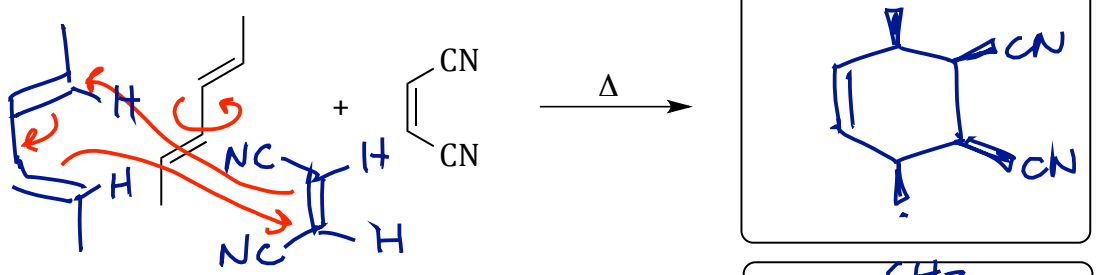
While you wait...

The Diels-Alder Reaction:
Test Yourself Now!

Consider the following dienes. Each one is heated with the dienophile *cis*-dicyanoethylene. For each diene, provide the product of the reaction; be sure to indicate **stereochemistry** where relevant. If no reaction will take place, write "no reaction" in the box. Then, **rank** the four dienes in terms of their rate of reaction with the dienophile, with 1 = fastest and 4 = slowest.

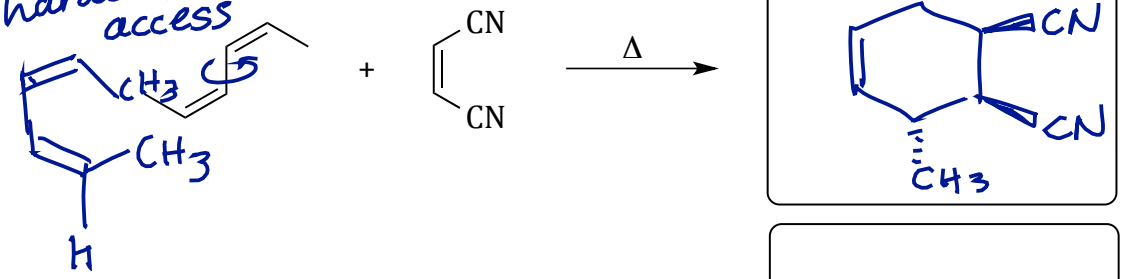
Ranking of reaction rate (1 = fastest)

S-cis



2

harder to access



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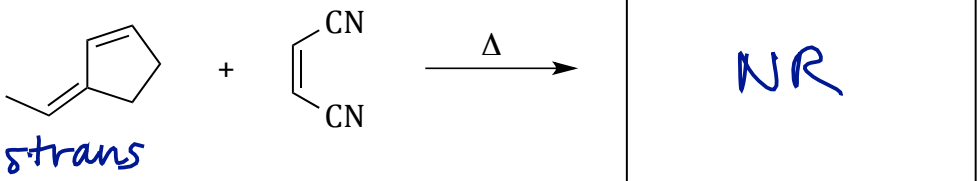
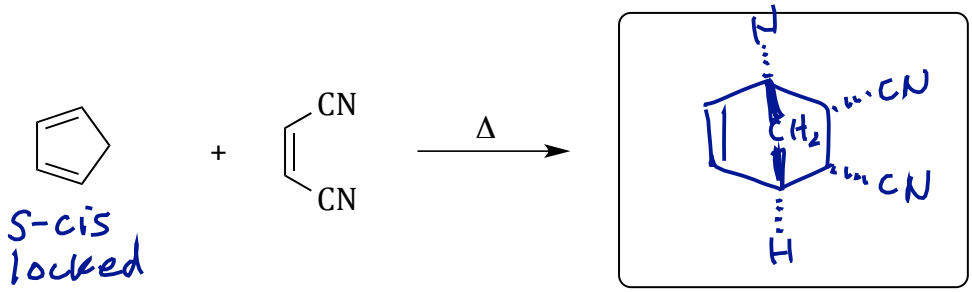


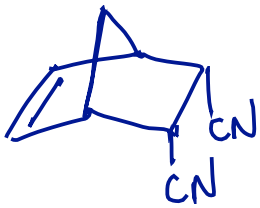
s-trans

4



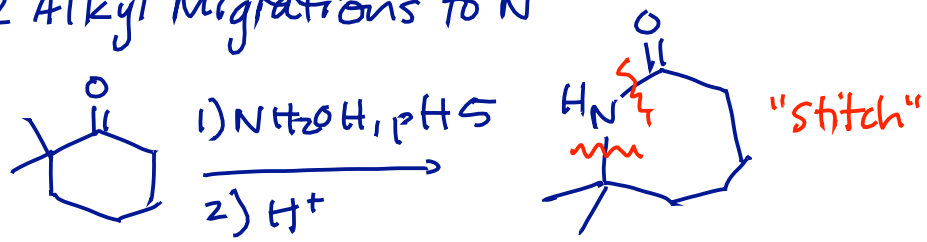
S-cis locked

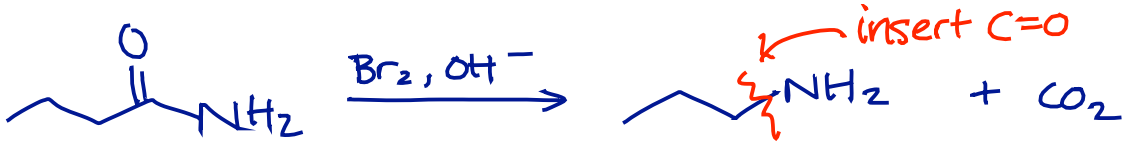
1

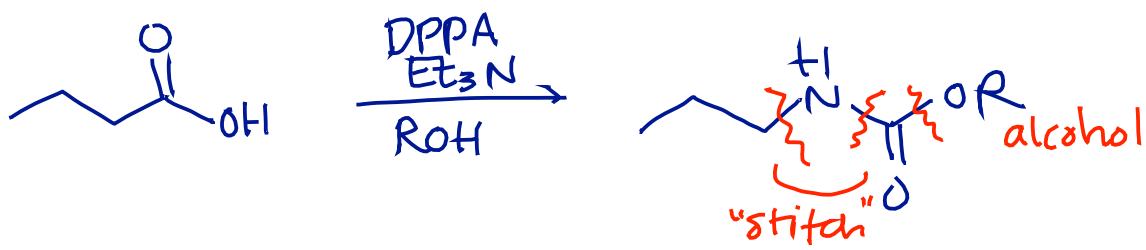


Recap:

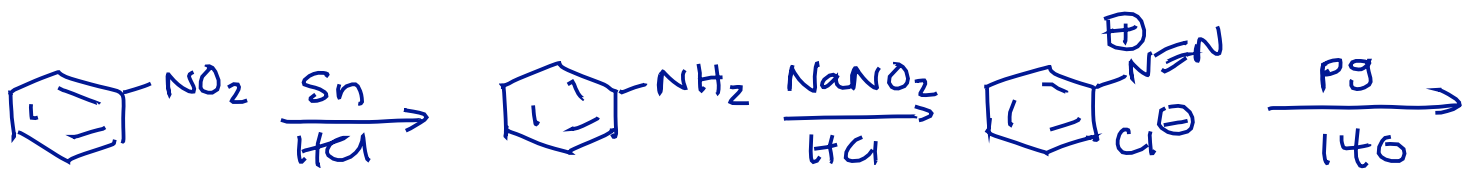
1) 1,2 Alkyl Migrations to N



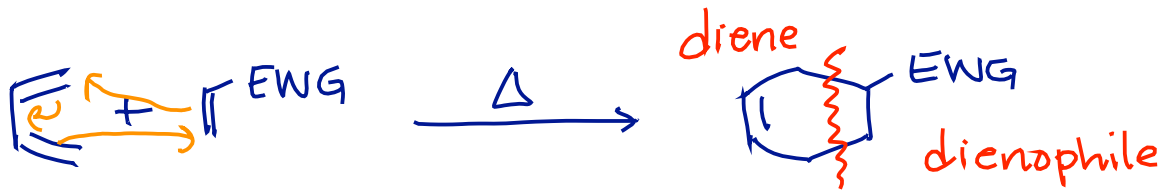




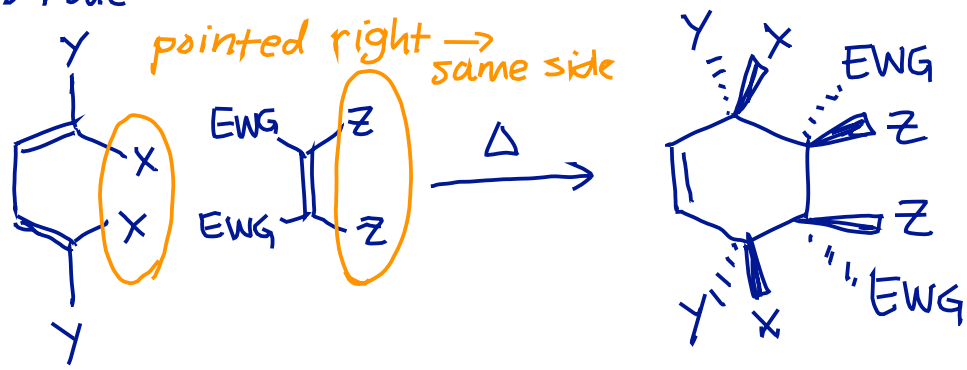
2) Diazonium Salts



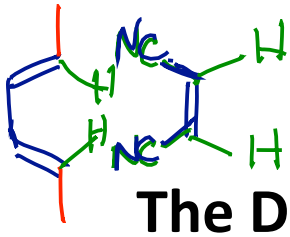
3) Diels Alder (DA) Rxn



- HOMO of diene + LUMO of dienophile
- diene & dienophile stereochem preserved
- "ends rule"



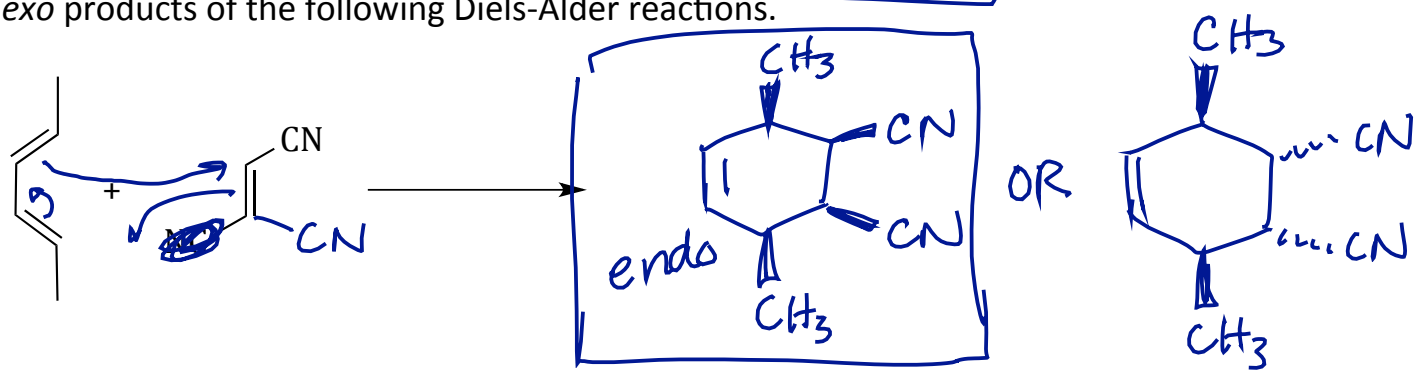
NET: lose 2 π bonds, Gain 2 σ bonds

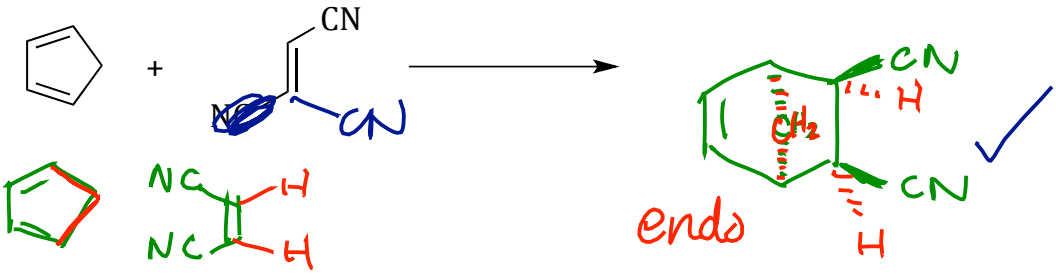
Week 6  → right = same side July 29, 2014

The Diels-Alder Reaction:

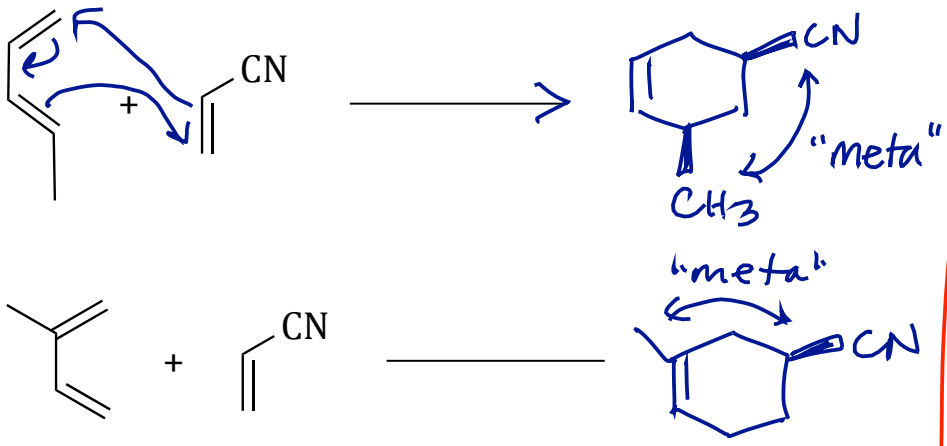
Stereo- and Regiochemistry

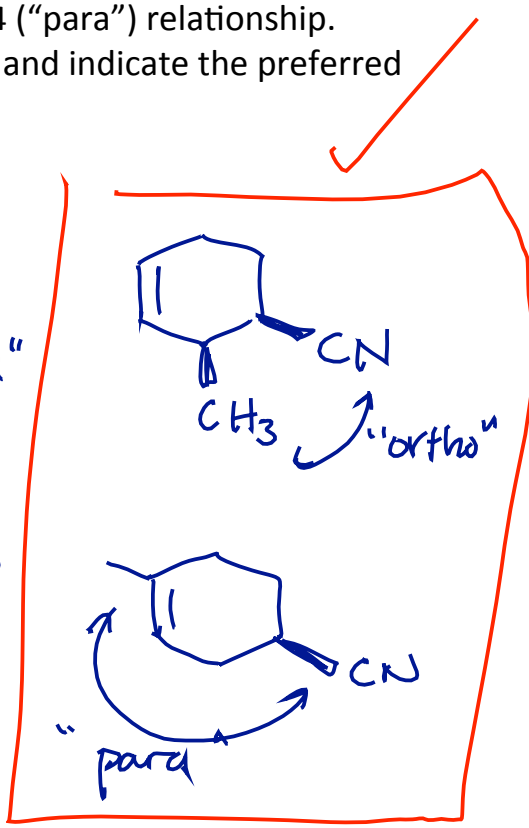
When relevant, the *endo* diastereomer is favored (the "*endo rule*"). Show the *endo* and *exo* products of the following Diels-Alder reactions.





Finally, when there are two possible regioisomers that can be formed, the preferred isomers usually have the substituents in a 1,2 ("ortho") or 1,4 ("para") relationship. Show both possible regioisomers for the following reactions, and indicate the preferred isomer:





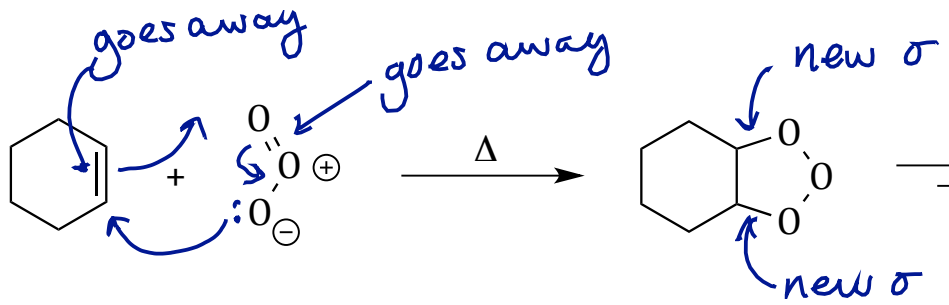
Reading: Section 15.3

loss of 2 π bonds
gain of 2 σ bonds

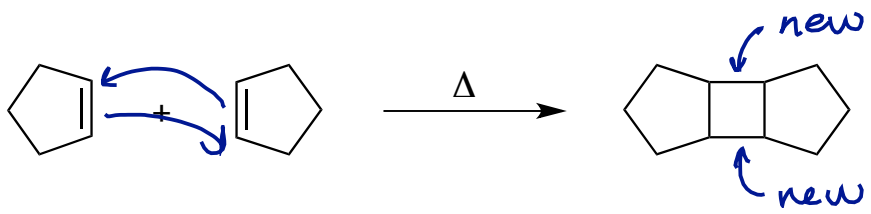
Week 6 July 30, 2014

Pericyclic Reactions 1:
Cycloadditions — 2 π-systems come together to make 1

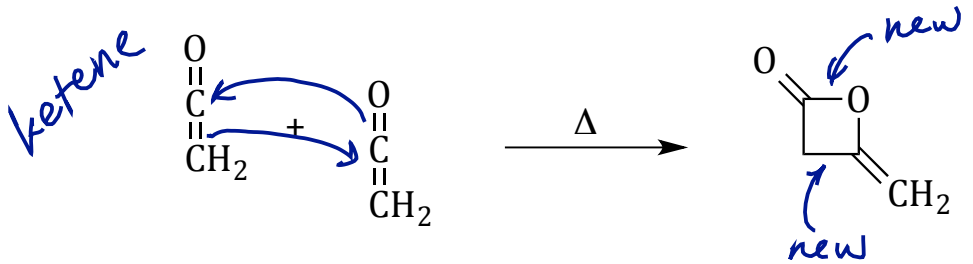
For each of the following "Diels-Alder-like" reactions, draw the curved-arrow mechanism.



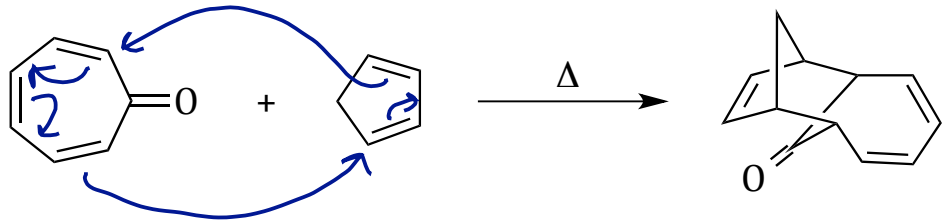
does *happen!*



does NOT *happen!*



does *happen!*



does *happen!*

Why do some reactions happen and others don't? Look at the ***frontier molecular orbitals…***

Reading: Section 27.3

[#s + #s/a]

s: suprafacial

a: antarafacial

Week 6

July 30, 2014

π e⁻

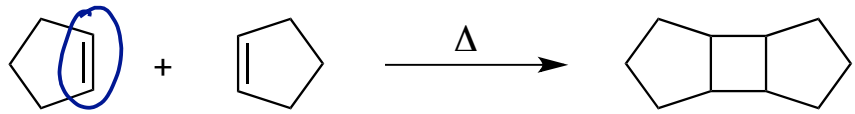
Cycloadditions:

Diels-Alder: thermal

[2s + 2s]

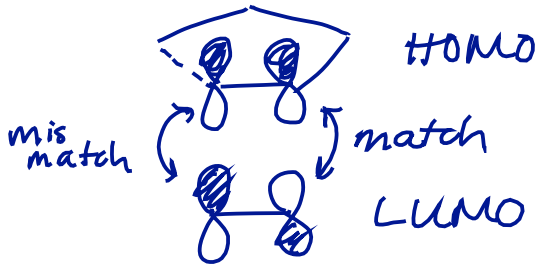
π EWG [4s + 2s]

Consider the following seemingly plausible reaction. Why doesn't it happen?



does NOT *happen!*

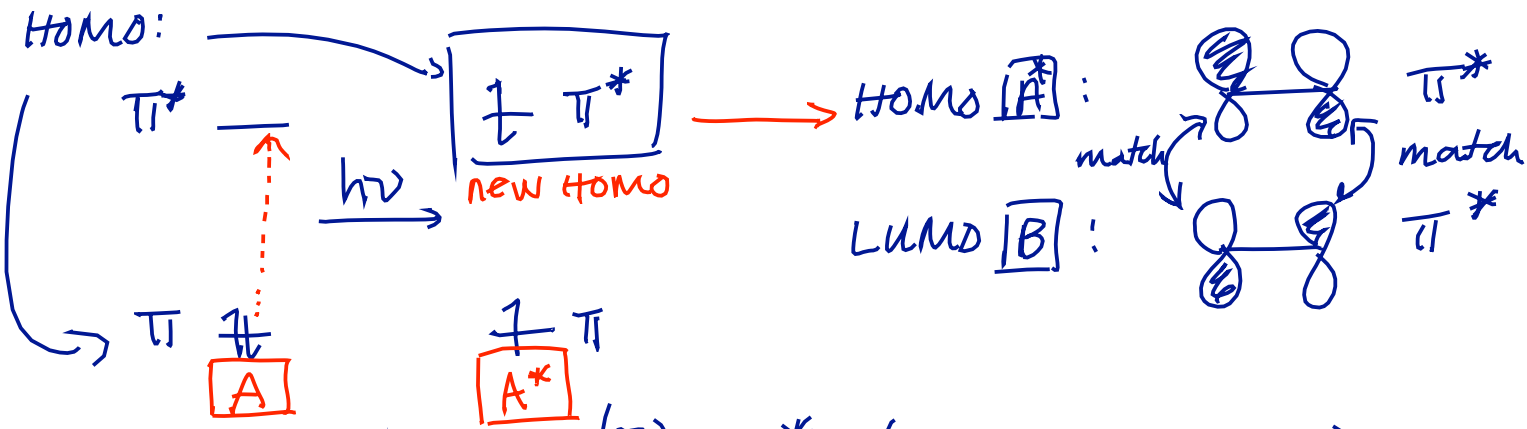
New bonds — filled-empty orb. interaction



No constructive orbital overlap

Forbidden by orbital symmetry

How can we *make* it happen? Change the frontier orbitals!



chemical $A \xrightarrow{h\nu} A^*$ (* = excited state)

Thus, we observe that [2s + 2s] cycloadditions are **thermally forbidden** but **photochemically allowed.**

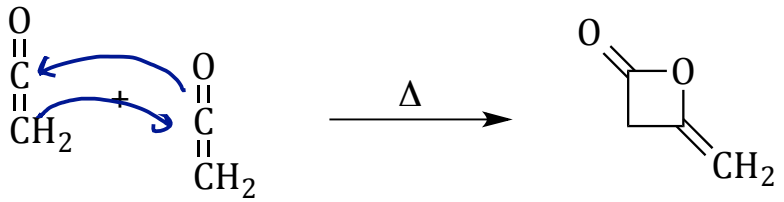
Reading: Section 27.3

cyclobutanes

Cycloadditions:

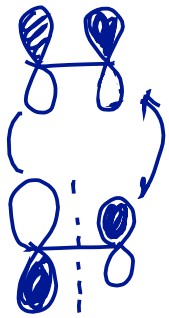
[2s + 2a] ← suprafacial/ antarafacial

Having said that [2s + 2s] cycloadditions are thermally forbidden, how can we explain the following *observed* reaction?



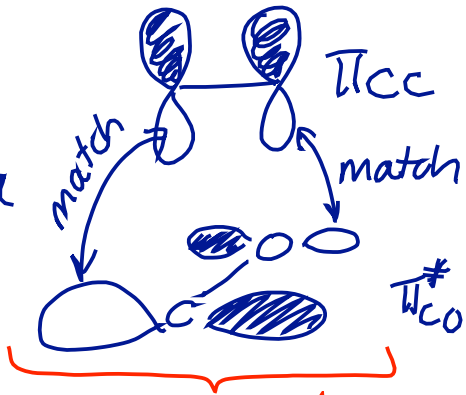
does *happen!*

"HOMO:" π_{CC} match



LUMO: π^*_{CO}

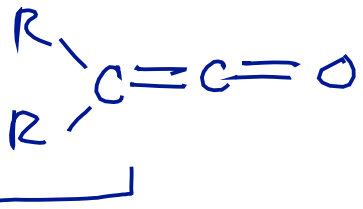
mismatch NO supra/supra



What are the requirements for **antarafacial** cycloadditions?

must have NO substituents on π-bonds

ONLY with ketenes



R must be small!

Reading: Section 27.3

2x # of arrows

Cycloadditions:
Putting it Together

πe^- Summarize the *selection rules* for cycloadditions:

6 → [4s + 2s] thermal — allowed

4 → [2s + 2s] photochemical — allowed

4 — [2s + 2a] thermal — allowed

General:

⬡ → 4n+2 e^- → thermally allowed, suprafacial

4n+2 e^- → photochemically, antarafacial ← rare

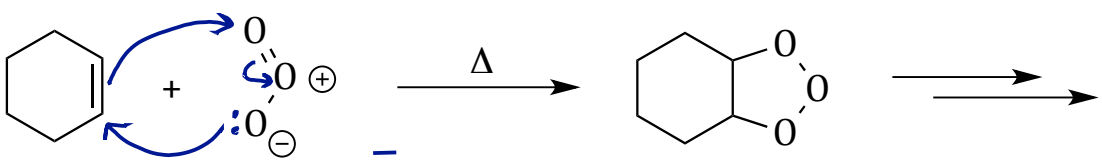
□ 4n e^- → thermal, antarafacial

→ 4n e^- → photochemical, suprafacial

Now analyze the following cycloadditions:

not in S-20

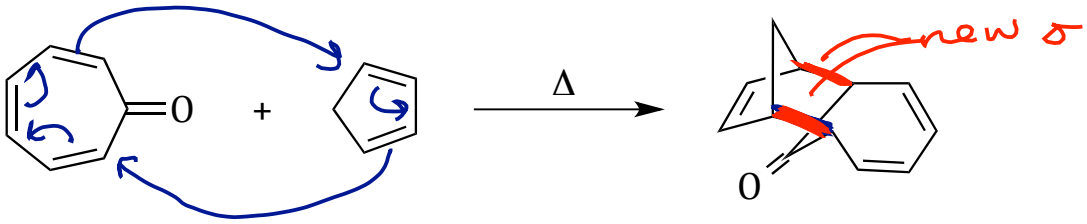
~~[3+2]~~



does *happen!*

3 arrows, 6 πe^-

[4s + 2s] thermal cycloaddition



does *happen!*

5 arrows → 10 πe^-

[6s + 4s] thermal cycloaddition

Reading: Section 27.3

Pericyclic – cyclic motion of e⁻

Week 6 ECRC/ECRO – a single π-system July 30, 2014

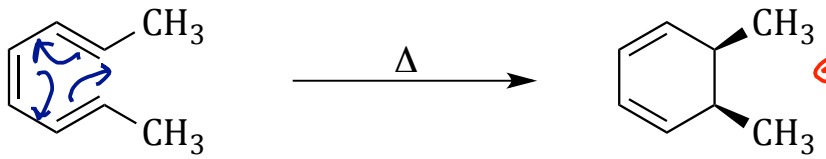
exchange of 1 π-bond for 1 σ-bond

snapping or shut

Pericyclic Reactions 2:
Electrocyclic Ring-Closing & Ring-Opening

Show the curved arrows for the following **electrocyclic reactions:**

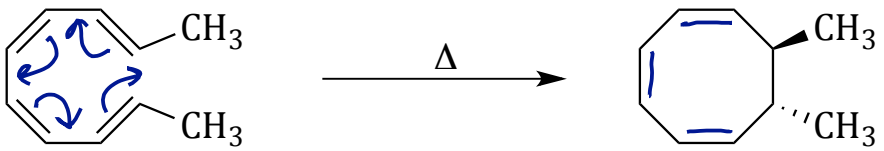
3 arrows (6 π e⁻)



← Stereochem!

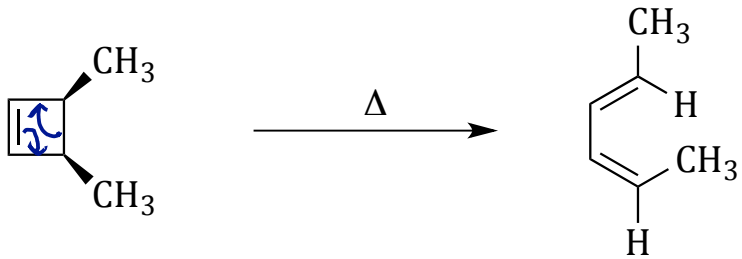
ECRC

4 arrows (8 π-e⁻)



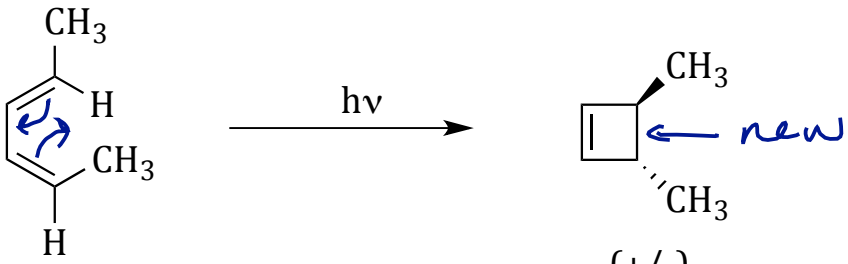
(+/-)

2 arrow 4 π e⁻



ECRO

2 arrow 4 π e⁻



← new

(+/-)

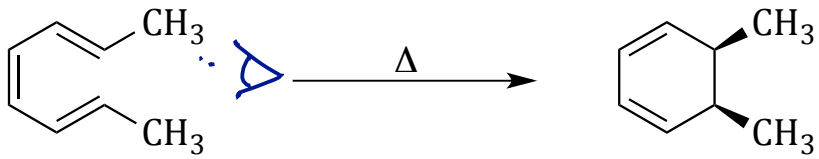
ECRC

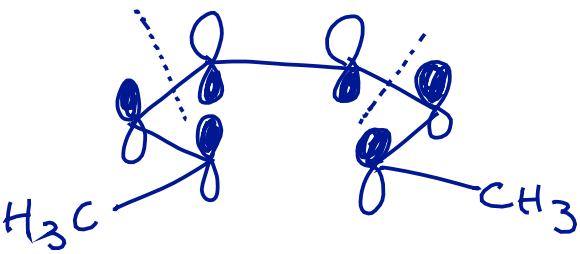
How can we explain the **stereochemistry**? Look at the **frontier molecular orbitals!**

Reading: Section 27.2

Electrocyclic Ring-Closing:
6 Electrons, Thermal

Explain the observed stereochemistry: 1 π system: look at HOMO

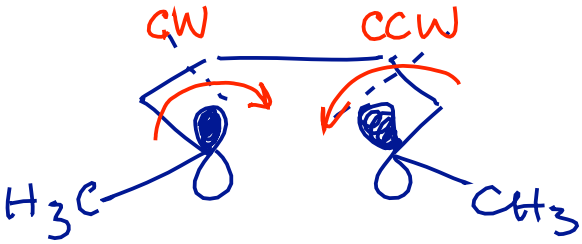




6 carbons – 6 p-orbitals

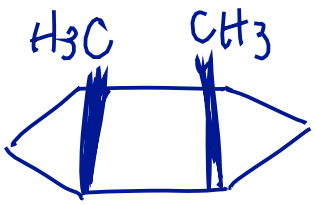
— 5
— 4
— 3
HOMO: $\boxed{\uparrow\uparrow \quad 2}$ nodes
$\uparrow\uparrow$ 1
$\uparrow\uparrow$ 0 nodes

Look just at end C:



DISROTATORY ← ring closure – opp direction

Disrotatory
6π e⁻
thermal
ECRC

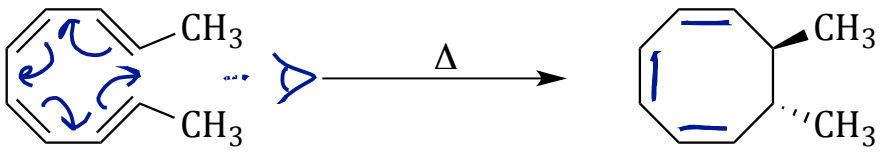


methyl groups

Reading: Section 27.2

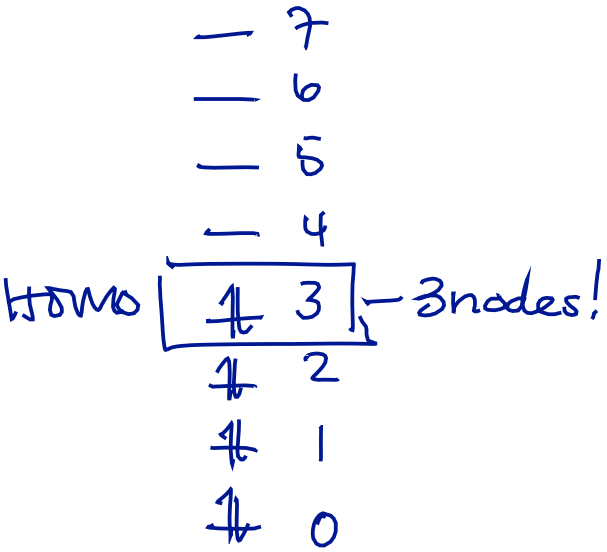
Electrocyclic Ring-Closing:
8 Electrons, Thermal

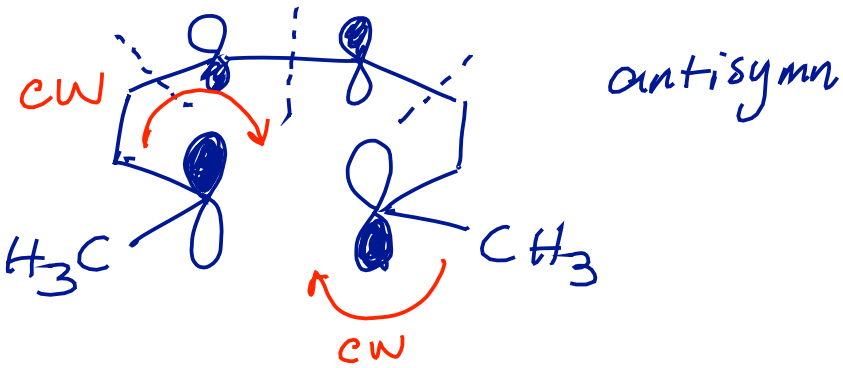
Explain the observed stereochemistry:



(+/-)

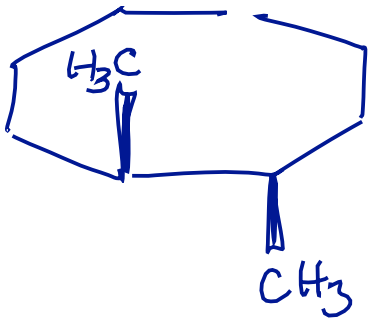
Look at HOMO





CONROTATORY RING CLOSURE

8πe⁻
thermal
conrotatory
ECRC

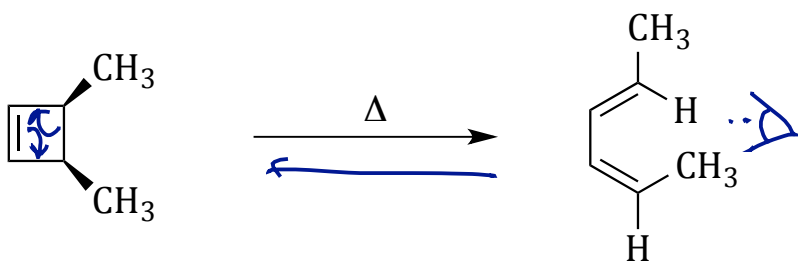


methyl groups trans

Reading: Section 27.2

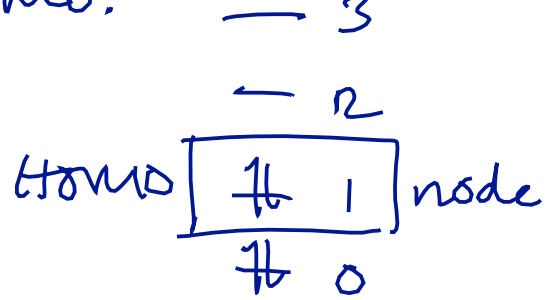
Electrocyclic Ring-Opening:
4 Electrons, Thermal

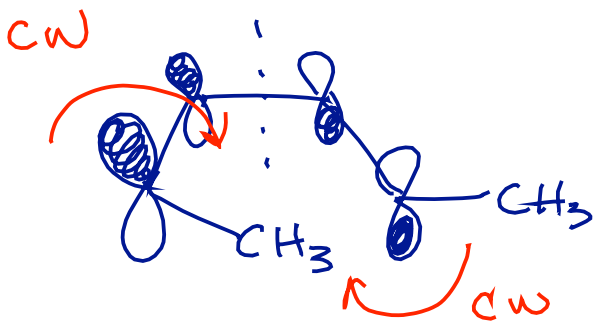
Explain the observed stereochemistry:



Ring Opening: Look at HOMO of product to see if dis or con rotatory

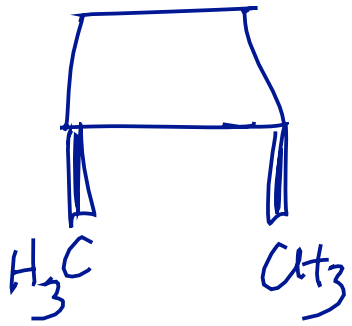
HOMO:





conrotatory

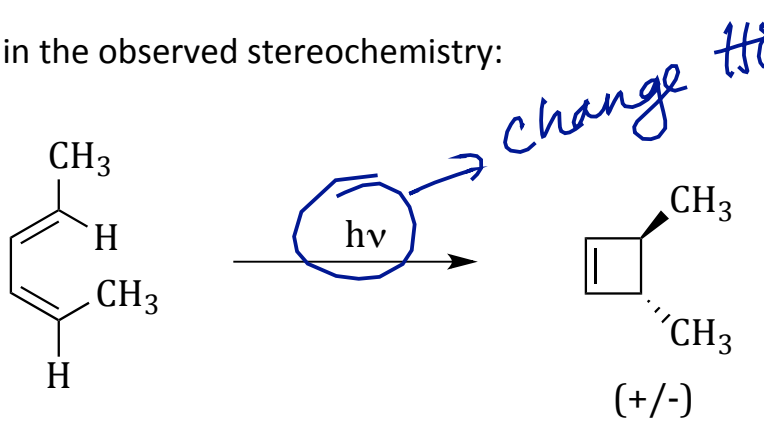
4 πe⁻
thermal
conrotatory
ECRO



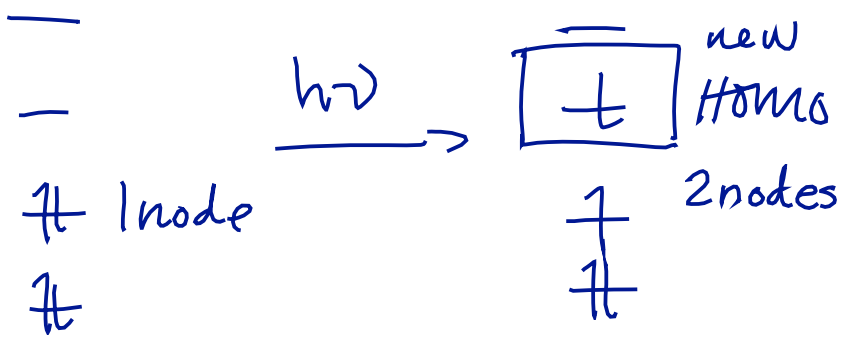
Reading: Section 27.2

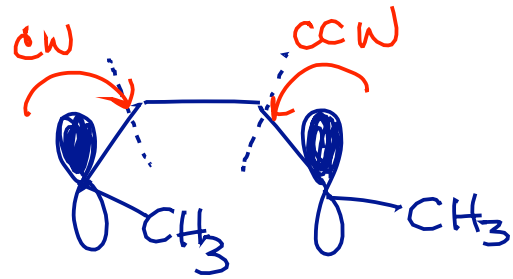
Electrocyclic Ring-Closing:
4 Electrons, Photochemical

Explain the observed stereochemistry:



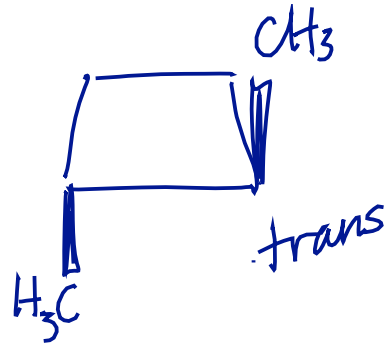
HOMO





DISROTATORY

4π e⁻
photochemical
disrotatory
ECRC



Ring-closing – make big rings (5–10 membered)

Ring-opening – open 3-4 membered ring 5

Reading: Section 27.2

Electrocyclic Reactions:
Putting It Together

Summarize the *selection rules* for electrocyclic reactions:

arrows eg.	# e⁻	Activation	Rot
3	4n+2	Thermal	disrotatory
even	4n	Thermal	conrotatory
odd	4n+2	hν	conrotatory
even	4n	hν	disrotatory

Mnemonic:

The Electrons Cycle Around

T ~ thermal
E ~ even # of arrows (4n e⁻)
C ~ conrotatory (for electrocyclic)
A ~ antarafacial for cycloadditions & σ-tropic rearrangements

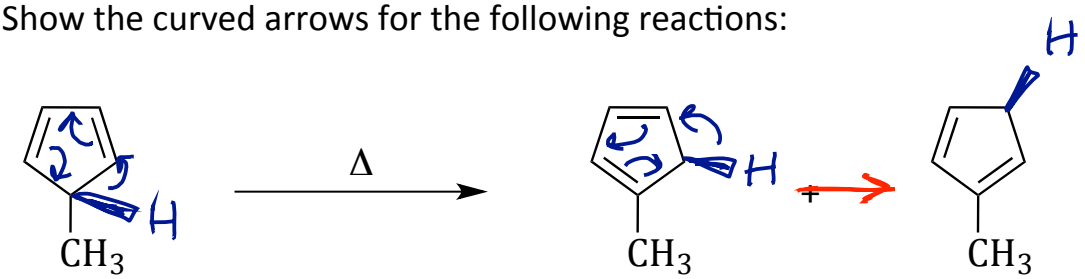
Reading: Section 27.2

Week 6 move a sigma bond from 1 place to another (and π bonds move) July 30, 2014

Pericyclic Reactions 3:
Sigmatropic Rearrangements

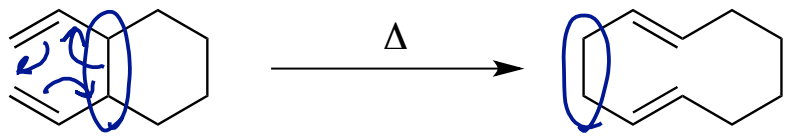
THERMAL

Show the curved arrows for the following reactions:

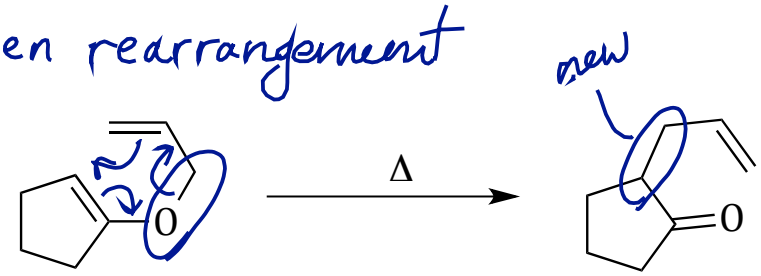


σ-tropic

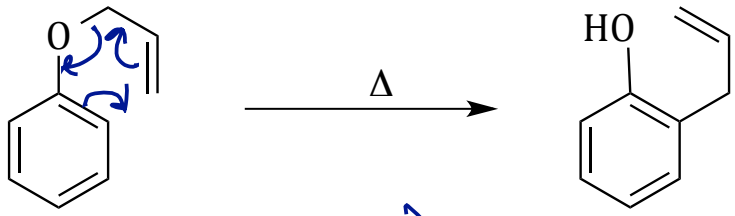
Cope rearrangement



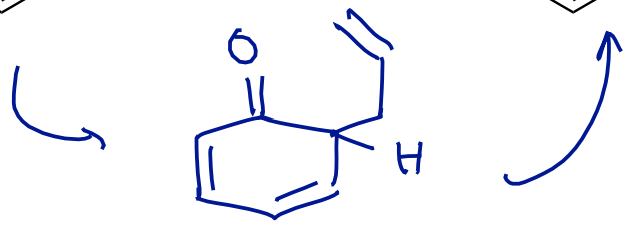
Claisen rearrangement



Claisen (II)



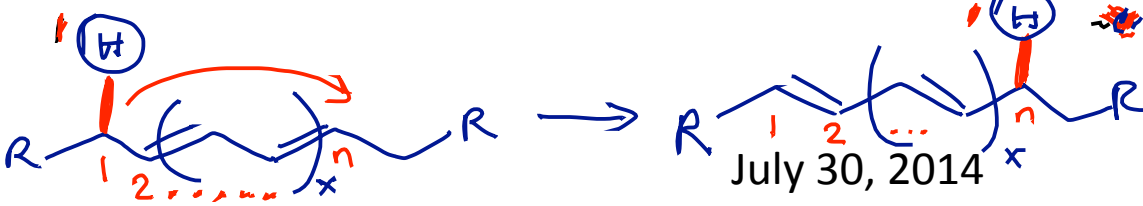
aromatic!



tautomerization

Reading: Section 27.4

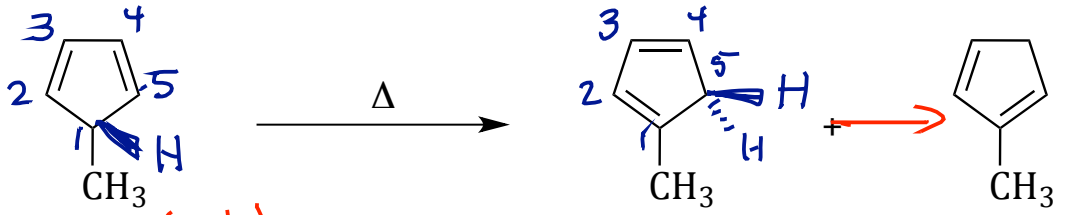
[#,#]



Week 6 July 30, 2014

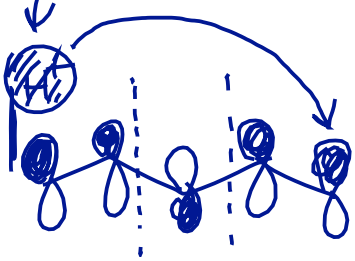
Sigmatropic Rearrangements: [1,n] & Stereochemistry

The following rearrangement is *suprafacial*. Why?



[1,5] sigmatropic rearr.

LUMO (H^+)

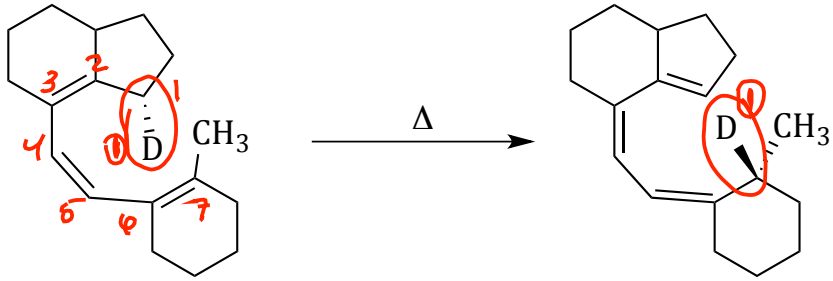


H^+

HOMO

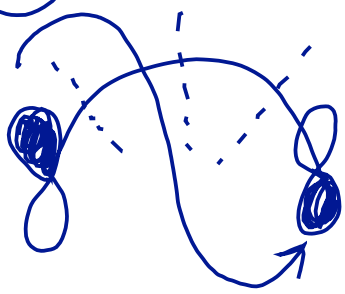
— 4
— 3
⇅ 2 ← HO MO
⇅ 1
⇅ 0

The following rearrangement is *antarafacial*. Why?



suprafacial [1,5] σ-tropic rearrangement thermally 6π e⁻

D^+



antisymmetric

HOMO

— 6
— 5
— 4
⇅ 3 — HOMO
⇅ 2
⇅ 1
⇅ 0 nodes

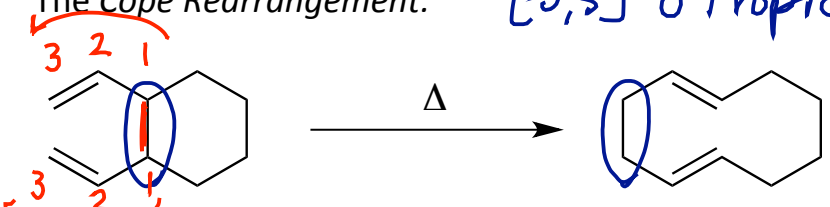
8π e⁻ antarafacial [1,7] σ-tropic rearrangement thermally

Reading: Section 27.4

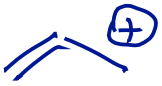
Sigmatropic Rearrangements:
MOs in [3,3] rearrangements = 6π e⁻

How can we understand the orbitals involved in the following rearrangements?

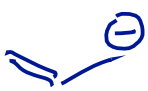
The *Cope Rearrangement:* [3,3] otropic rearrangement



1,5-diene



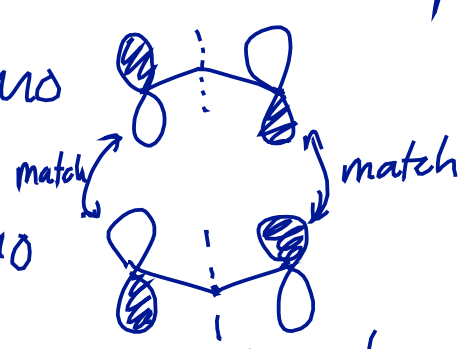
allyl cation



allyl anion

LUMO

HOMO

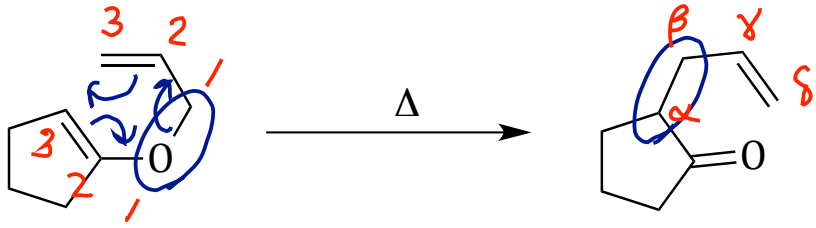


suprafacial

3 p-orb
LUMO — 1 nodes
⇅ 0 nodes

HOMO ⇅ 1 nodes (2)
⇅ 0

The *Claisen Rearrangement:*



[3,3] otropic rearrangement
thermal
suprafacial

Cope:
1,5-diene → 1,5 diene

Claisen rearr:
allyl vinyl ether
→ γ,δ-~~non~~ unsat. ketone

phenyl allyl ether → o-allyl phenol

Reading: Section 27.4

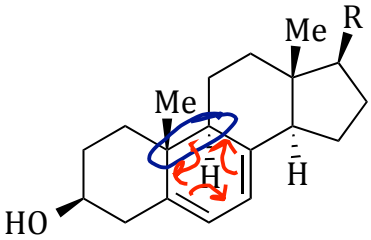
Sigmatropic Rearrangements:
Putting it Together

Summarize the *selection rules* for sigmatropic rearrangements:

By Far, most important!

#e⁻			
4n+2	thermal	→	suprafacial
4n	thermal	→	antara
4n+2	photochem.	→	antara
4n	photochem	→	suprafacial

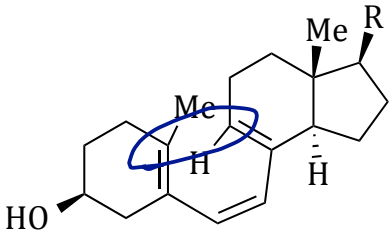
Let's examine the biosynthesis of Vitamin D. Why is sunlight required?



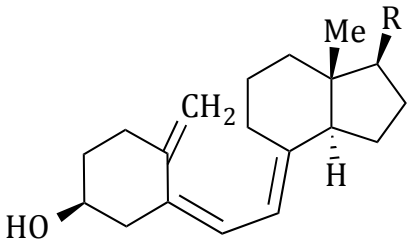
7-dehydrocholesterol

hν

ECRO
6πe⁻
conrotatory
photo

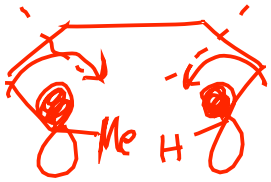


previtamin D_3



vitamin D_3

dis



THERMAL
HOMO

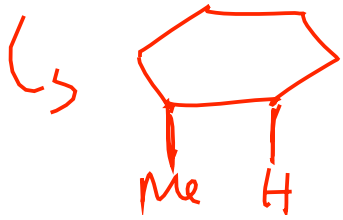
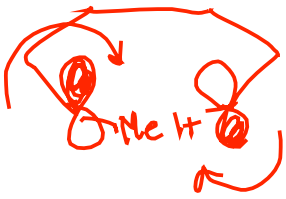


PHOTO
HOMO



Reading: Section 27.7