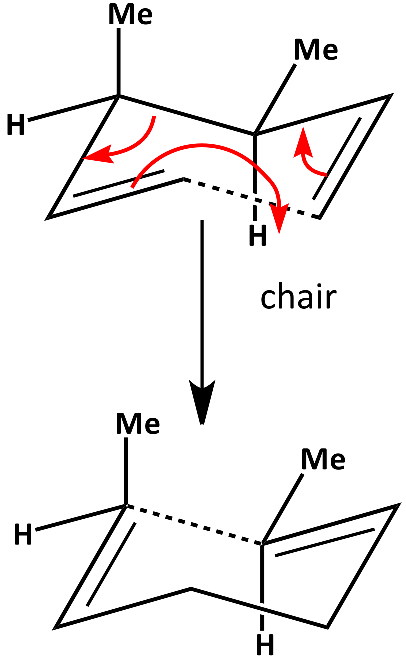
$(4r)_a = 0$

Total = 3

odd ✓

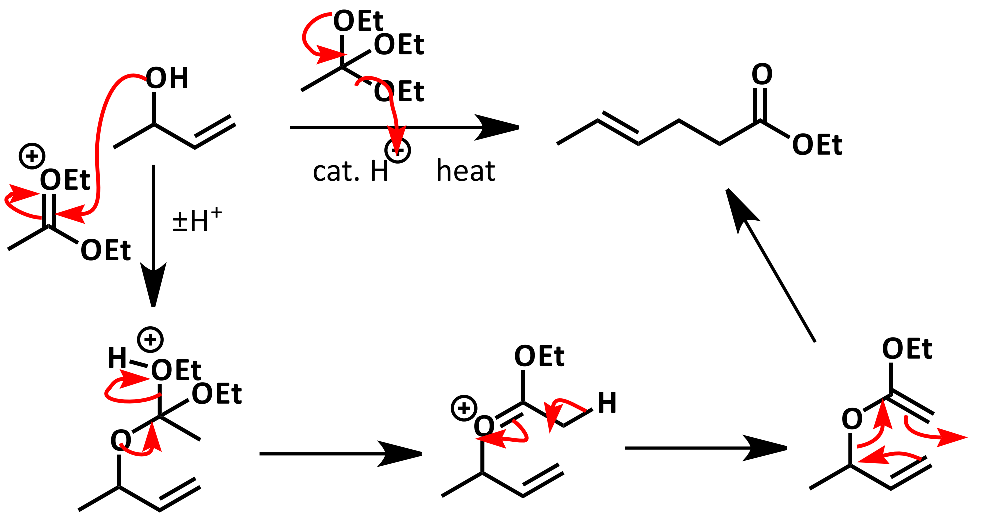
allowed

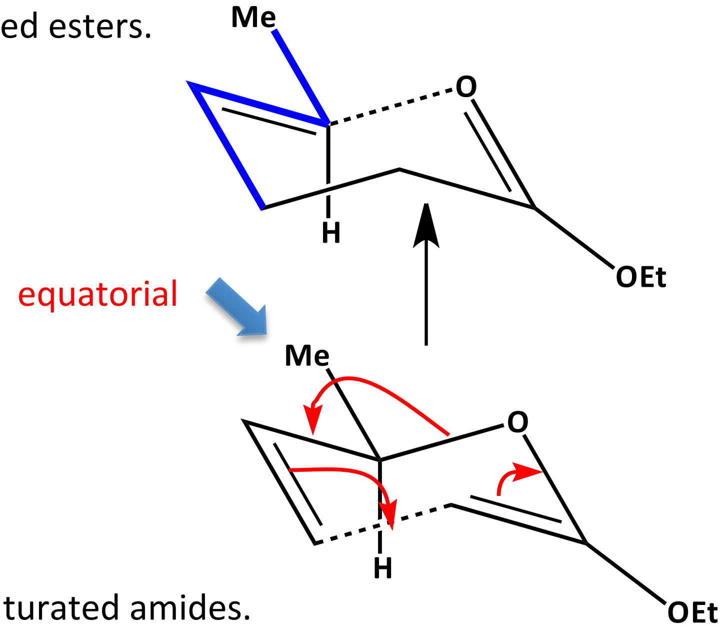




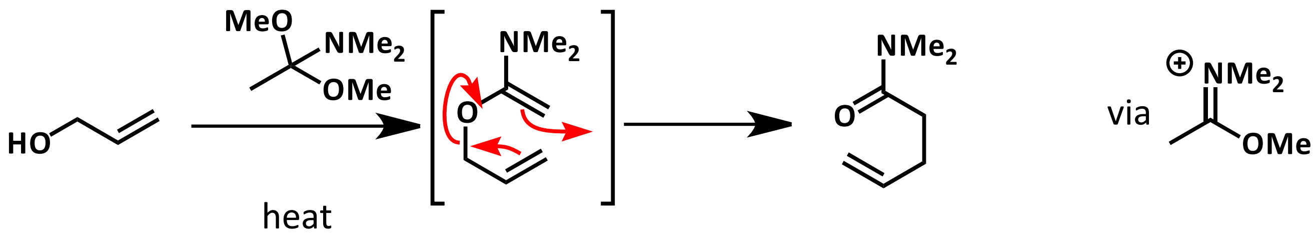
cis, trans

- Claisen rearrangement - variants.
- Johnson-Claisen rearrangement - synthesis of γ,δ-unsaturated esters.

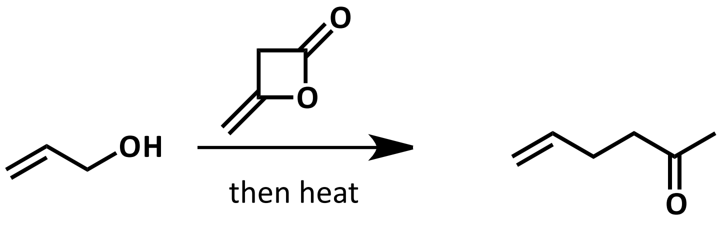


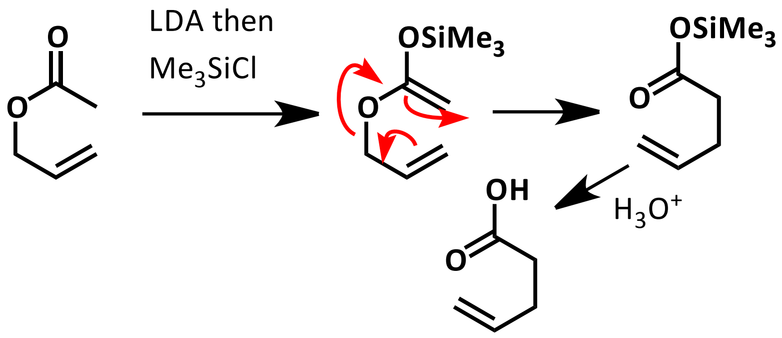


- Eschenmoser-Claisen rearrangement - synthesis of γ,δ-unsaturated amides.

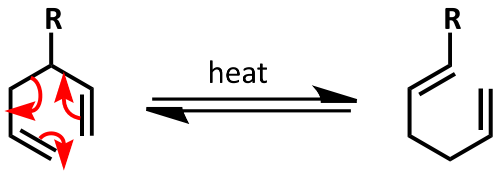


- Carroll rearrangement - synthesis of γ,δ-unsaturated methyl ketones.
- Ireland Claisen rearrangement.

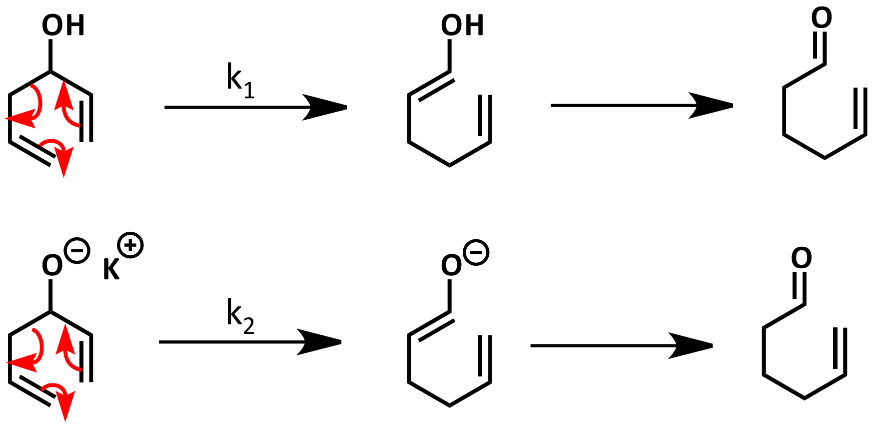




- Oxy-Cope rearrangement.
- Generally the Cope rearrangement requires very high temperatures > 200 °C.



- The anionic oxy-Cope can be conducted at low temperature (0 °C).

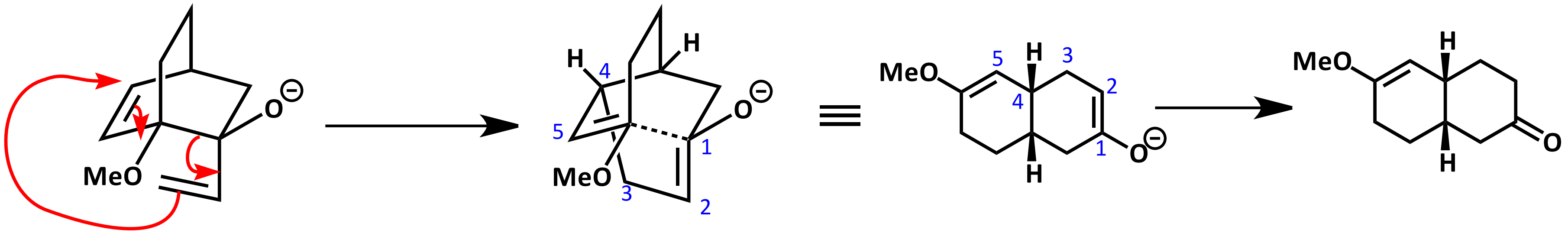


oxy-Cope

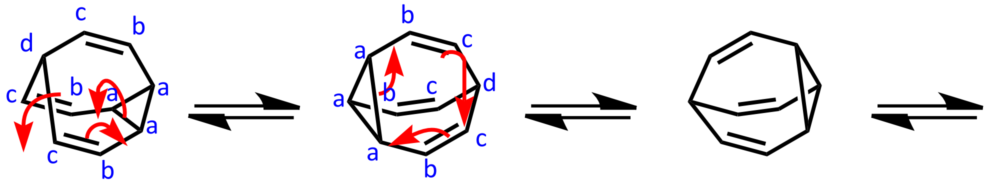
k_2/k_1 ~$10^{10} - 10^{17}$

anionic oxy-Cope

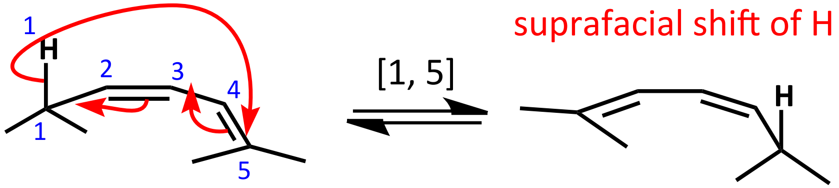
- Useful method for the synthesis of *cis*-decalins.

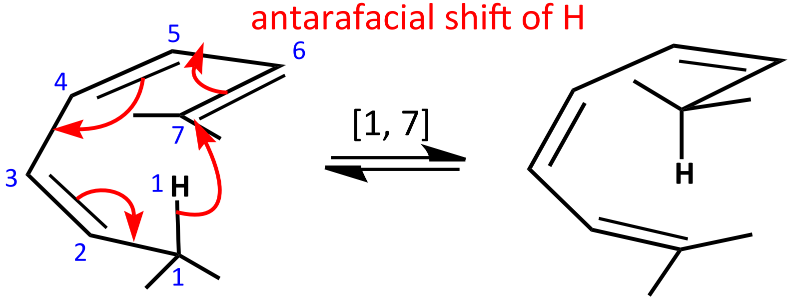


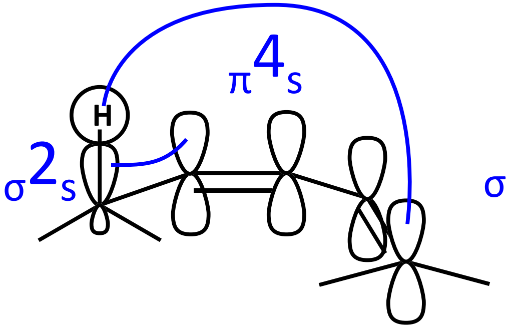
- Bulvalene - valence isomers interconvert by degenerate Cope rearrangements.



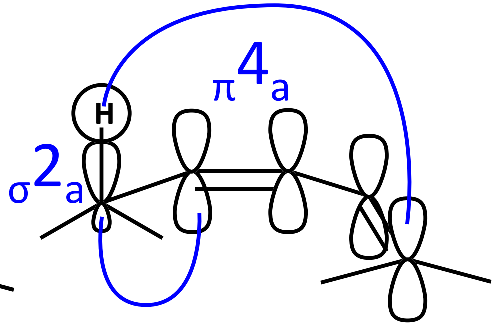
- 1,n-Hydride shifts.
- A *suprafacial* 1,n-hydride shift involves the hydrogen moving from one end of the conjugated system to the other across one face of the conjugated system.
- An *antarafacial* 1,n-hydride shift involves the hydrogen moving from one end of the conjugated system to the other and moving from one face of the conjugated system to the opposite face.



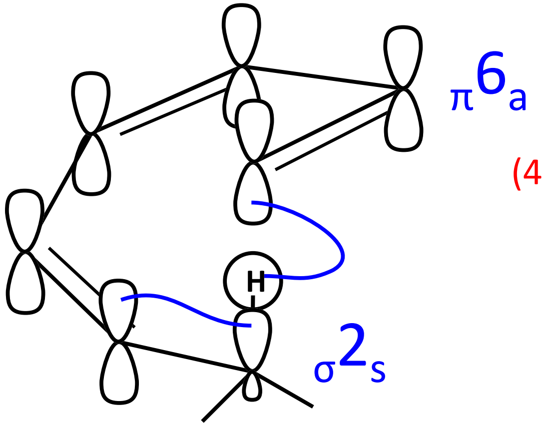




$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

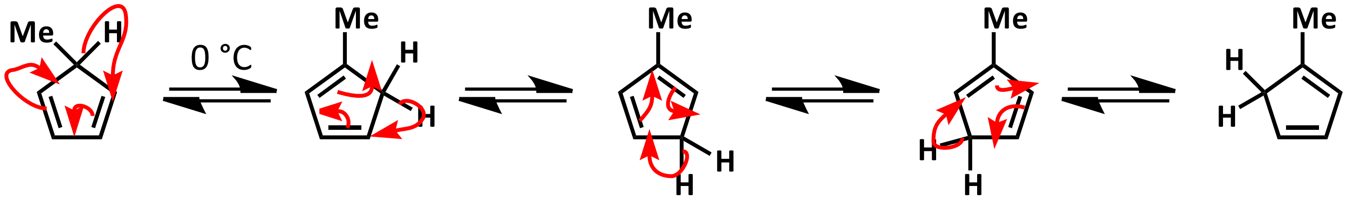


$(4q + 2)_s = 0$
$(4r)_a = 1$
Total = 1
odd ✓
allowed

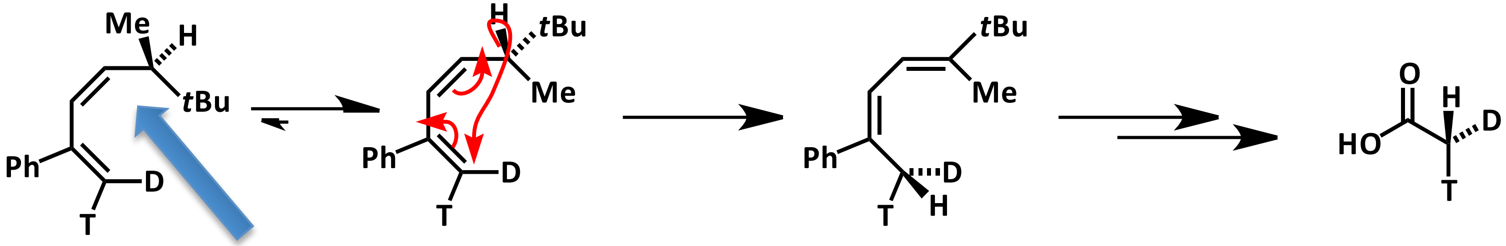


$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

- 1,5-Hydride shifts occur readily when the two ends of the diene are held close.

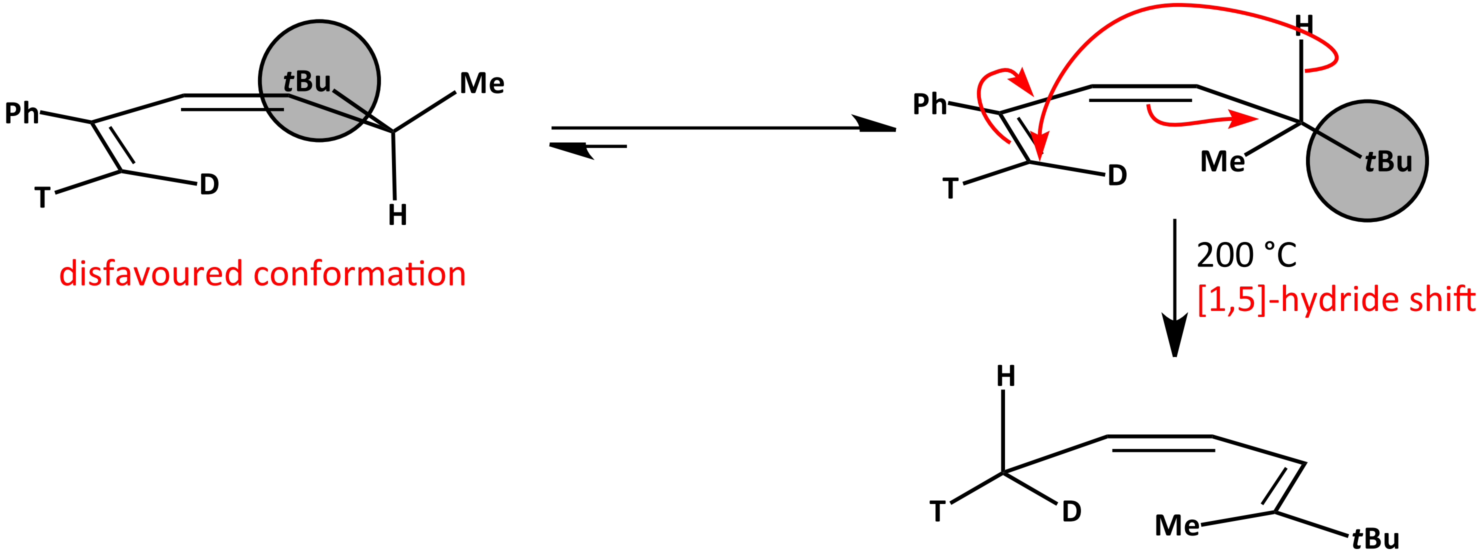


- In acyclic systems 1,5-hydride shifts can be much slower.



chiral acetic acid

allylic strain

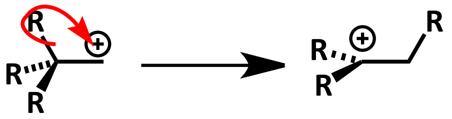


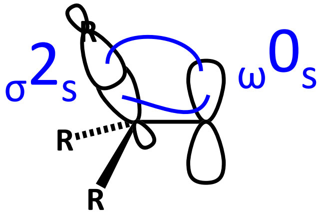
disfavoured conformation

200 °C
[1,5]-hydride shift

- 1,2-Shifts of alkyl groups can also be pericyclic.

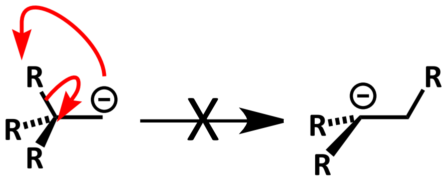
- Carbocations readily undergo allowed 1,2-shifts.

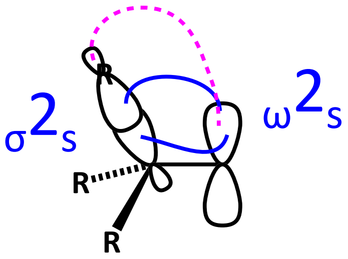




$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

- Allowed, concerted 1,2-shifts of carbanions are geometrically impossible.

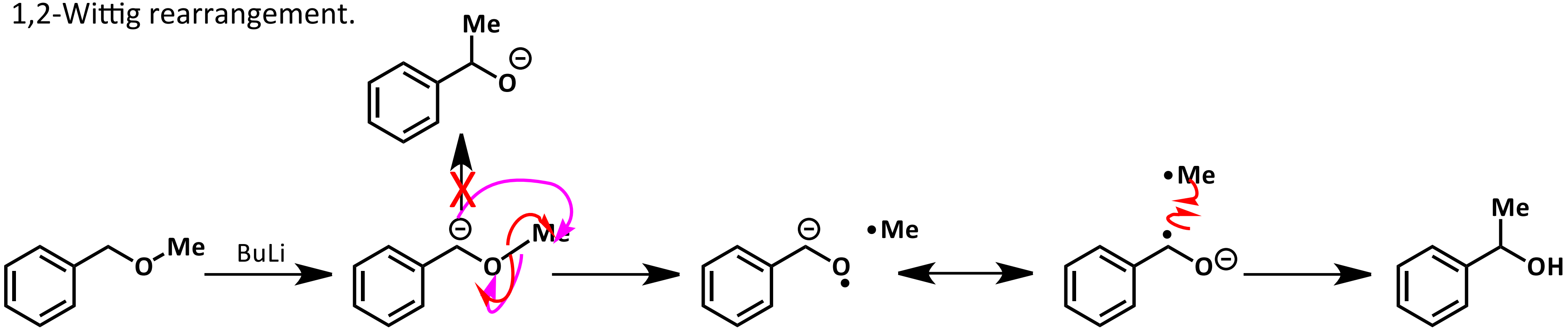




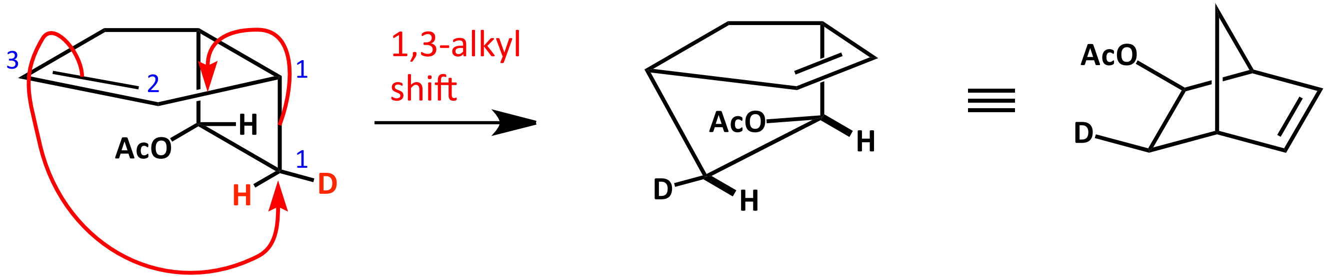
$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 2
even ✗
forbidden

- 1,2-Shifts of carbanions occur by a radical mechanism – 1,2-Wittig, 1,2-Stevens and related rearrangements.

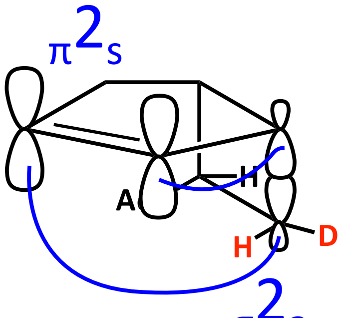
- 1,2-Wittig rearrangement.

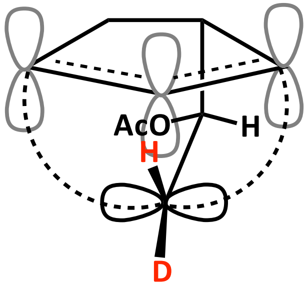


- Thermal [1,3]-alkyl shifts occur with inversion of configuration in the migrating group.

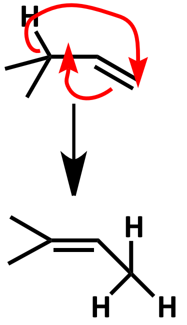


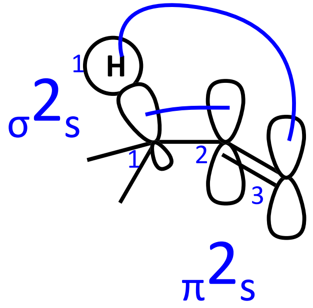
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed



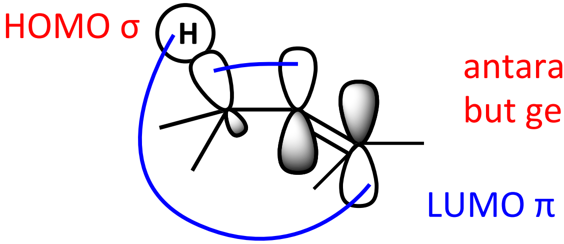


- Thermal 1,3-shift of hydrogen is only geometrically reasonable in a suprafacial sense which is thermally disallowed.





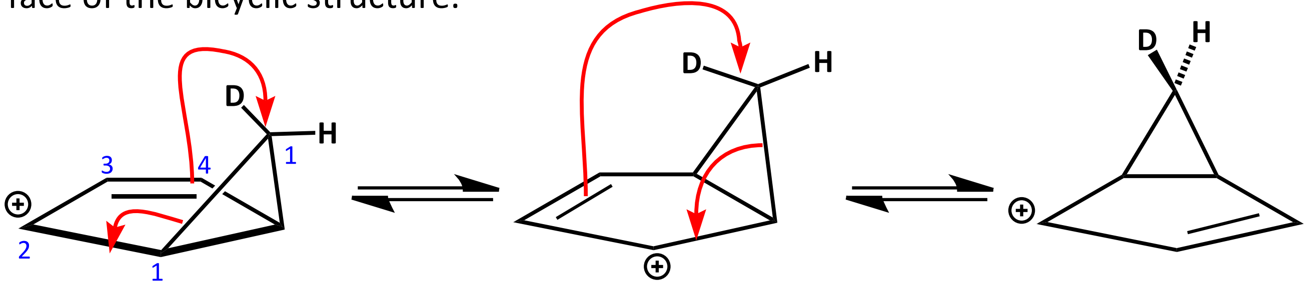
$(4q + 2)_s = 2$
$(4r)_a = 0$
Total = 0
even ✗
forbidden



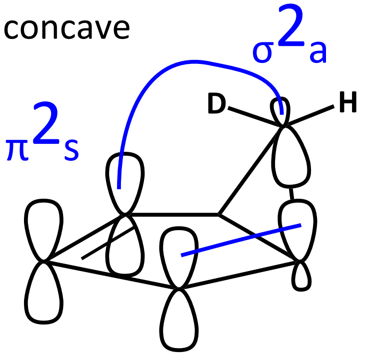
antarafacial shift allowed
but geometrically unreasonable

constructive overlap ✓

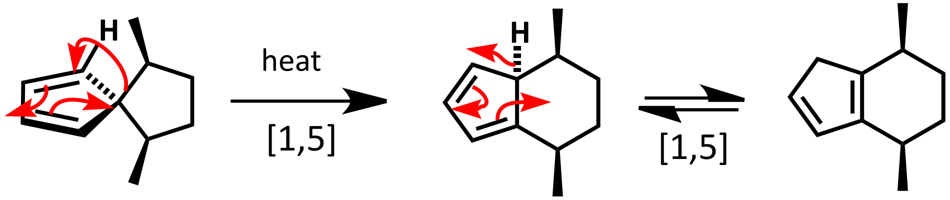
- In the following [1,4]-shift, migration occurs with inversion of configuration with D always on the concave face of the bicyclic structure.

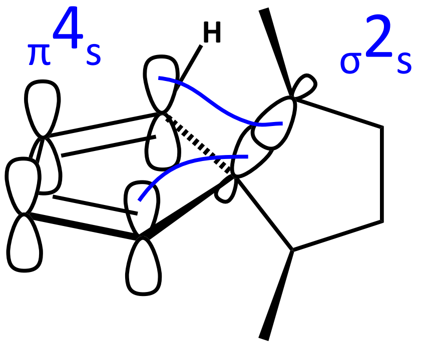


$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed



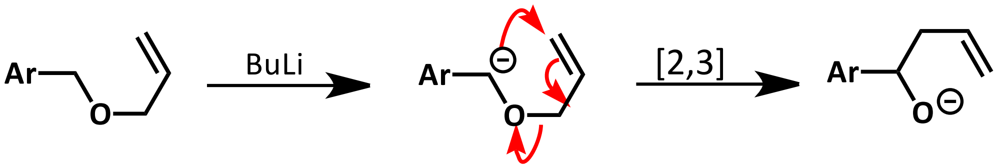
- 1,5-Alkyl shift with retention of configuration in the migrating group.

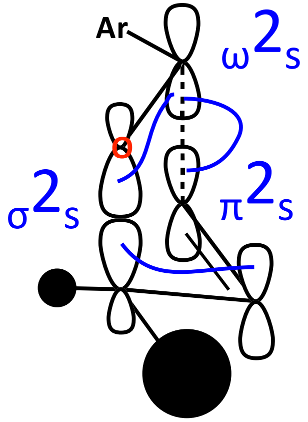




$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

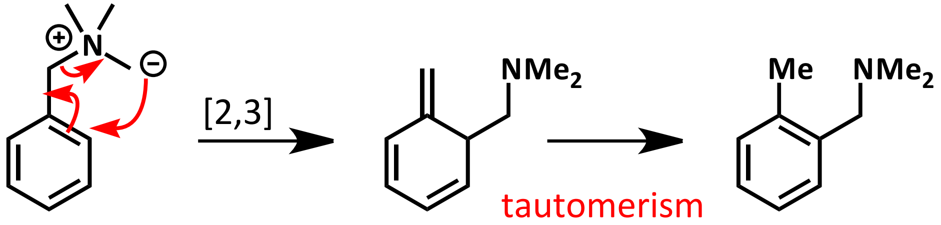
- A number of [2,3]-sigmatropic shifts are useful synthetically.
- [2,3]-Wittig rearrangement – most likely proceeds via an envelope transition state; large groups at the allylic position will tend to occupy a pseudo-equatorial position.



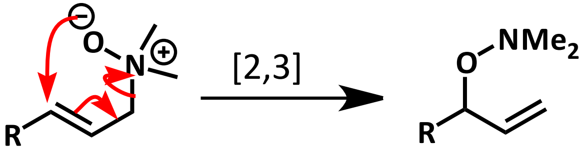


$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed

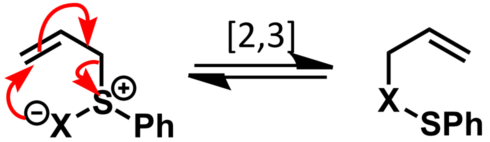
- Sommelet-Hauser rearrangement.



- Meisenheimer Rearrangement.

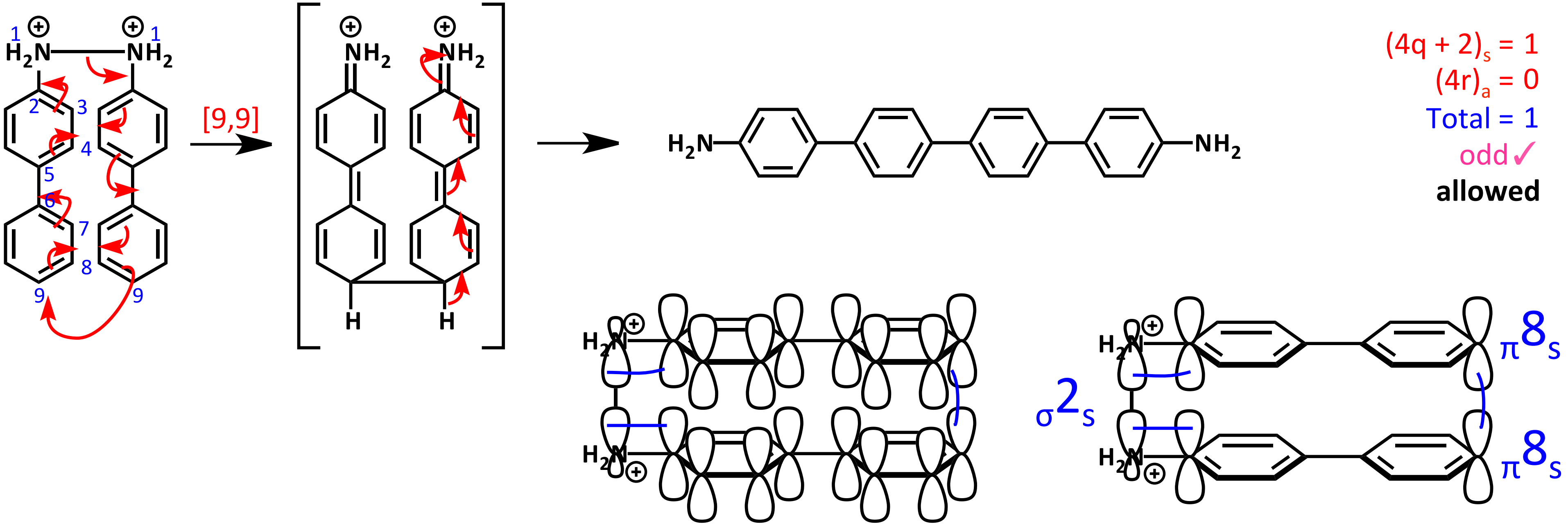


- Rearrangement of allyl sulfoxides, sulfinimines and sulfonium ylids.



X = O, NTs, CH_2

- A [9,9]-sigmatropic shift.



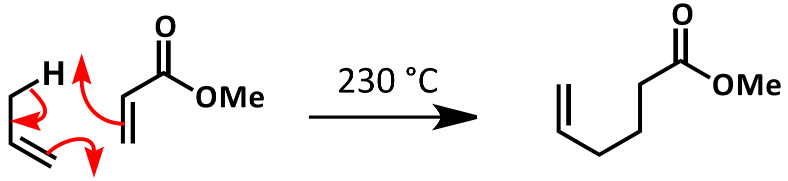
$(4q + 2)_s = 1$
$(4r)_a = 0$
Total = 1
odd ✓
allowed

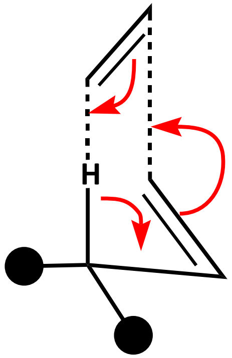
- Group transfer reactions.

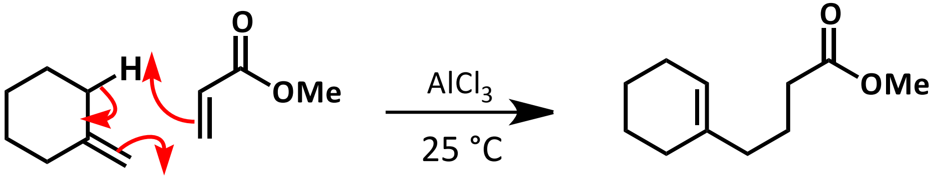
- Group transfer – appear to be a mix of a sigmatropic rearrangement and a cycloaddition.

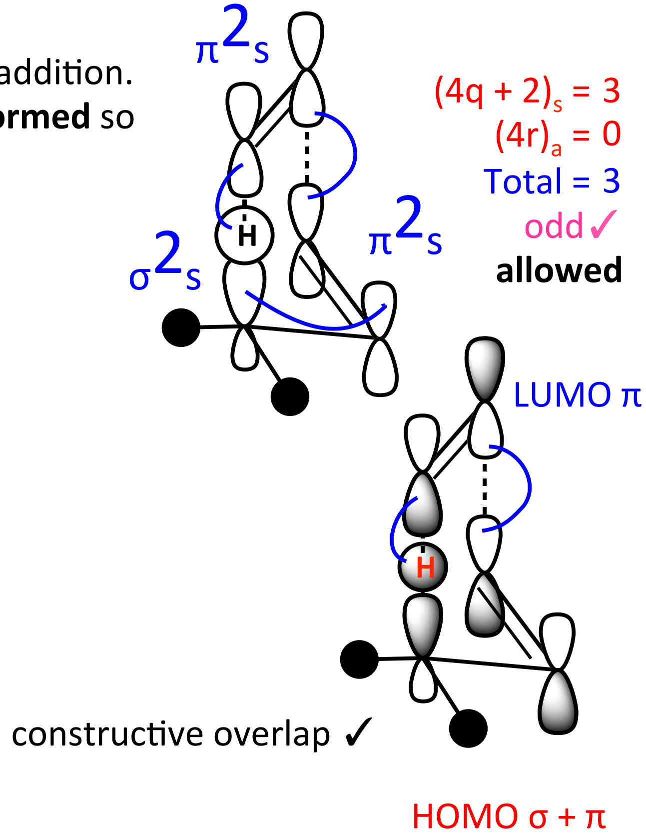
They are **bimolecular** and so are not sigmatropic rearrangements, and **no ring is formed** so they are not cycloadditions.

- Alder ene reaction







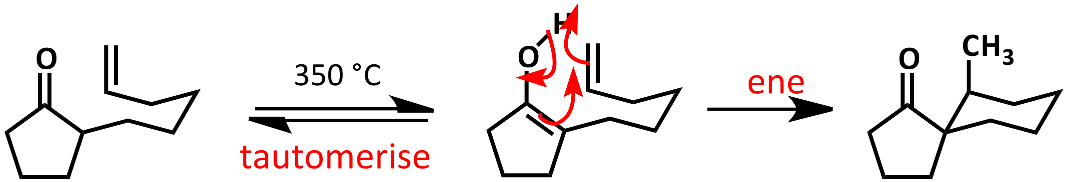


$(4q + 2)_s = 3$
$(4r)_a = 0$
Total = 3
odd ✓
allowed

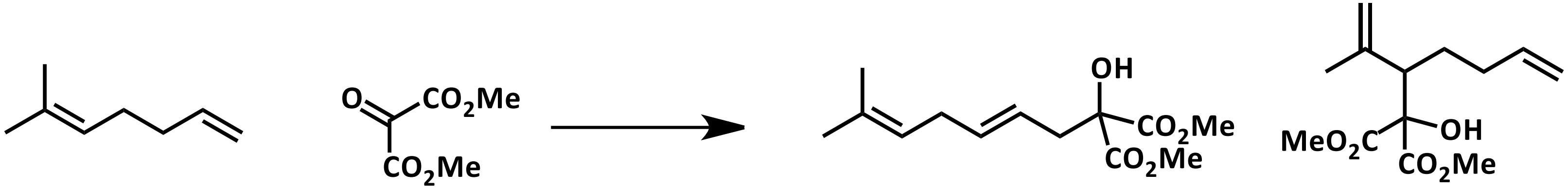
constructive overlap ✓

HOMO σ + π

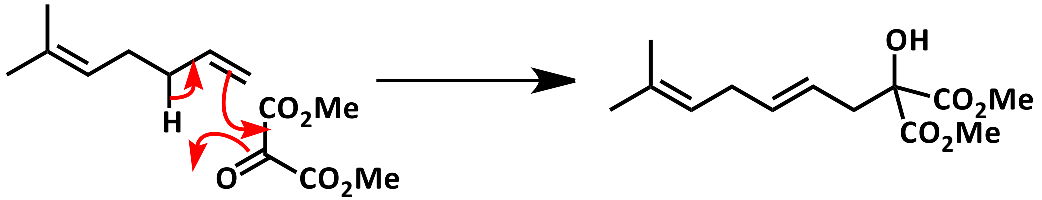
- Conia-ene reaction.



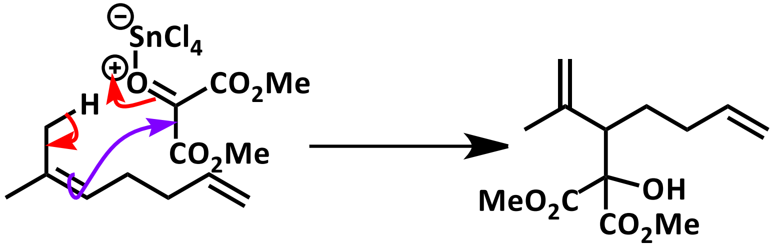
- Carbonyl-ene reaction - frequently catalysed by Lewis acids.



180 °C, 48 h	92	8
$SnCl_4$, 0 °C	2.5	97.5

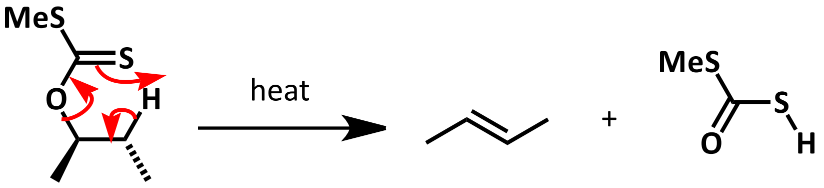


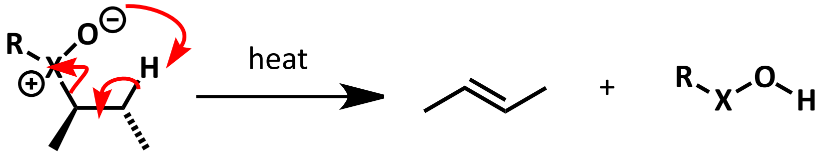
- Thermal carbonyl ene reaction, sterics are important.



- In the Lewis acid-catalysed reaction significant positive charge develops in the “eneophile”.

- Retro-ene and retro group transfer reactions are common.





retro-ene

retro group transfer: X = S, Se, or NR (Cope elimination)

- Pericyclic reaction summary:

- Four classes:

  Cycloadditions (chelotropic reactions); Electrocyclic reactions; Sigmatropic rearrangements; Group transfer.

- Woodward-Hoffmann rules:

A ground state pericyclic reaction is symmetry allowed when the total number of $(4q + 2)_s$ and $(4r)_a$ components is odd (q and r must be integers).

A pericyclic change in the first electronically excited state (i.e. a photochemical reaction) is symmetry-allowed when the total number of $(4q + 2)_s$ and $(4r)_a$ components is even.

For thermal cycloadditions and group transfers:

- If the total number of electrons is (4n + 2) both components can be used in a suprafacial manner.
- If the total number of electrons is (4n) one of the components is suprafacial and the other antarafacial.

For electrocyclic reactions:

- Thermal electrocyclic processes will be *conrotatory* if the total number of electrons is 4n and *disrotatory* if the total number of electrons is (4n +2).

- And just because you can draw a pericyclic curly arrow mechanism does not necessarily mean the reaction is pericyclic.