

Pericyclic Reactions (McM chapt 30)

•Polar react. (nucleophiles and electrophiles) $\text{Nu} : \curvearrowright \text{E}^{\oplus}$

•Radical react. $\text{R} \cdot \curvearrowright \curvearrowleft \cdot \text{R}'$

•Pericyclic react. (concerted, cyclic TS[#])

•Electrocyclic react.

•Cycloadditions (*i.e.* Diels Alder)

•Sigmatropic rearrangement

•Pericyclic react. (concerted, cyclic TS#)

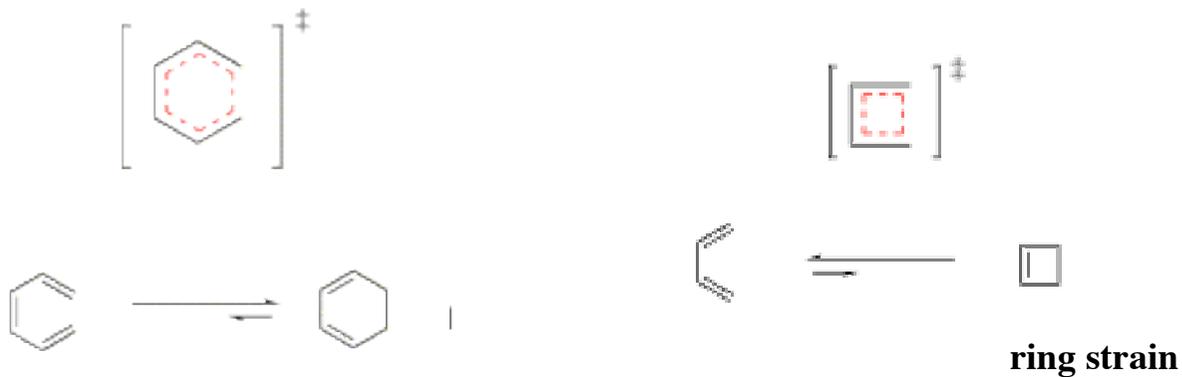
•Electrocyclic react. \longrightarrow

•Cycloadditions (*i.e.* Diels Alder)

•Sigmatropic rearrangement

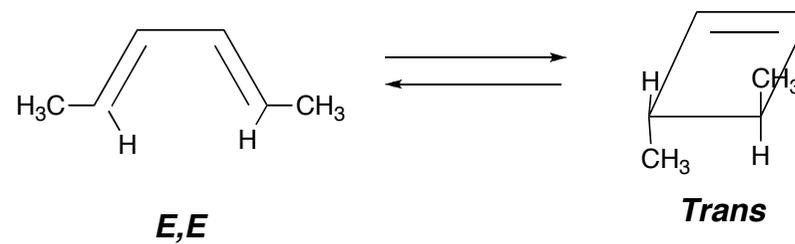
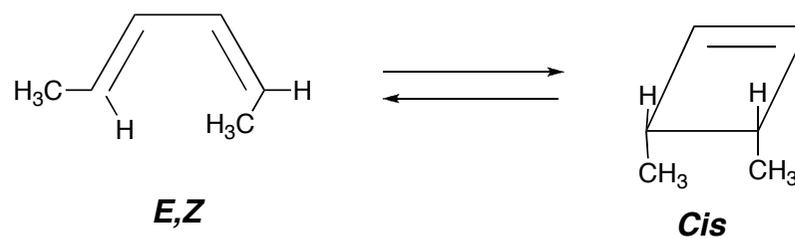
•Rearrangement of polyene

•Thermal (react. in ground state)
or photochemical
(react of excited state)



Electrocyclic react. - Stereospecific react.

Thermal cond.:



Opposite stereochem. under photochem. cond.

Pericyclic react. are symmetry allowed react.

Woodward Hoffmann rules

**Symmetry in reactants are preserved during pericyclic react.
Maximum bonding interactions by transferring electrons between
molecular orbitals of the same symmetry in reactant and products.**

**The lobes of the reactant MOs must be of the correct algebraic sign
for bonding to occur in the TS**

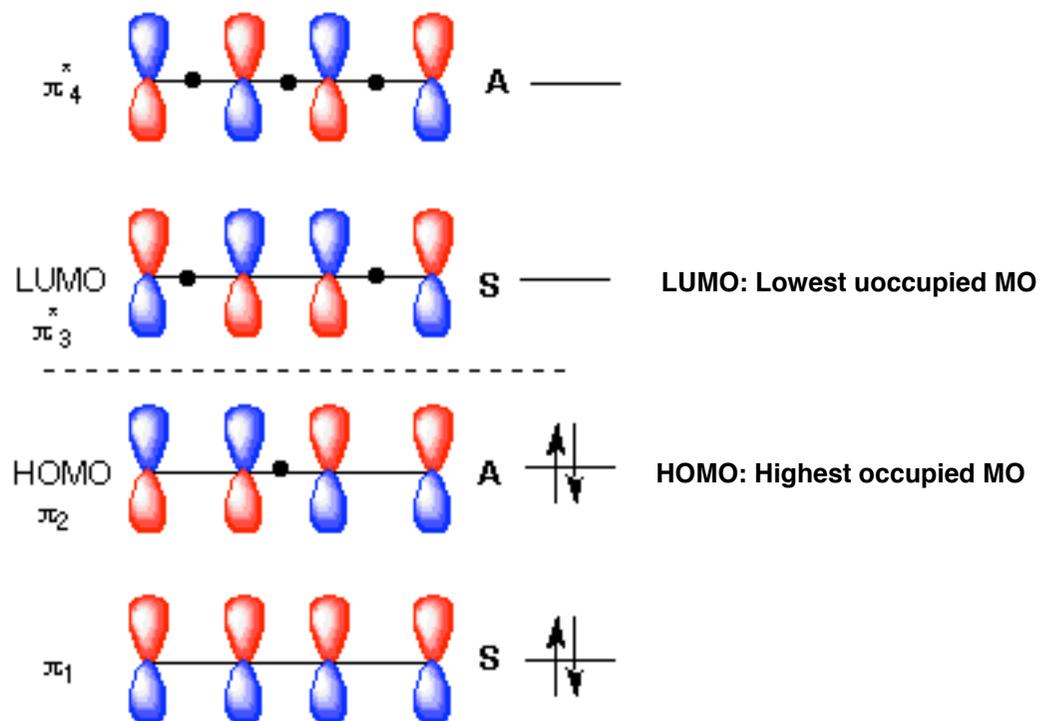
**Results can generally be predicted just by looking at Front Molecular Orbitals
(FMO; HOMO and LUMO) - Fukui**

Symmetry allowed react.

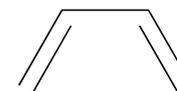
Woodward Hoffmann rules

Symmetry in reactants are preserved during pericyclic react.

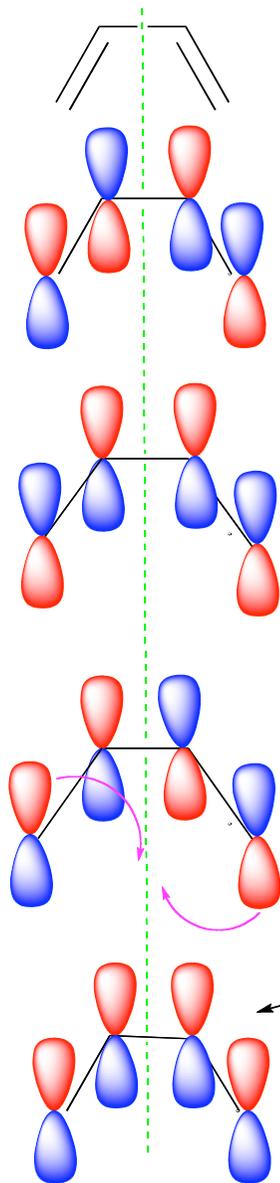
Results can generally be predicted just by looking at Front Molecular Orbitals (FMO; HOMO and LUMO) - Fukui



Butadiene
(ground state)



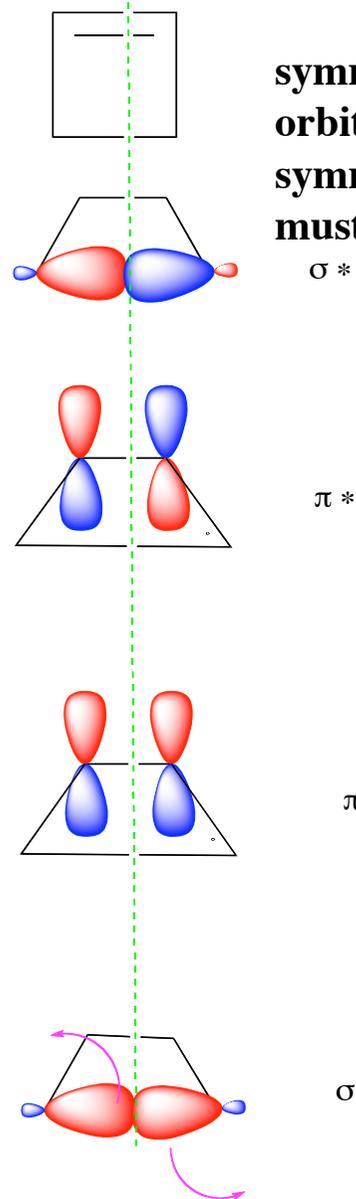
Conrotatory movement - symmetry allowed



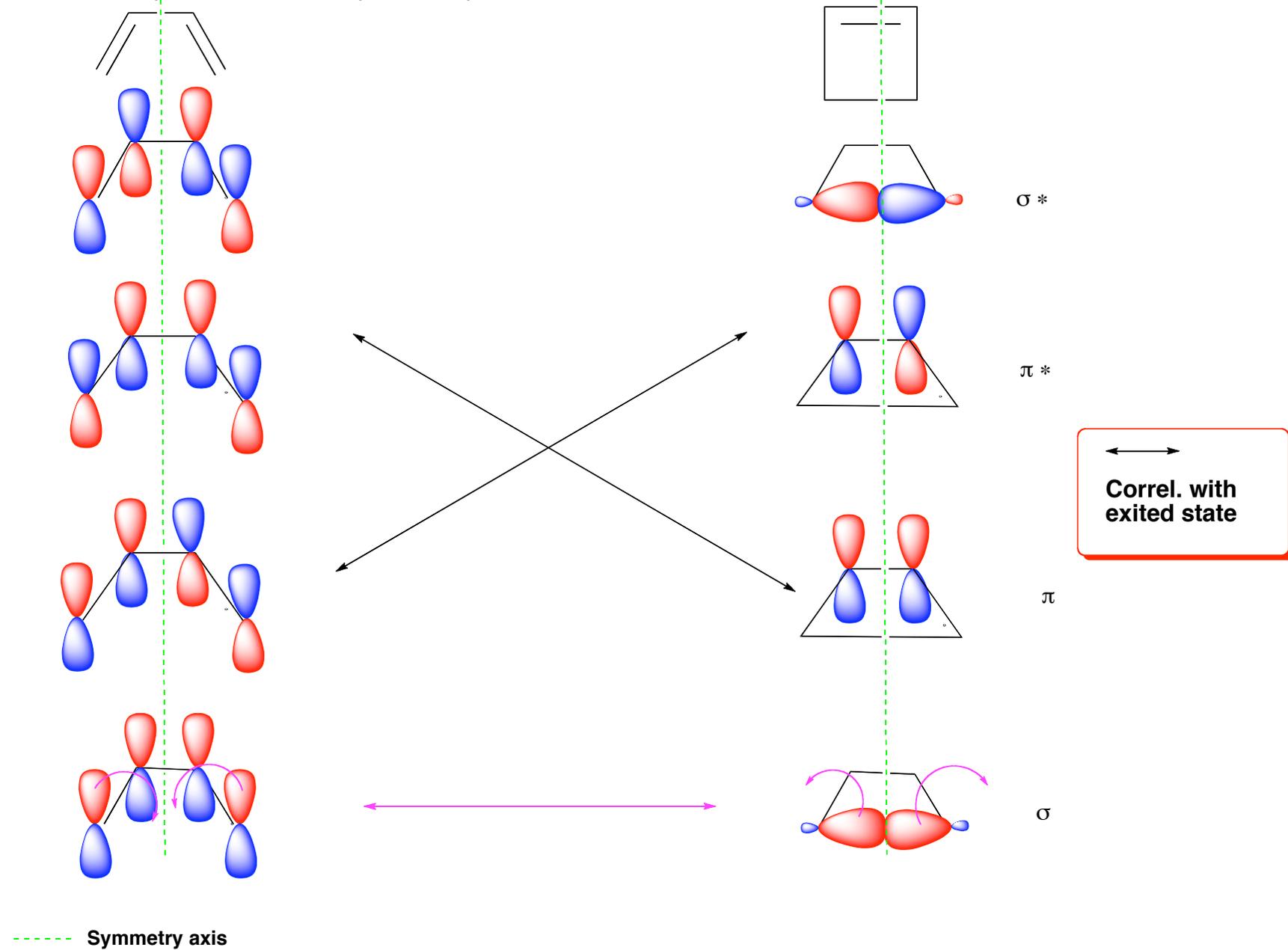
--- Symmetry axis

Woodward - Hoffmann

symmetries of the changing orbitals relative to the overall symmetry of the system must be retained

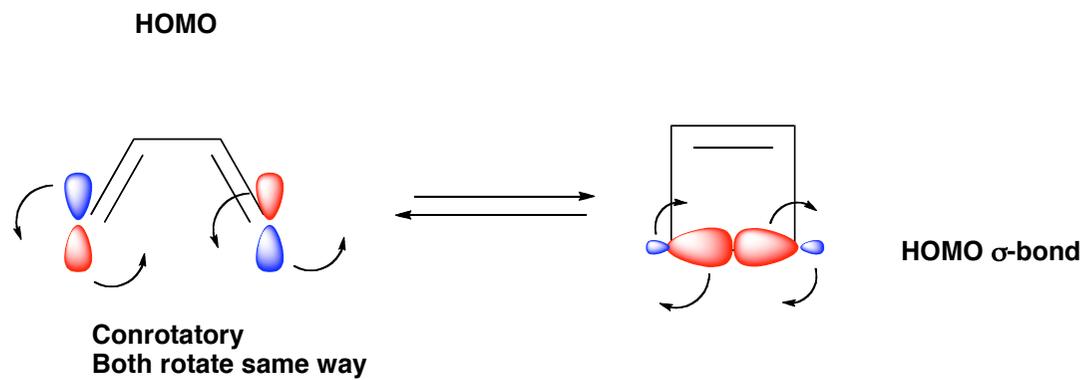


Disrotatory movement - symmetry forbidden

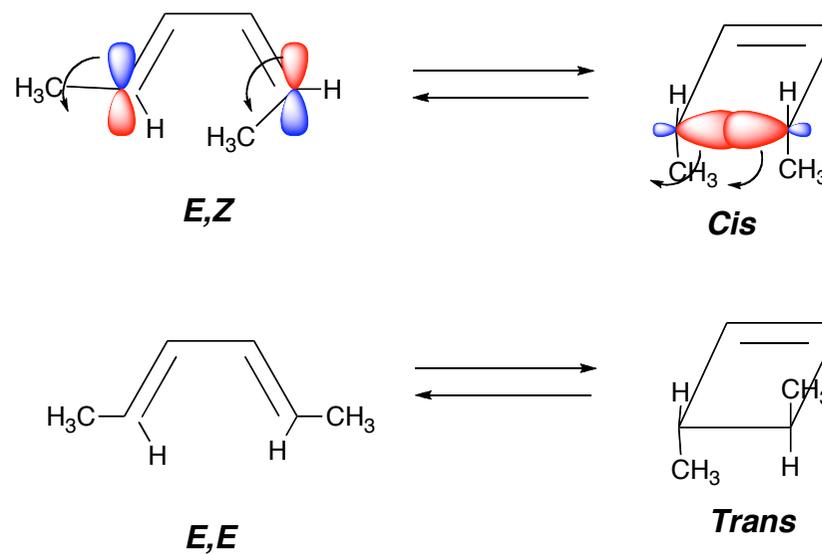


Fukui

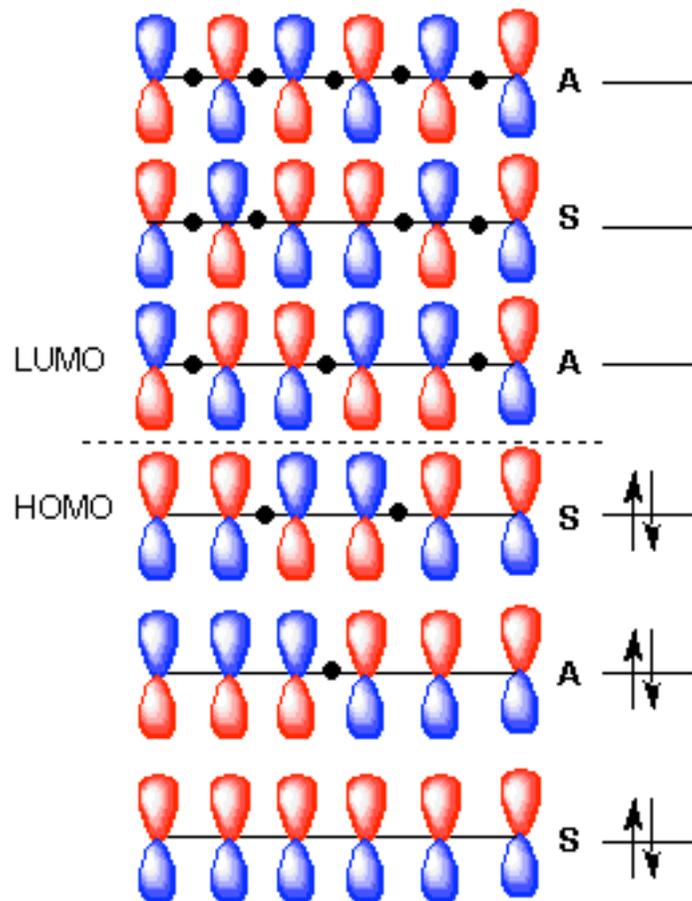
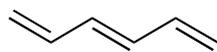
The HOMO controls the course of the reaction



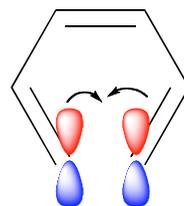
Stereospecific react.



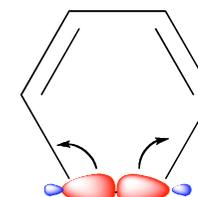
Molecular orbitals hexatriene



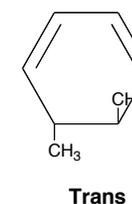
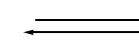
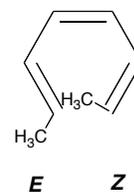
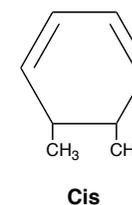
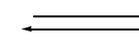
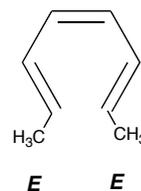
HOMO



Disrotatory
Rotation opposite way



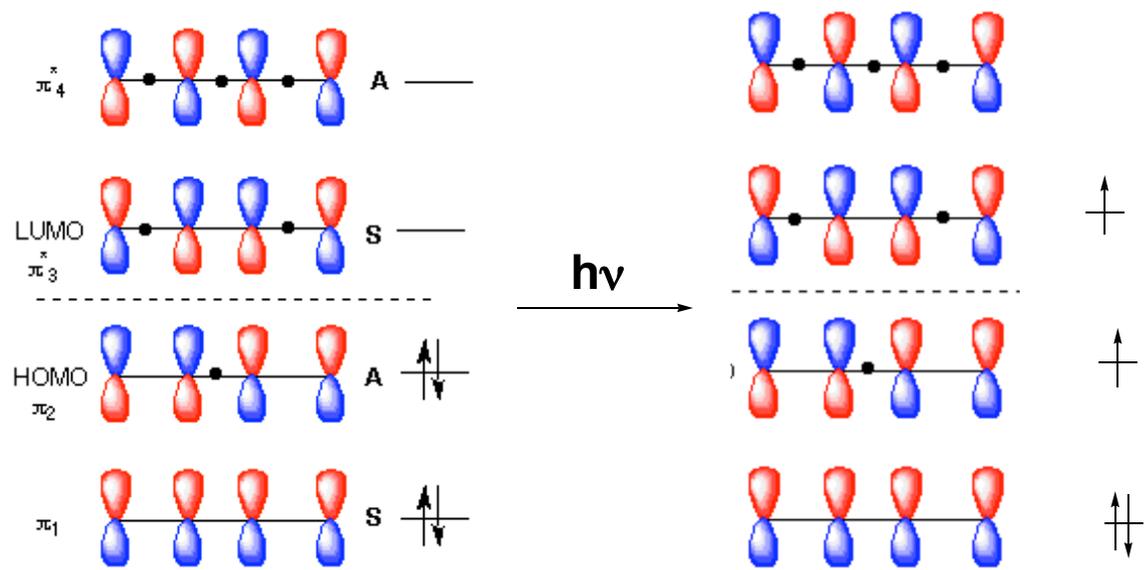
HOMO σ -bond



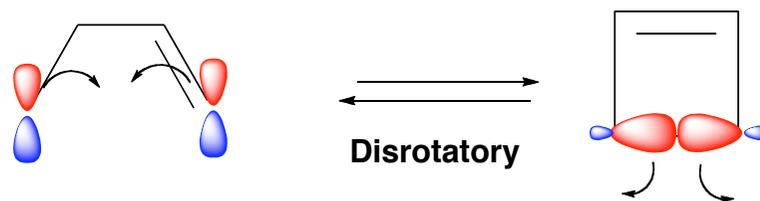
Electrocyclic react. -Symmetry allowed

| No. of electrons | Reactions in the ground state |
|------------------|-------------------------------|
| 4n | Conrotatory |
| 4n + 2 | Disrotatory |

Photochemical electrocyclic react.

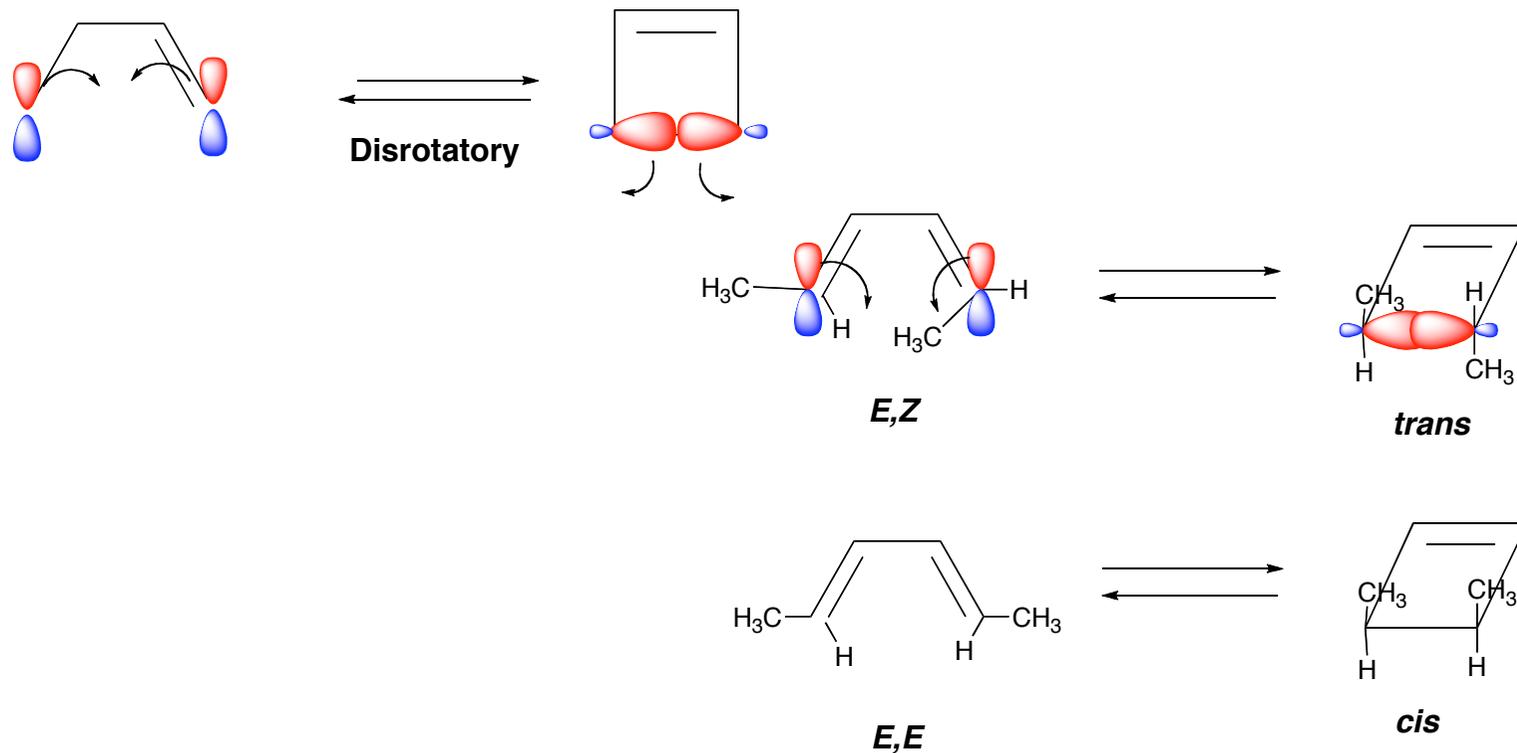


HOMO excited state
(= LUMO ground state)

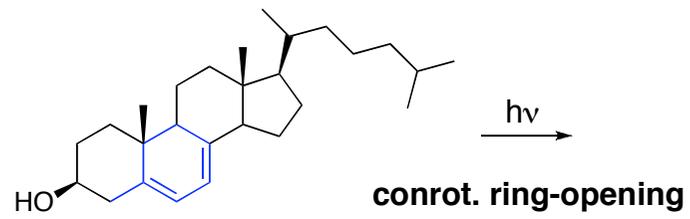
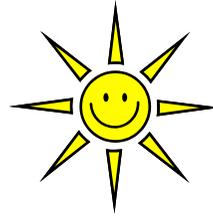


Photochemical electrocyclic react. - opposite stereochemistry

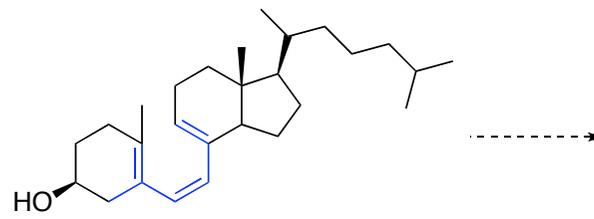
HOMO excited state
(= LUMO ground state)



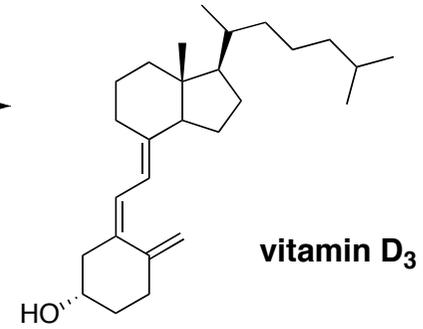
| No. of electrons | Reactions in the ground state (thermal) | Reactions in excited state (Photochem.) |
|------------------|---|---|
| 4n | Conrotatory | Disrotatory |
| 4n + 2 | Disrotatory | Conrotatory |



7-dehydrocholesterol
cyclohexadiene



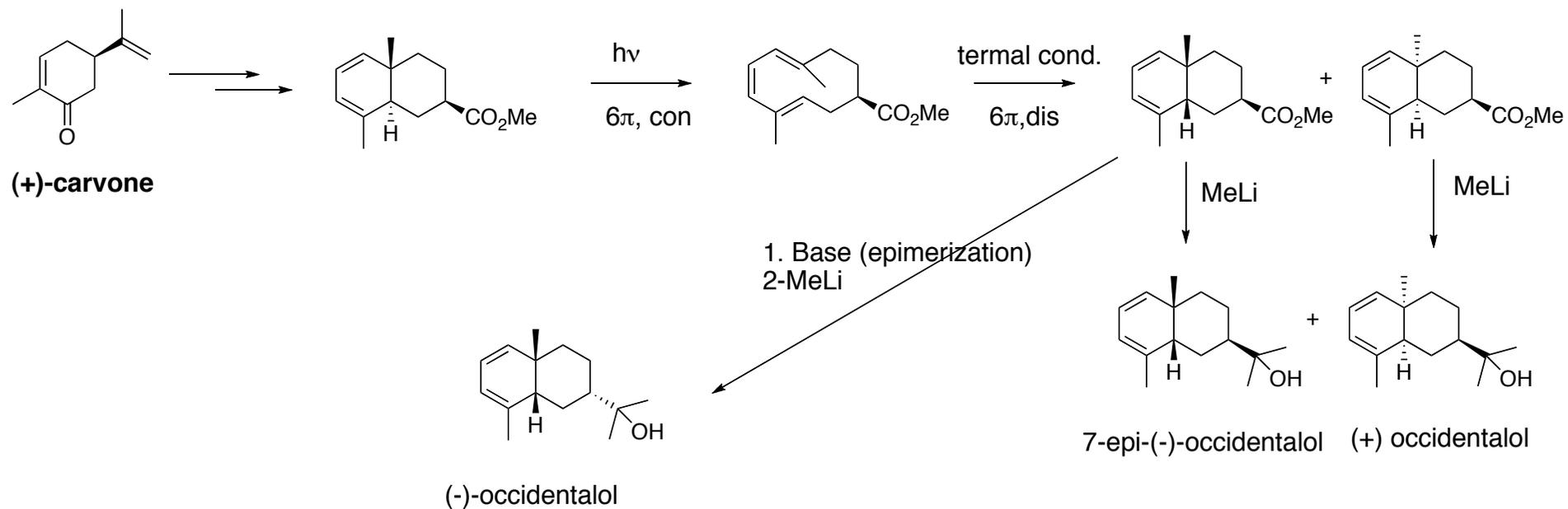
previtamin D₃



vitamin D₃

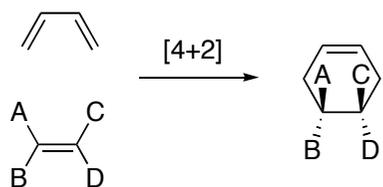
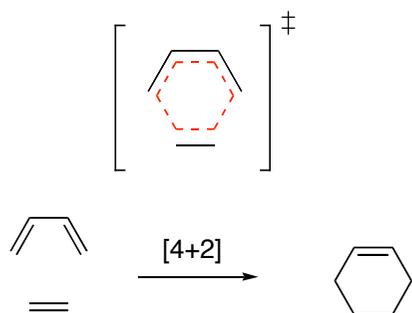
Applications in synthesis - Synthesis of occidentalol

J. Org. Chem. 1973, 38, 728



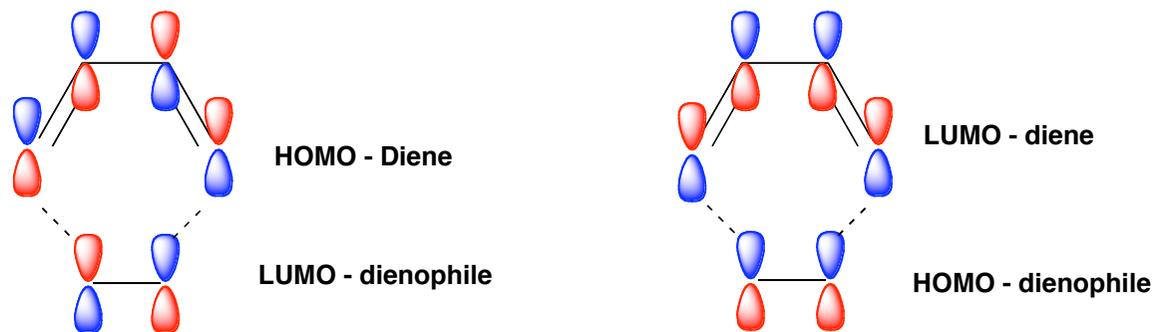
Cycloadditions (i.e. Diels Alder)

[4+2] add. thermal cond.



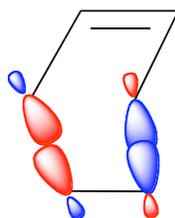
Stereospecific react.

Suprafacial cycloadd.



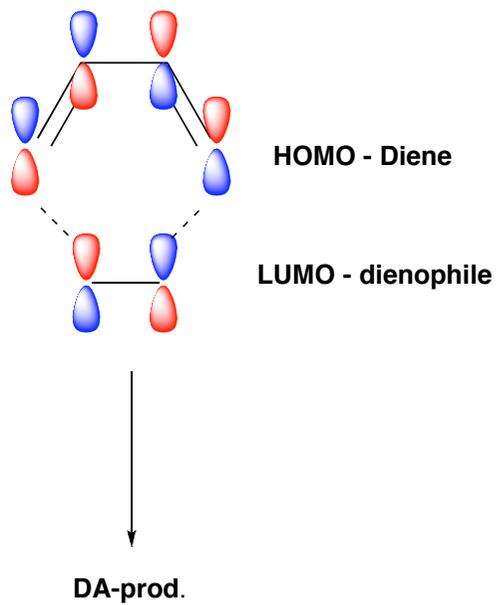
Both interact. may lead to product

In reality, the electron rich species reacts via its HOMO and the electron poor species via its LUMO.

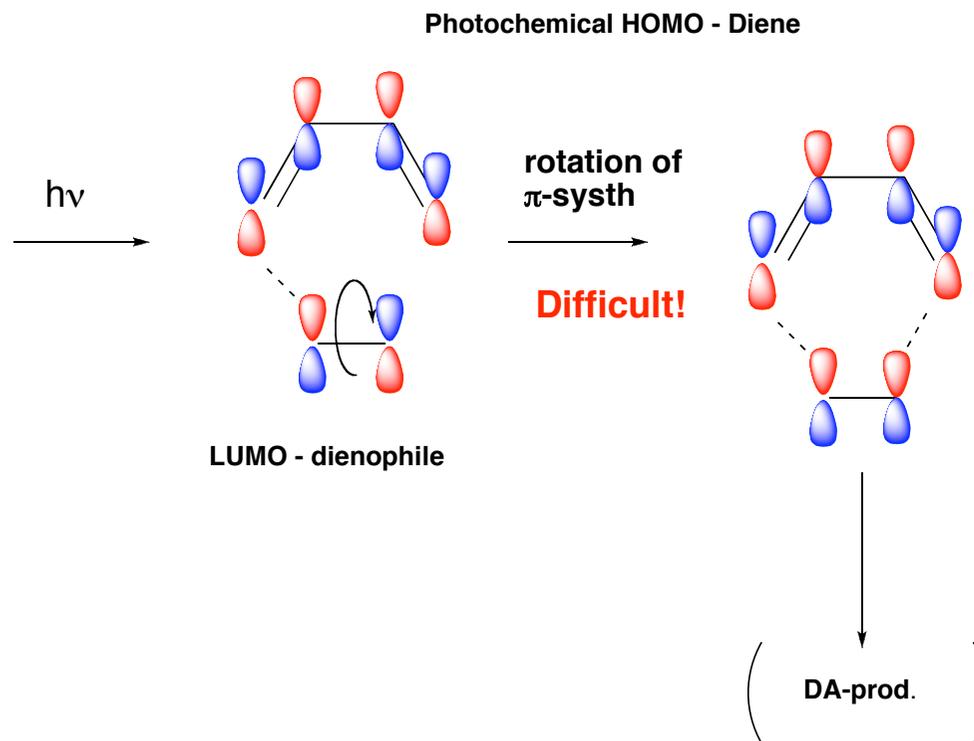


Suprafacial and antarafacial cycloadd.

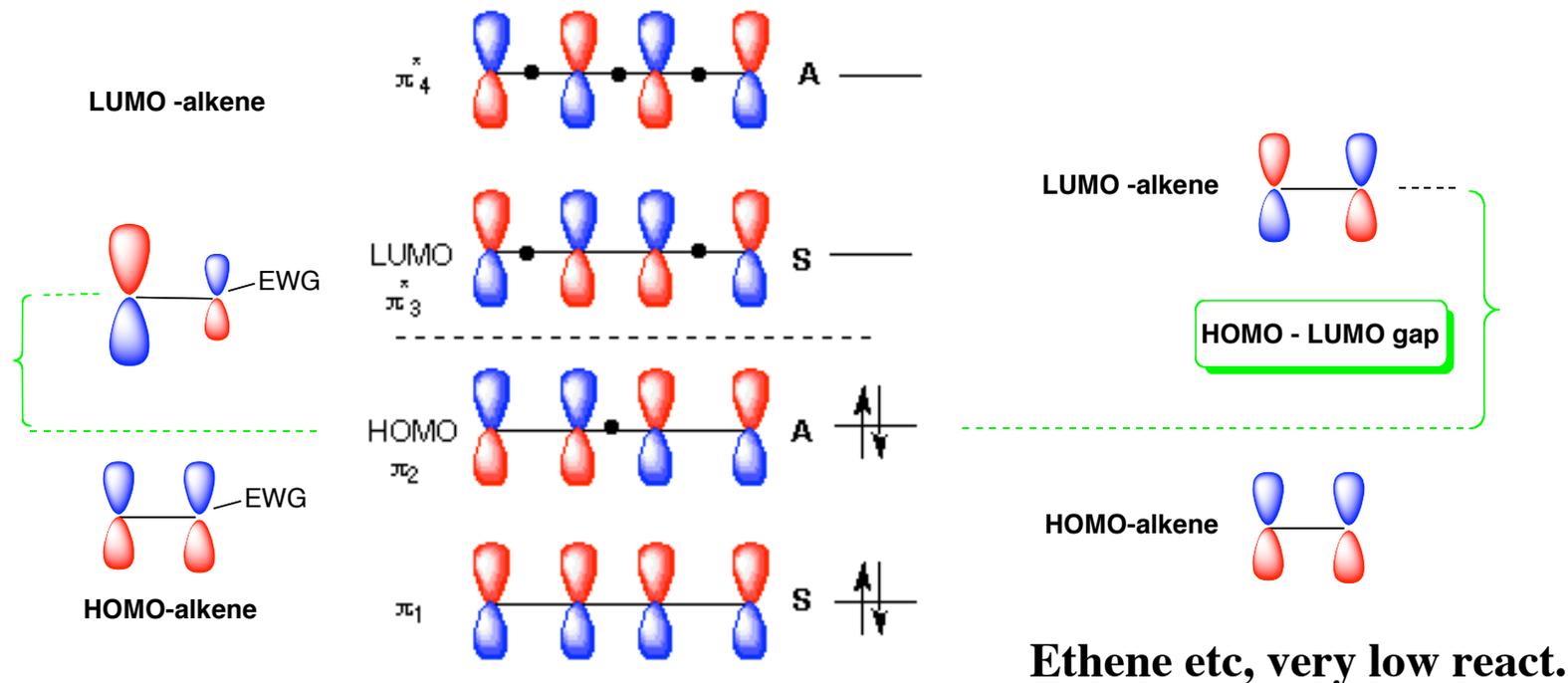
Suprafacial cycloadd.



Antarafacial cycloadd

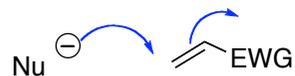


Normal electron demand DA - Electron poor dienophile (Michael accept.)

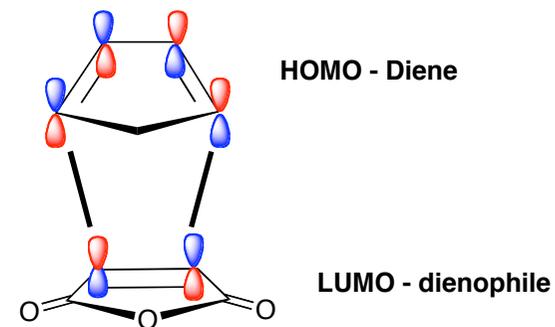
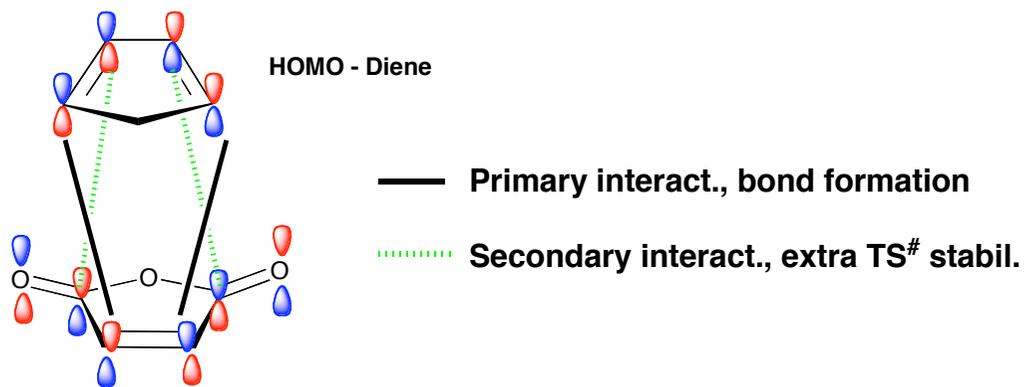
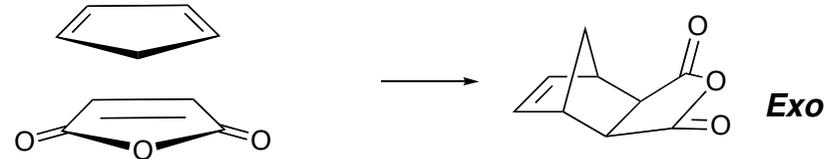
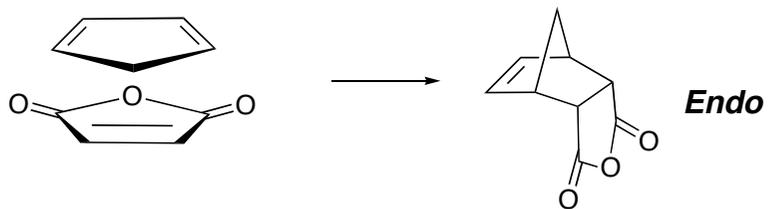


Michael accept.
Lower LUMO, largest coefficient on β -carbon

C.f. conjugate addition, β -carbon attacked by Nu

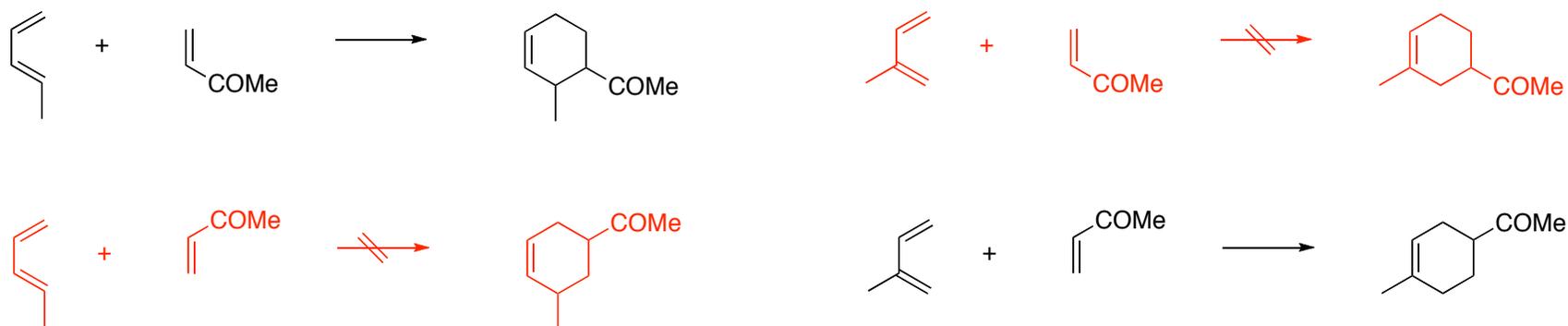


endo - exo selectivity (Not in McM)

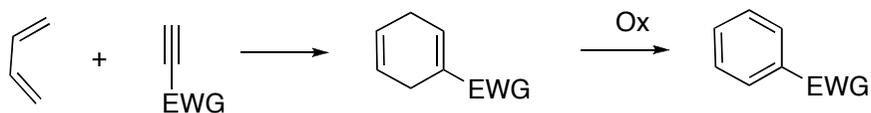


Regioselectivity in Diels Alder (Not McM)

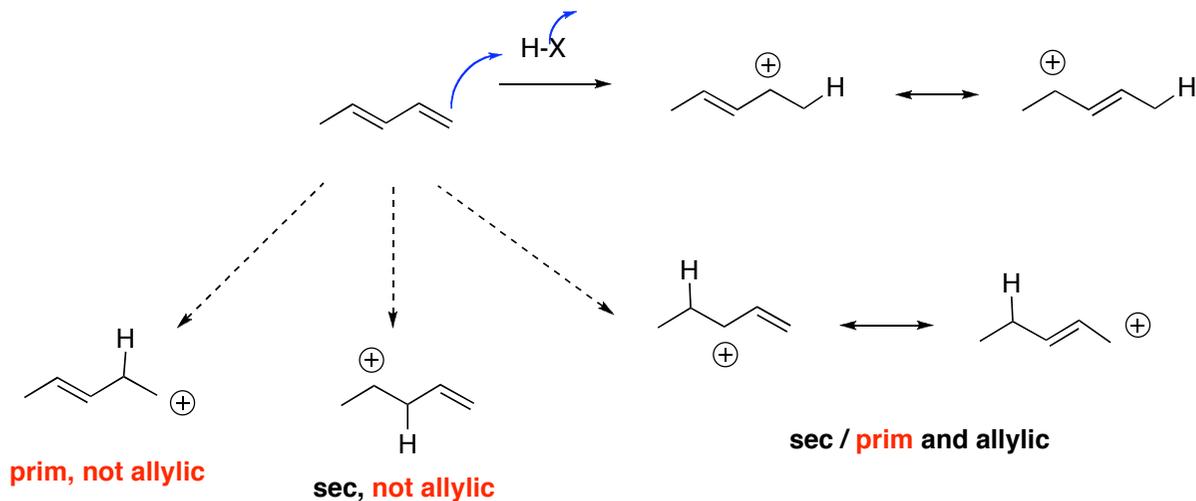
DA is “ortho - para directing”



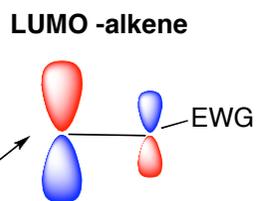
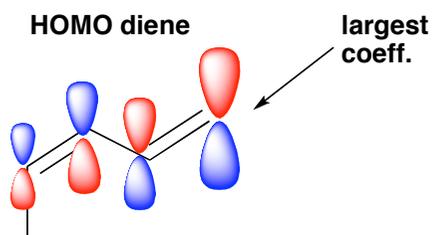
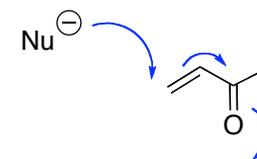
Also alkynes, and arynes, can be dienophiles



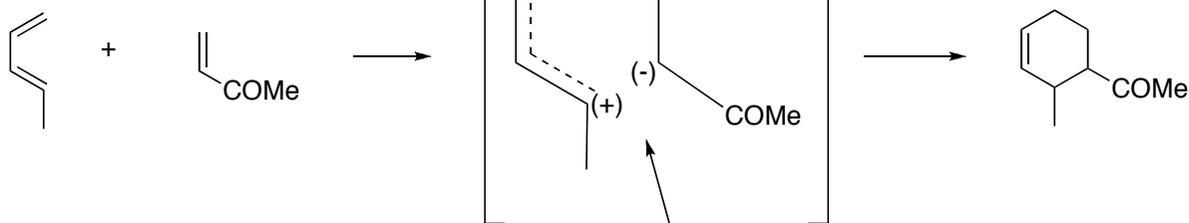
Reactivity of diene as nucleophile



Reactivity of alkene as electrophile



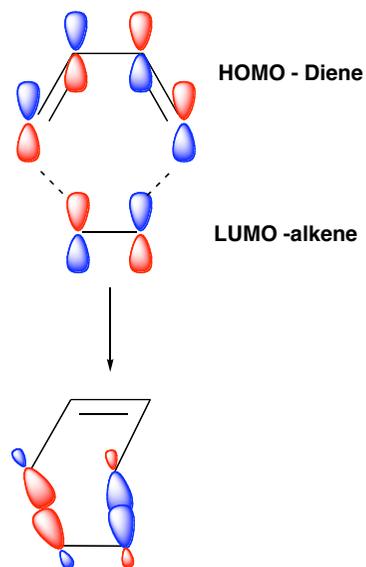
Bond formation almost complete in TS
Interact between the largest HOMO and LUMO coeff
(or between most nucleophilic C in diene,
and most electrophilic C in alkene)



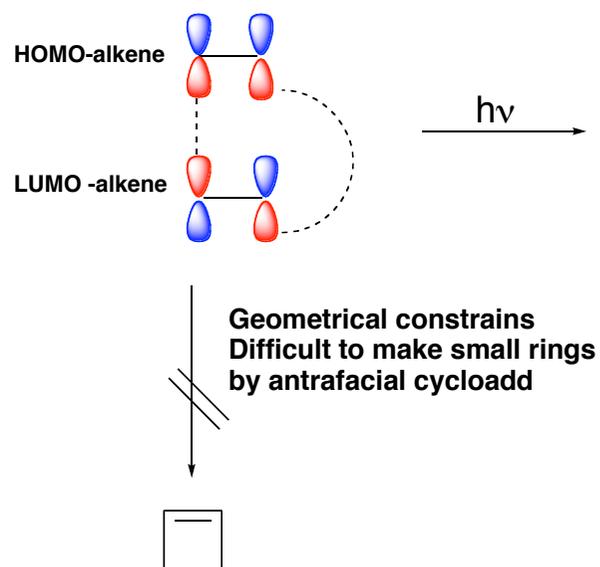
almost no bond formation
in TS

[2+2] Cycloadditions

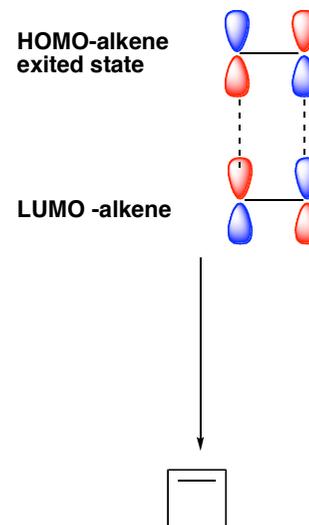
Suprafacial cycloadd.



Antarafacial cycloadd. (termal cond.)



Suprafacial cycloadd. (photochem. cond.)



No. of electrons

$4n$

$4n + 2$

Reactions in the ground state
(termal)

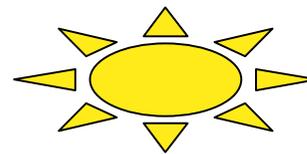
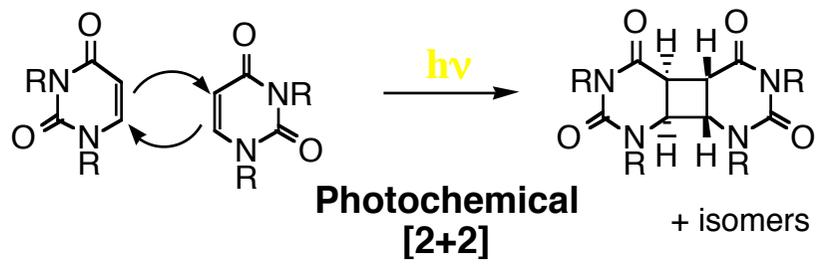
Antarafacial

Suprafacial

Reactions in exited state
(Photochem.)

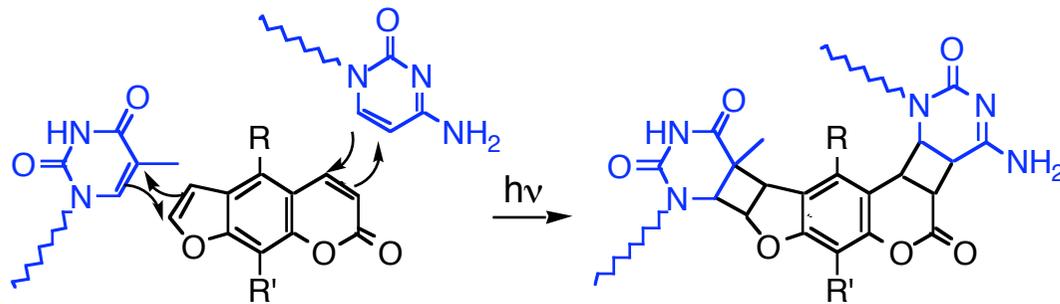
Suprafacial

Antarafacial



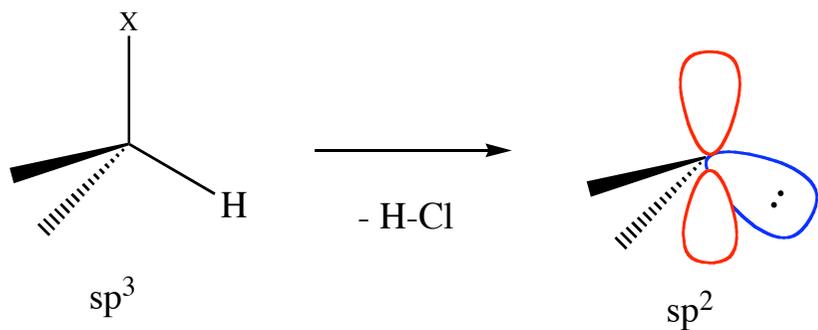
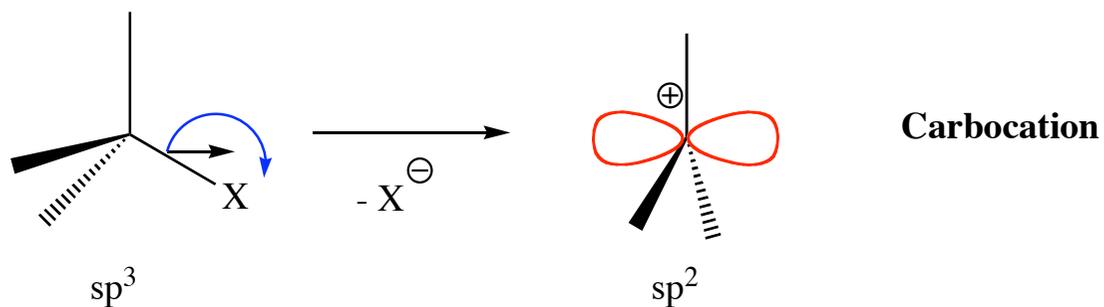
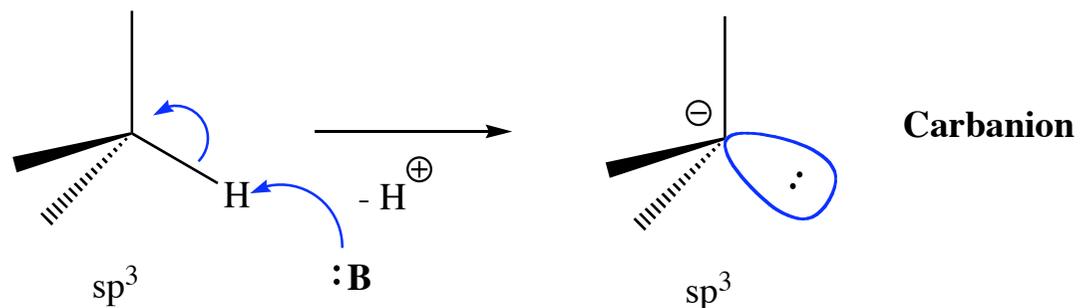
Cancer

Psoralenes - Psoriasis



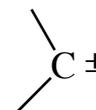
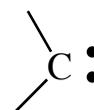
Carbenes

McM chapt 7.6, lab ex. 7



Carbene

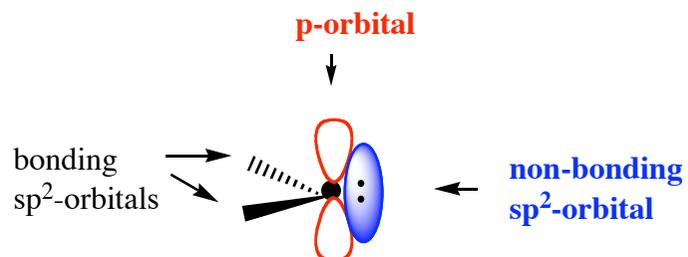
**Neutral
Divalent**



6 valence electrons - Highly reactive $t_{1/2} < 1$ s

Electron deficient / electrophilic properties

singlet carbene



electron pair, opposite spin
cation / anion properties

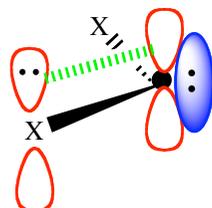
triplet carbene



2 half-filled p-orbitals
electrons with parallel spin

diradical properties
Gives triplet signal in esr spektrum

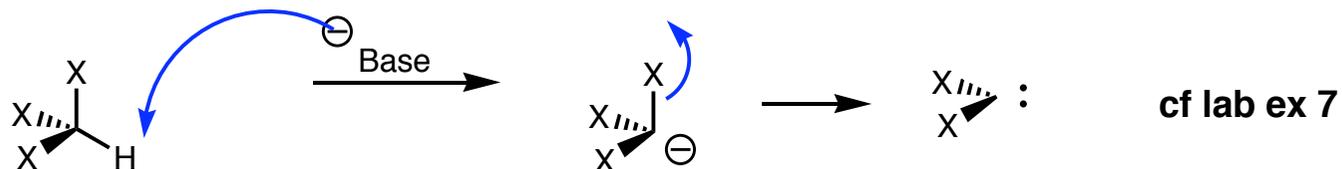
Triplet normally somewhat more stable than singlet
Singlets more reactive



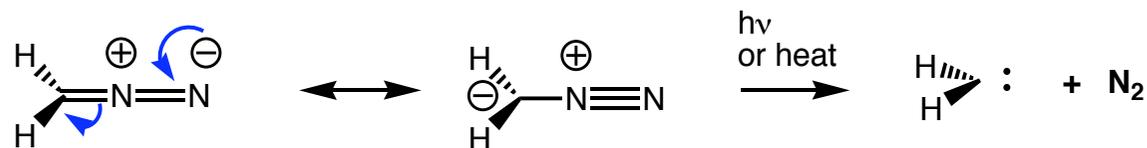
dihalocarbene
Stabilizing overlap
in singlet state

Carbenes and carbenoids in synthesis

Generation of carbenes



Not in McM

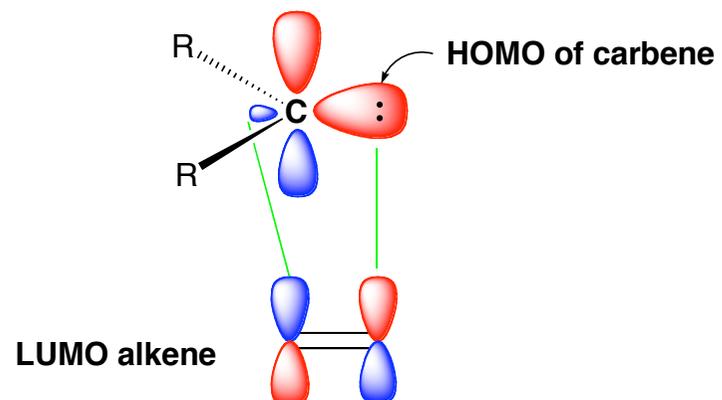
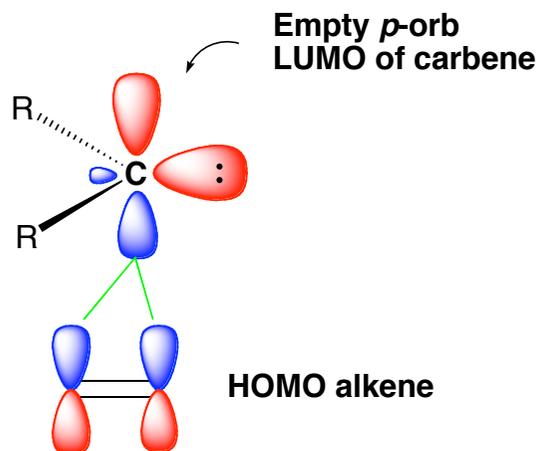
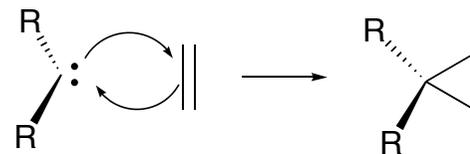
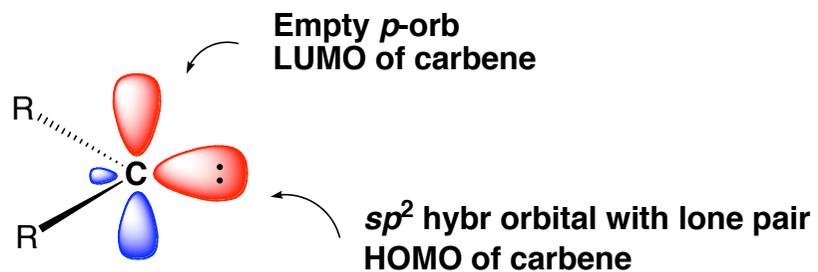


Diazomethane
(toxic, explosive)

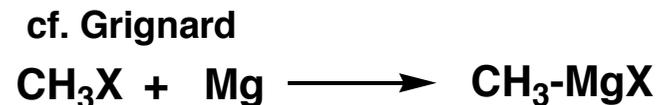
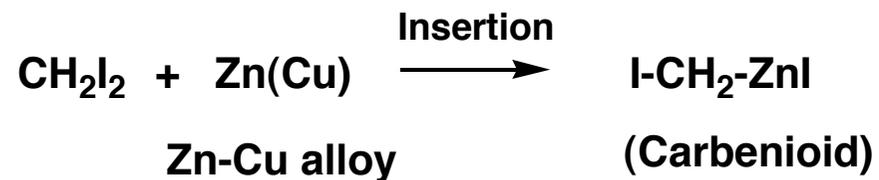
(From Hg-species)

Carbene Cycloadditions

Singlet Carbene

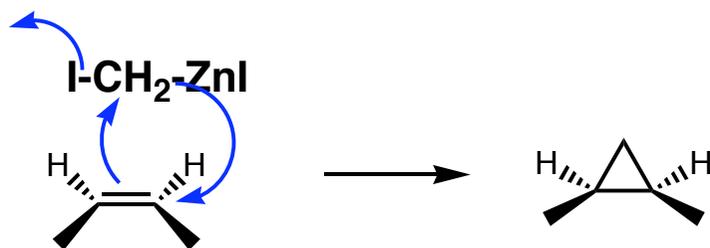


Carbenoids - Simmons Smith reaction



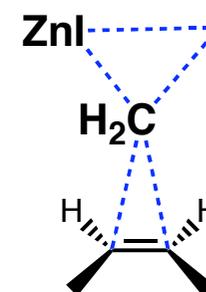
Other methods

| reactants | active reagent |
|---|---|
| Et ₂ Zn, CH ₂ I ₂ | EtZnCH ₂ I or Zn(CH ₂ I) ₂ |
| EtZnI, CH ₂ I ₂ | IZnCH ₂ I |
| TFA, Et ₂ Zn, CH ₂ I ₂ | CF ₃ COOZnCH ₂ I |
| Sm(Hg), CH ₂ I ₂ | ISmCH ₂ I |
| R ₃ Al, CH ₂ I ₂ | R ₂ AlCH ₂ I |
| ZnX ₂ , CH ₂ N ₂ | Zn(CH ₂ I) ₂ |

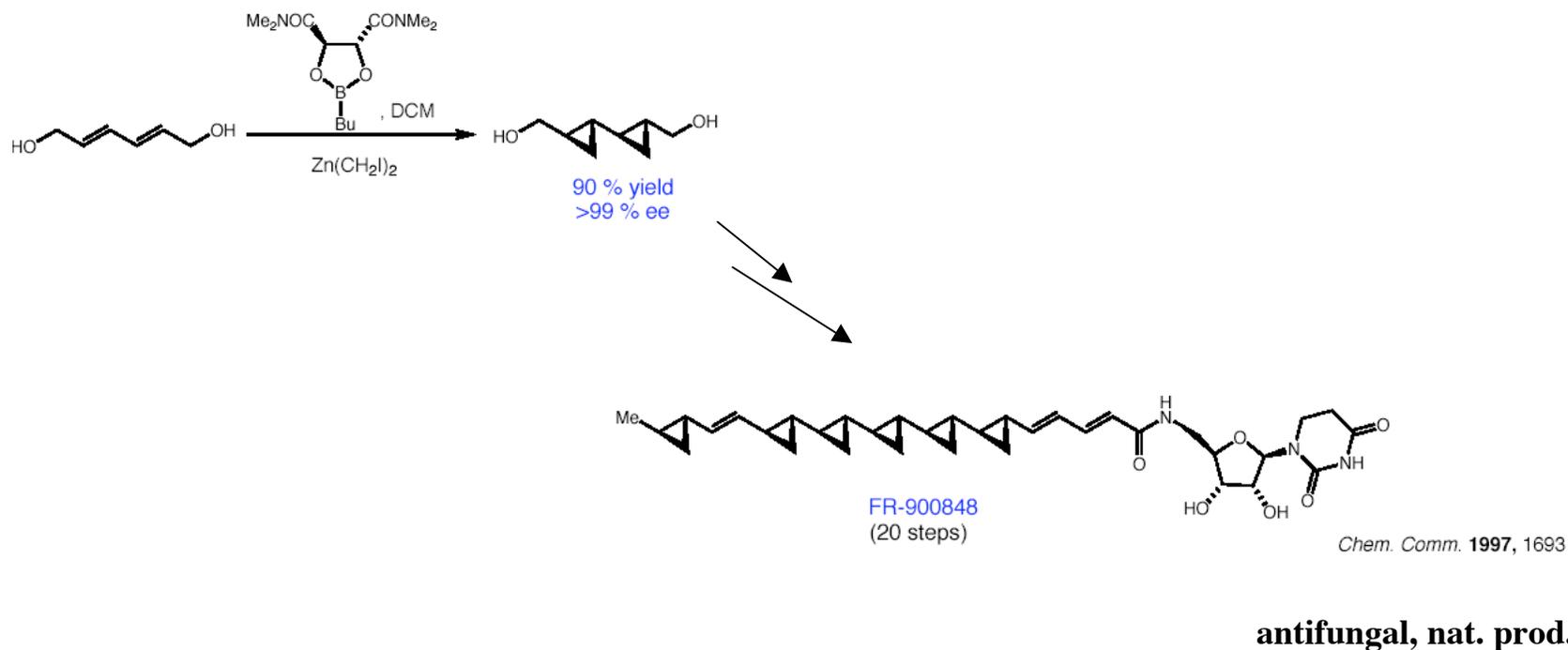


- One-step - Concerted
- Stereospecific

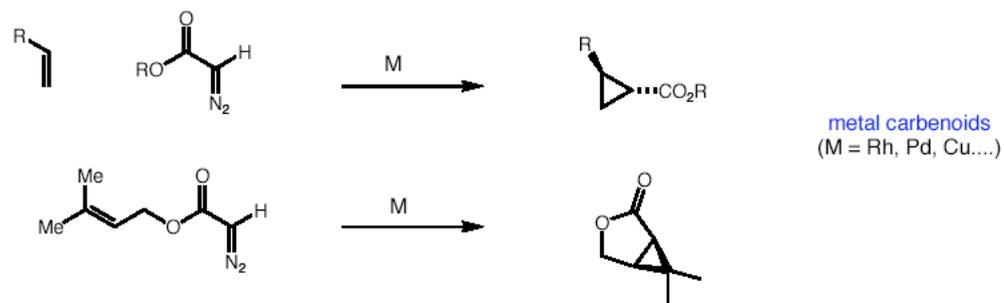
TS# ?



Enantioselective Simmons Smith Allylic alcohols (Chiral auxiliary or catalyst)

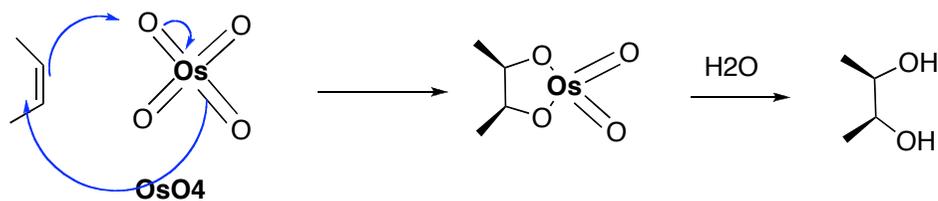
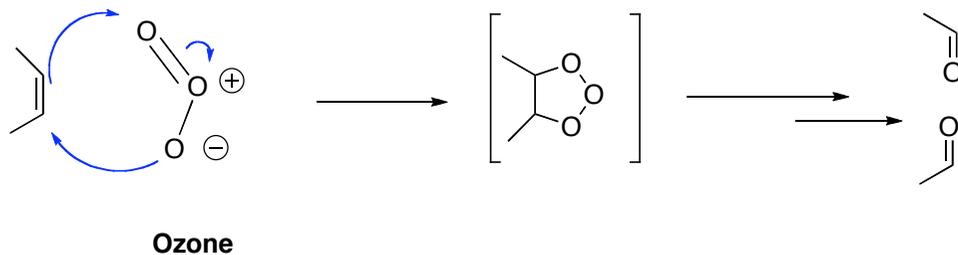


Other carbenoids

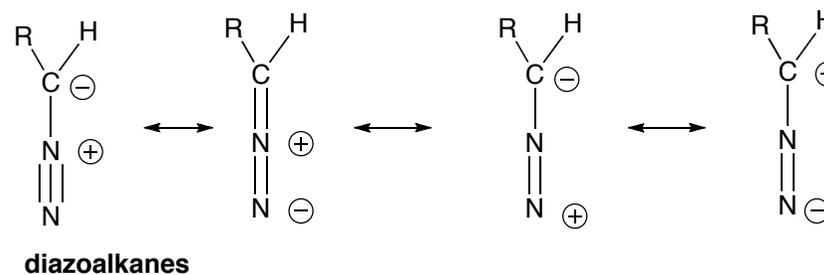
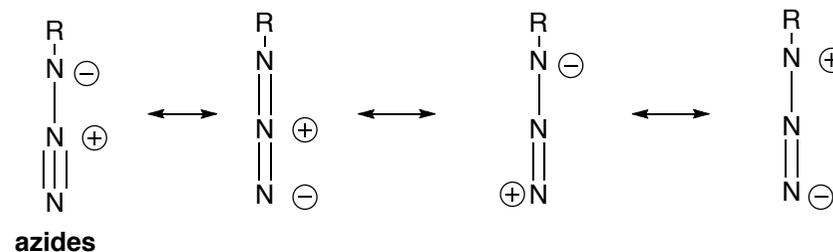


Cycloadditions with 1,3-dipolar reagents

[4+2] cycloadd. Not in McM



Other ex of 1,3-dipoles

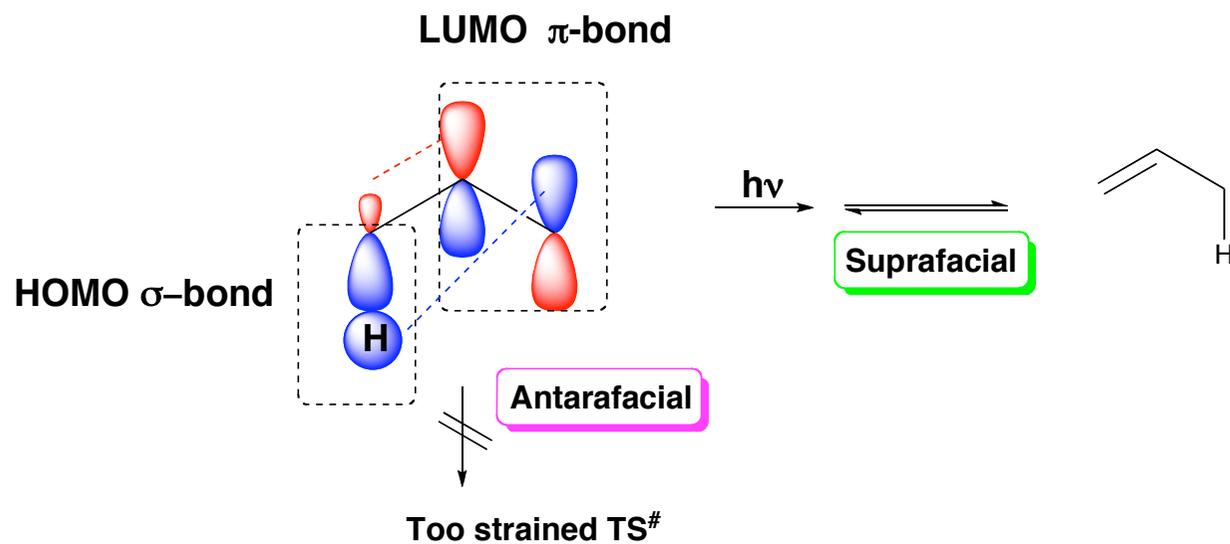
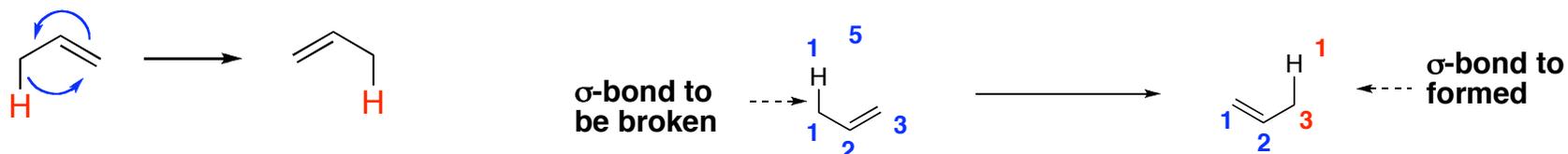


Synthesis of heterocycles

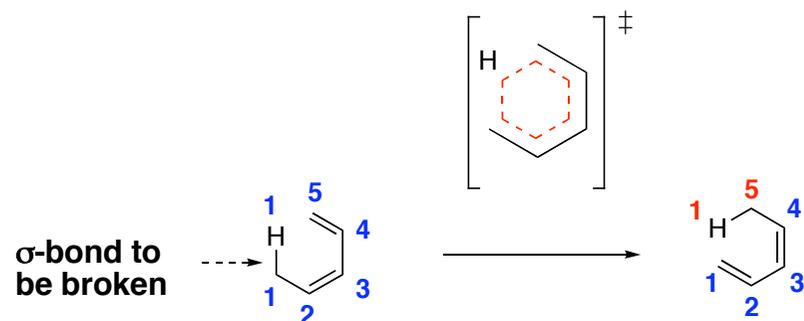
Sigmatropic Rearrangements

σ -bonded subst migrates accross a π -electron system

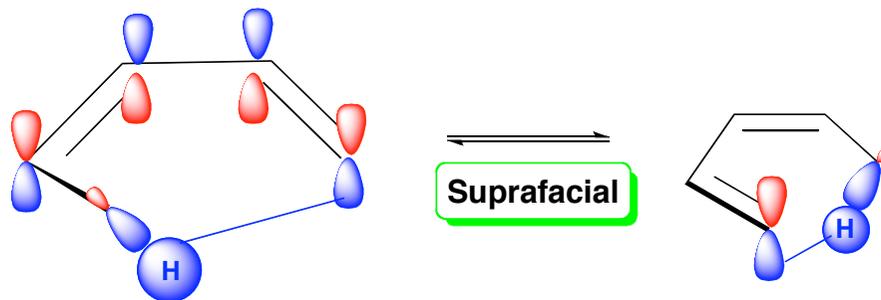
[1,3] Rearrangement (H-shift)



[1,5] Rearrangement (H-shift)

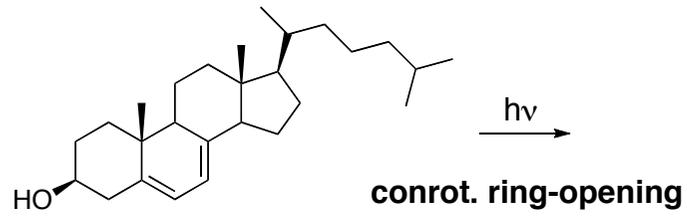
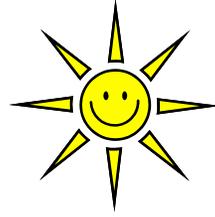


LUMO π -system butadiene

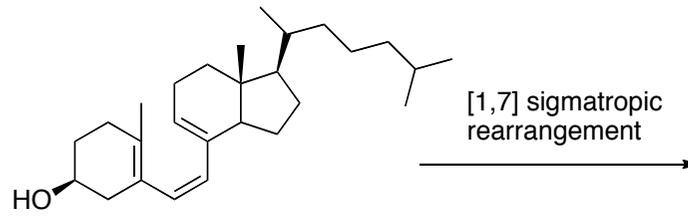


HOMO σ -bond

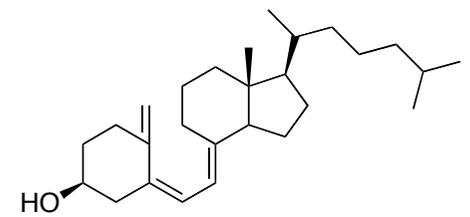
| No. of electrons | Reactions in the ground state (thermal) | Reactions in excited state (Photochem.) |
|------------------|---|---|
| $4n$ | Antarafacial | Suprafacial |
| $4n + 2$ | Suprafacial | Antarafacial |



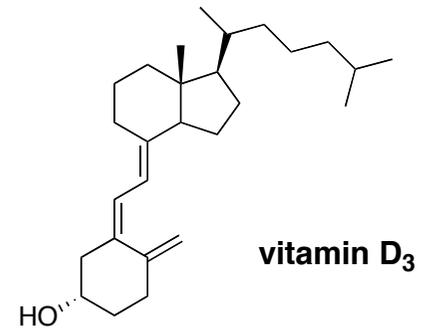
**7-dehydrocholesterol
cyclohexadiene**



previtamin D₃



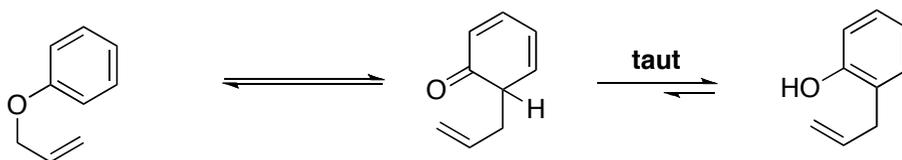
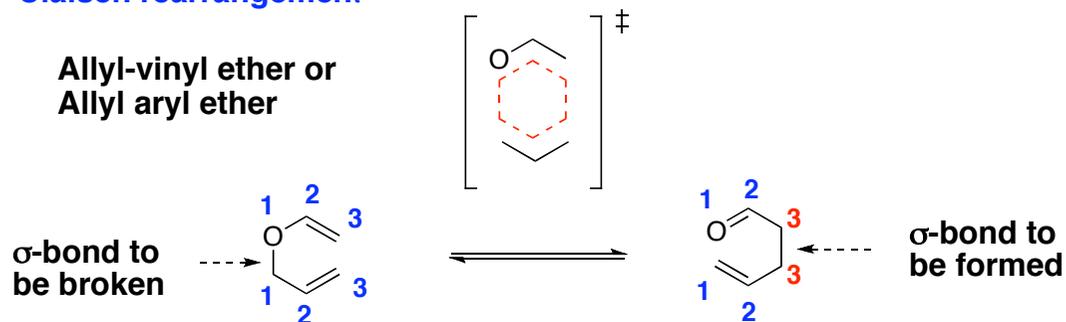
|||



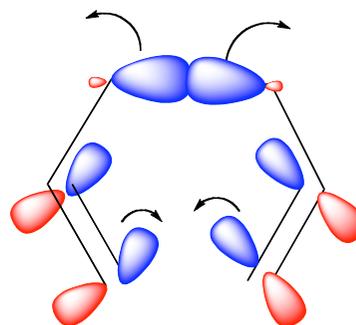
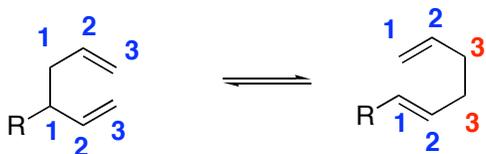
[3,3] Rearrangements; Claisen rearrang. etc.

Claisen rearrangement

Allyl-vinyl ether or
Allyl aryl ether

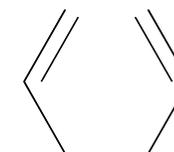


Cope rearrangement



Suprafacial
Disrotatory

6 electrons
($4n+2$)



Oxy-Cope rearrangement

