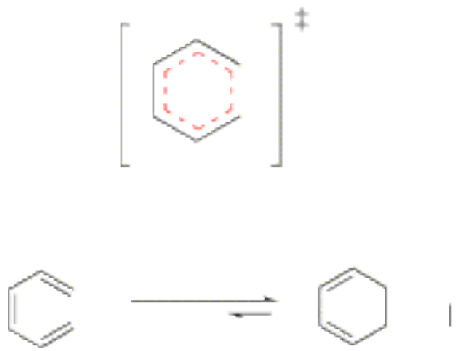
Pericyclic Reactions (McM chapt 30)

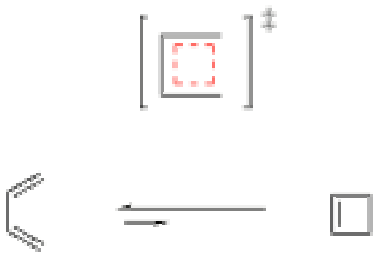
- **Polar react. (nucleophiles and electrophiles)** 

- **Radical react.** 

- **Pericyclic react. (concerted, cyclic TS$^{\#}$)**
  - **Electrocyclic react.**
  - **Cycloadditions (*i.e.* Diels Alder)**
  - **Sigmatropic rearrangement**

- **Pericyclic react. (concerted, cyclic TS[#])**
  - **Electrocyclic react.** →
    - **Rearrangement of polyene**
    - **Termal (react. in ground state) or photochemical (react of exited state)**
  - **Cycloadditions (*i.e.* Diels Alder)**
  - **Sigmatropic rearrangement**

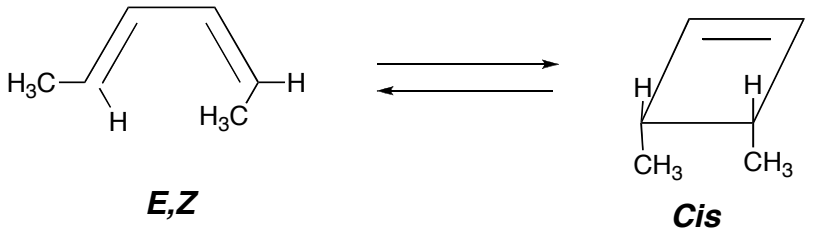




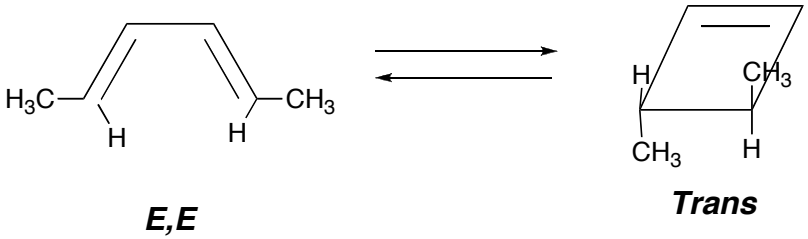
ring strain

Electrocyclic react. - Stereospesific react.

Termal cond.:



E,Z ***Cis***



E,E ***Trans***

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

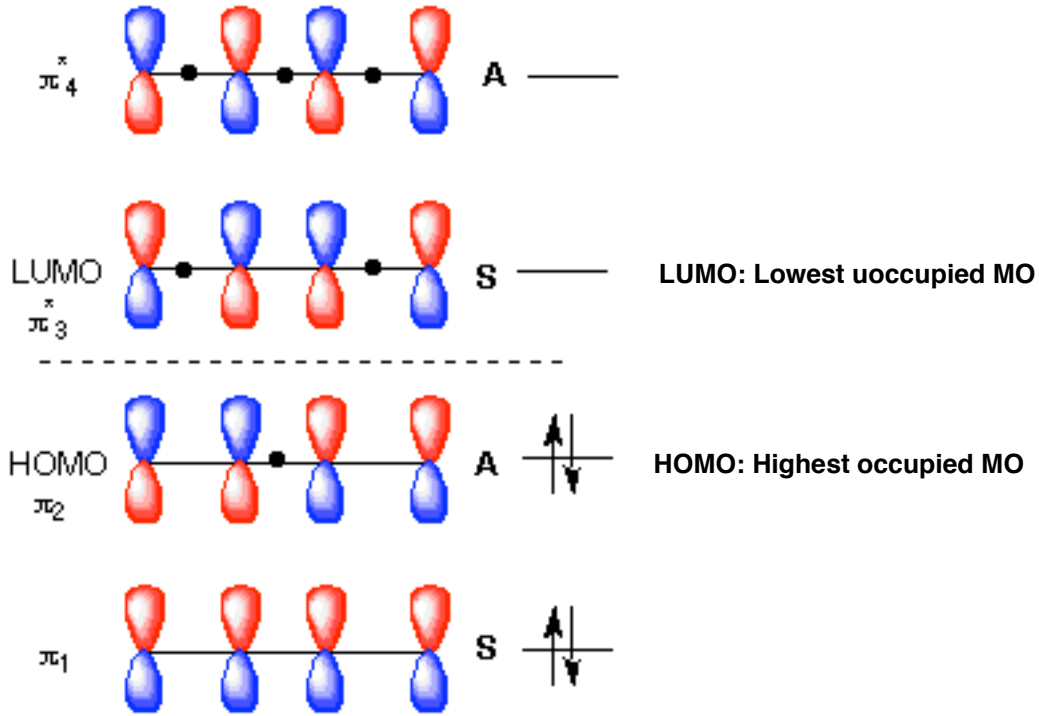
Results can generally be predicted just by looking at Front Molecular Orbitals (FMO; HOMO and LUMO) - Fukui

Symmetry allowed react.

Woodward Hoffmann rules

Symmetry in reactants are preserved during pericyclic react.

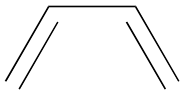
Results can generally be predicted just by looking at Front Molecular Orbitals (FMO; HOMO and LUMO) - Fukui



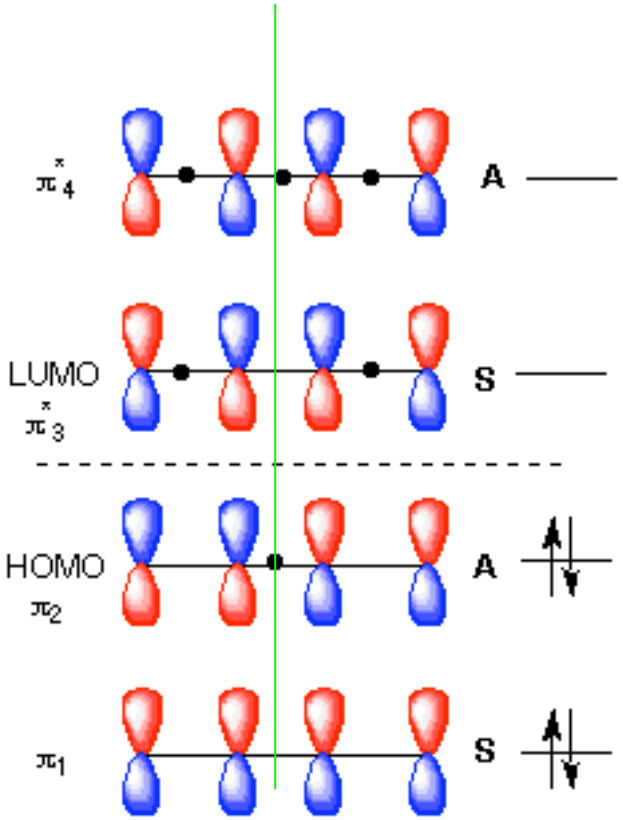
LUMO: Lowest uoccupied MO

HOMO: Highest occupied MO

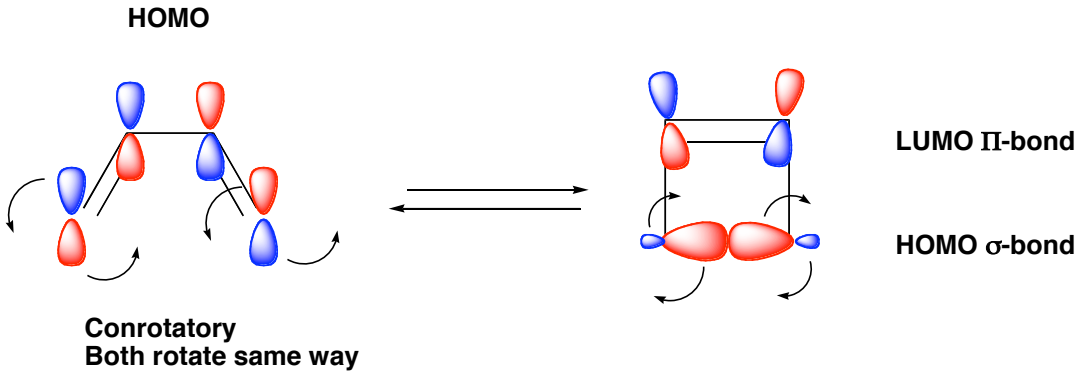
Butadiene (ground state)



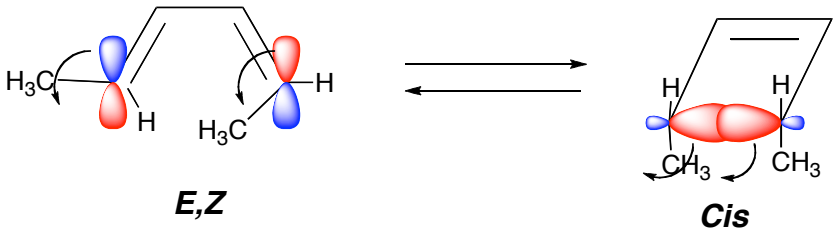
Molecular orbitals 1,3-butadiene



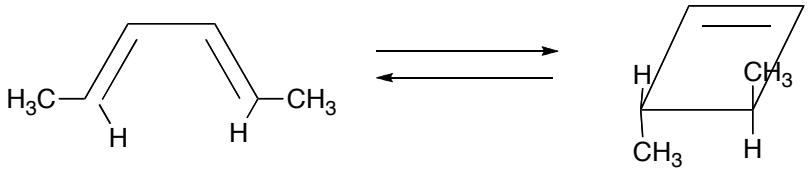
S: Symmetric
A: Antisym.



Stereospesific react.

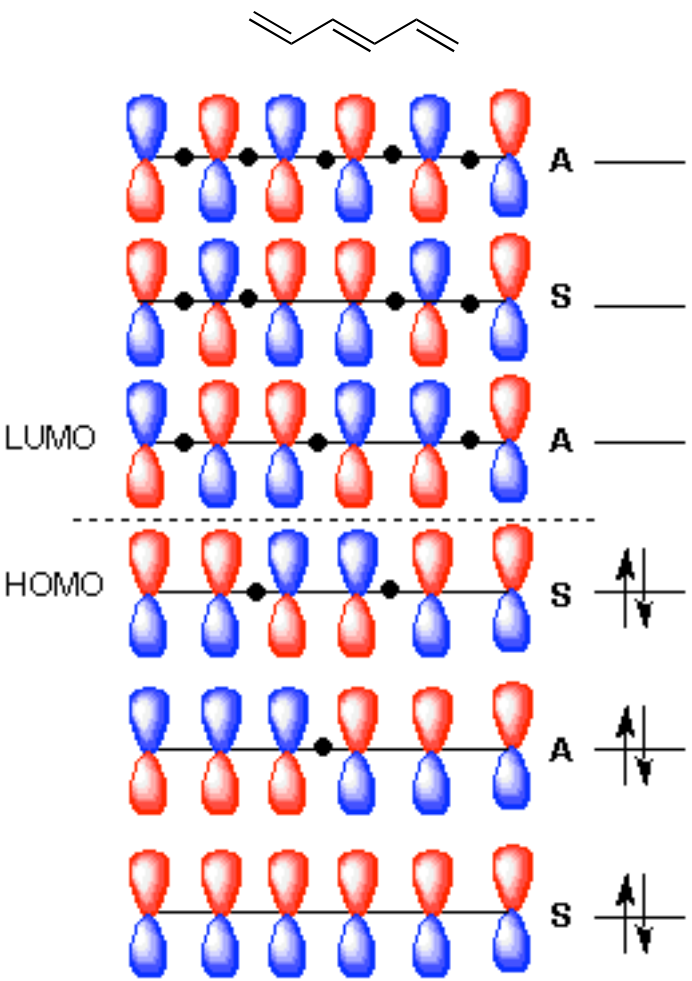


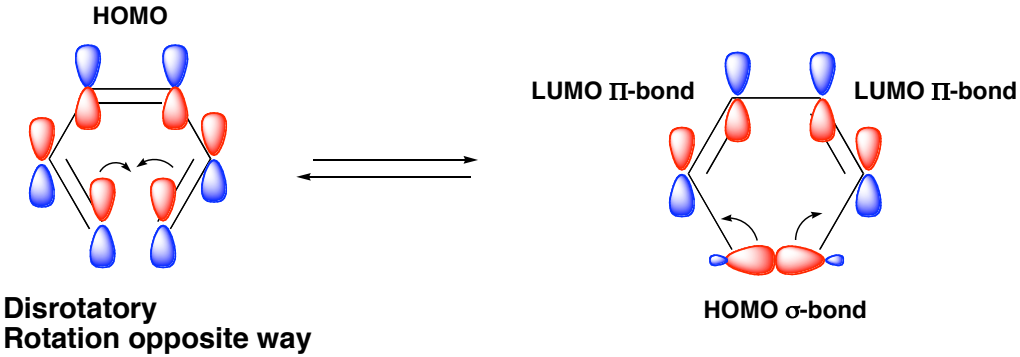
E,Z *Cis*



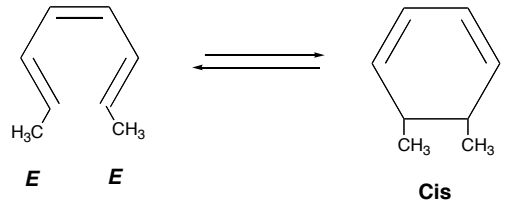
E,E *Trans*

Molecular orbitals hexatriene

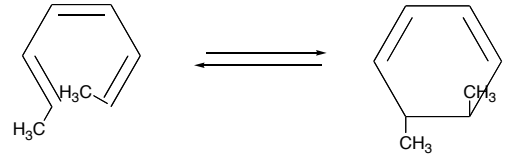




Disrotatory
Rotation opposite way



E *E* Cis

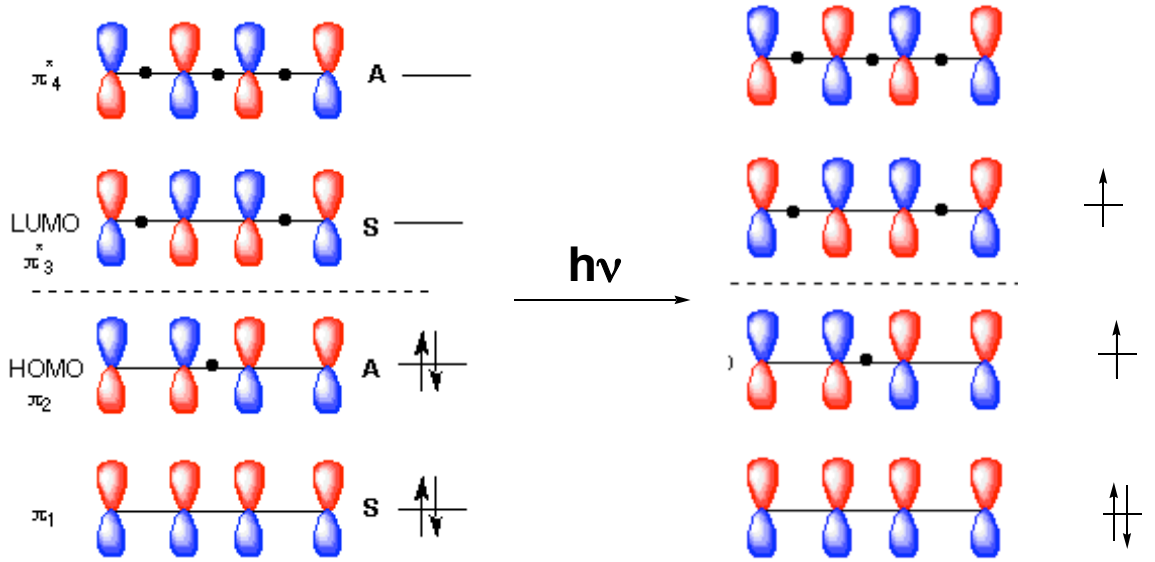


E *Z* Trans

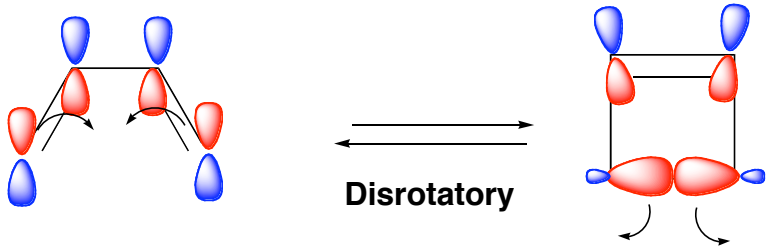
Electrocyclic react. -Symmetry allowed

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

Photochemical electrocyclic react.

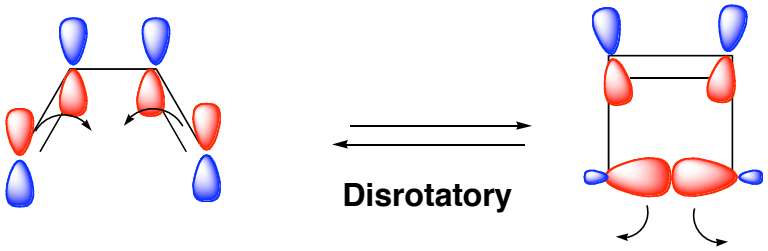


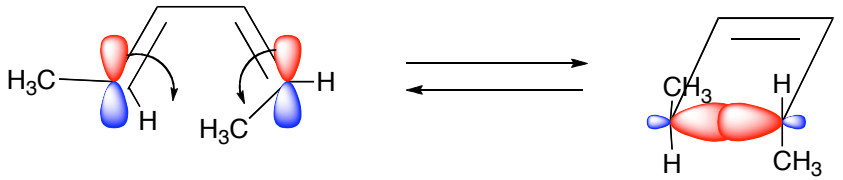
HOMO exitet state
(= LUMO ground state)



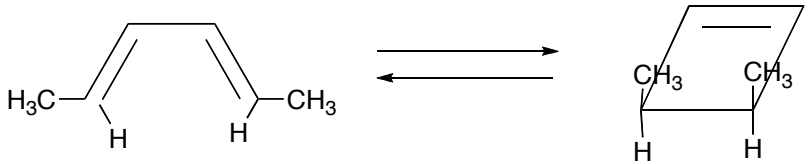
Photochemical electrocyclic react. - opposite stereochemistry

HOMO exitet state
(= LUMO ground state)



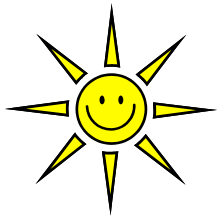


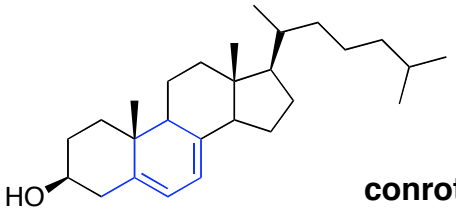
E,Z ***trans***



E,E ***cis***

No. of electrons	Reactions in the ground state (termal)	Reactions in exited state (Photochem.)
4n	Conrotatory	Disrotatory
4n + 2	Disrotatory	Conrotatory

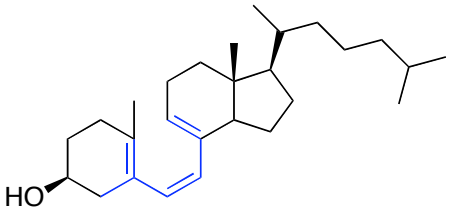




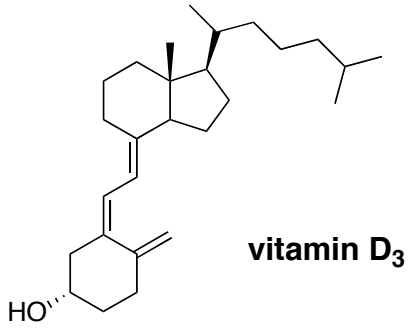
7-dehydrocolestol
cyclohexadiene

hν

conrot. ring-opening



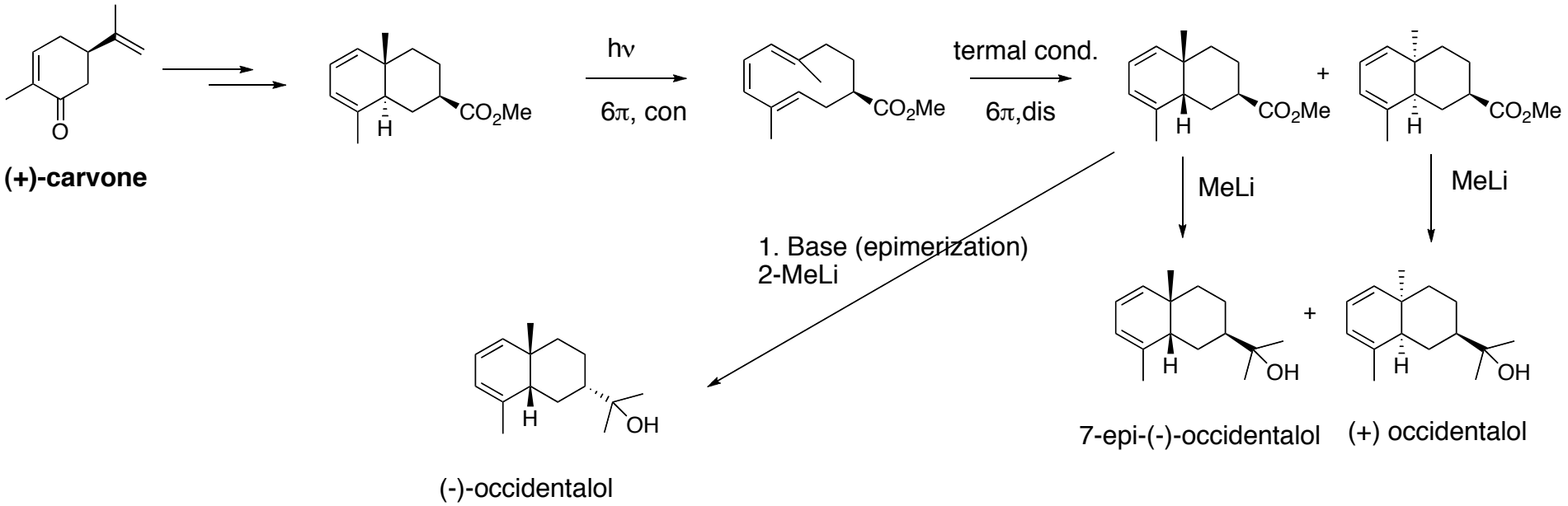
previtamin D_3



vitamin D_3

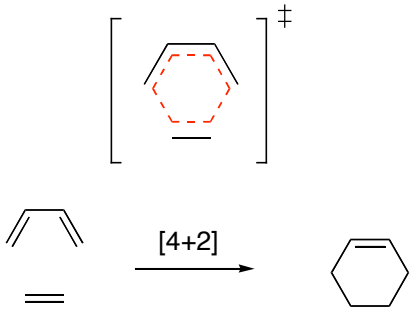
Applications in synthesis - Synthesis of occidentalol

***J. Org. Chem.* 1973, *38*, 728**



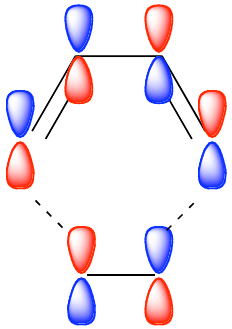
Cycloadditions (i.e. Diels Alder)

[4+2] add. termal cond.



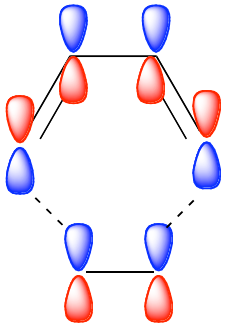
Stereospecific react.

Suprafacial cycloadd.



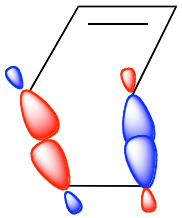
HOMO - Diene

LUMO - dienophile



LUMO - diene

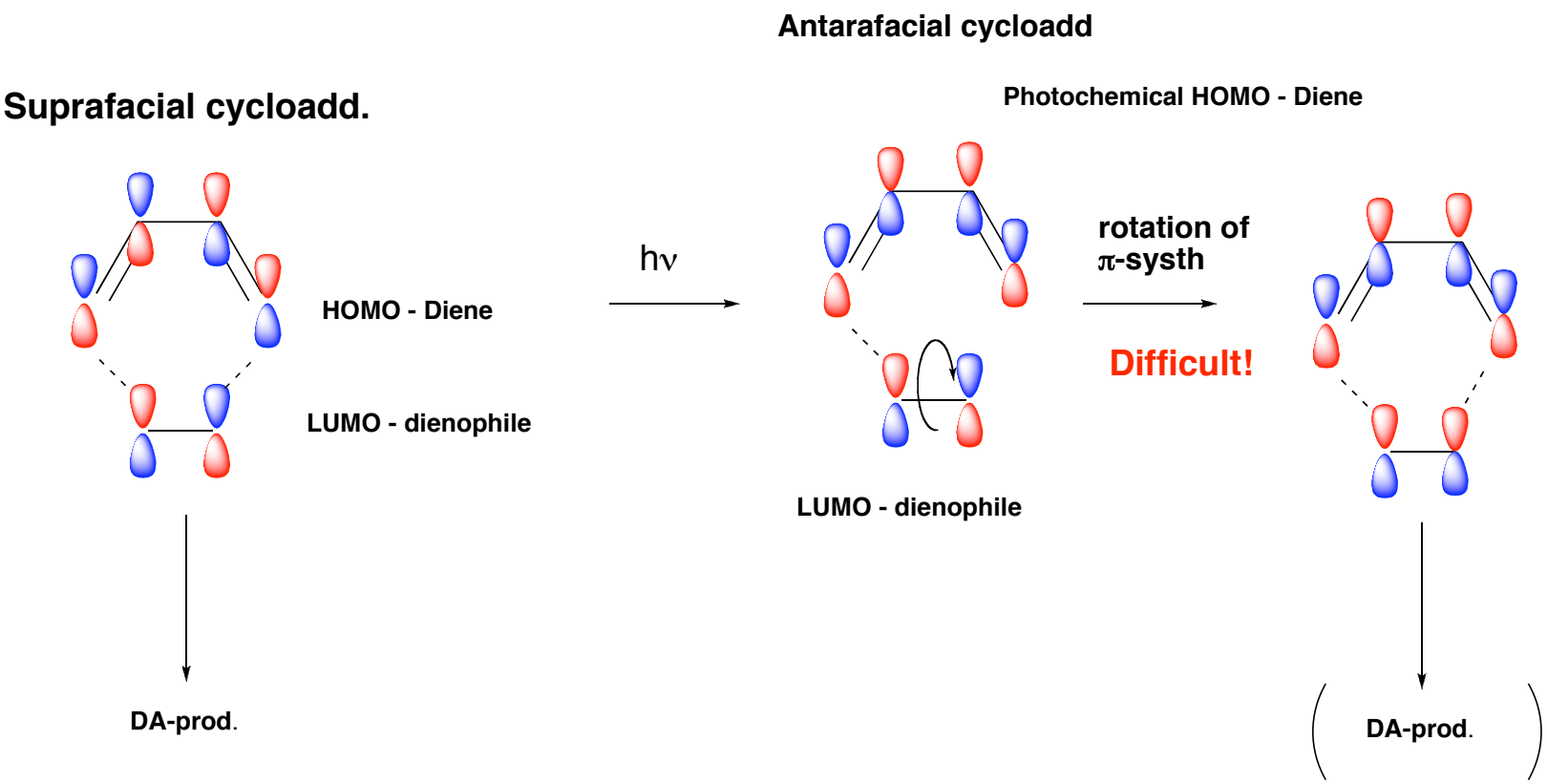
HOMO - dienophile



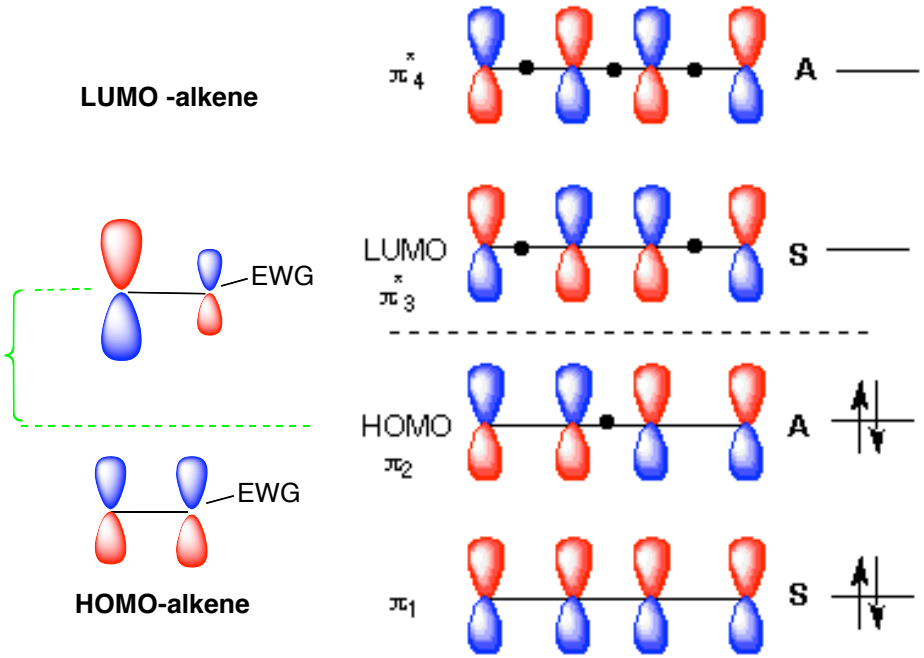
Both interact. may lead to product

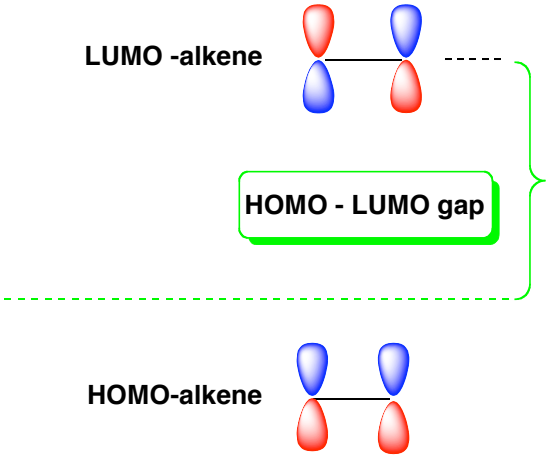
In reality, the electron rich species reacts via its HOMO and the electron poor species via its LUMO.

Suprafacial and antarafacial cycloadd.



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

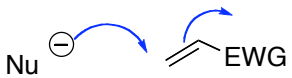




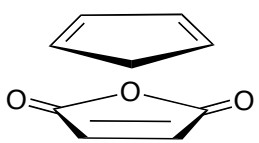
Ethene etc, very low react.

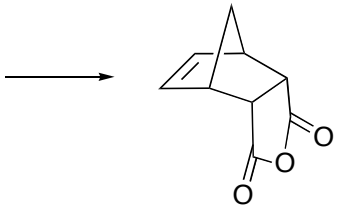
Michael accept.
Lower LUMO, largest coefficient on β-carbon

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

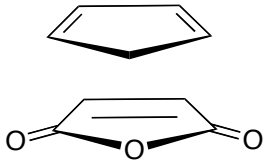


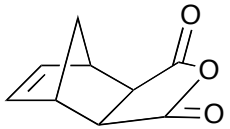
endo - exo selectivity (Not in McM)



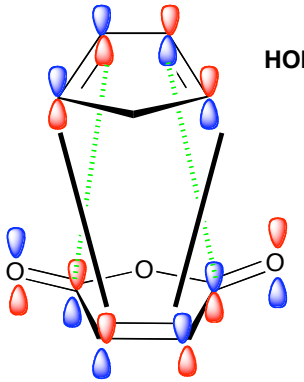


Endo





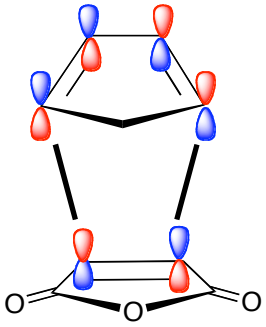
Exo



HOMO - Diene

Primary interact., bond formation

Secondary interact., extra TS$^{\#}$ stabil.

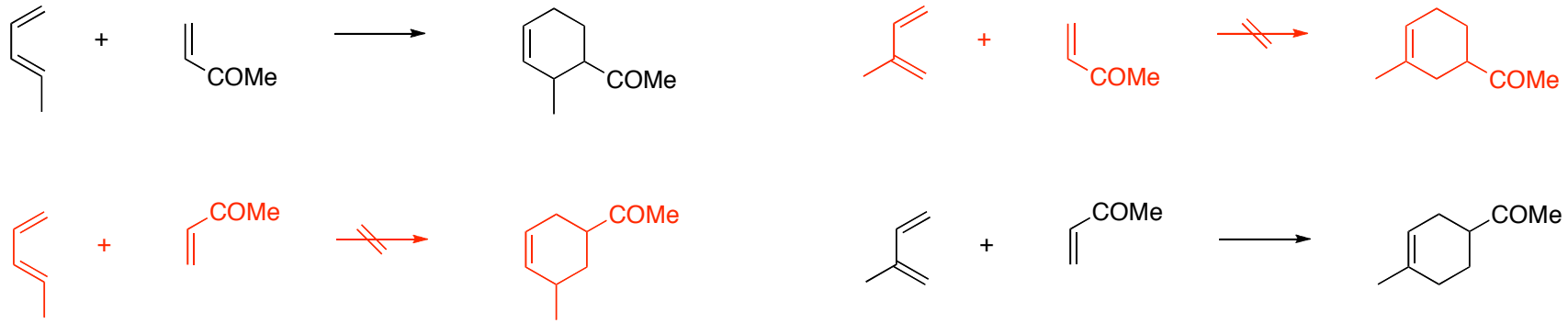


HOMO - Diene

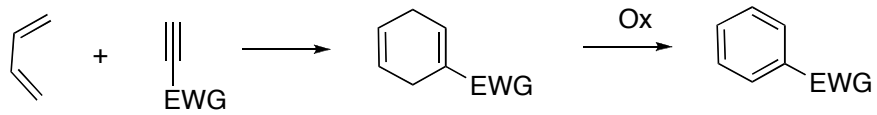
LUMO - dienophile

Regioselectivity in Diels Alder (Not McM)

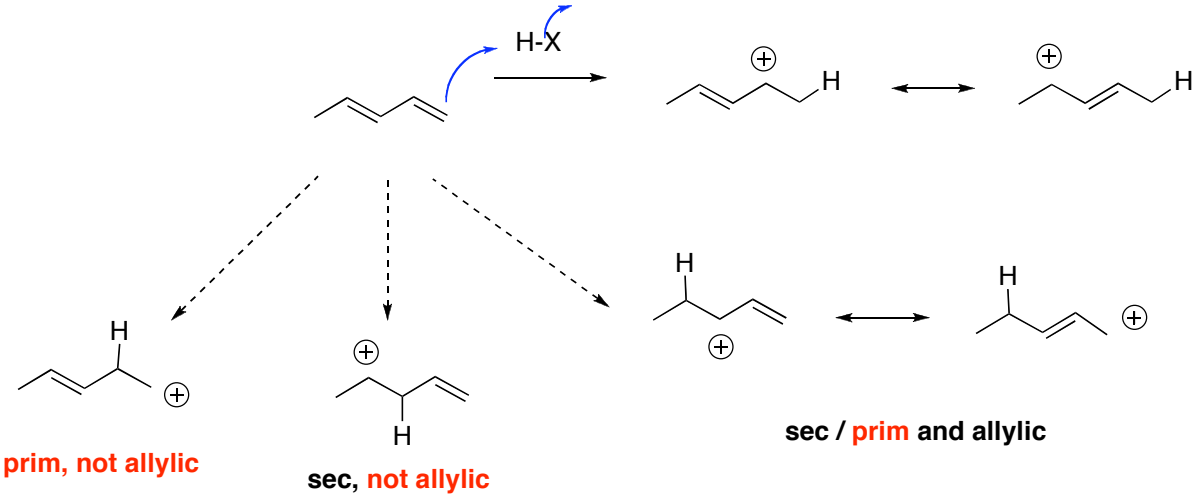
DA is “ortho - para directing”



Also alkynes, and arynes, can be dienophiles

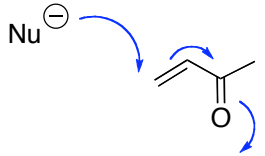


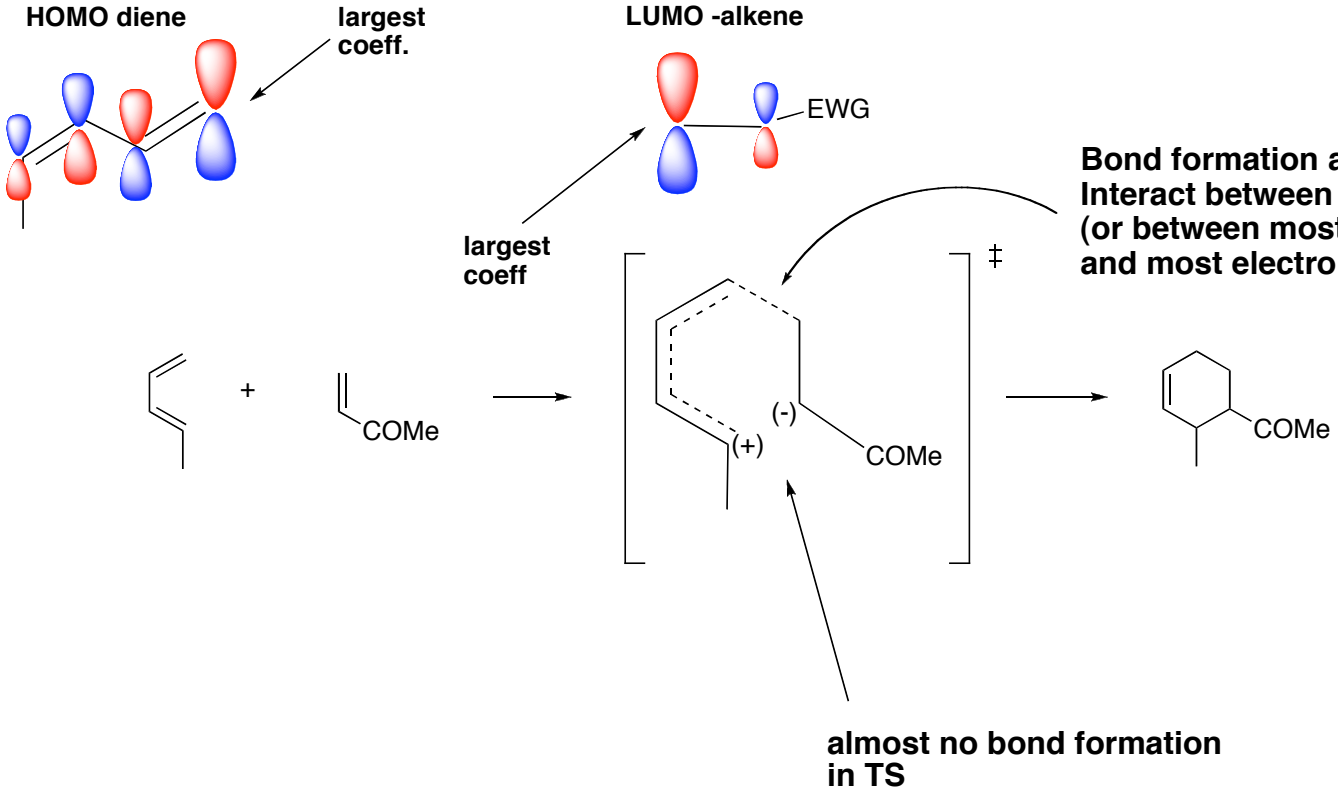
Reactivity of diene as nucleophile



sec and allylic

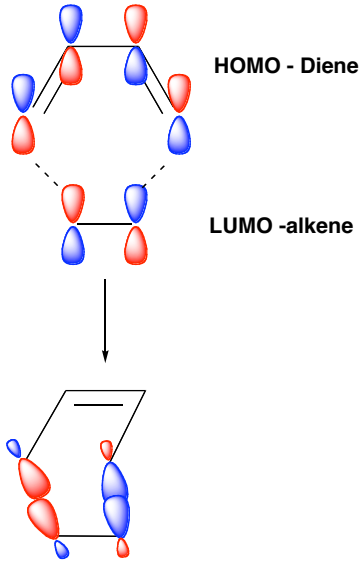
Reactivity of alkene as electrophile



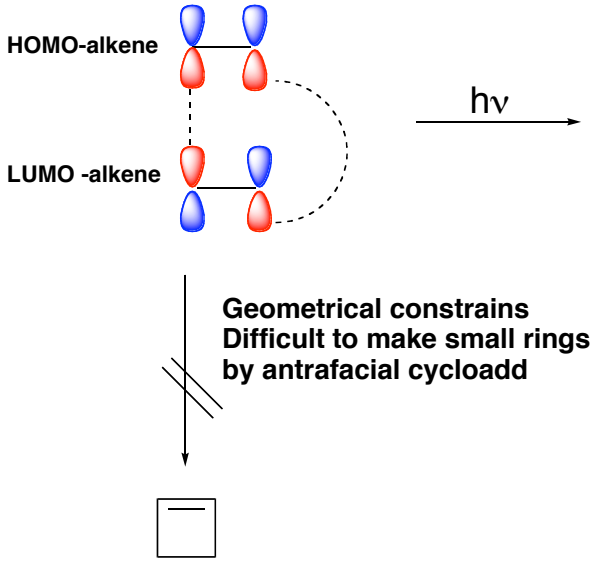


[2+2] Cycloadditions

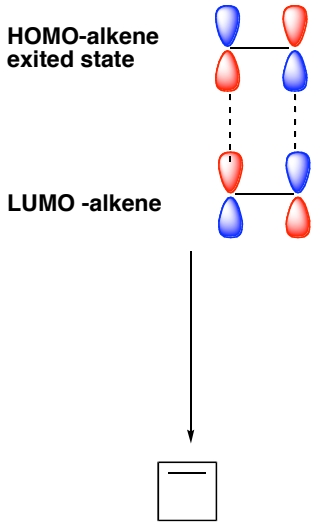
Suprafacial cycloadd.



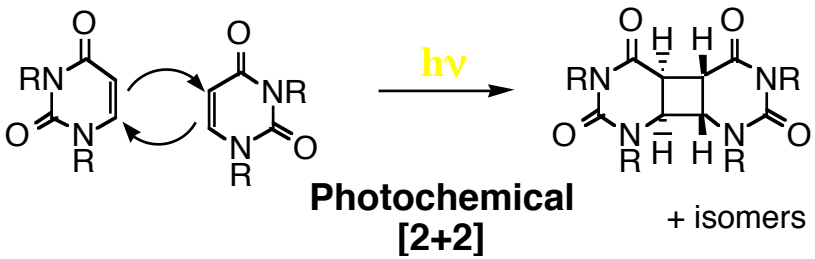
Antarafacial cycloadd. (termal cond.)

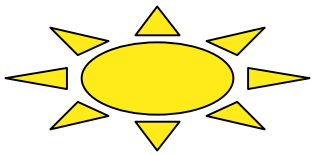


Suprafacial cycloadd. (photochem. cond.)



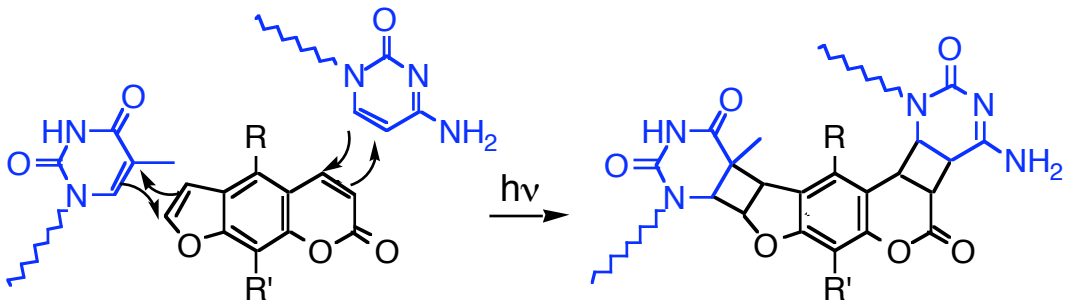
No. of electrons	Reactions in the ground state (termal)	Reactions in exited state (Photochem.)
4n	Antarafacial	Suprafacial
4n + 2	Suprafacial	Antarafacial





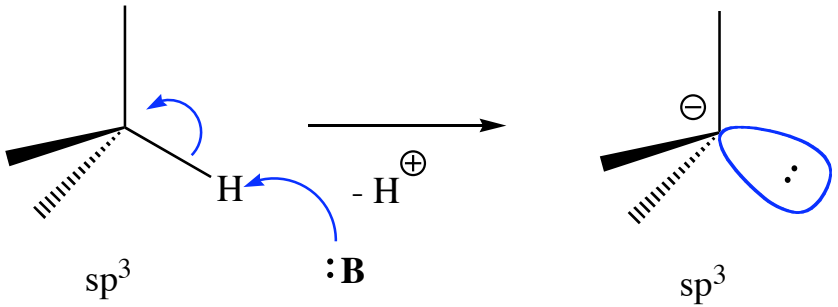
Cancer

Psoralenes - Psoriasis

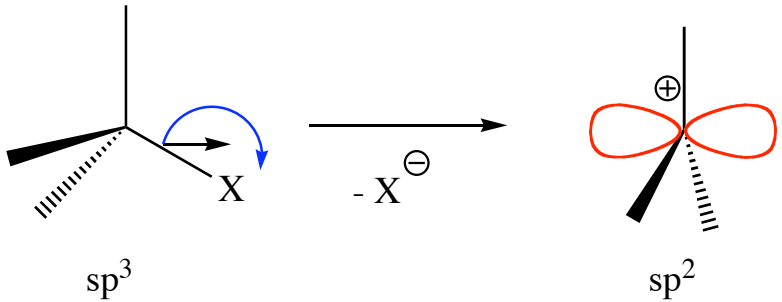


Carbenes

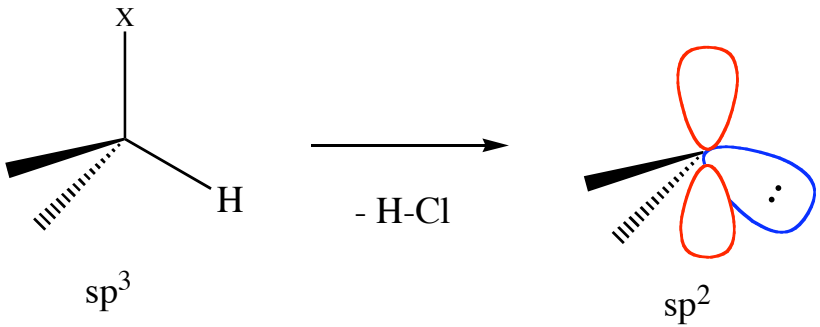
McM chapt 7.6, lab ex. 7



Carbanion



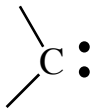
Carbocation

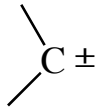


Carbene

Neutral

Divalent

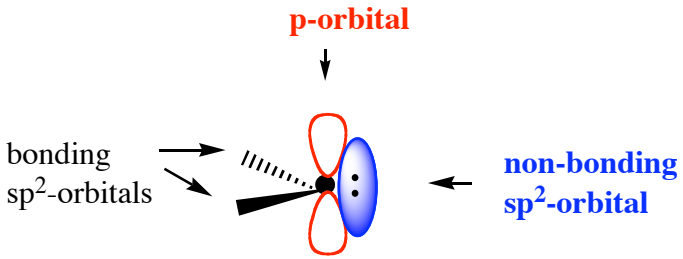




6 valence electrons - Highly reactive $t_{1/2} < 1$ s

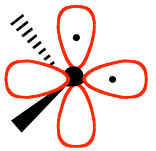
Electron deficient /electrophilic properties

singlet carbene



electron pair, opposite spin
cation / anion properties

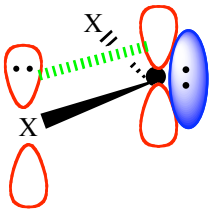
triplet carbene



2 half-filled p-orbitals
electrons with parallell spin

diradical properties
Gives triplet signal in esr spektrum

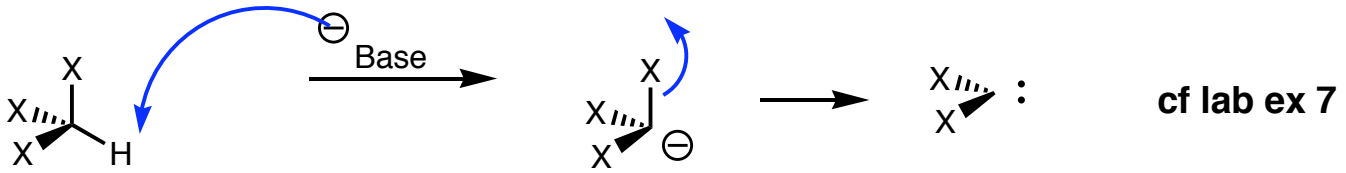
Triplet normally somewhat more stable than singlet
Singlets more reactive



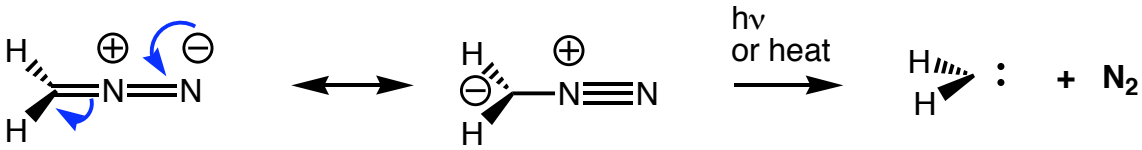
dihalocarbene
Stabilizing overlap
in singlet state

Carbenes and carbeniods in synthesis

Generation of carbenes



Not in McM

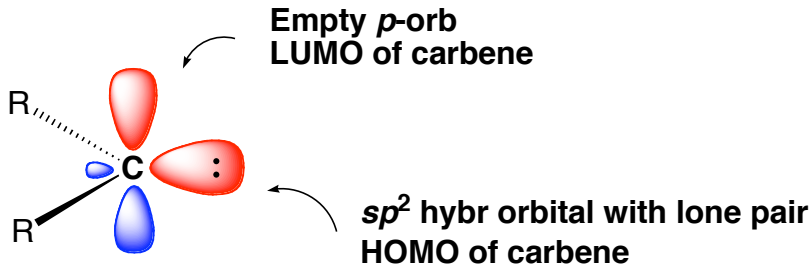


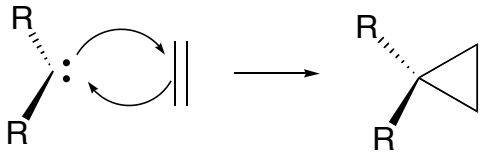
Diazomethane
(toxic, explosive)

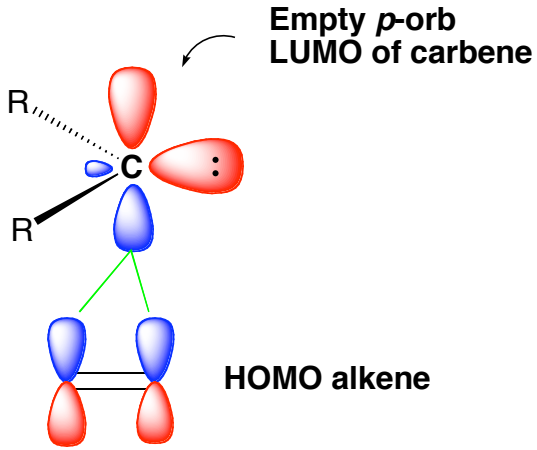
(From Hg-species)

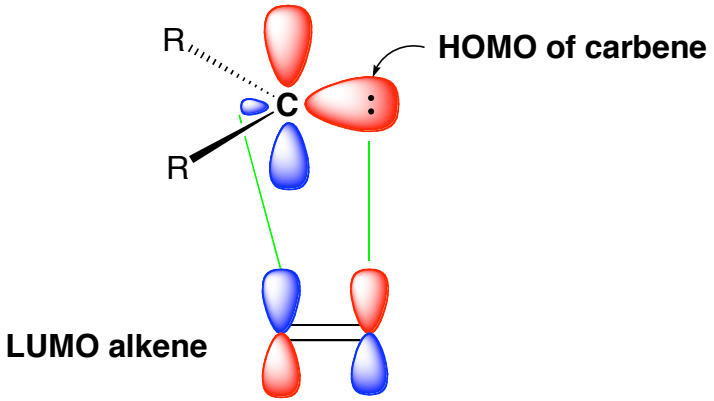
Carbene Cycloadditions

Singlet Carbene

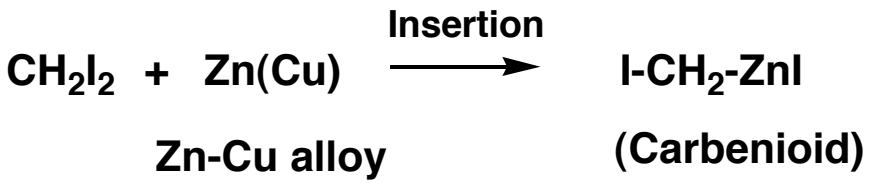




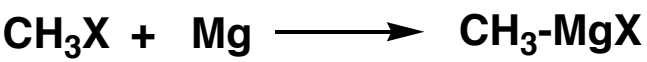




Carbenoids - Simmons Smith reaction

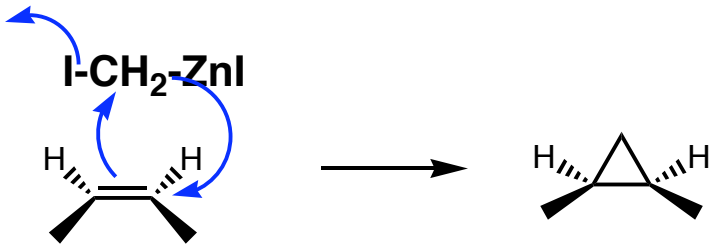


cf. Grignard



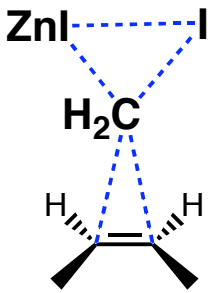
Other methods

reactants	active reagent
Et_2Zn, CH_2I_2	$EtZnCH_2I$ or $Zn(CH_2I)_2$
EtZnI, CH_2I_2	$IZnCH_2I$
TFA, Et_2Zn,CH_2I_2	$CF_3COOZnCH_2I$
Sm(Hg), CH_2I_2	$ISmCH_2I$
R_3Al, CH_2I_2	R_2AlCH_2I
ZnX_2, CH_2N_2	$Zn(CH_2I)_2$

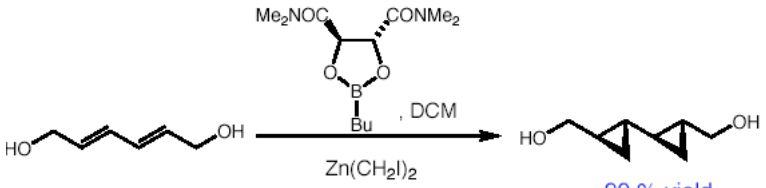


- **One-step - Concerted**
- **Stereospesific**

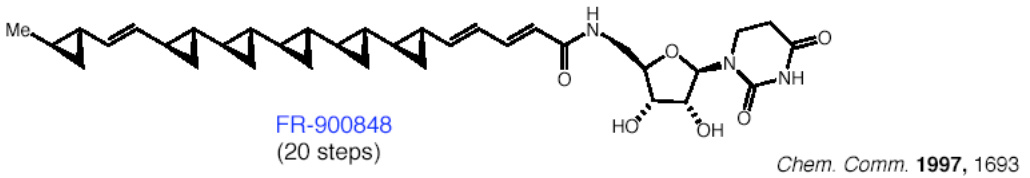
$TS^{\#}$?



Enentioselective Simmons Smith
Allylic alcohols (Chiral auxilary or catalyst)



90 % yield
>99 % ee

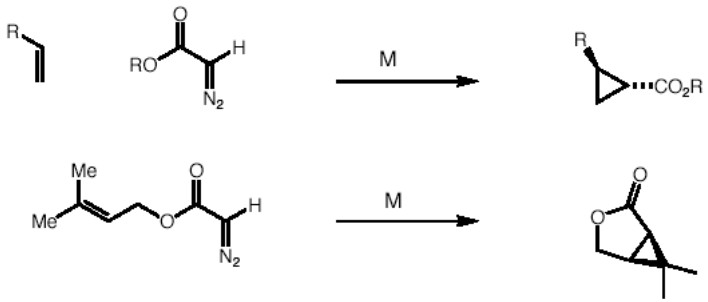


FR-900848
(20 steps)

Chem. Comm. **1997,** 1693

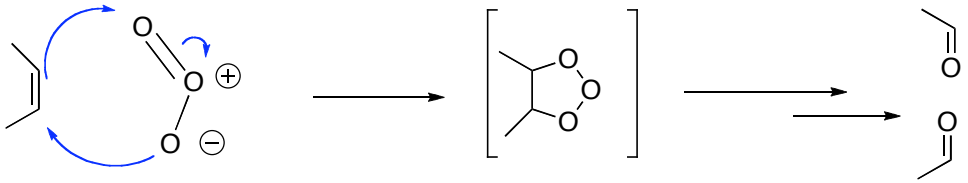
antifungal, nat. prod.

Other carbenoids

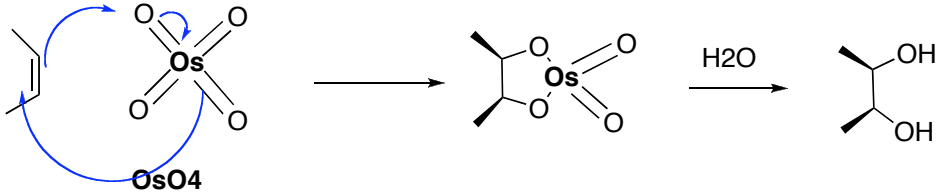


metal carbenoids
(M = Rh, Pd, Cu....)

Cycloadditions with 1,3-dipolar reagents
[4+2] cycloadd. Not in McM

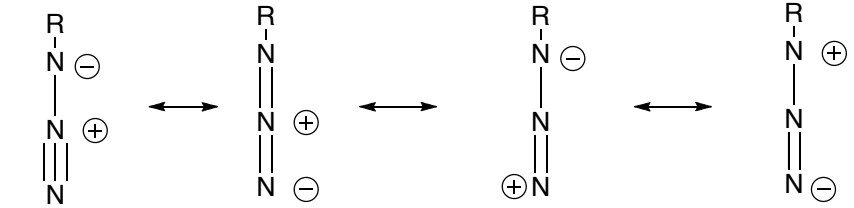


Ozone

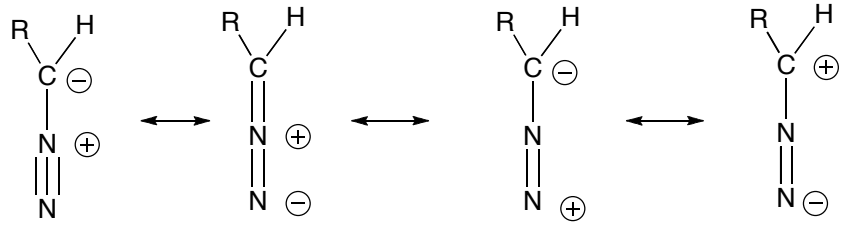


OsO4

Other ex of 1,3-dipoles



azides



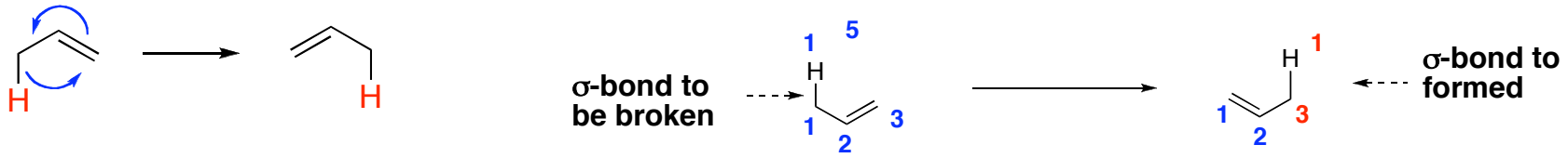
diazoalkanes

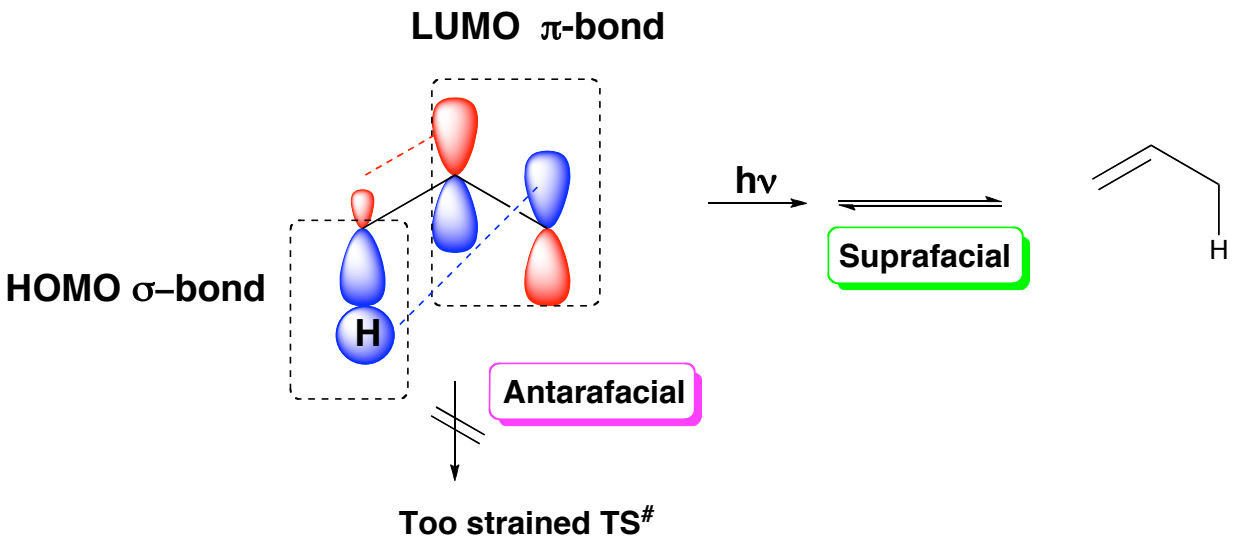
Synthesis of heterocycles

Sigmatropic Rearrangements

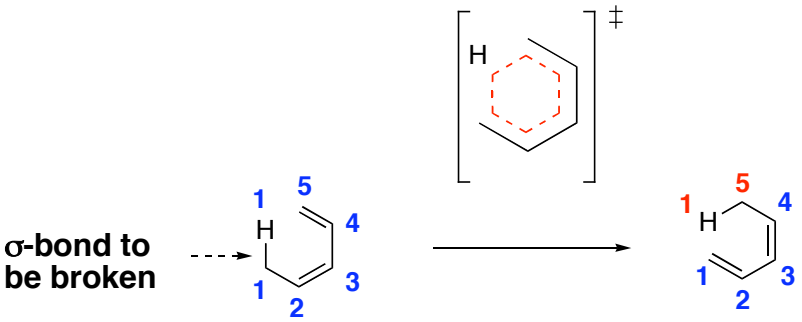
σ-bonded subst migrates accross a π-electron systhem

[1,3] Rearrangement (H-shift)

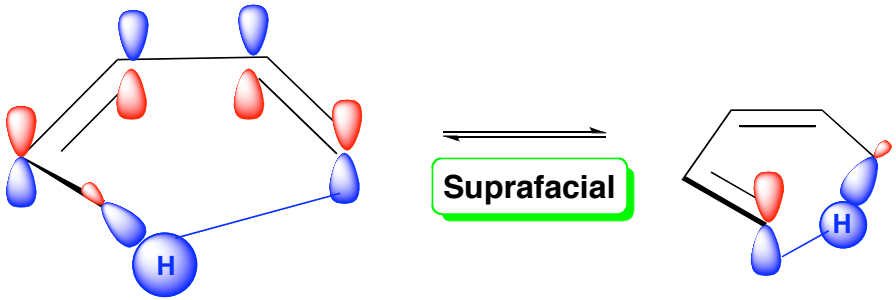




[1,5] Rearrangement (H-shift)

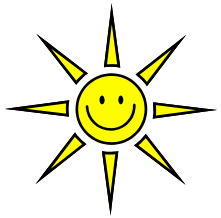


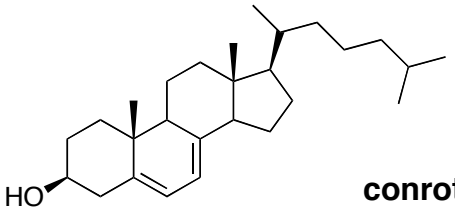
LUMO π-systhem butadiene



HOMO σ–bond

No. of electrons	Reactions in the ground state (termal)	Reactions in exited state (Photochem.)
4n	Antarafacial	Suprafacial
4n + 2	Suprafacial	Antarafacial

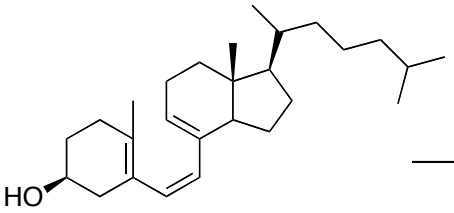




7-dehydrocolestol cyclohexadiene

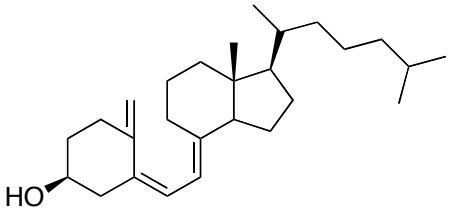
hν

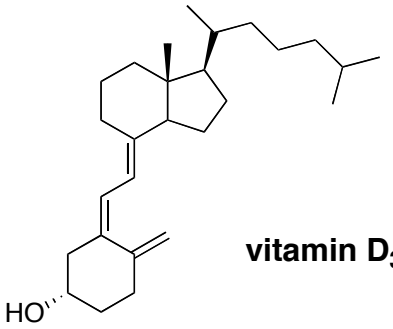
conrot. ring-opening



previtamin D_3

[1,7] sigmatropic rearrangement



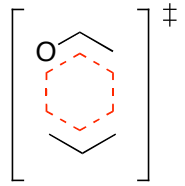


vitamin D_3

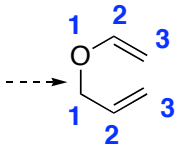
[3,3] Rearrangements; Claisen rearrang. etc.

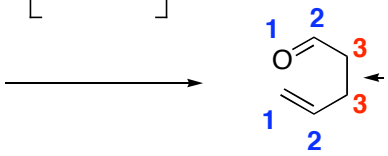
Claisen rearrangement

Allyl-vinyl ether or
Allyl aryl ether

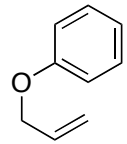


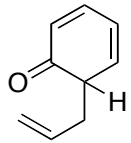
σ-bond to be broken



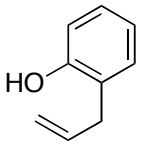


σ-bond to be formed

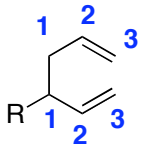


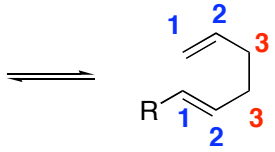


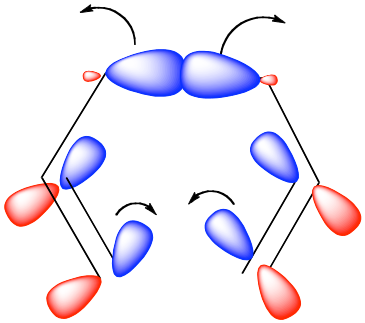
taut



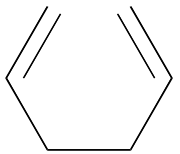
Cope rearrangement





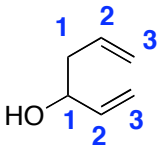


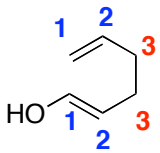
Suprafacial
Disrotatory



6 electrons
(4n+2)

Oxy-Cope rearrangement





taut