# Chap. 8 Réactions péricycliques

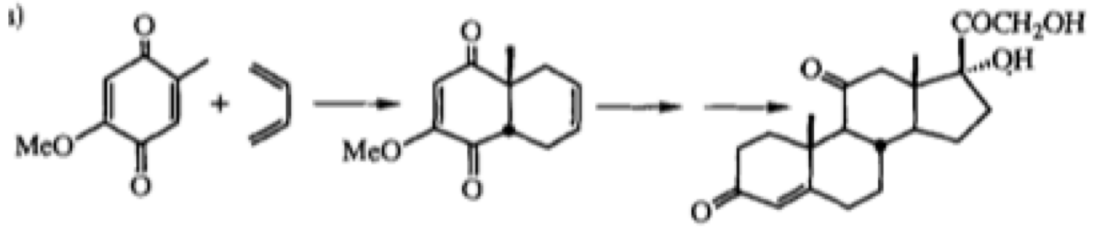
## 8.1- Historique

R. Woodward :

The Nobel Prize in Chemistry 1965
Robert B. Woodward

Synthèses totales où réactions de Diels-Alder, réarrangements de Cope, Claisen, etc…

Pb de compréhension et donc de prédiction



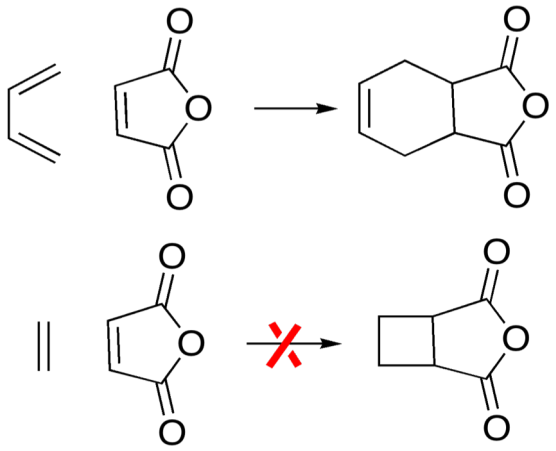

eg synth Cortisone
*JACS* **1952**, *74*, 4223

Réactions peu influencées par :

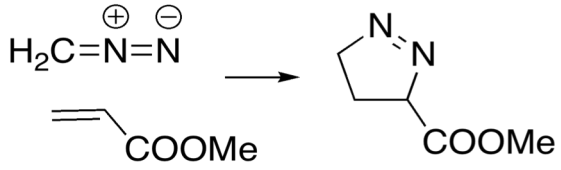
- charges
- solvant
- effet stériques

pb de réactivité

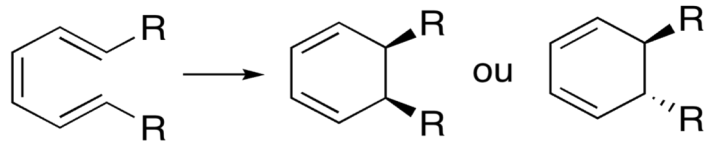
pb de régio & stéréosélectivité

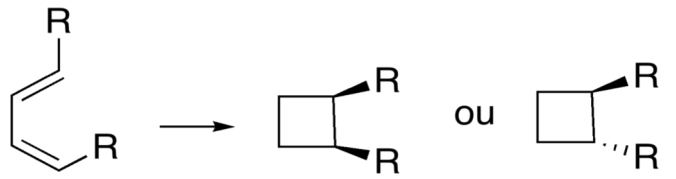


cycloaddition

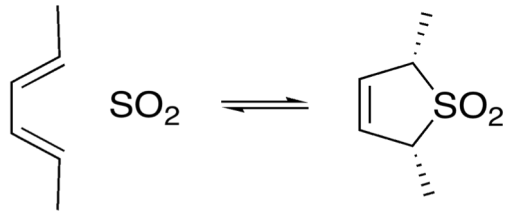


cycloaddition

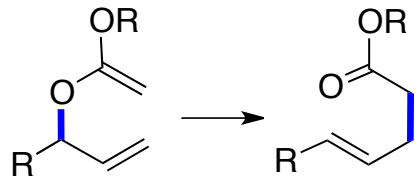




électrocyclisation



réactions chélétropiques



sigmatropie

⇒ Théorie ?

R. Hoffmann

OF, etc … de K. Fukui

K. Fukui
*Tetrahedron Lett.* **1965**, 2009 & 2427
*Acc. Chem. Res.* **1971**, *4*, 57

⇒ Théorie OF, etc … de K. Fukui

K. Fukui
*Tetrahedron Lett*. **1965**, 2009 & 2427
*Acc*. *Chem*. *Res*. **1971**, *4*, 57

Woodward-Hoffmann : R. B. Woodward, R. Hoffmann

*J*. *Am*. *Chem*. *Soc*. **1965**, *87*, 395 & 2046 & 2511 & 4389
*Angew*. *Chem*. *I*. *E*. **1969**, *8*, 781

- Def. Réactions péricycliques :

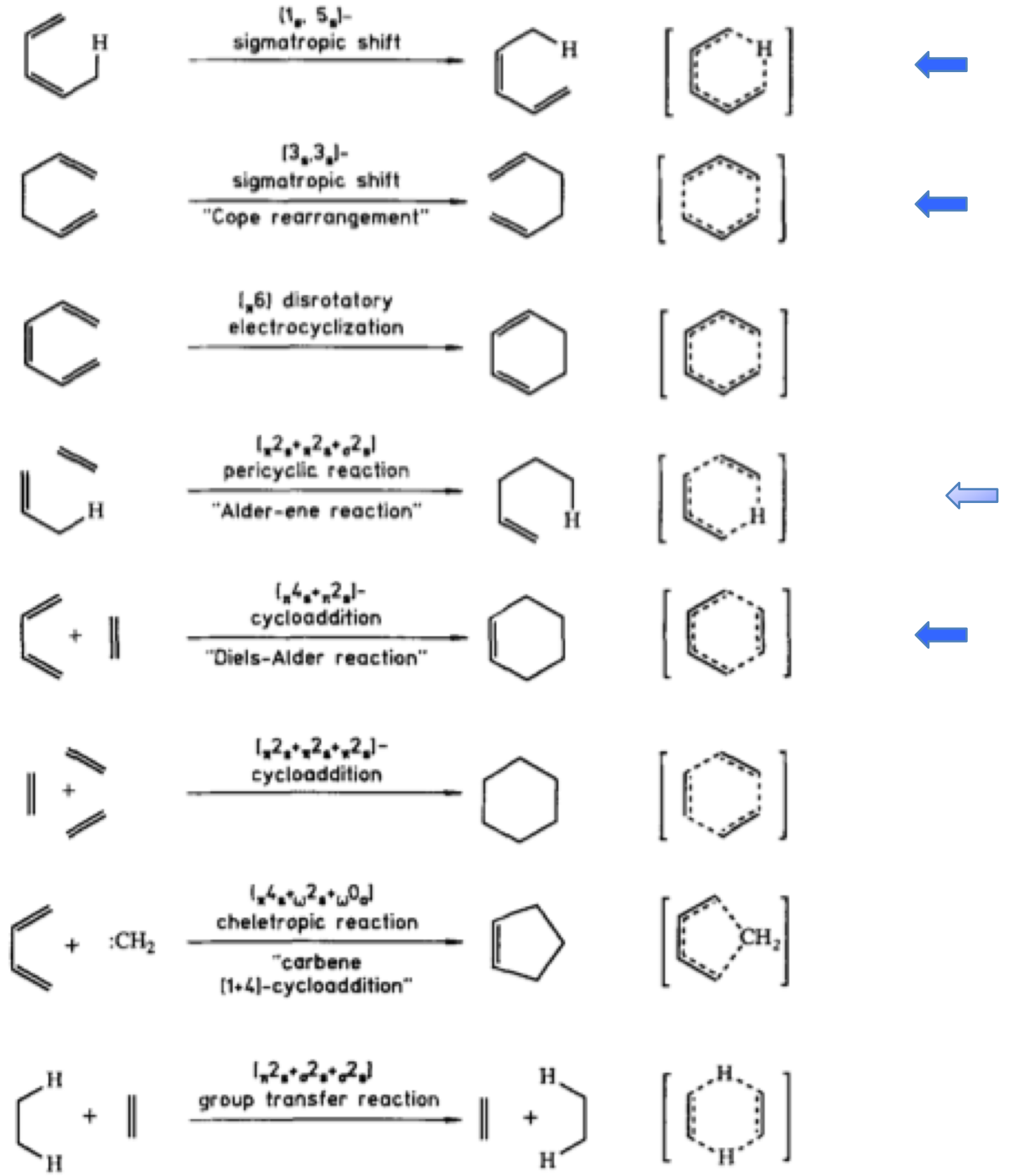
" reactions in which all 1st-order changes in bonding relationships take place in concert on a closed curve "

Formation ou migration de liaison σ à partir de liaisons C=C via un mécanisme concerté avec un mouvement cyclique des électrons

- 5 catégories :
  - cycloaddition
  - réactions électrocycliques
  - sigmatropies
  - réactions chélétropiques
  - réactions de transfert de groupe

Réactions péricycliques :

à 6 e



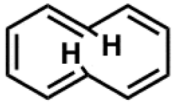

K. N. Houk et al.
*Angew. Chem. I. E.* **1992**, *31*, 682

TS aromatique

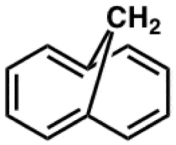
Aromaticité ?

Règle de Huckel (1931) : 4n+2 e π

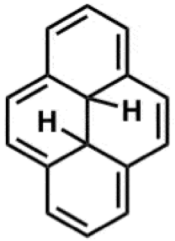
mais




not aromatic

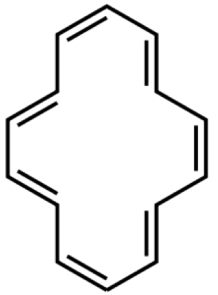



aromatic !



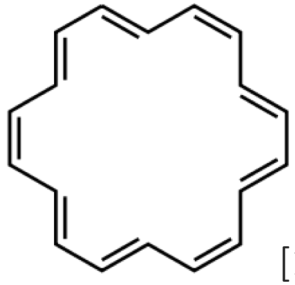

Aromatic!

14 pi electrons, cyclic, ring carbons conjugated, flat.



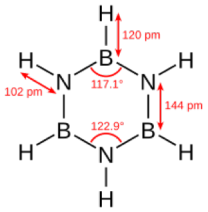
[14]annulene

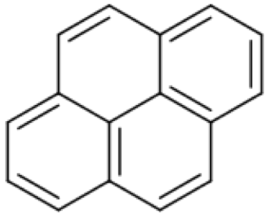
[n]annulenes

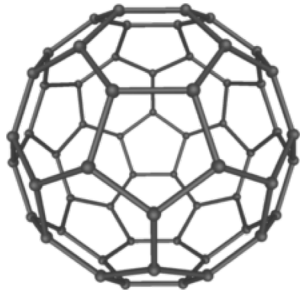


[18]annulene

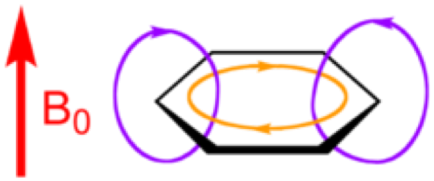
pas limité au C

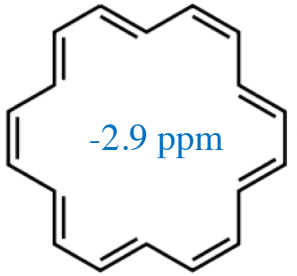




RMN: ‘courant de cycle’



Réactions péricycliques

The Nobel Prize in Chemistry 1981
Kenichi Fukui, Roald Hoffmann

In the mid-1960s, Fukui and Hoffmann discovered - almost simultaneously and independently of each other - that symmetry properties of **frontier orbitals** could explain certain reaction courses that had previously been difficult to understand (Nobel Pr).

R. B. Woodward, R. Hoffmann
*The Conservation of Orbital Symmetry*
Verlag Chemie: Weinheim **1970**

K. Fukui
*Orbital Symmetry papers*
ACS **1976**

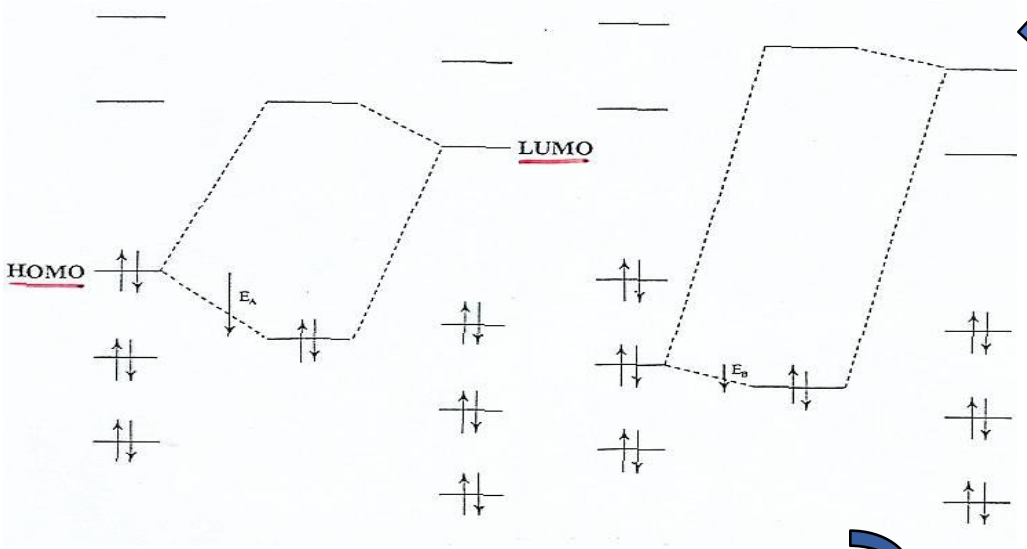
OF de Fukui

"règles" de Woodward-Hoffmann

# 8.2- Rappels OF

**Réactivité Klopman-Salem**

$$\Delta E = \underbrace{-\sum_{ab}(q_a + q_b)\beta_{ab}S_{ab}}_{\textit{first term}} + \underbrace{\sum_{k<l}\frac{Q_k Q_l}{\varepsilon R_{kl}}}_{\textit{second term}} + \underbrace{\sum_{r}^{occ.}\sum_{s}^{unocc.} - \sum_{s}^{occ.}\sum_{r}^{unocc.}\frac{2(\sum_{ab} c_{ra}c_{sb}\beta}{E_r - E_s}}_{\textit{third term}}$$




etc...

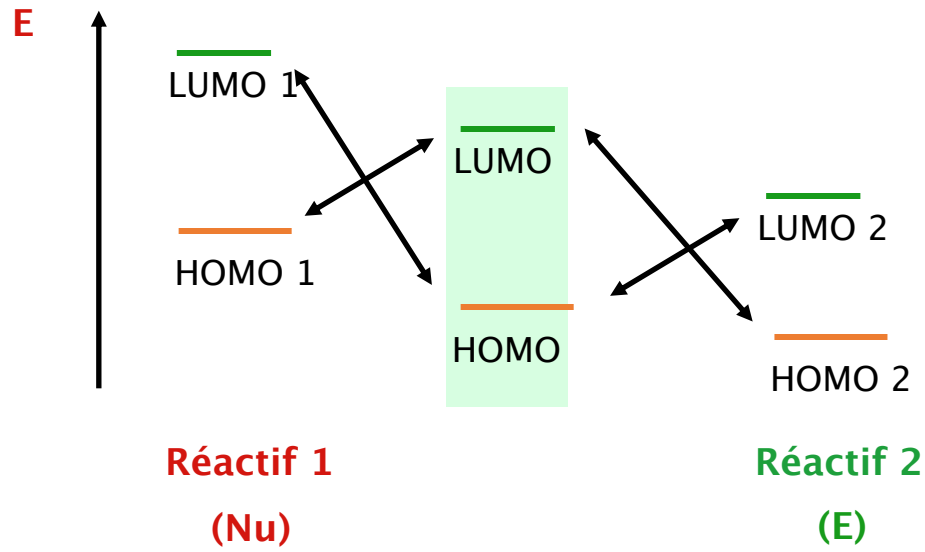
**Interaction HOMO-LUMO Prépondérante (Fukui)**

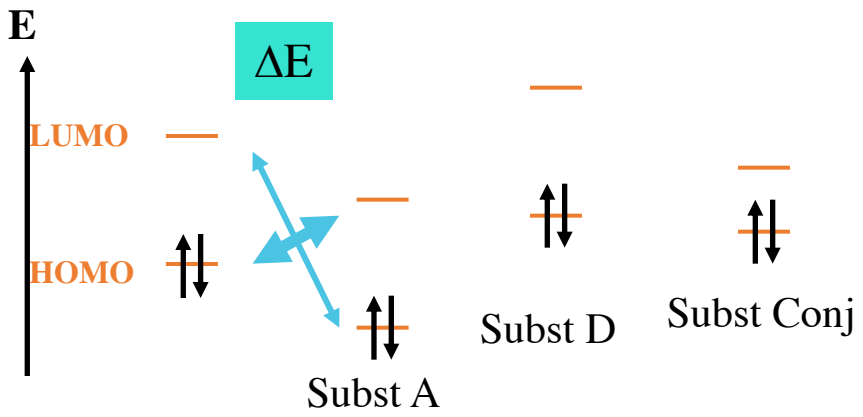
$$\Delta E = \underbrace{-\frac{Q_{nuc.}\,Q_{elec.}}{\varepsilon R}}_{\textit{The Coulombic term}} + \underbrace{\frac{2(c_{nuc.}\,c_{elec.}\,\beta)^2}{E_{HOMO\,(nuc.)} - E_{LUMO\,(elec.)}}}_{\textit{The frontier orbital term}}$$

**Interactions électrostatiques** **orbitalaires**

-«Théorie HSAB (acide/base dur/mou) »
- Mécanismes réactionnels
- Règles de Baldwin
- Base de synthèse asymétrique
- Réactions péricycliques

# Interaction HOMO-LUMO: relatif



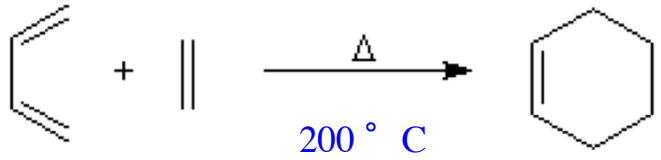

*Plus le couple HO-BV sera proche en énergie plus l'interaction sera favorable.*

cf eq. $\Delta E = Q + \dfrac{2(c_i.c_{ii}.\beta)^2}{E_{HO} - E_{LU}}$

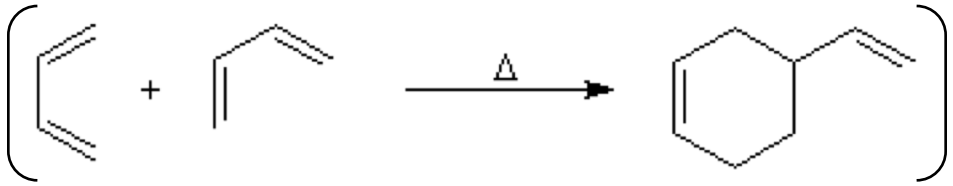
# 8.3- Réaction de Diels-Alder

The Nobel Prize in Chemistry 1950
Otto Diels, Kurt Alder

en 1928 :

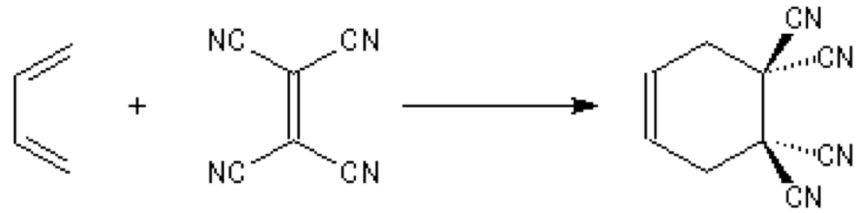



pb de réactivité

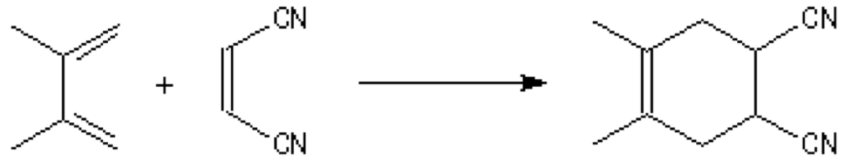


## 8.3.1 Réaction de Diels-Alder : effet de substituant

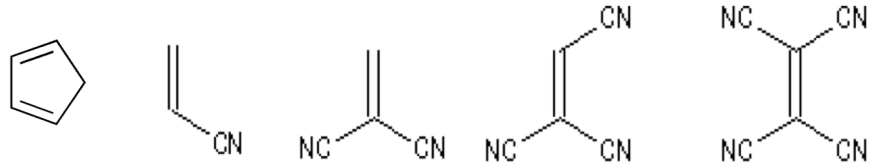
facilitée - si le diènophile porte un ou plusieurs groupes attracteurs d'électrons.




- si le diène porte des groupes donneurs d'électrons.




⇒ **"Règle" d'Alder :** la vitesse (d'une réaction de D-A) croît si l'un des partenaires est enrichi et l'autre appauvri en électrons



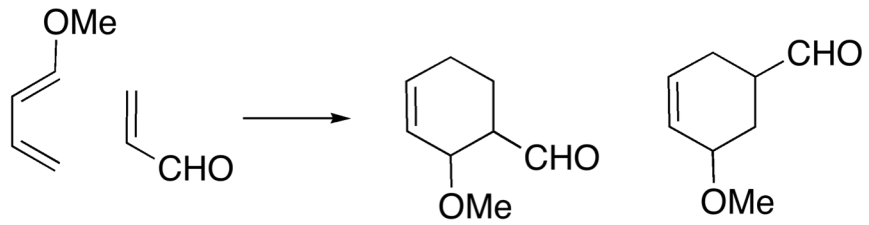

*K* 1 $45{,}5\ 10^3$ $48{,}0\ 10^4$ $43{,}0\ 10^6$

- Idem si acide (Lewis)

➡ pb de réactivité ?

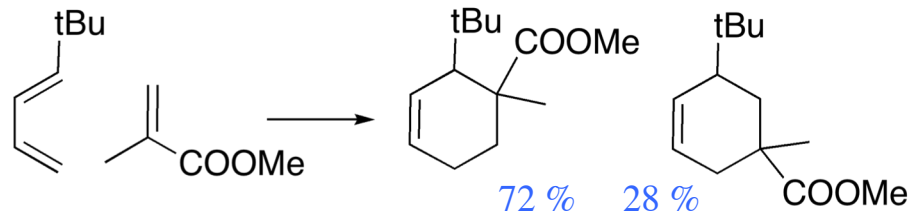
## 8.3.2 Réaction de Diels-Alder : régiosélectivité

pb de régiosélectivité :



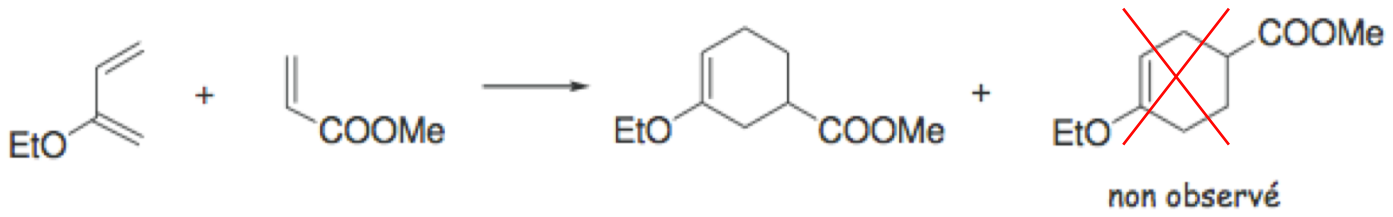

91 % 9 %

Adduit le + encombré formé
⇒ pas stérique

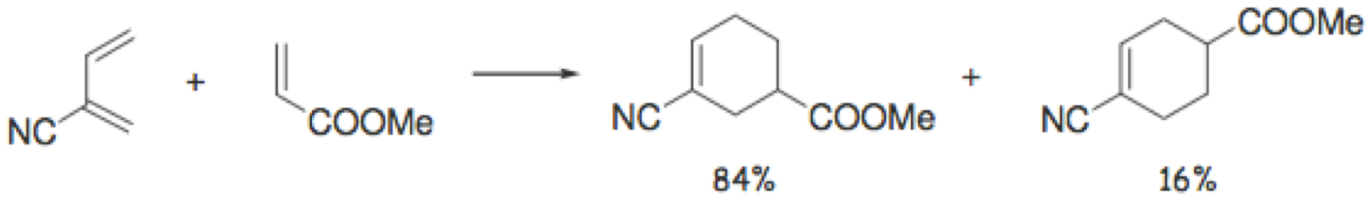



72 % 28 %

même régiosélectivité qqs le subst (D ou A)

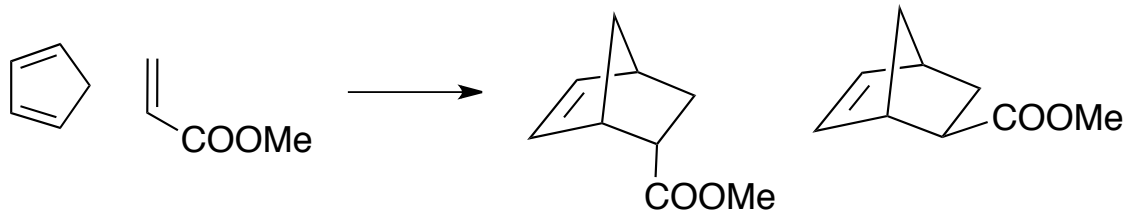



NB: ne "colle" pas avec mésomérie



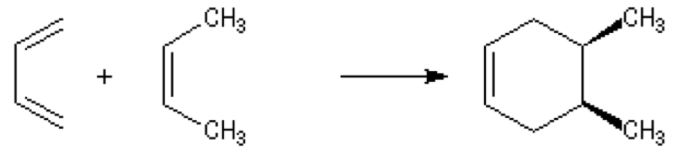
## 8.3.3 Réaction de Diels-Alder : stéréochimie

pb de stéréosélectivité :

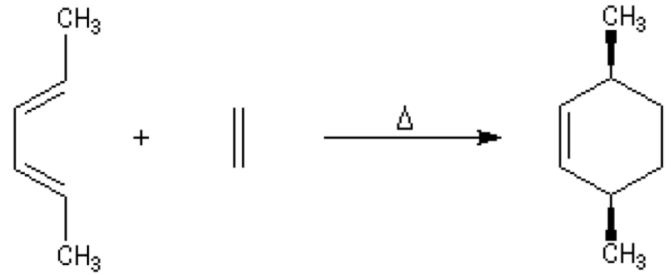



| *endo* | *exo* | |
|---|---|---|
| 78 | 22 | ⇒ **Règle endo d'Alder** |

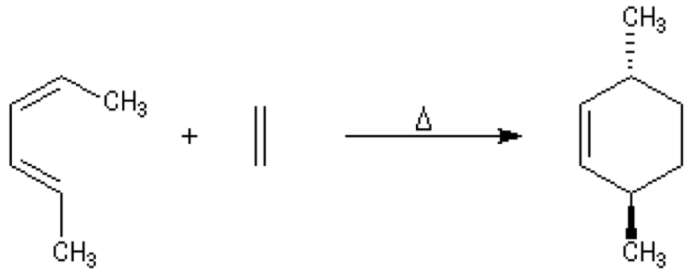
stéréospécificité :




| | |
|---|---|
| *Z* | cis |
| *E* | trans |

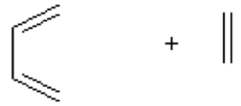


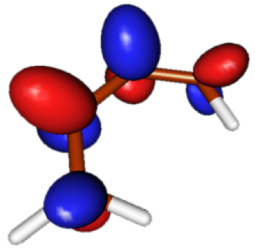

*E, E* cis



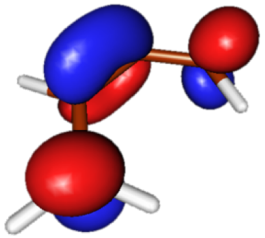

*E, Z* trans

# 8.3.4 Réaction de Diels-Alder : mécanisme par recouvrement d'orbitales, OF

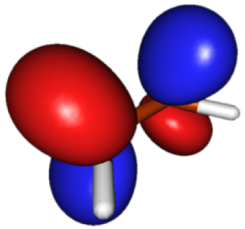




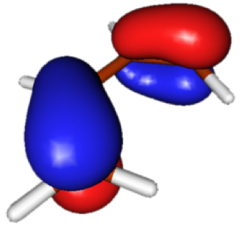
LU+1



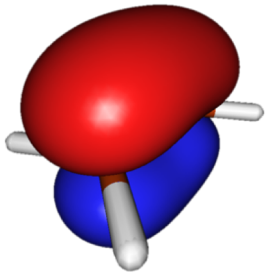
LU



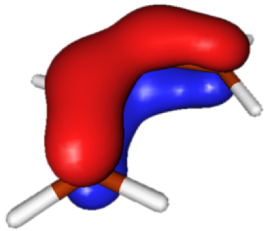
LU



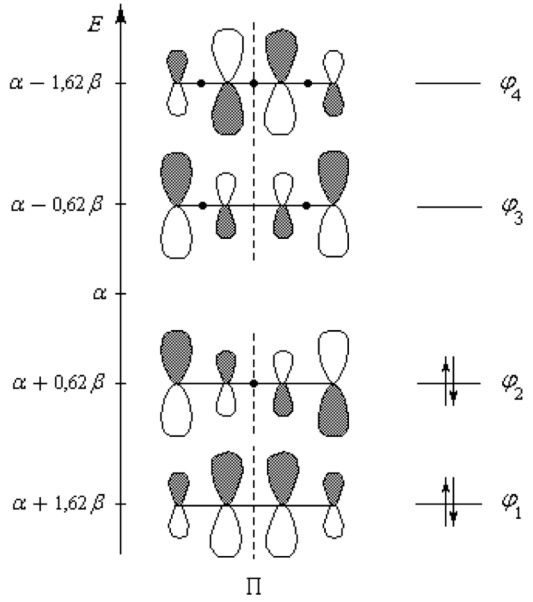
HO

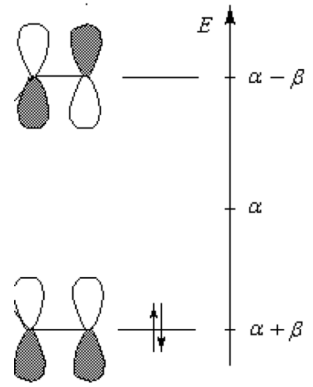


HO

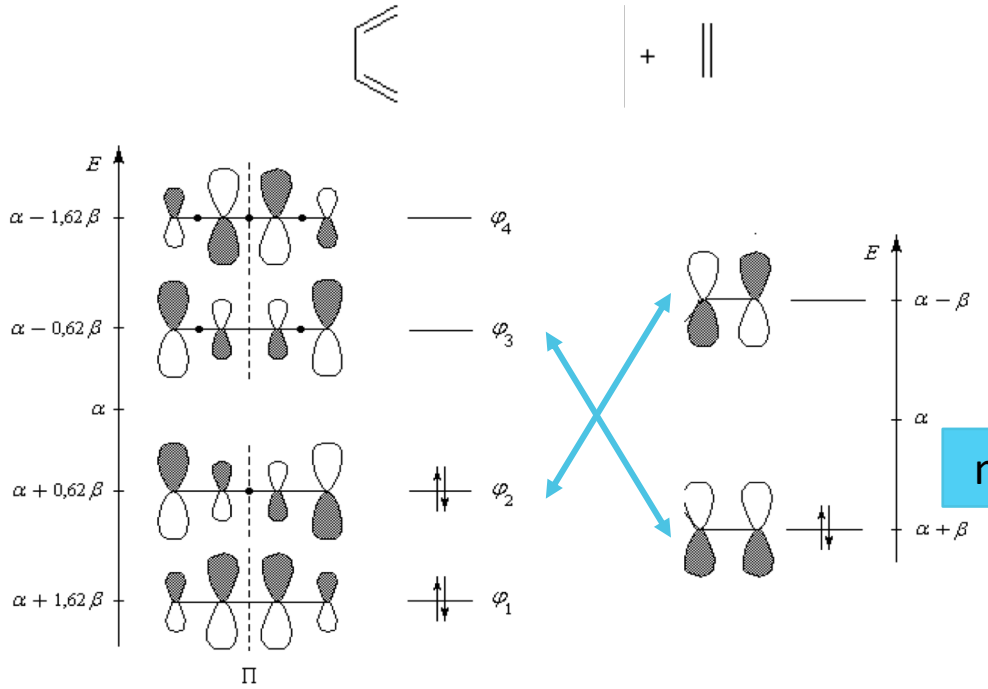


HO-1

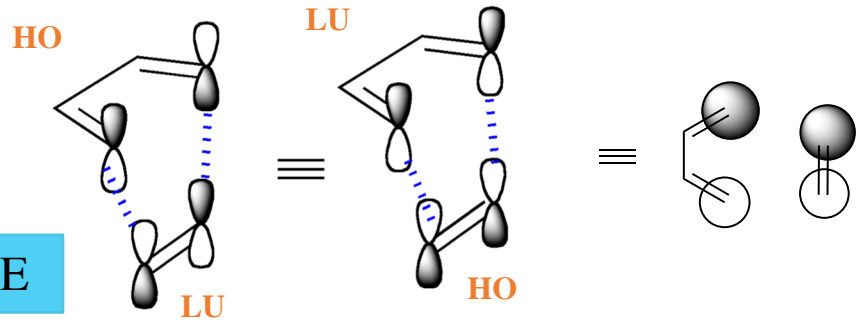


# mécanisme par recouvrement d'orbitales, OF




⇒ même ΔE

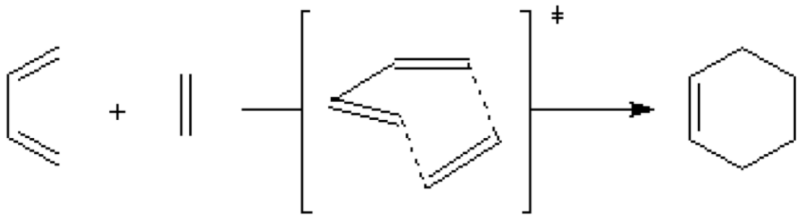


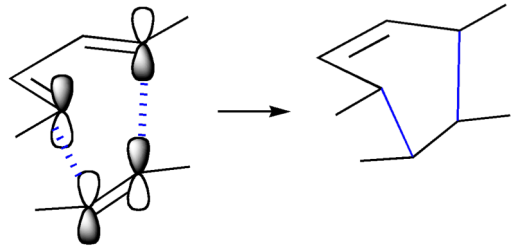

Interaction supra-supra

la ***réaction ds l'état fondamental est permise par symétrie***

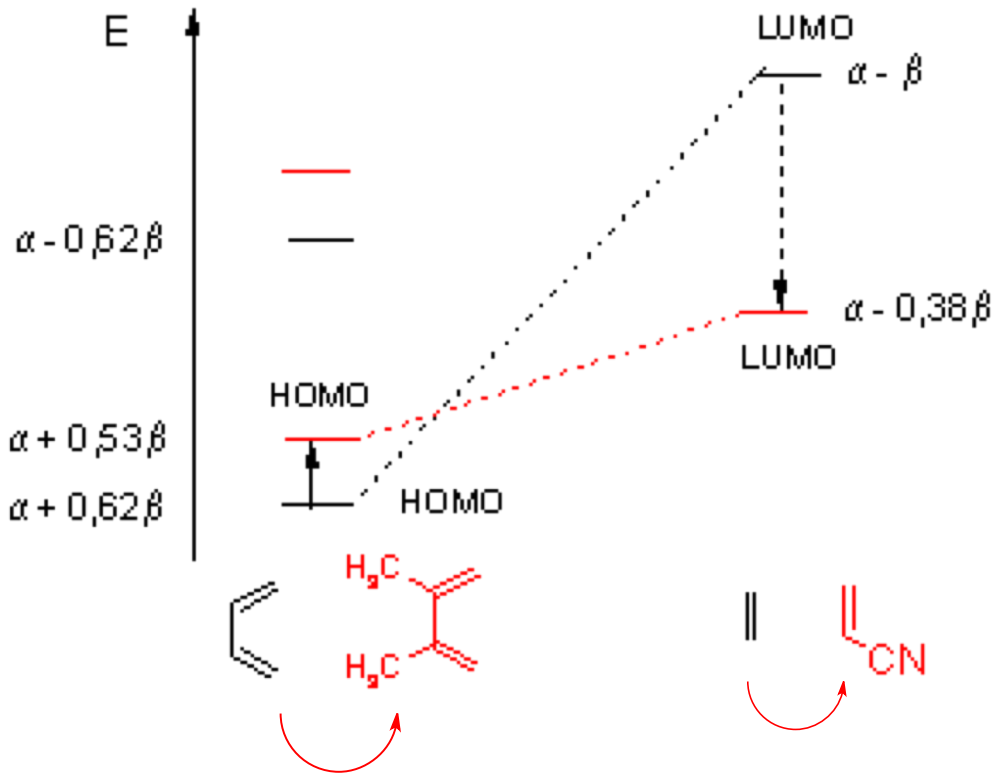
NB 1: Symétrie des OF : compatibles

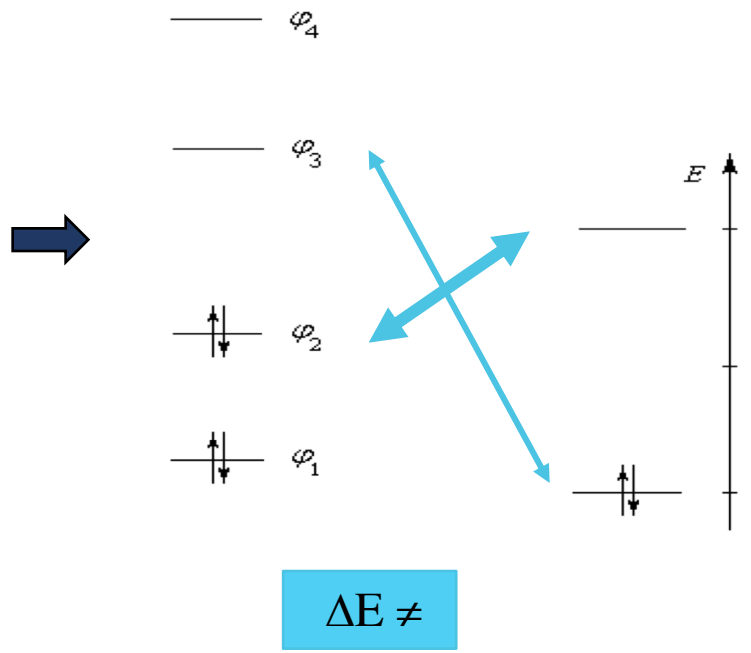
même signes ⇒ recouvrements possibles





**Effet substituant**
**ou acide (Lewis) :** - substituant

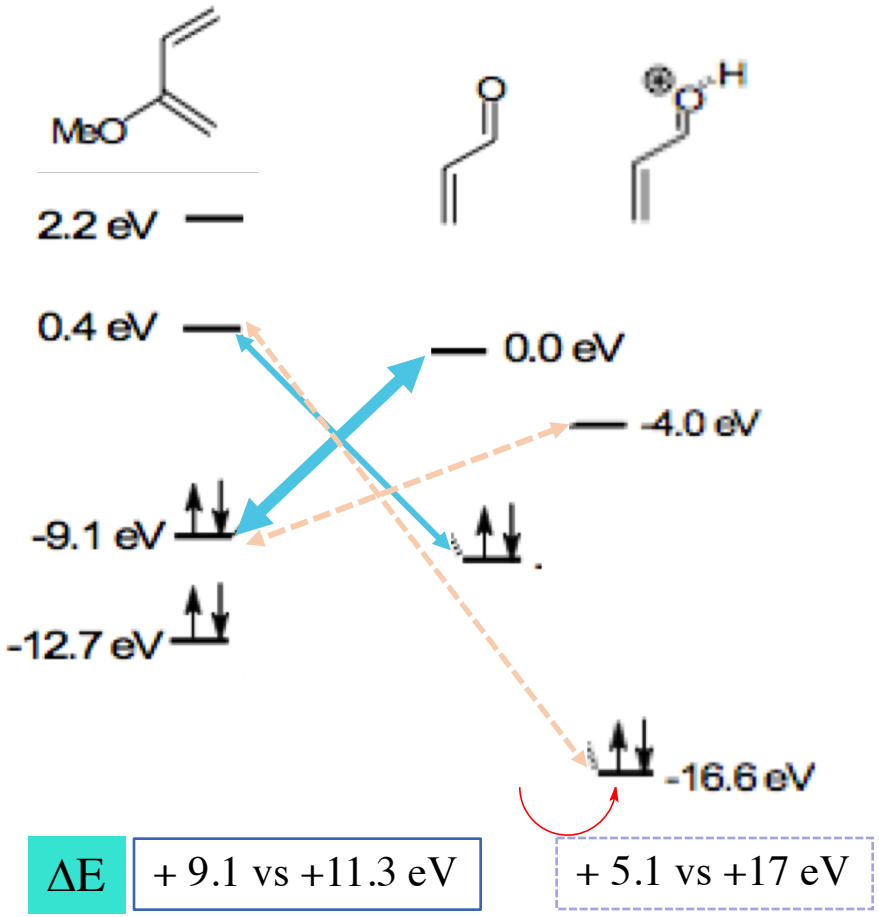



cf avant (effets électroniques)
= En. OM changent

⇒ Interaction HOMO (diène)-LUMO (dièNophile)
prépondérante & + efficace

**Effet substituant ou acide (Lewis) :** - acide

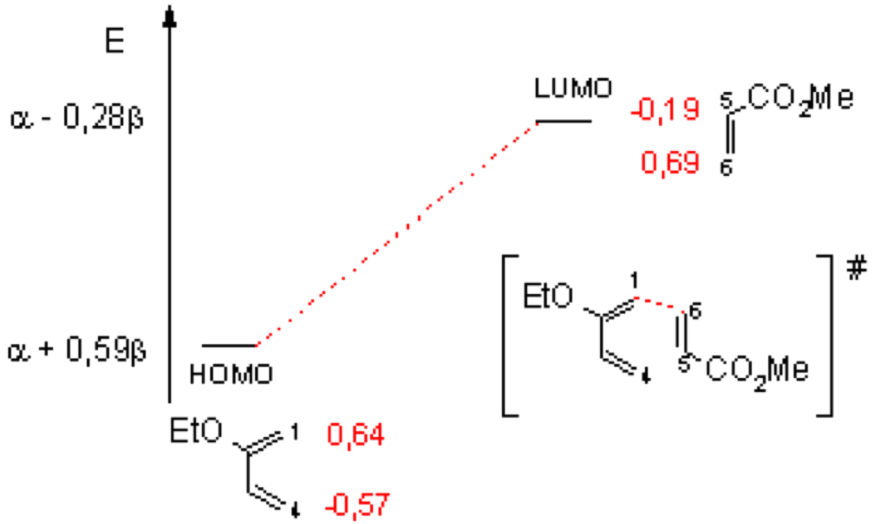


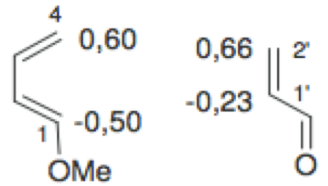

| ΔE | + 9.1 vs +11.3 eV | + 5.1 vs +17 eV |
|---|---|---|

⇒ Interaction HOMO (diène)-LUMO (dièn**o**phile) prépondérante & + efficace

**Régiosélectivité :** = déterminer quelle est l'interaction qui a la plus forte probabilité de s'établir en premier, via OF

= rendre le recouvrement *S* maximal = trouver la meilleure géométrie d'approche







$E = \alpha + 0{,}465\beta$ $E = \alpha - 0{,}347\beta$

liaison 4-2' $P = 0{,}60 \times 0{,}66 \times \beta = 0{,}396\beta$

liaison 1-2' 0,330β

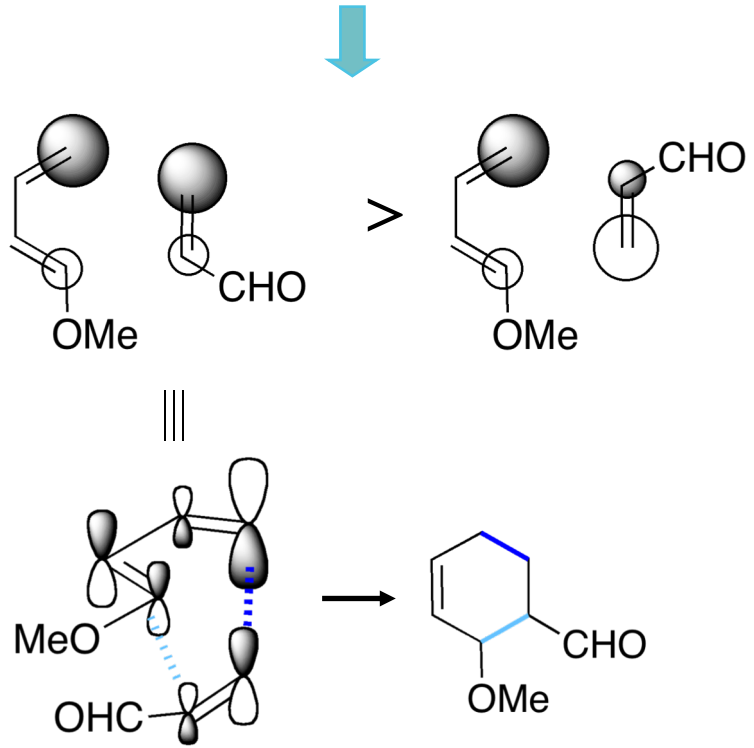
liaison 4-1' 0,138β

liaison 1-1' 0,115β

***principe du recouvrement maximum***

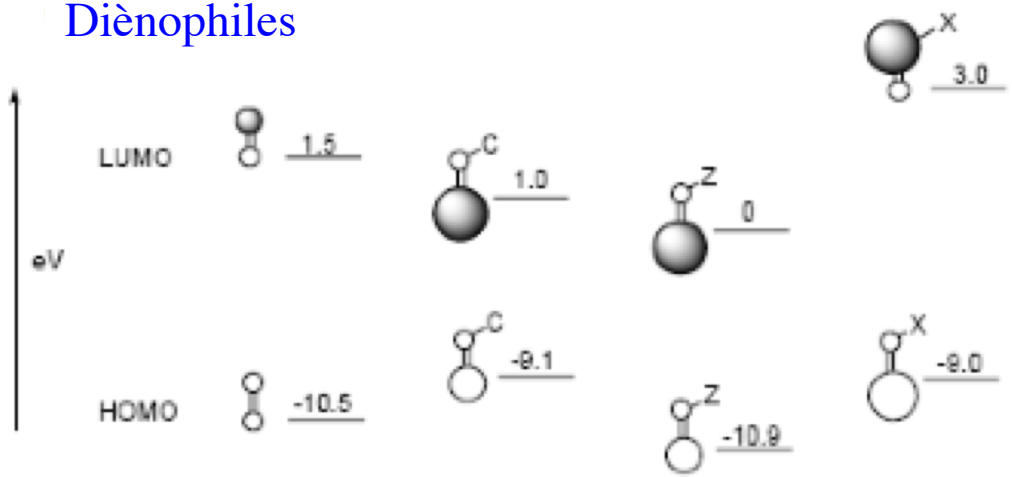
méthodes de Hückel : l'énergie de formation de la liaison C1-C6 est **la plus exothermique** avec 0,283β.

Les liaisons vont se former entre les atomes avec les plus **grands coefficients** (C1: 0,64; C-6: 0,69)

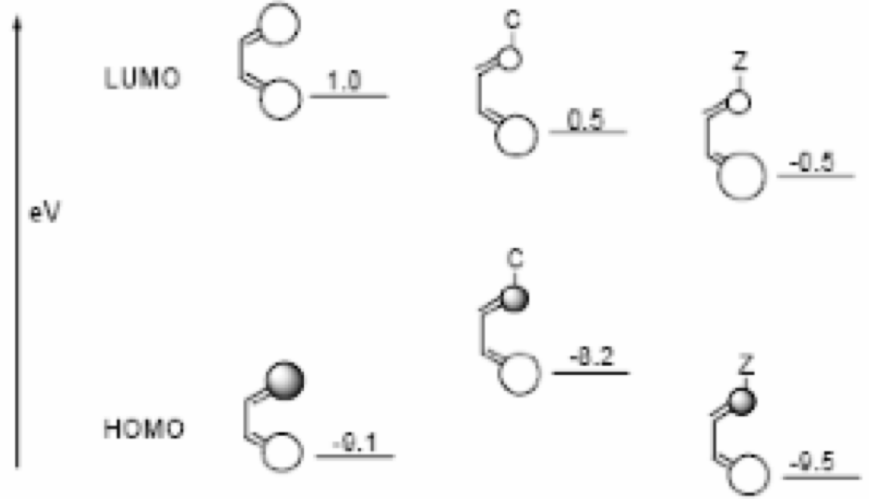


**Effet substituant ou acide (Lewis) :**

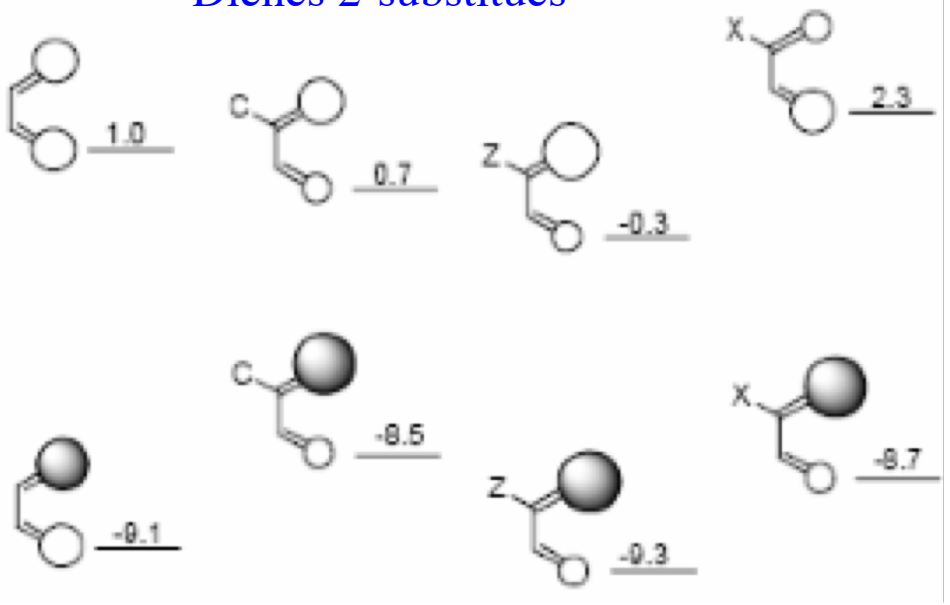
## Dièenophiles




## Dièenes 1-substitués



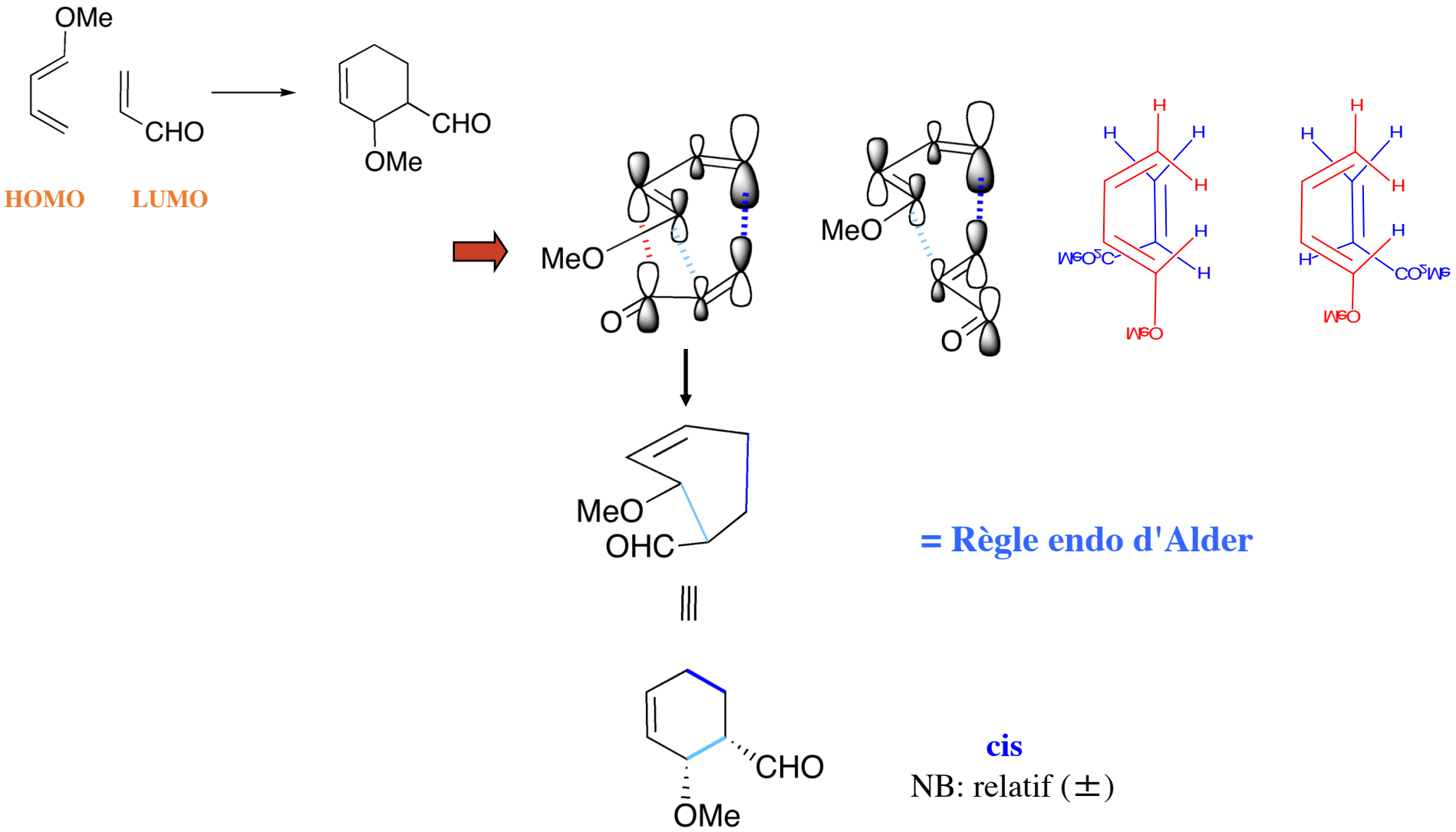

## Dièenes 2-substitués




Sauer et Sustmann, *Angewandte Chemie International edition in English*, **1980**, *19*, 779-807.

**Stéréosélectivité :** = rendre le recouvrement β (*S*) maximal, et si possible d' autres recouvrements

***recouvrement secondaire d'orbitales***

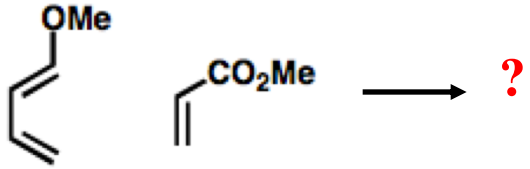



**= Règle endo d'Alder**

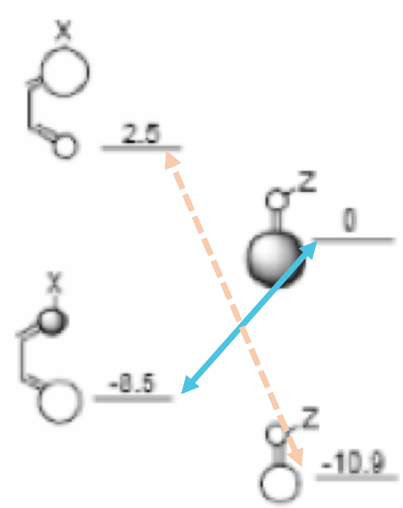
**cis**

NB: relatif (±)

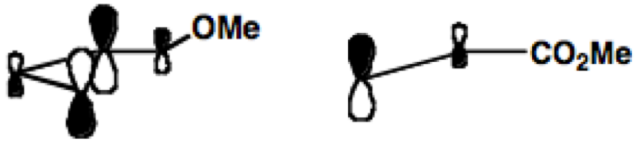
**Démarche :**



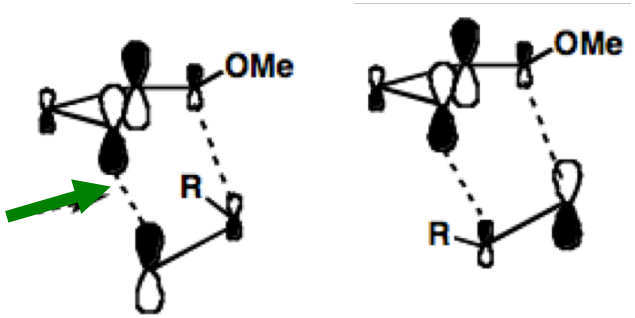

Tables



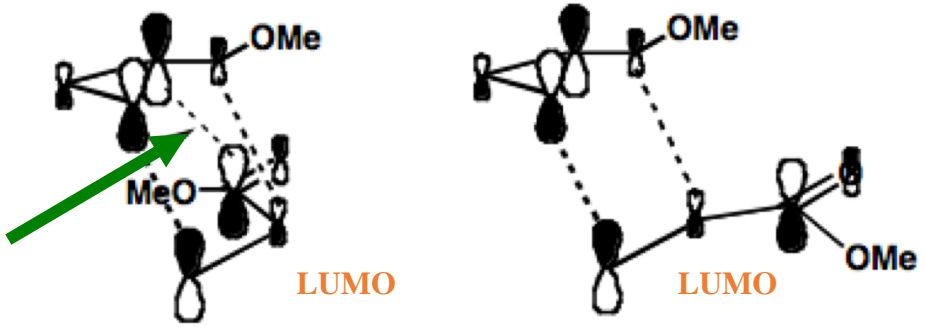

HOMO LUMO

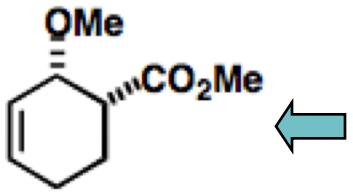



2 recouvrements possibles (= régiosélectivité)



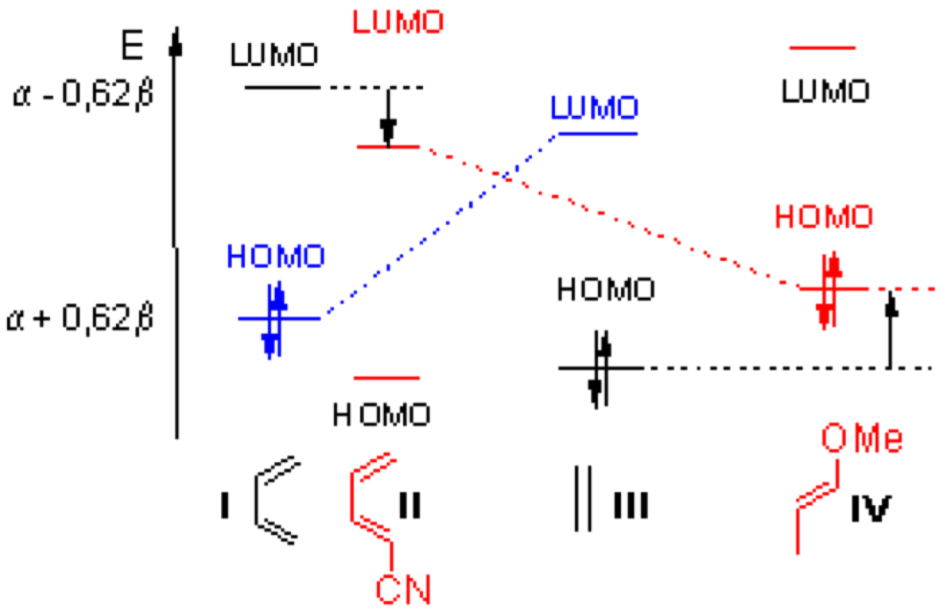

2 géométries possibles (= stéréosélectivité - relative)

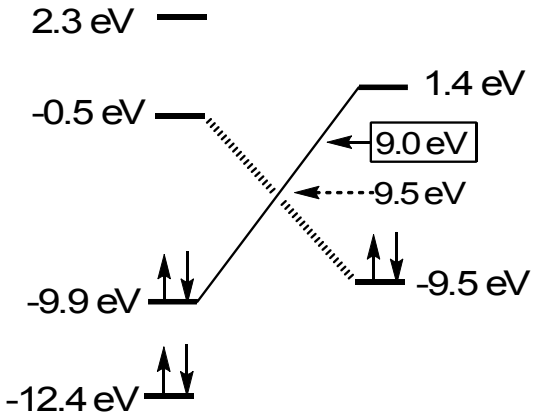


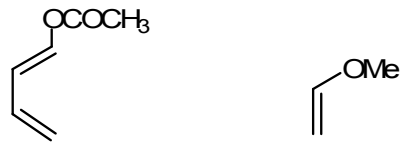



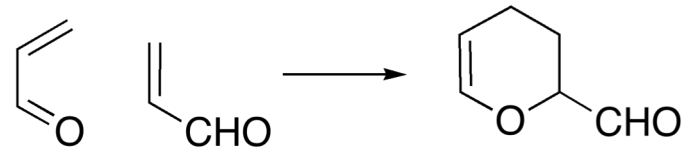

NB: relatif (±)

# D-A à demande (électronique) inverse

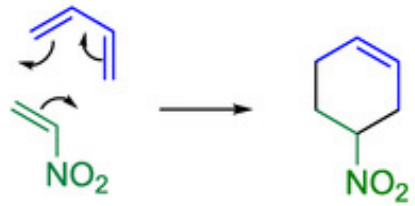


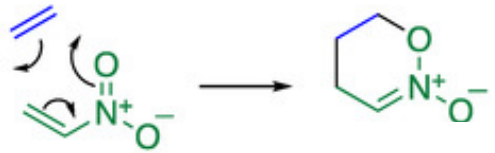



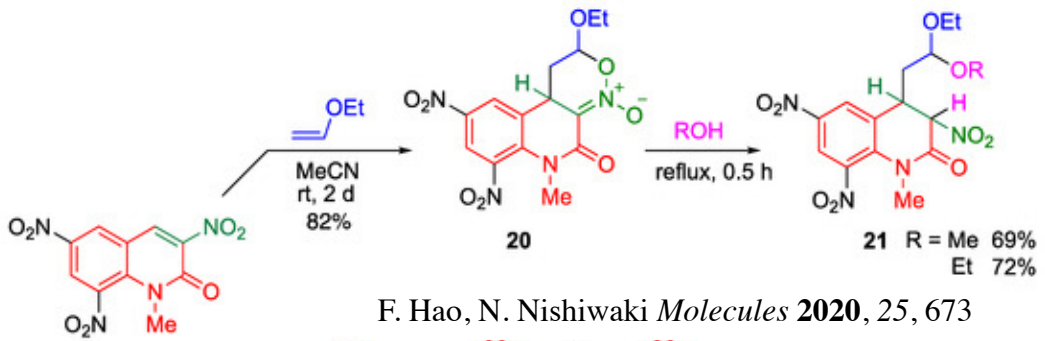



As a dienophile

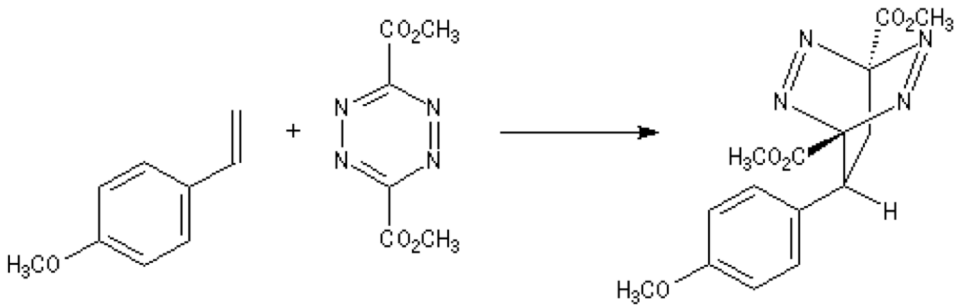



As a heterodiene

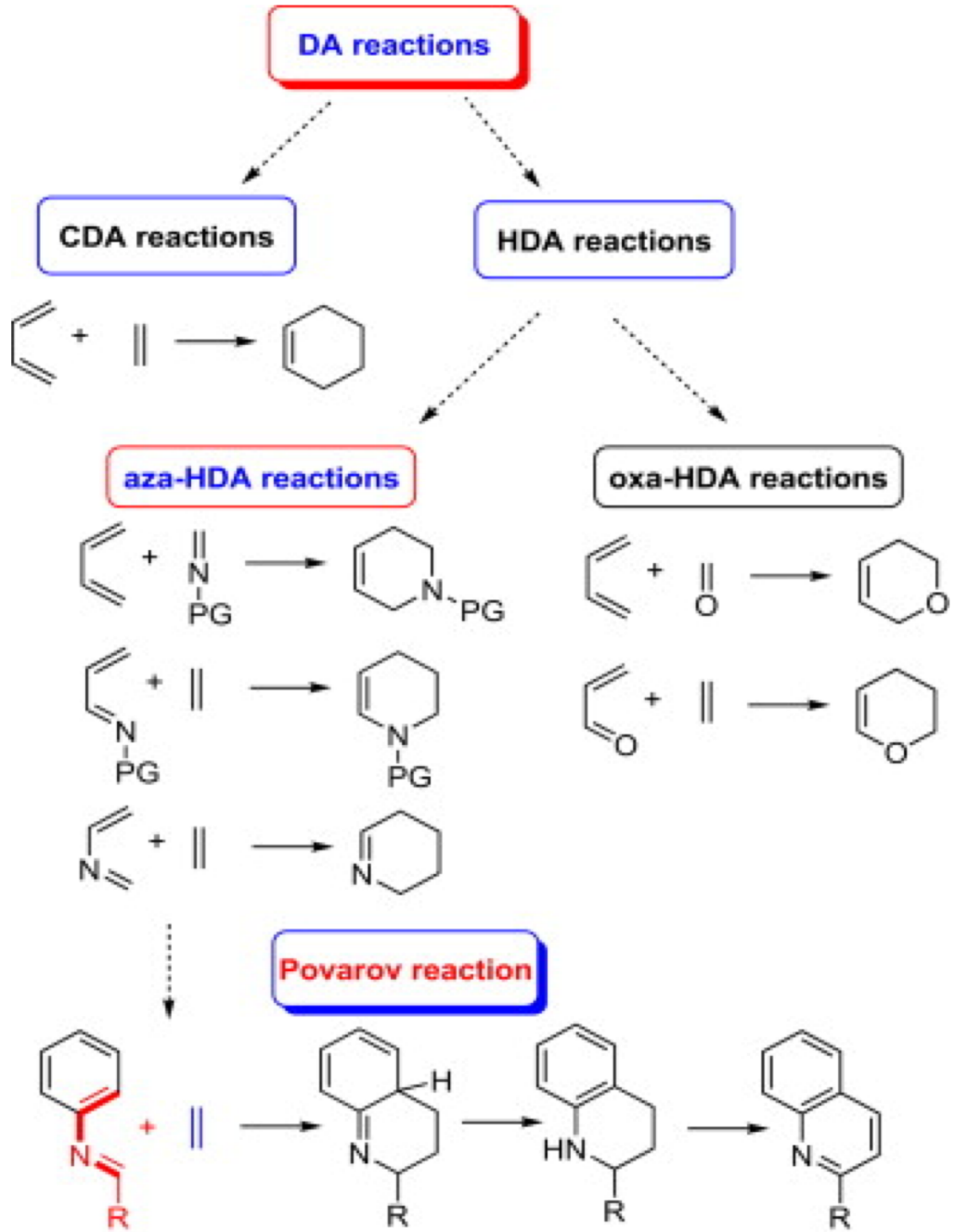



F. Hao, N. Nishiwaki *Molecules* **2020**, *25*, 673



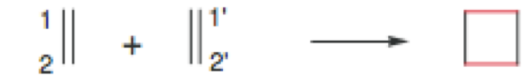
# Diversité des D-A



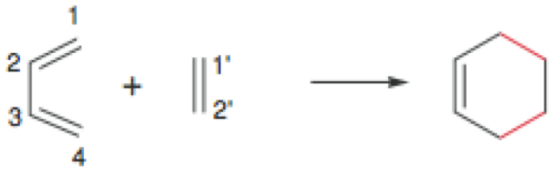
# 8.4 Cycloadditions

Diels-Alder : cas de cycloaddition

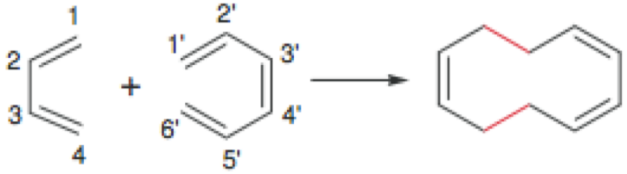
Général :



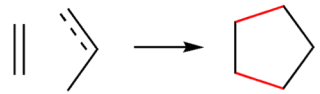
cycloaddition [2+2]



cycloaddition [4+2]



cycloaddition [4+6]

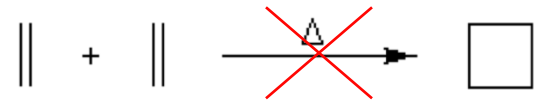


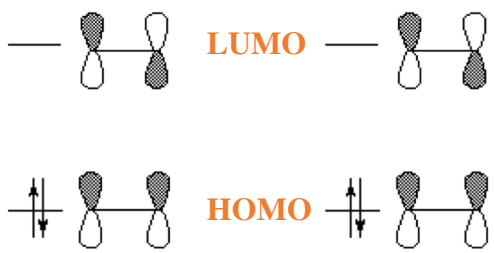
[3+2]

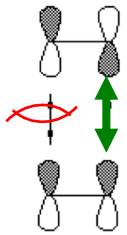
Etc…

Mais certaines cycloadditions possibles, d'autres pas

CA [2+2]





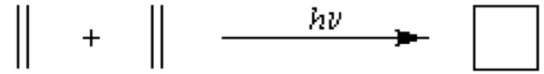



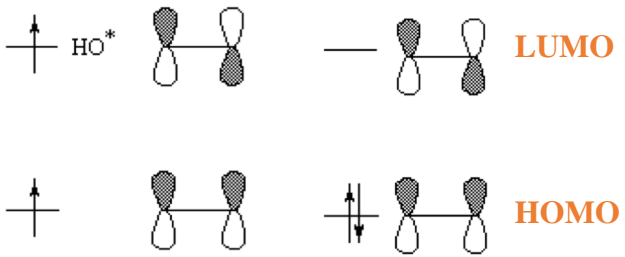
Pas de recouvrement
Réact. concertée pas favorable

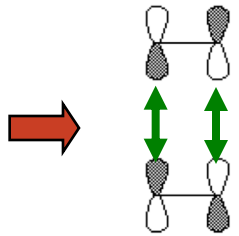
hν

Interaction supra-antara

[π2s+π2a]



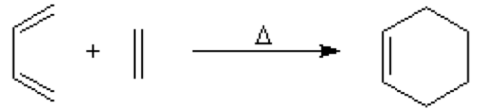



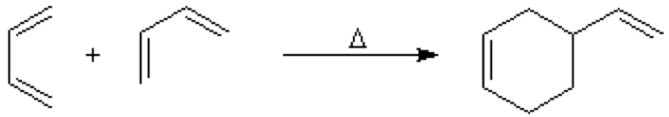
recouvrement

Interaction supra-supra

la ***réaction photochimique (ds l'état excité)***
***est permise par symétrie***

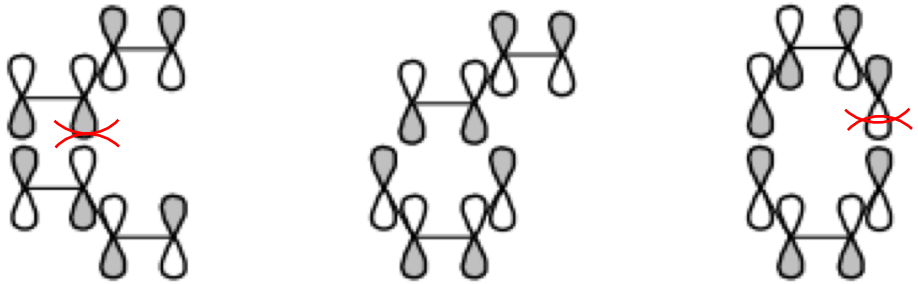
Général :
explique la réactivité

cf avant : 

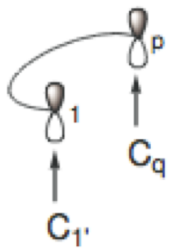
plutôt: 

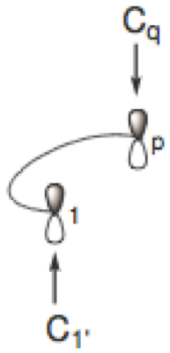
pourquoi pas [2+2], [4+4] ?

périsélectivité

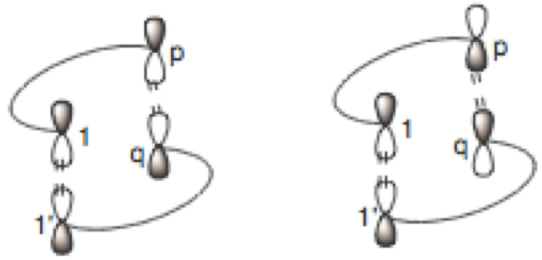


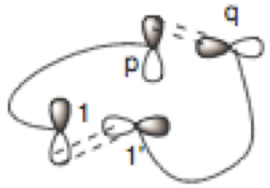

Général :
classement par
type d'interactions

supra-supra 

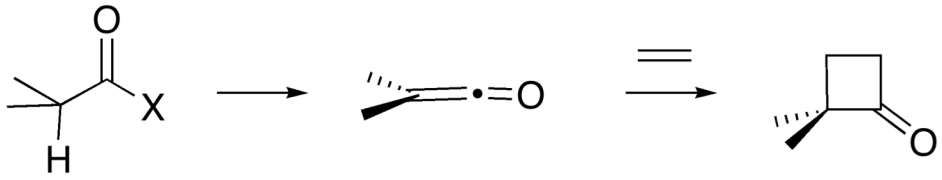

supra-antara

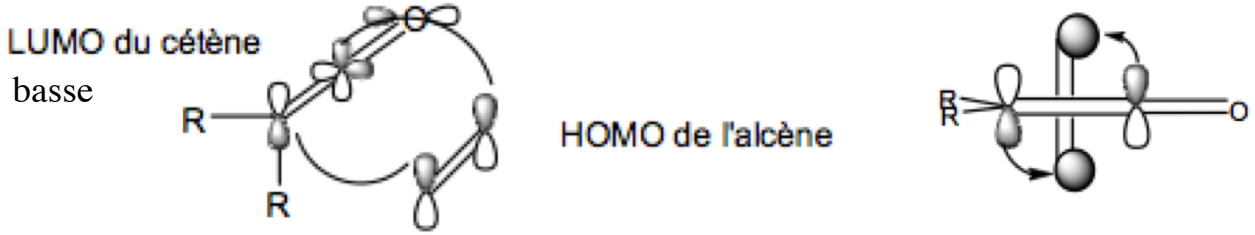


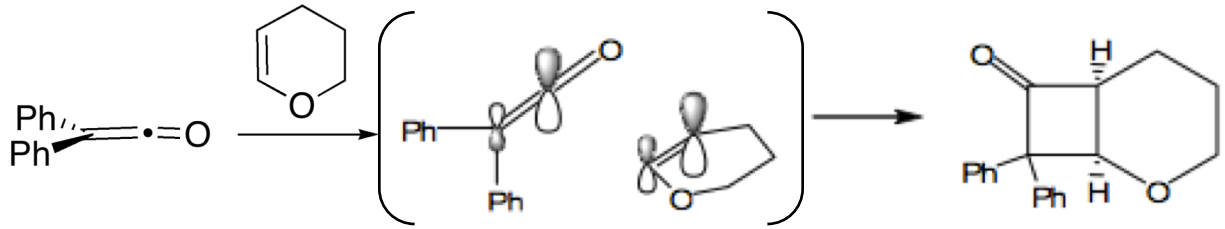
Qq cas de CA [2+2] thermiques:

- Cétènes :

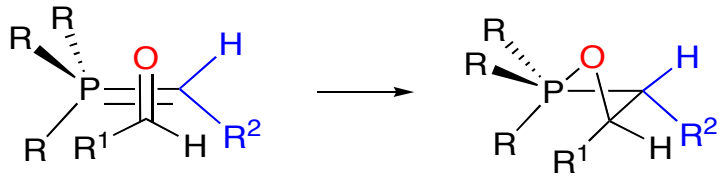


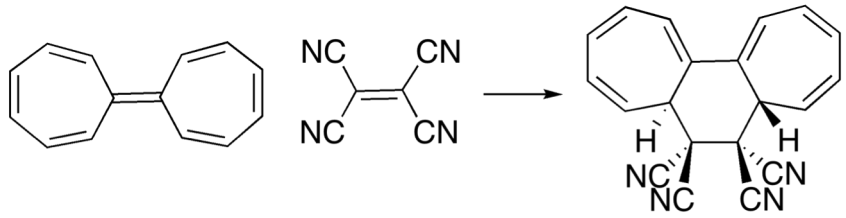

Régiosel. : cf coeff.

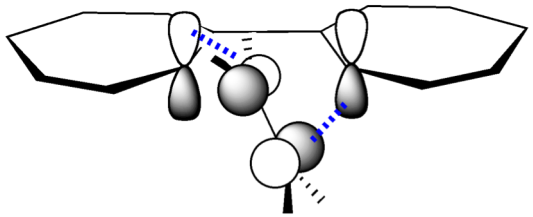



- Ylures de phosphore :



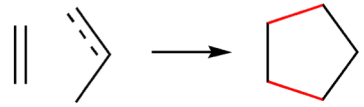

- Cas :



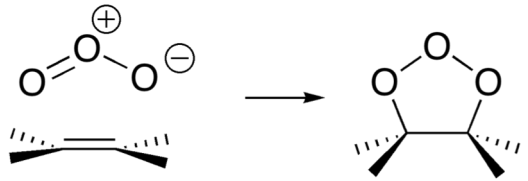



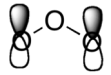
[π14a+π2s]

CA [3+2]

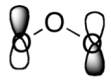


Stéréochimie ?
Thermique /photochimique ?

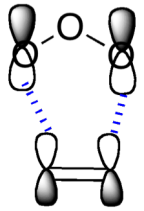


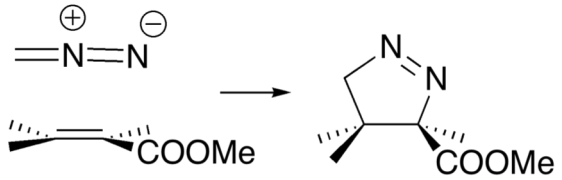


**LUMO** - 2.2 eV



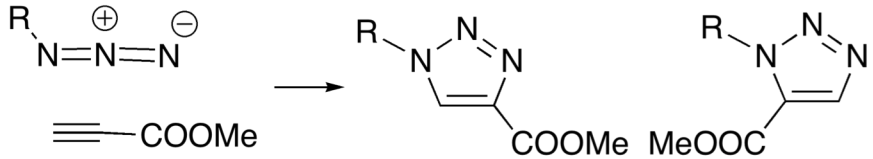
**HOMO** - 13.5 eV

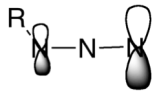




**LUMO** - 1.8 eV

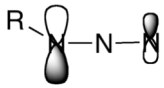
**HOMO** - 9.0 eV



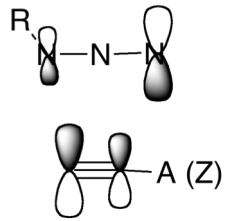


**LUMO** - 0.1 eV

(R = H)



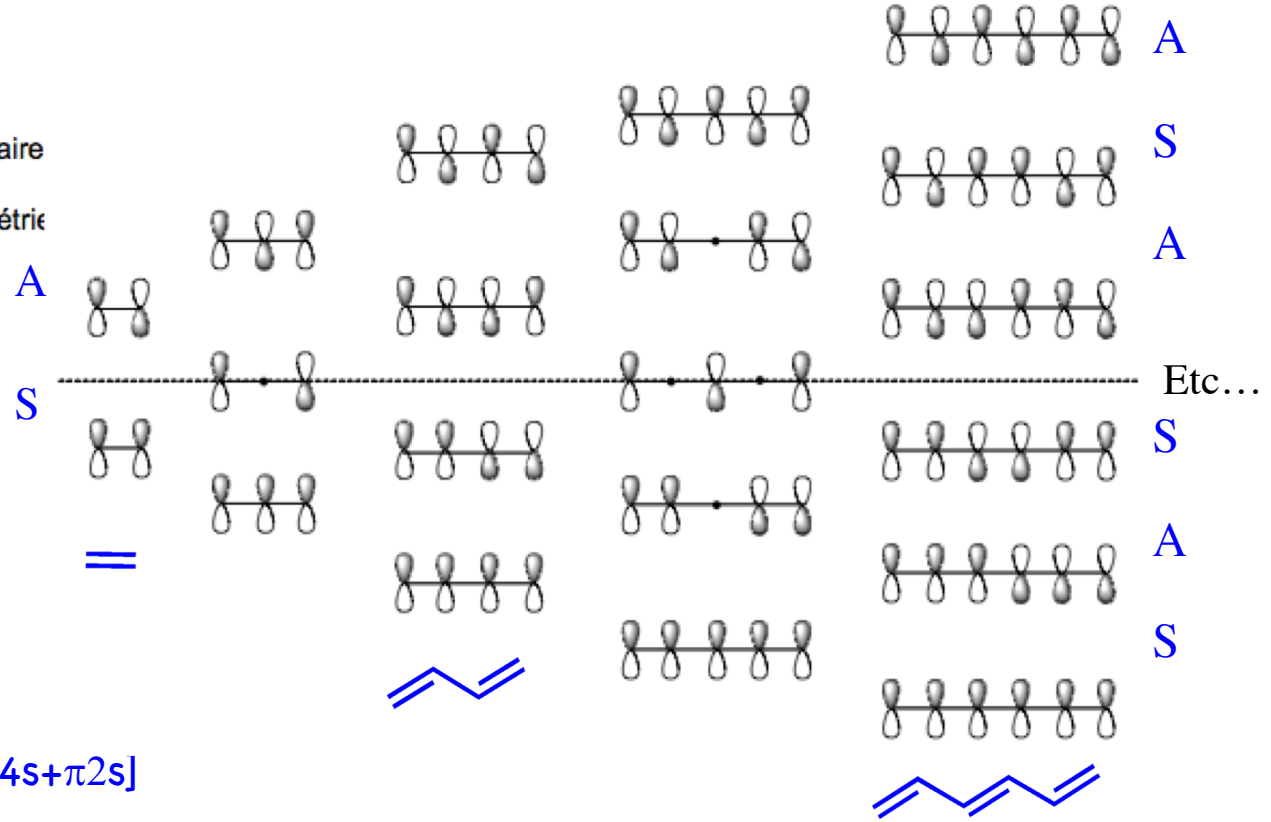
**HOMO** - 11.5 eV

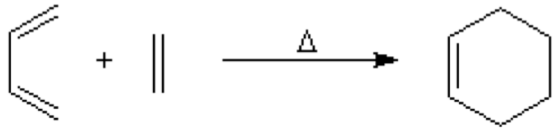


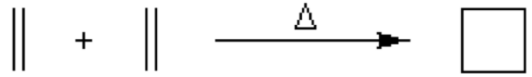

Cyclisation de Huisgen

# Interactions & Symétrie des OM

- n orbitales atomiques = n orbitales moléculaires
- OM de plus basse énergie = toutes les OA en phase.
- Chaque niveau d'énergie supérieur = 1 noeud supplementaire d'ou Ψn = (n-1) noeuds.
- Ψn : n impair = 1 plan de symétrie; n pair = 1 centre de symétrie




[4+2]  [π4s+π2s]

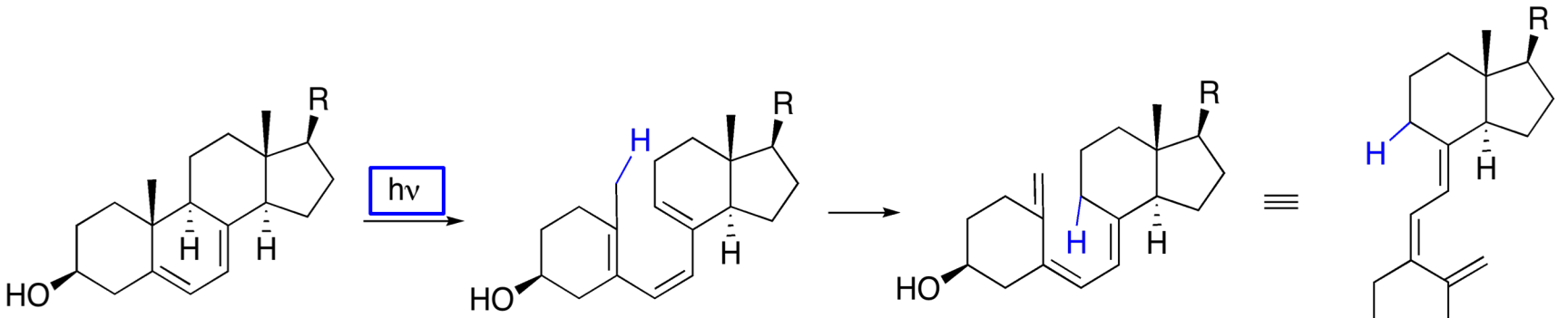
[2+2]  [π2s+π2a]

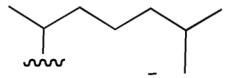
"règles" de Woodward-Hoffmann

| Electrons | Stereochemical Course: Thermal Mode | Stereochemical Course: Photochemical Mode |
|---|---|---|
| 4n + 2 | [s + s] | [s + a] |
| 4n | [s + a] | [s + s] |

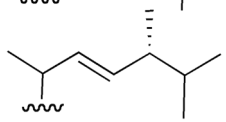
http://en.wikipedia.org/wiki/Woodward–Hoffmann_rules

# 8.5 Electrocyclisations



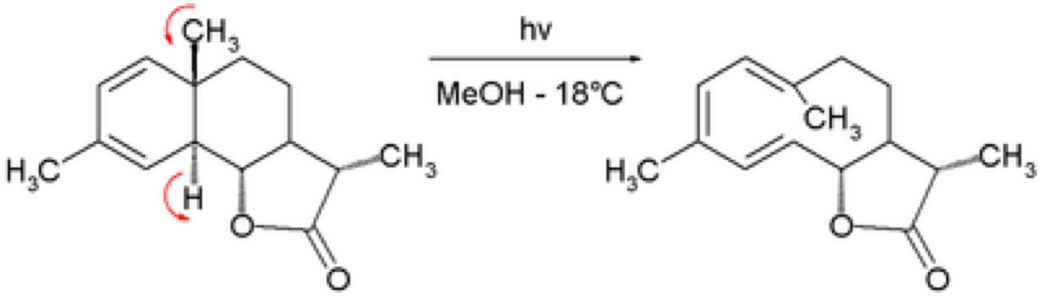

R = 

7-dehydrocholestérol — provitamine D3

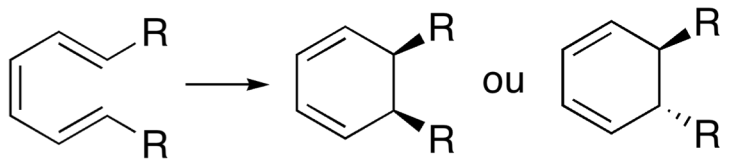
R = 

Ergostérol — provitamine D2

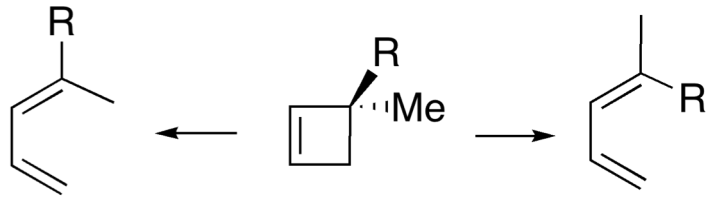
Cholecalciférol
(vit. D3)




Dehydrocostunolide
JACS 1963, 85, 4022
JACS 1965, 87, 5736








out in

R = Et in/out 2.1
R = iPr in/out 1.9

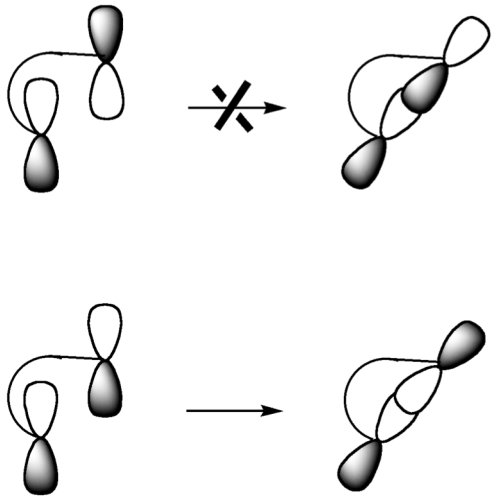
Pas stérique

Stéréochimie ?
Possible / pas possible ?
(thermique / photochimique ?)

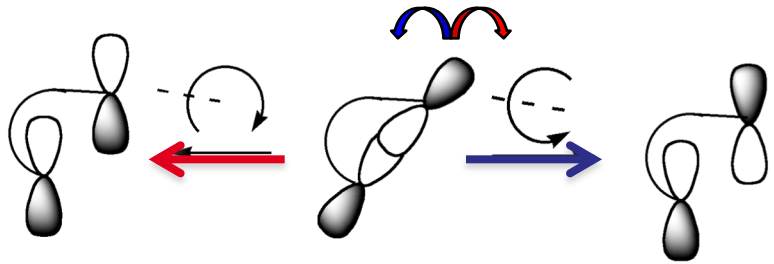
OF & symétrie

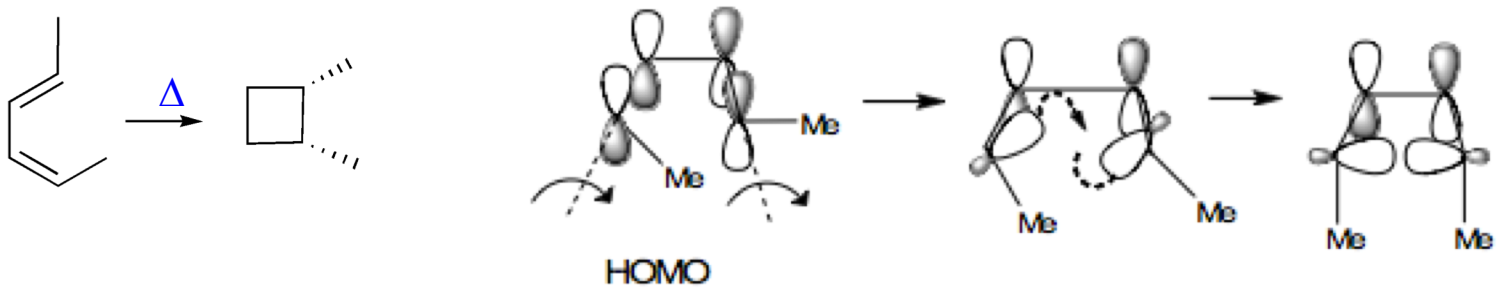
# OF & symétrie

Electrocyclisation
Fermeture de cycle

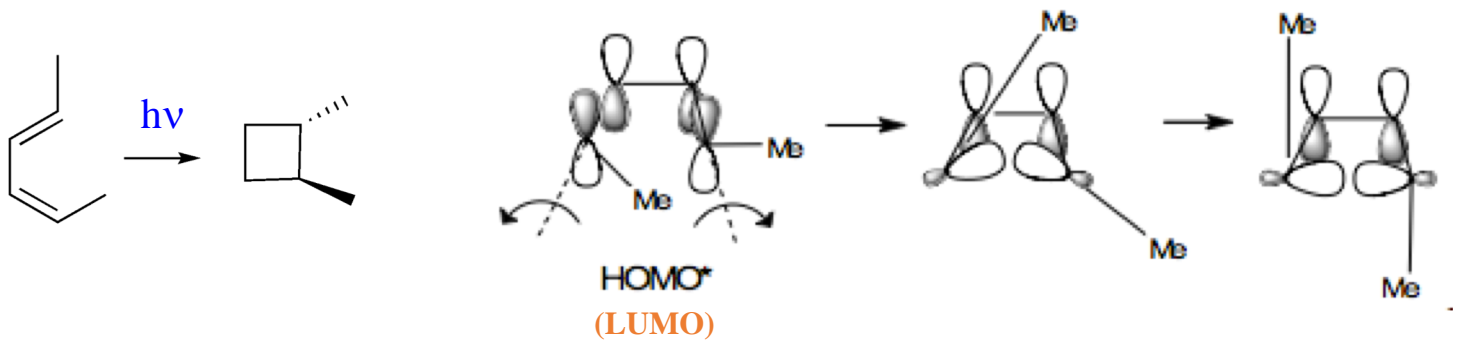


Electrocyclisation
Ouverture de cycle

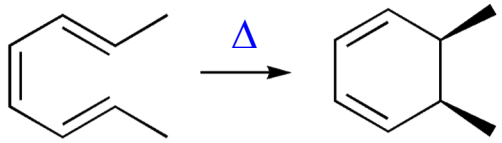


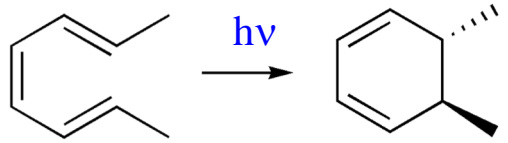



conrotatoire



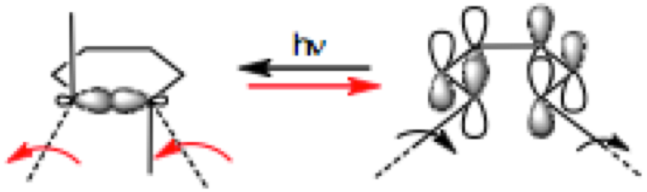

disrotatoire

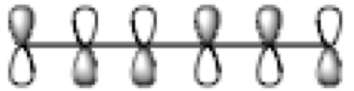


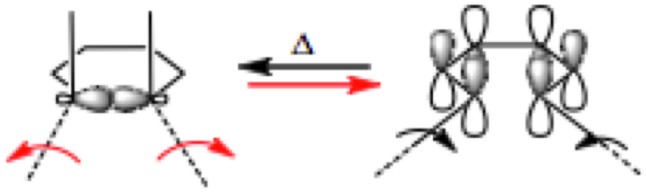

HOMO*
(LUMO)

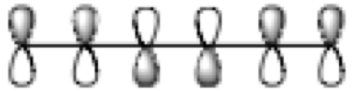
conrotatoire



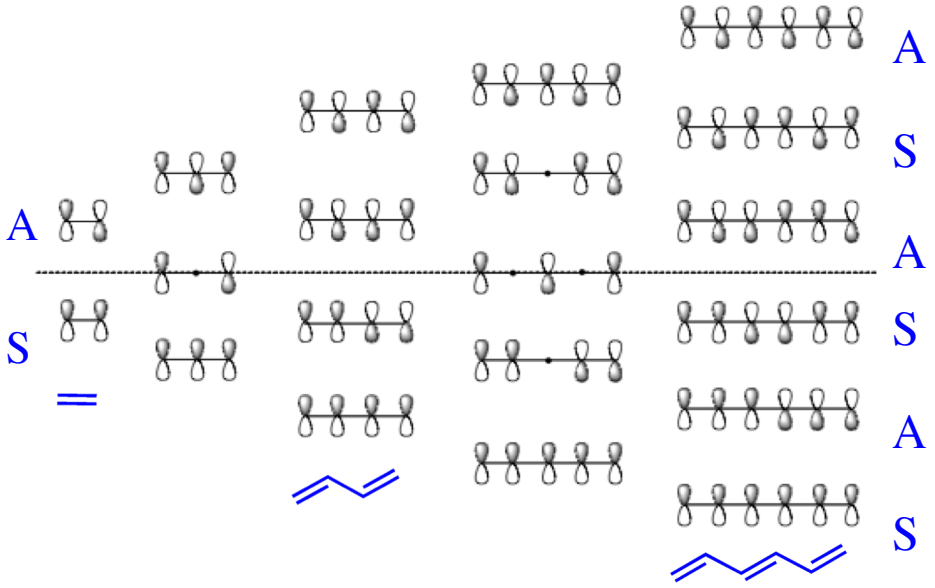



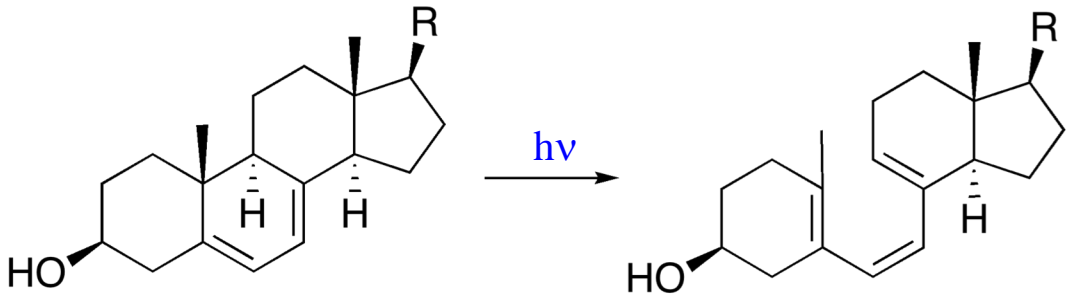
disrotatoire



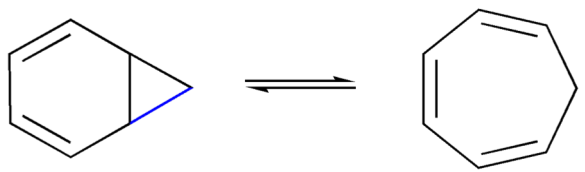



HOMO

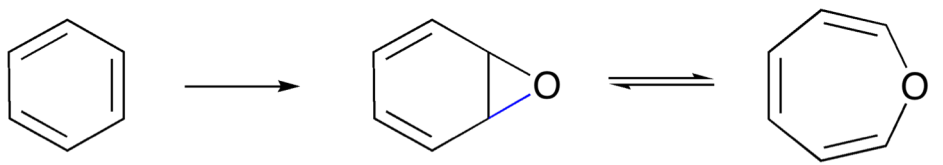





7-dehydrocholestérol provitamine D3



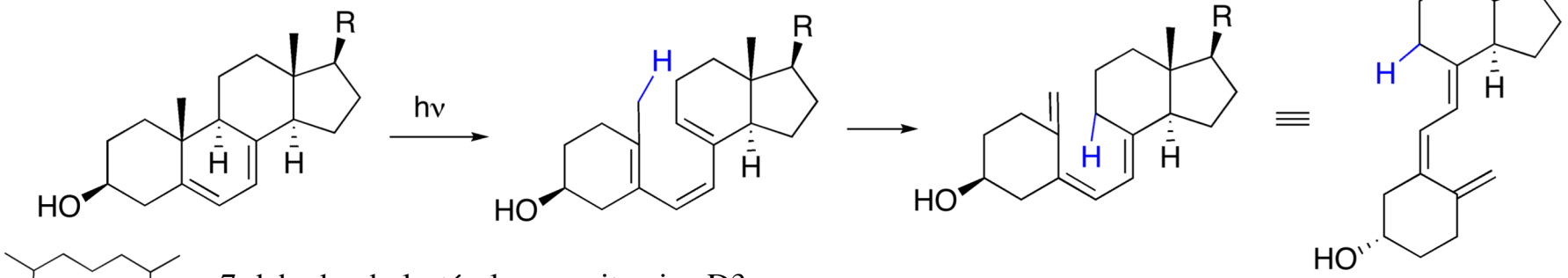
Norcaradiene

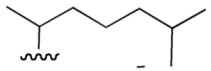


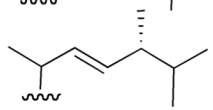

Détectable à – 110°

# 8.6 Sigmatropies

Migration de liaison σ  liaisons σ  C-H, C-C, etc



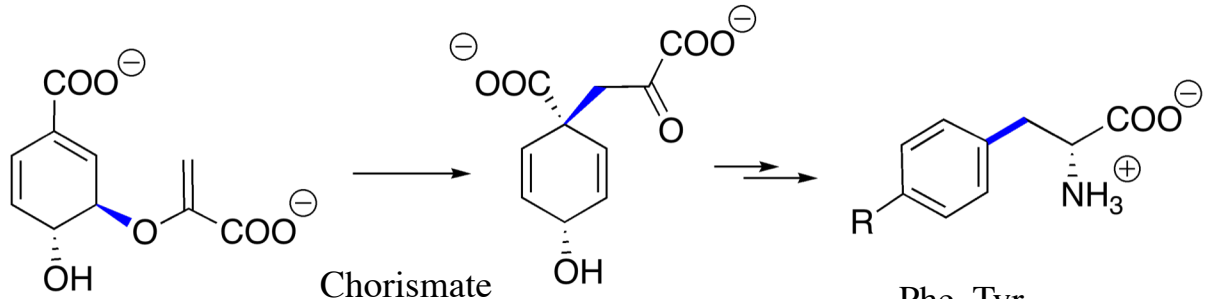

R =   7-dehydrocholestérol  provitamine D3

R =   Ergostérol  provitamine D2

Cholecalciférol
(vit. D3)

Migration σ  C-H

Stéréochimie

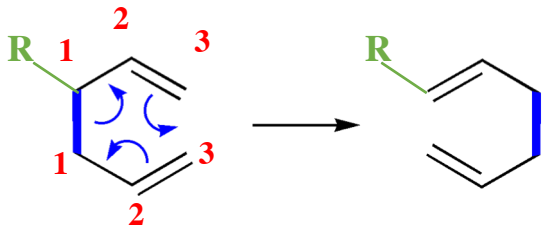


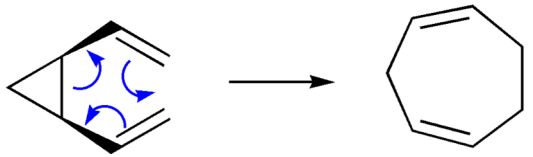

Migration σ  C-O/C-C

## 8.6.1 Migration de liaison C-C

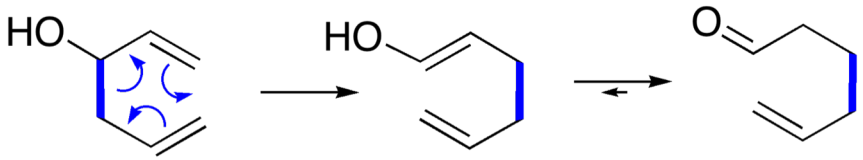
### σ [3,3] C–C

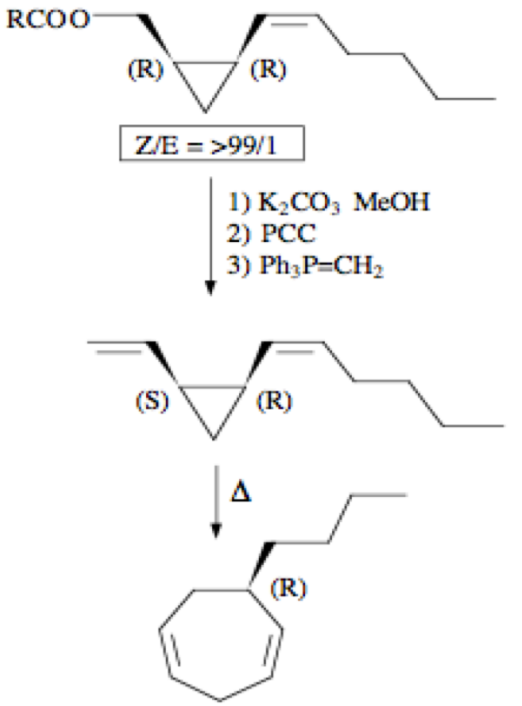
-Réarrangement de Cope



Réarrᵗ d'oxy-Cope, aza-Cope

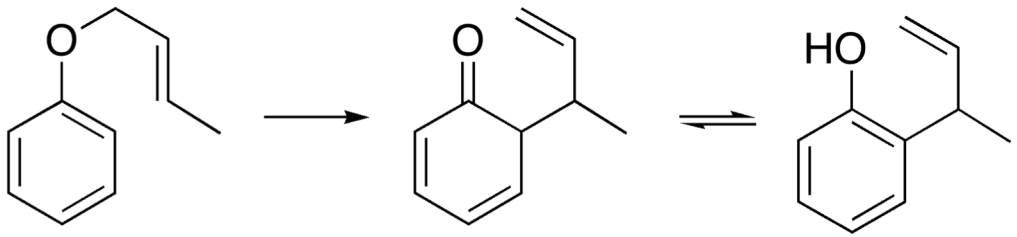


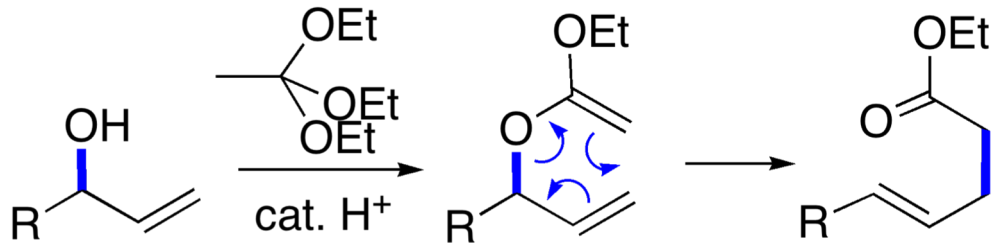

D. Grandjean, P. Pale, J. Chuche
*Tetrahedron* **1991**, *47*, 1215

σ [3,3] C–C

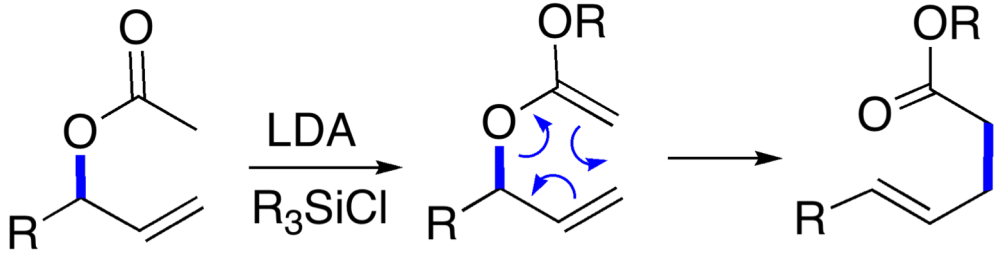
-Réarrangement de Claisen



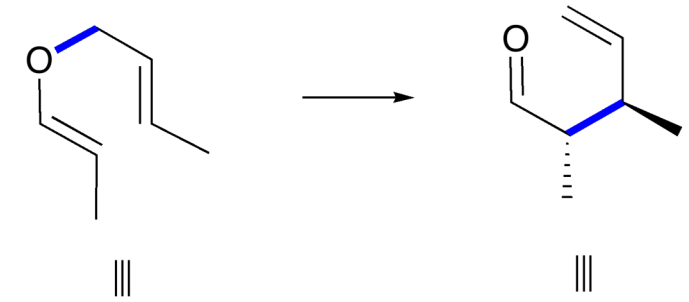

Réarrᵗ de Johnson-Claisen

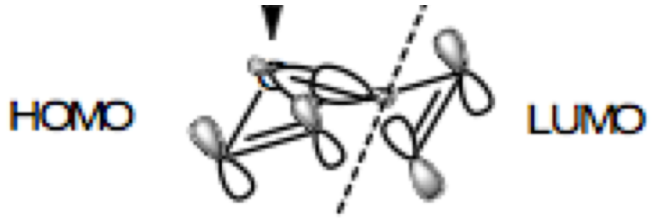


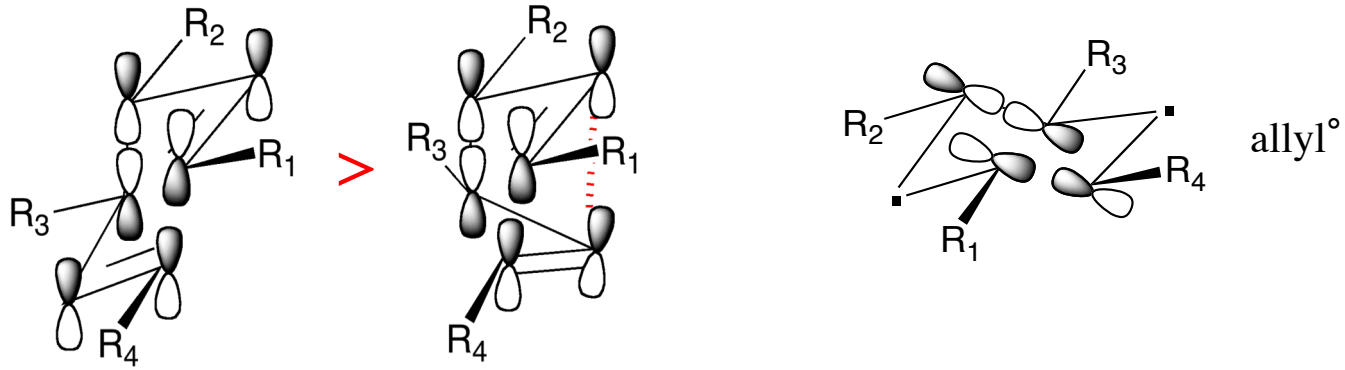

Réarrᵗ d'Ireland-Claisen



Réarrangement de Cope, Claisen, etc : Stéréochimie

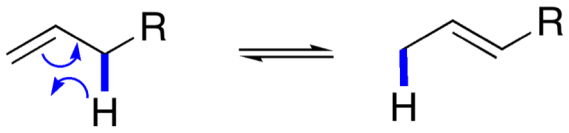


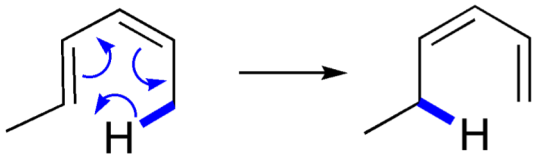




HOMO 'Diene'/LUMO Ene  Interaction antiliante

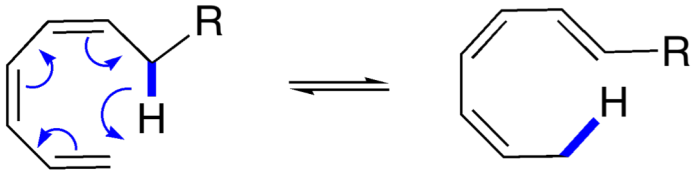
## 8.6.2 Migration de liaison C-H




σ [1,3]

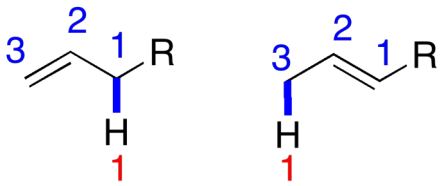



σ [1,5]




σ [1,7]

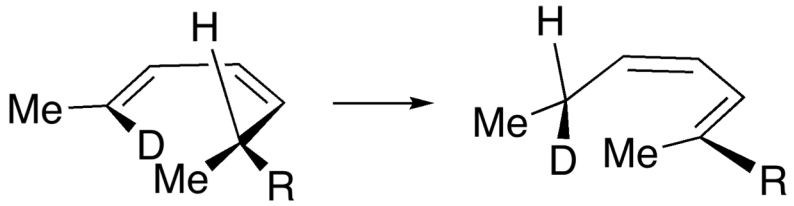
NB: numérotation




Stéréochimie ?
Possible / pas possible ?
(thermique / photochimique ?)

Migration de liaisons σ C-H

Stéréochimie ?
Possible / pas possible ?
(thermique / photochimique ?)

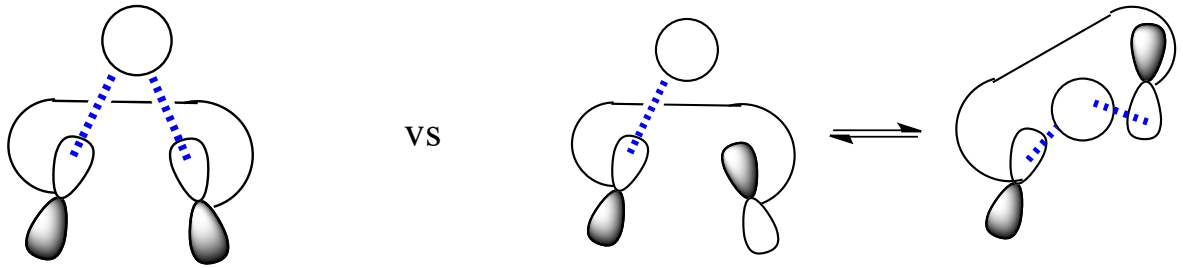



Interaction liaison C-H avec (di)ene ?

Migration " continue » ?

OF & symétrie

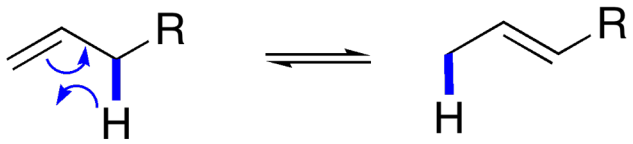
2 cas possibles :



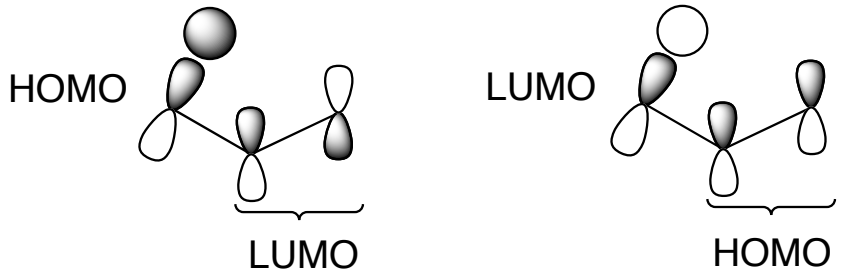

supra

antara facial

σ [1,3] C–H




Interaction d'une liaison C-H avec syst. π




thermique

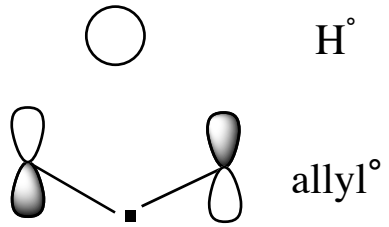
antarafacial

peu envisageable

(pb géométrie)

Pas favorable

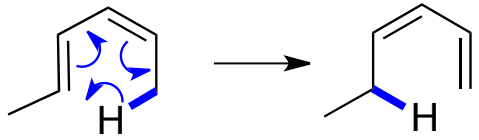
Interaction de 2 radicaux



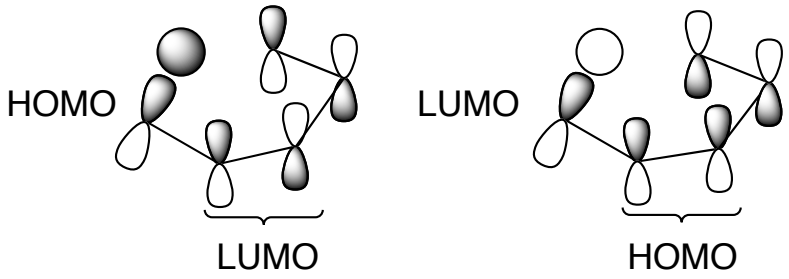

antarafacial

cf tautomérie

σ [1,5] C–H




Interaction d'une liaison C-H avec syst. π



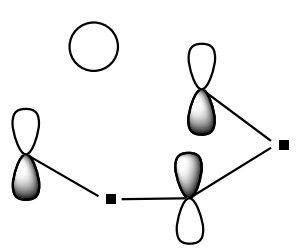

thermique

suprafacial

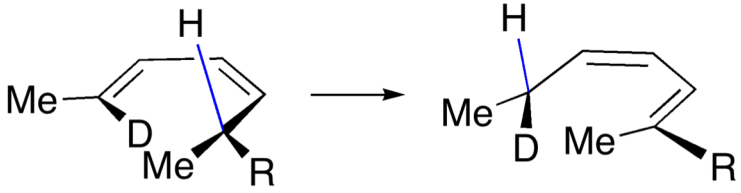
Géométrie OK

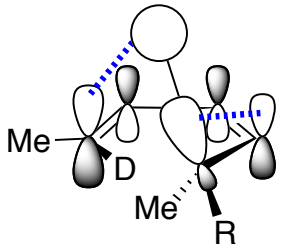
favorable

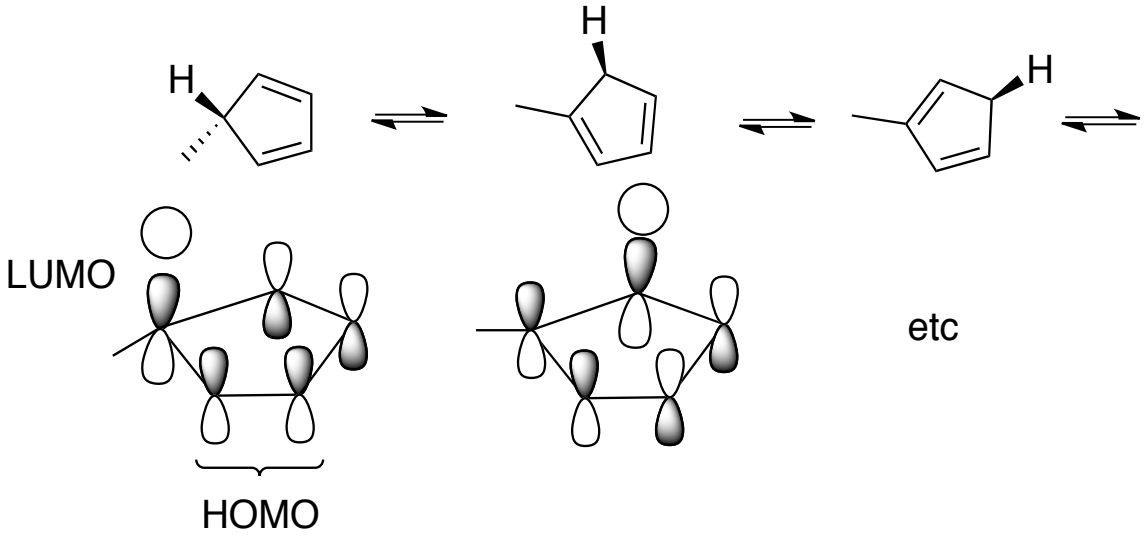
Interaction de 2 radicaux




suprafacial

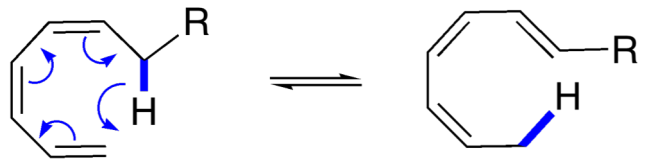


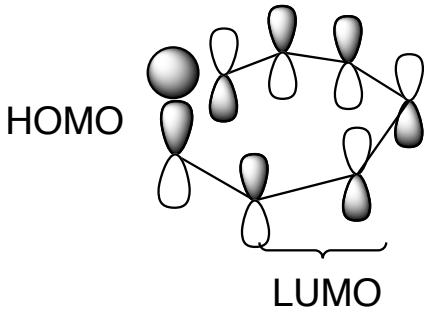




suprafacial

σ [1,7] C–H




Interaction d'une liaison C-H avec syst. π



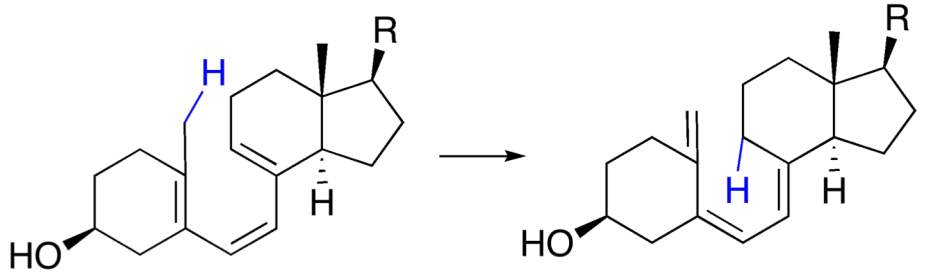

thermique

antarafacial

A priori peu envisageable

(pb géométrie)

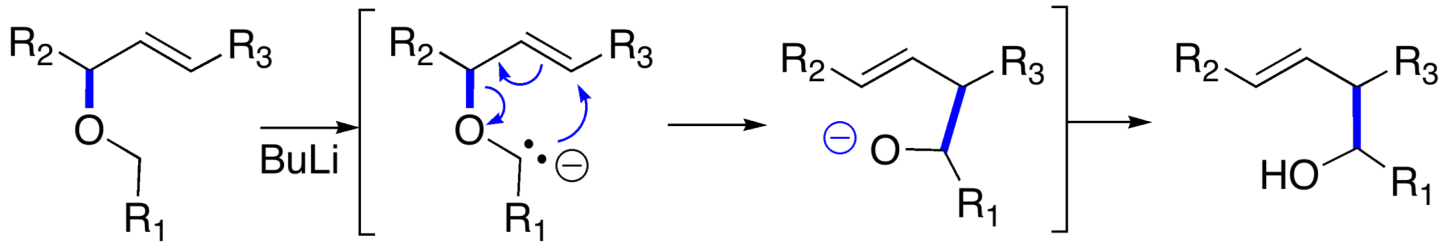
± favorable



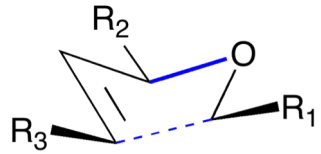

envisageable si molécule flexible

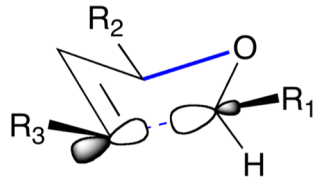
## 8.6.3 Autres Migrations

Réarrangement de Wittig  σ [2,3] C–C

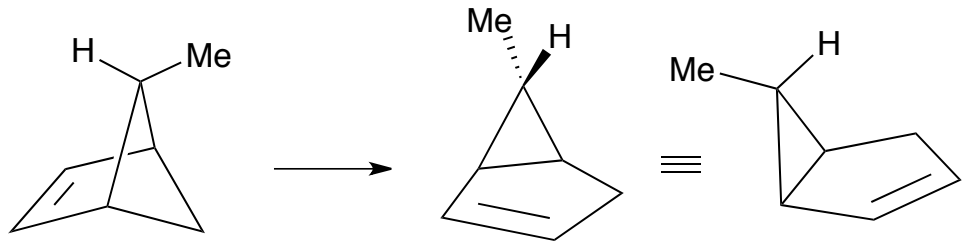


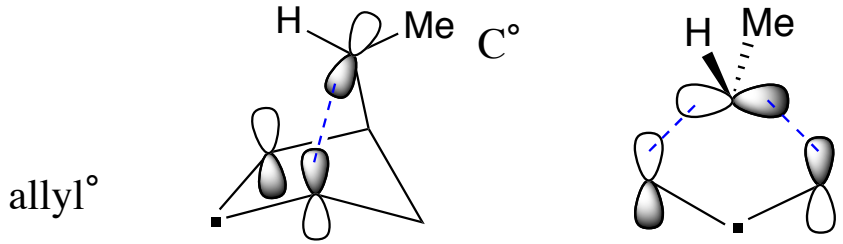

via

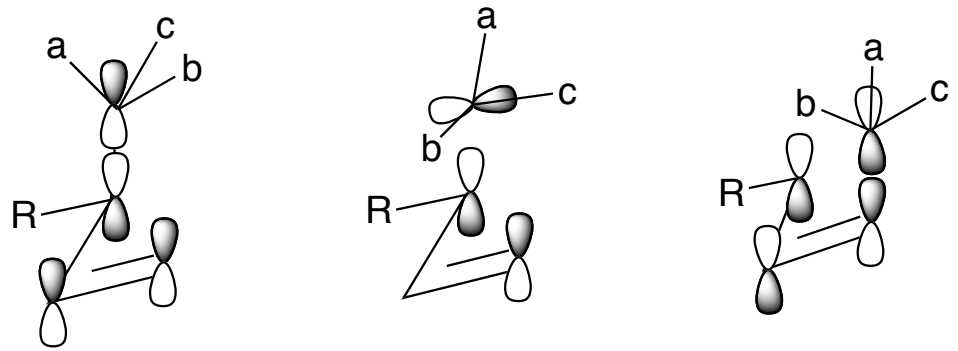


σ [1,3] C–X



# "règles" de Woodward-Hoffmann

| i+j | s-s<br>a-a | s-a<br>a-s |
|---|---|---|
| 4q | therm. defav. | therm. fav. |
| 4q+2 | therm. fav. | therm. defav. |