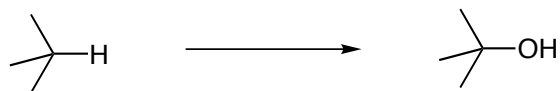


## Selective Oxidations

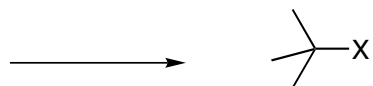
SUBSTRATE

REAGENT

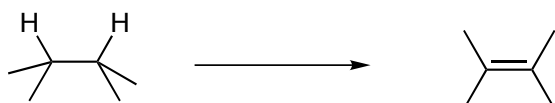
### Non-activated Carbon Atoms



Bugs, enzymes



$X_2 / h\nu$

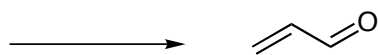


$X_2 / h\nu$  or  $ArICl_2$

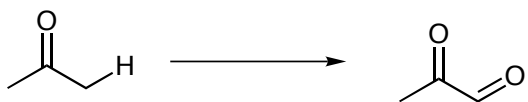
### Activated Non-functionalized Carbon Atoms



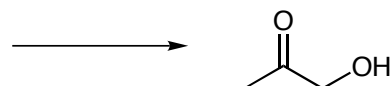
$SeO_2$



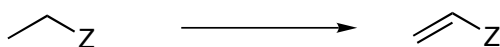
$SeO_2$ , PDC



$SeO_2$

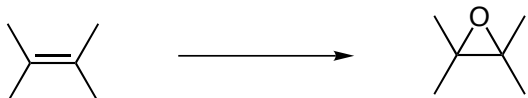


$KO^tBu / (EtO)_3P / O_2$   
or  
 $LDA / Mo(VI)O(O_2)_2 / HMPA / py$   
( $MoOOPH$ )

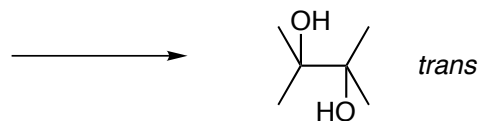


$SeO_2$   
or (i)  $LDA / PhSeBr$  (ii)  $H_2O_2$   
 $/NaIO_4$

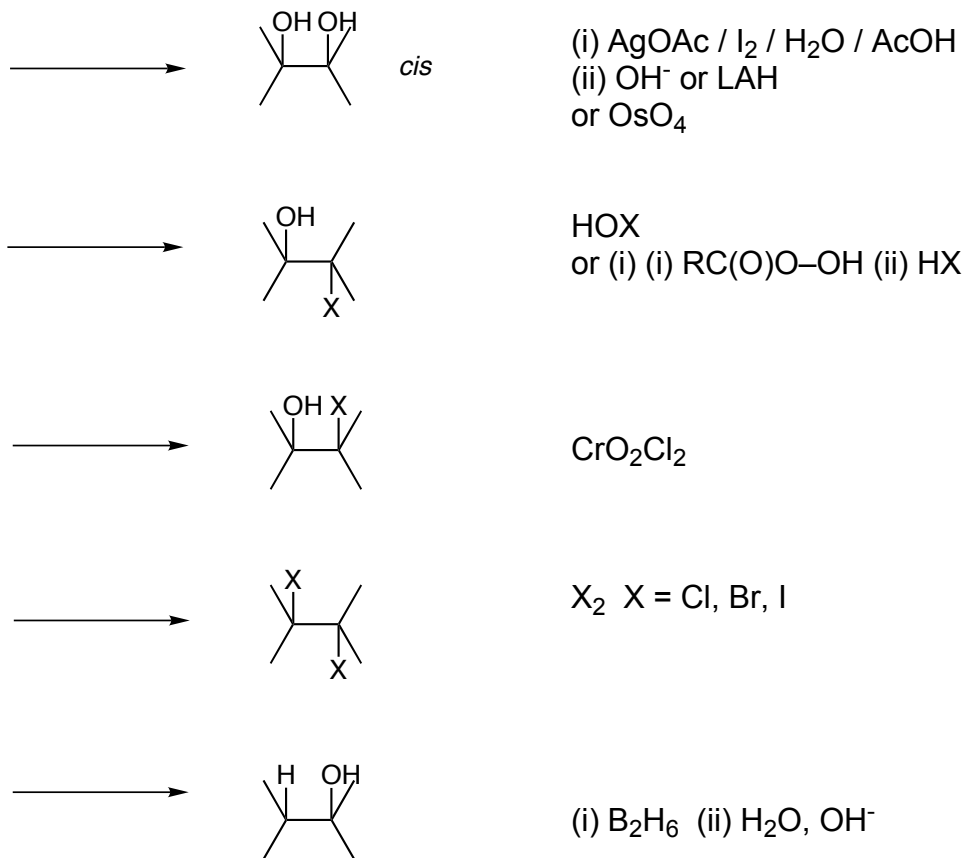
### Carbon Atoms of C-C Double Bonds



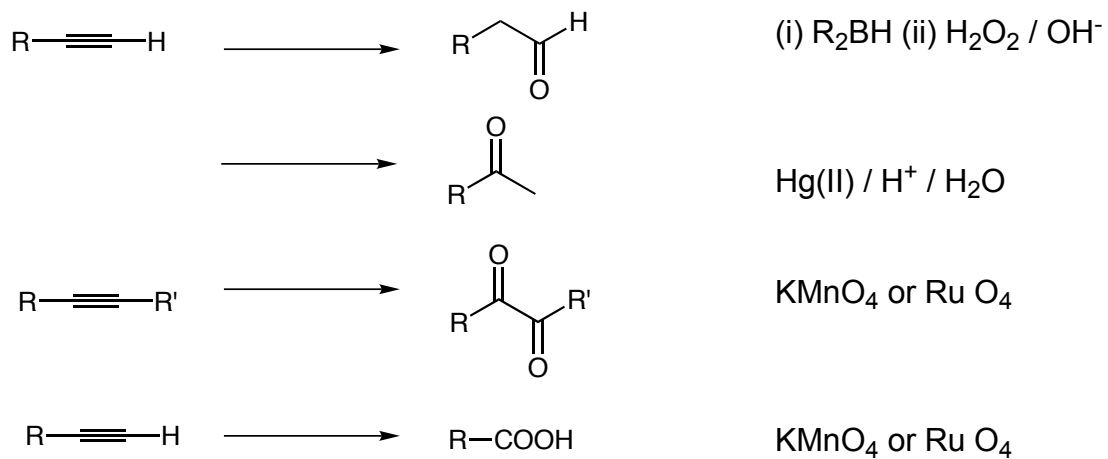
(i)  $HOX$  (ii)  $OH^-$   
or  $RC(O)O-OH$



(i)  $RC(O)O-OH$  (ii)  $OH^-$   
or (i)  $AgOAc / I_2$  (ii)  $OH^-$  or  $LAH$



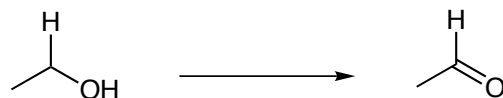
### Carbon Atoms of C-C Triple Bonds



## Oxygen Containing Functional Groups



PDC or PCC  
 or  $\text{Me}_2\text{CO} / \text{Al}(\text{OiPr})_3$   
 or  $\text{DMSO} + \text{E}^+$   
 $\text{E}^+ = \text{DCC}$  or  $\text{Ac}_2\text{O}$  or  $\text{SO}_3$  or  $\text{P}_4\text{O}_{10}$  or  
 $\text{COCl}_2$  or  $(\text{COCl})_2$



$\text{Ag}_2\text{CO}_3$  or  $\text{Pb}(\text{OAc})_4$



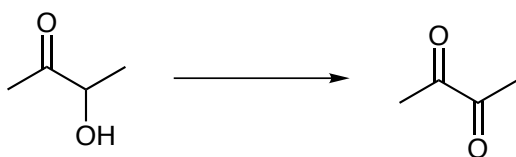
Most strong [O]



$\text{RuO}_4$

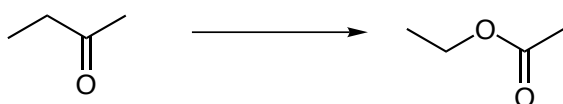


$\text{MnO}_2$  or DDQ

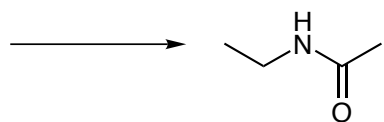


$\text{Cu}(\text{OAc})_2$

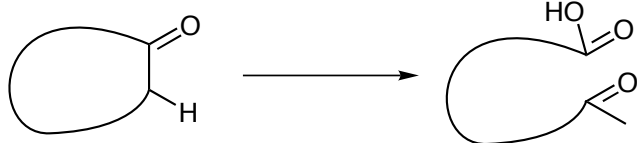
## Rearrangements & Cleavages



$\text{RC}(\text{O})\text{OOH}$



(i)  $\text{NH}_2\text{OH}$  (ii)  $\text{H}^+$



$\text{CrO}_3$  or  $\text{KMnO}_4$   
 or  
 (i)  $\text{SeO}_2$  (ii)  $\text{HIO}_4$

## REDUCTION

One of the most important Functional Group Interconversions which is very frequently performed in organic synthesis is that of reduction. Modern organic synthesis depends very heavily on a range of reducing agents, amongst the most useful of which are the hydride-donor reducing reagents. A selection of the more commonly used reagents are shown below, along with the substrates with which they react, and the products which are obtained.

REDUCING AGENT	SUBSTRATE		PRODUCTS			
	$R-\overset{\text{O}}{\parallel}-Cl$	$RCHO$	$R-\overset{\text{O}}{\parallel}-R$	$R-\overset{\text{O}}{\parallel}-OR$	$R-\overset{\text{O}}{\parallel}-NR$	$RCOO^{\ominus}$
$LiAlH_4$	$RCH_2OH$	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$RCH_2OH$	$RCH_2NR$	$RCH_2OH$
$LiAl[O-t-Bu]_3$	$RCHO$	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$RCH_2OH$	$RCHO$	$NR$
$NaBH_4$	-	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$NR$	$NR$	$NR$
$NaBH_3CN$	-	$RCH_2OH$	$NR$	$NR$	$RCH_2NR$	$NR$
$B_2H_6$	-	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$NR$	$RCH_2NR$	$RCH_2OH$
$AlH_3$	$RCH_2OH$	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$RCH_2OH$	$RCH_2NR$	$RCH_2OH$
$H_2BH$	-	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$NR$	$RCHO$	$NR$
$\text{Cyclohexane ring}-AlH$ (Dilute)	-	$RCH_2OH$	$R-\overset{\text{OH}}{\mid}-R$	$RCHO$	$RCHO$	$RCH_2OH$

## THIRD YEAR ORGANIC CHEMISTRY - REVISION COURSE Lecture 4

## MOLECULAR REACTIVITY 3: ORBITAL SYMMETRY AND PERICYCLIC REACTIONS

Books: Carey and Sundberg, Part A, Ch 10.

Lowry and Richardson, "Mechanism and Theory in Organic Chemistry", Ch 10 and 11.

Fleming OCP 67

Fleming, "Frontier Orbitals and Organic Chemical Reactions", Sections 2.1 and 2.2.

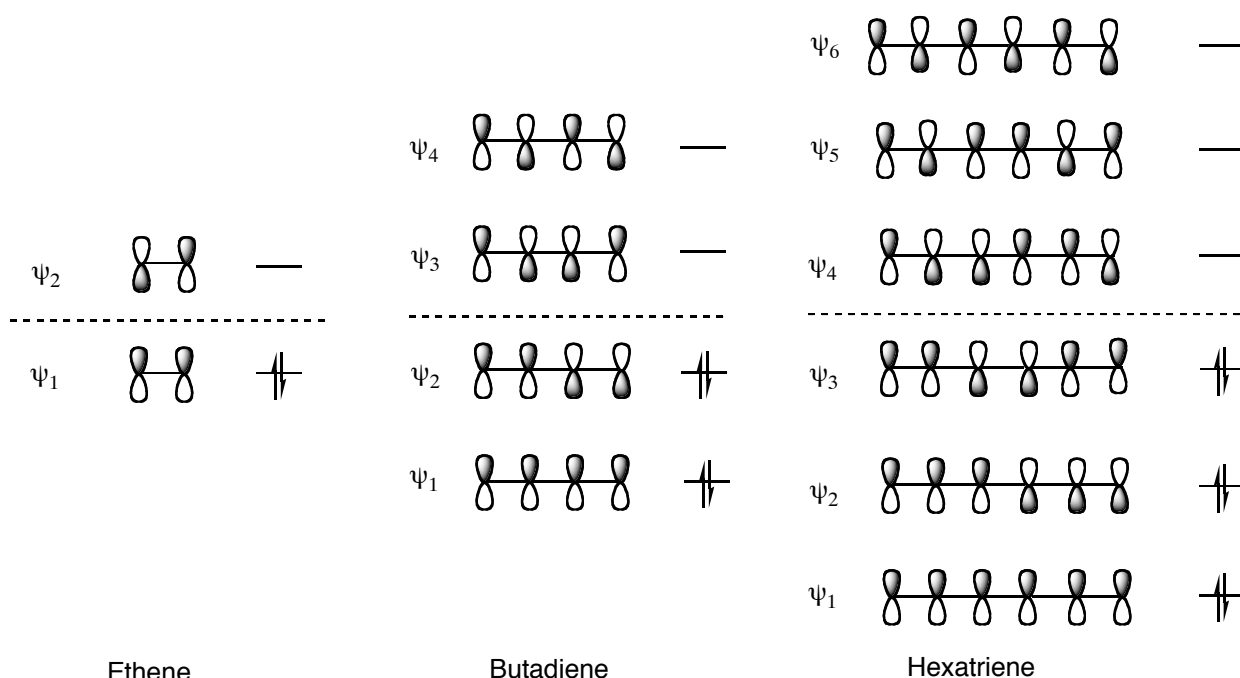
Gilchrist and Storr, "Organic Reactions and Orbital Symmetry", Ch 2, and sections in Ch 4, 5, 6, 7.

Morrison and Boyd, Organic Chemistry, 6th Edn, Ch 28.

## 1. MOLECULAR ORBITALS

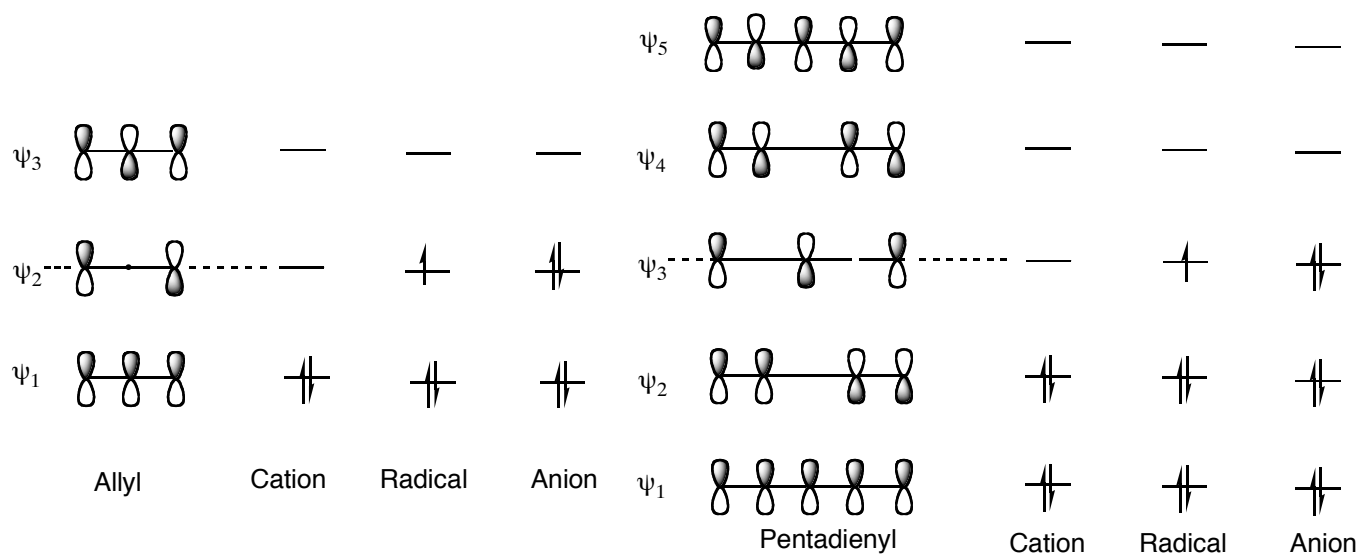
MOs for extended  $\pi$ -systems by Linear Combination of Atomic Orbitals (LCAO).

ethene ( $\pi$  and  $\pi^*$ ), butadiene ( $\psi_1, \psi_2, \psi_3, \psi_4$ ), hexatriene ( $\psi_1, \psi_2, \psi_3, \psi_4, \psi_5, \psi_6$ ):



- NB:
- (i) The  $n$ th orbital has  $n-1$  nodes symmetrically distributed around the midpoint;
  - (ii) The orbitals are alternately symmetric and antisymmetric with regard to a mirror plane at the midpoint;
  - (iii) The orbitals are alternately antisymmetric and symmetric with regard to a two-fold rotational axis of symmetry at the midpoint;

This analysis is applicable to systems with odd numbers of atoms: here one MO is non-bonding (i.e. energetically neutral), and has nodes at the nuclei (this is why electron deficiency or electron density lies at the end of the molecule), e.g. allyl and pentadienyl systems (cation, radical and anion)



**The Frontier Molecular Orbital Approach (FMO):** considers the interactions of HOMO (electron donor) and LUMO (electron acceptor) (bonding arises only when orbitals of the same phase overlap) to determine the feasibility of any given reaction.

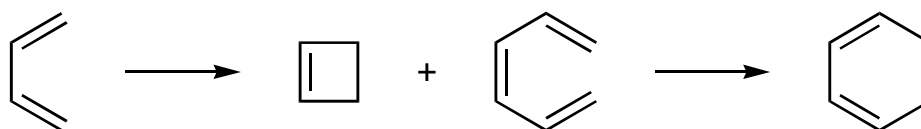
The easiest path (i.e. lowest  $E_{act}$ ) for a reaction is one which maximises the bonding during the reaction process; since bonding results from orbital overlap, we require maximum overlap which can only be achieved when orbitals are of the same phase. Thus, concerted reactions can either be *symmetry allowed* or *symmetry forbidden*. This can easily be decided by a consideration of the Frontier Molecular Orbitals, which contain the "valence electrons" of the molecules.

## 2. PERICYCLIC REACTIONS

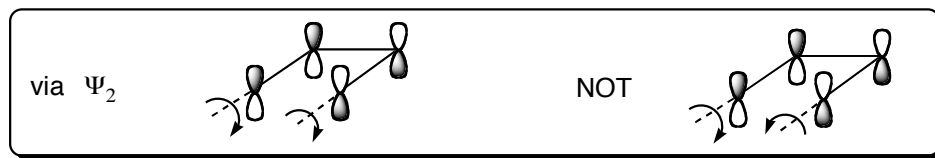
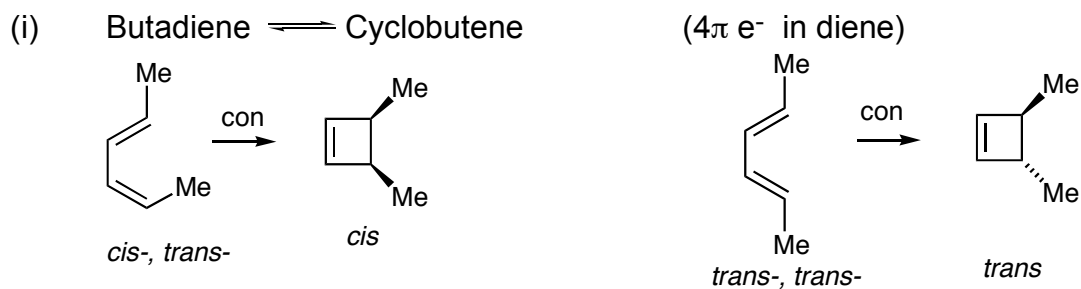
- a concerted reaction that proceeds via a cyclic TS (concerted = simultaneous bond making/breaking)

- characteristics:
- \*  $\Delta S^\ddagger \ll 0$
  - \* highly stereospecific
  - \* reversible

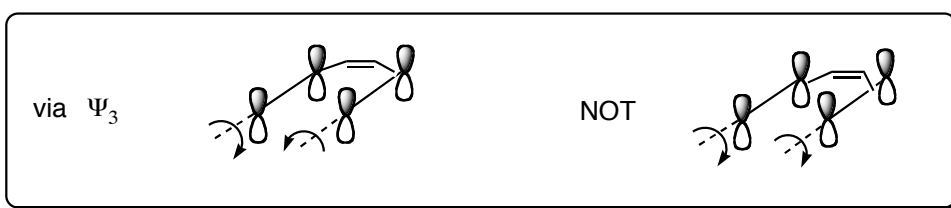
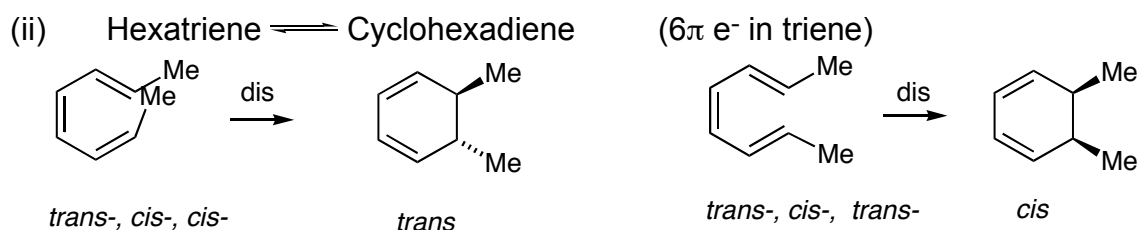
A) Electrocyclic Reactions - a pericyclic reaction that involves ring opening or ring closure, by bond formation/cleavage between the ends of a linear system of  $\pi$  electrons



But the reaction is of much greater interest when there are substituents on the polyene termini: we can understand the mode of ring closure (conrotatory or disrotatory) by a consideration of the FMO, in particular the HOMO of the polyene; ring closure is symmetry allowed only when orbital overlap of the same phase.



thermal = conrotatory  
photochemical = disrotatory



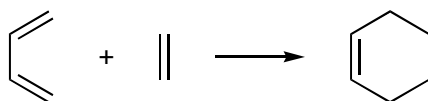
thermal = disrotatory  
photochemical = conrotatory

These results are generalised in the following Selection Rules:

No. of $e^-$ in ring closure	Reaction	
	Photochemical	Thermal
$4n$	<b>Dis</b>	<b>Con</b>
$4n+2$	<b>Con</b>	<b>Dis</b>

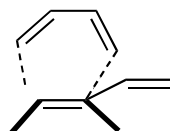
B) Cycloaddition Reactions - a reaction in which two unsaturated molecules react to form a cyclic compound; the  $\pi$  electrons are used to form two new  $\sigma$  bonds.

**[4+2]**

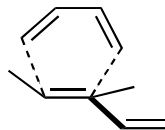


Require \* *s-cis* conformation of the diene

\* addition is stereospecifically *syn* -with respect to the alkene dienophile (suprafacial)



*endo-*

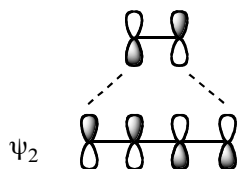


*exo-*

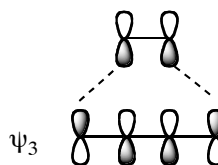
\* *endo-* additions is kinetically preferred, due to secondary orbital interactions

\* FMO analysis permits either

a) HOMO( $\psi_2$  diene)-LUMO( $\pi^*$  dienophile) This is promoted by ERG substituents on diene and EWG (-M type) on dienophile



Diels-Alder

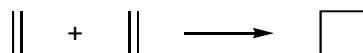


Inverse Demand Diels Alder

b) LUMO( $\psi_3$  diene)-HOMO( $\pi$  dienophile) Inverse demand D-A; This is promoted by EWG substituents on diene and ERG on dienophile

\* reversible, and this can lead to equilibration of product mixtures

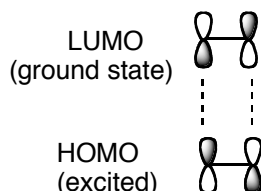
## [2+2]



\* Favoured only under photochemical conditions, by supra-supra overlap

\* Irradiation excites an electron from HOMO of the ground state, and then FMO analysis permits

HOMO( $\pi^*$  excited ene)-LUMO( $\pi^*$  ground state ene)



### Woodward-Hofmann Rules for the Facial Selectivity of [i+j] Cycloadditions

$i+j$	<i>Thermal</i>	<i>Photochemical</i>
$4n$	s,a (or a,s)	s,s (or a,a)
$4n+2$	s,s (or a,a)	s,a (or a,s)

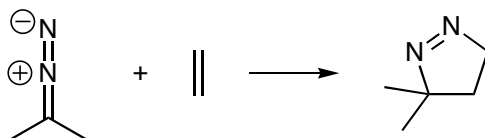
## [3+2]

1,3-Dipolar Cycloadditions - FMO description of cycloadditions of 1,3- dipoles to double bonds (called the "dipolarophile"). Examples of 1,3-dipoles, their synthesis and synthetic utility:

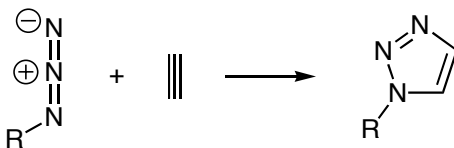


Some useful types of 3+2:

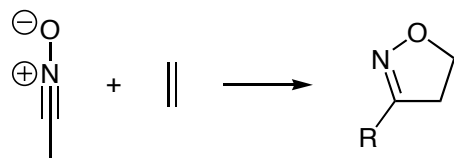
1. Diazomethane -----> pyrazolines



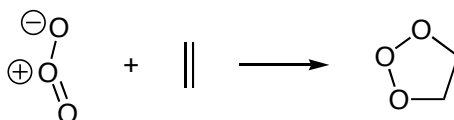
2. Azides -----> triazoles



3. Nitrile oxides -----> isoxazolines



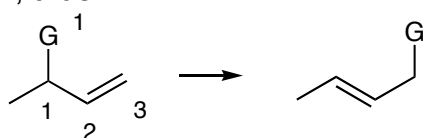
4. Ozone -----> molozonides (primary ozonides)



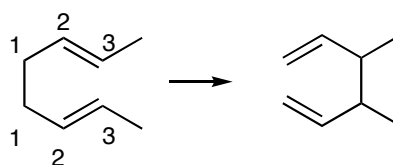
### C) Sigmatropic Reactions

- a migration, in an uncatalysed intramolecular process, of a  $\sigma$ -bond, adjacent to one or more  $\pi$ -systems, to a new position in the molecule, with the  $\pi$ -system reorganised in the process

- the process is given an [i,j] descriptor, with each terminus of the bond being broken given the number 1, thus:

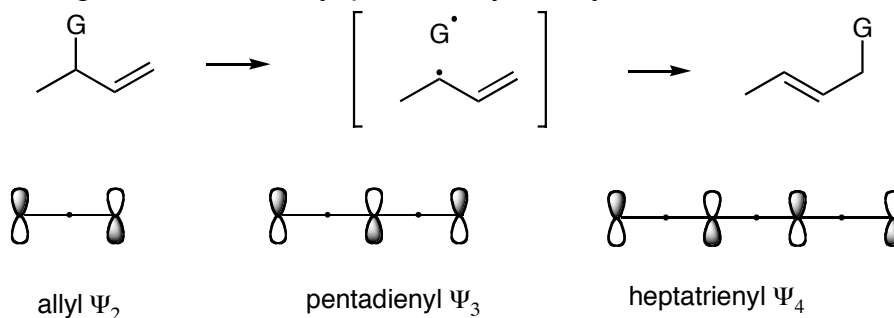


[1,3]



[3,3] Cope Rearrangement

- the FMO approach treats the reaction **formally** as a radical process, and uses the singly occupied non-bonding orbital of the allyl/pentadienyl/etc system:



(i) [i,j] Sigmatropic migrations

1. HYDROGEN SHIFTS: here we consider overlap with  $H_{1s}$

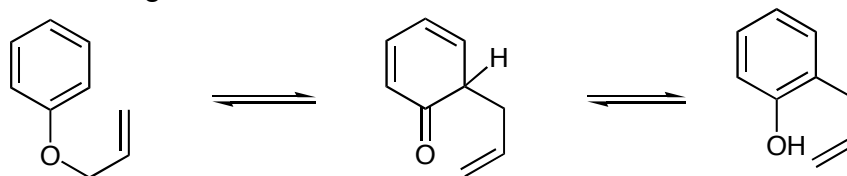
- [1,3] are thermally allowed (antarafacial) but sterically impossible
- [1,5] are thermally allowed (suprafacial) since the  $H_{1s}$  can overlap simultaneously with the end orbitals of  $\psi_3$ , which are of the same phase
- [1,7] are thermally allowed (antarafacial), e.g. in the Vitamin D series.

2. CARBON SHIFTS: here we consider overlap with  $C_{2p}$  (much more complex than for H)

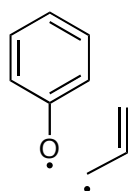
- [1,3] are thermally allowed (suprafacial)
- [1,5] are thermally allowed (suprafacial)

(ii) [i,j] Sigmatropic rearrangements

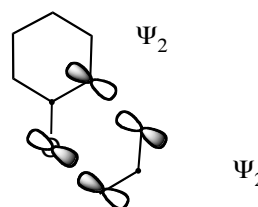
- \* Cope Rearrangement (see above)
- \* Claisen Rearrangement



Consider as



i.e.



D) Cheletropic Reactions - reactions in which 2  $\sigma$  bonds that terminate at a single atom are made or broken in concert.



E) Group Transfer - reactions in which one  $\pi$  is used to form one new  $\sigma$  bonds. e.g. *ene*