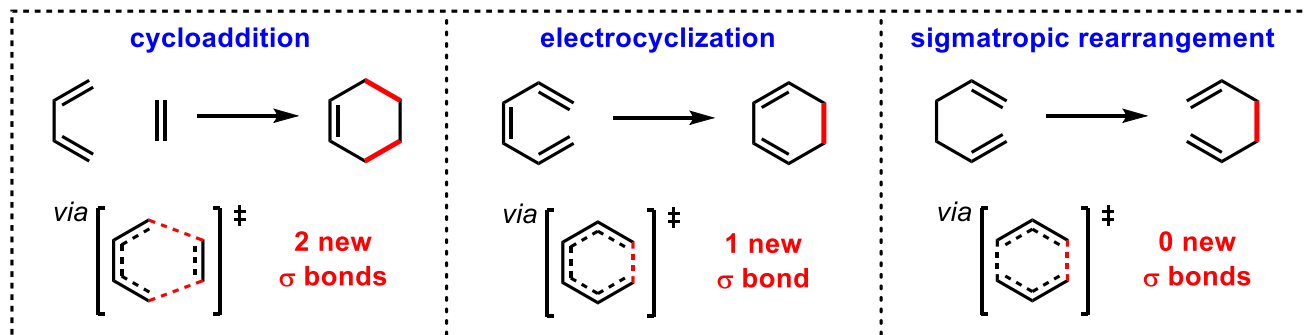


Woodward–Hoffmann Rules: Pericyclic Reactions

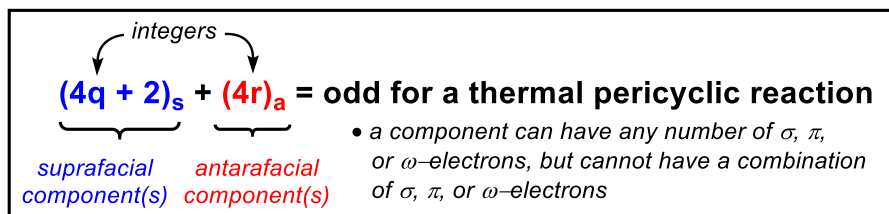
Woodward–Hoffmann rules and Frontier Molecular Orbital Theory (investigated by Kenichi Fukui) are used to analyze *pericyclic reactions*.

- Hoffmann and Fukui were awarded the Nobel Prize in 1981 for their seminal studies in predicting chemical reactivities and understanding reaction mechanisms.



- Pericyclic reactions have concerted transition states and no reaction intermediates

Woodward and Hoffmann considered the fundamental correlation between the symmetry of all the orbitals in the starting material and product, which can be summarized by:



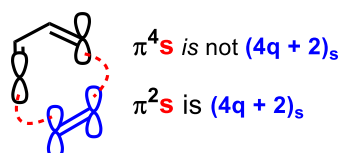
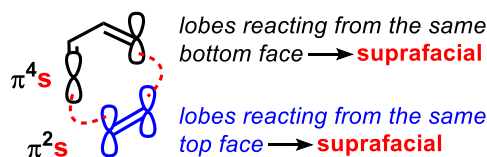
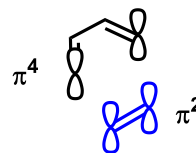
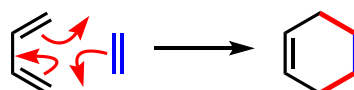
A) Cycloadditions

a) Diels–Alder [4 + 2] reaction

- Assign the components, including all and only the bonds that are transforming.
- Draw the components approaching in a reactive conformation, including orbitals at the end of each component. It is not necessary to shade the orbitals (cf. FMO theory)
- Join the components between the newly forming bonds and label *s* or *a*
- Determine the number of $(4q + 2)_s$ and $(4r)_a$ components.

$$(4q + 2)_s + (4r)_a = 1 + 0 = 1 \text{ (odd)}$$

[4 + 2] cycloadditions are thermally allowed

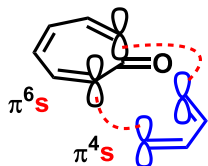
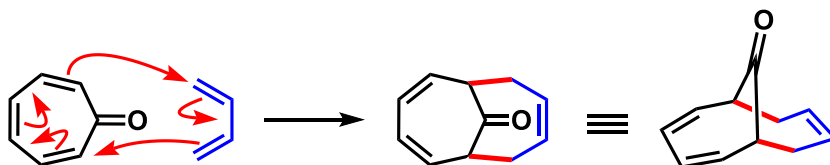


there are no $(4r)_a$ components

Woodward–Hoffmann Rules: Pericyclic Reactions

Cycloadditions (cont.)

b) [6 + 4] Cycloaddition

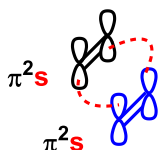
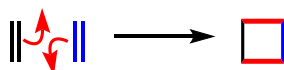


π^6_s is $(4q + 2)_s$
 π^4_s is not $(4q + 2)_s$

$$(4q + 2)_s + (4r)_a = 1 + 0 = 1 \text{ (odd)}$$

[6 + 4] cycloadditions are thermally allowed

c) [2 + 2] Cycloaddition

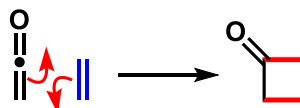


π^2_s is $(4q + 2)_s$

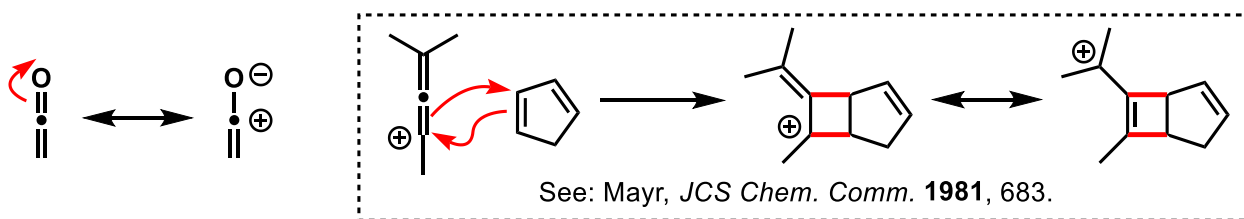
$$(4q + 2)_s + (4r)_a = 2 + 0 = 2 \text{ (even)}$$

[2 + 2] cycloadditions are not thermally allowed

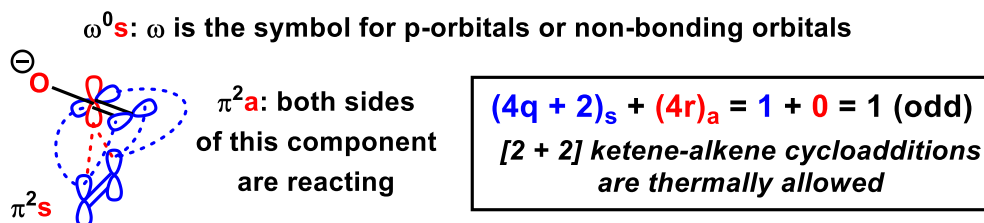
d) [2 + 2] Ketene-alkene cycloaddition



- Some WH analyses are derived from an FMO analysis or simply suggest ketene [2 + 2] cycloadditions are exceptions to the WH rules
- The analysis below uses the ketene in the form of its vinyl cation resonance structure. This is a valid assumption because vinyl cations are reported to undergo [2 + 2] cycloadditions:



- Since the carbonyl electrons are held on oxygen, which is not involved in the cycloaddition, it is not included in our WH analysis:

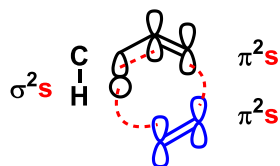
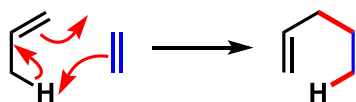


- ω^0_s and π^2_a components are irrelevant in the equation because they do not represent $(4q + 2)_s$ or $(4r)_a$ components
- Refer to class notes for the orthogonal approach between the ketene and alkene

Woodward–Hoffmann Rules: Pericyclic Reactions

Cycloadditions (cont.)

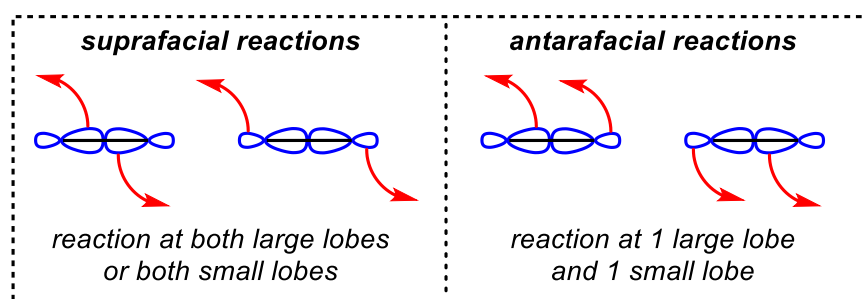
e) Alder–ene reaction



$$(4q + 2)_s + (4r)_a = 3 + 0 = 3 \text{ (odd)}$$

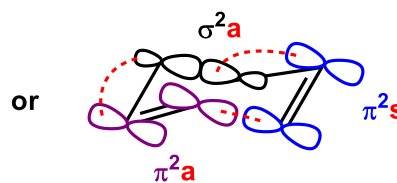
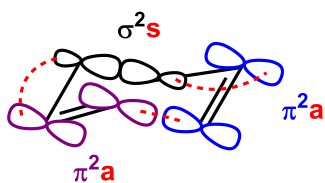
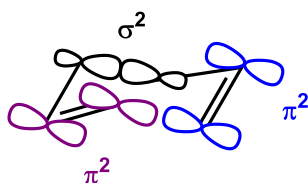
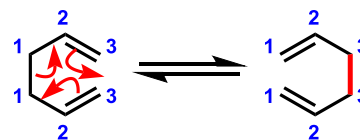
**Alder–ene reactions
are thermally allowed**

- Deducing whether σ -components react suprafacially or antarafacially are less obvious than with π -components
- Hydrogens have no nodes (1s orbital); therefore, C(sp³)–H(s) bonds simply react suprafacially



B) Sigmatropic Rearrangements

a) [3,3] sigmatropic rearrangement (e.g., Cope rearrangement)

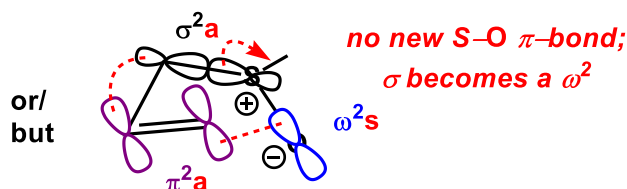
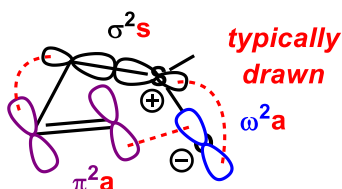
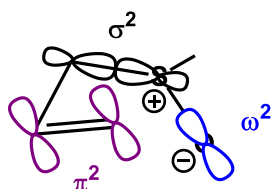
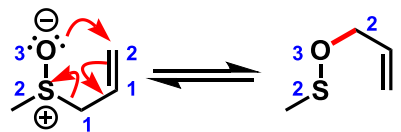


$$(4q + 2)_s + (4r)_a = 1 + 0$$

$$(4q + 2)_s + (4r)_a = 1 + 0$$

- Even though different orbitals are joined in the two analyses above, joining any of the geometrically-aligned orbitals at the ends of each components will result in the same outcome

b) [2,3] sigmatropic rearrangement (e.g., Mislow rearrangement)



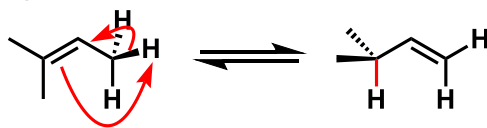
$$(4q + 2)_s + (4r)_a = 1 + 0$$

$$(4q + 2)_s + (4r)_a = 1 + 0$$

Woodward–Hoffmann Rules: Pericyclic Reactions

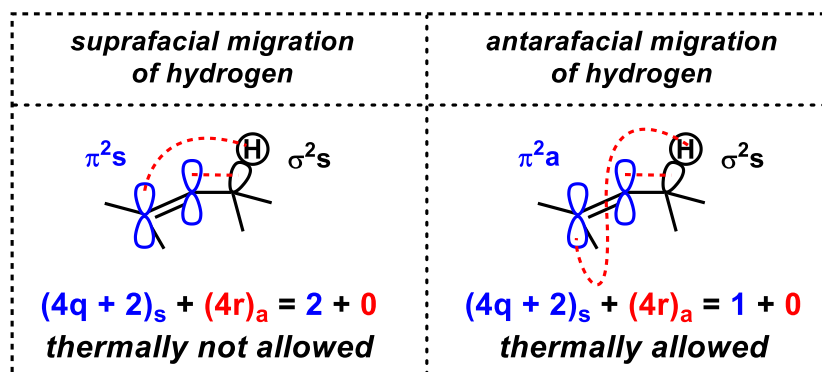
Sigmatropic Rearrangements (cont.)

c) [1,3] hydrogen shift



- Shifting of hydrogen across the same face of the π -system termed **suprafacial migration**
- Shifting of hydrogen across the opposite face of the π -system termed **antarafacial migration**

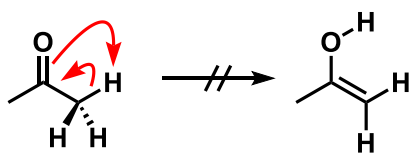
Note: Suprafacial/antarafacial hydrogen migrations does not refer to the σ -, π -, ω -components reacting suprafacially or antarafacially; both need to be considered



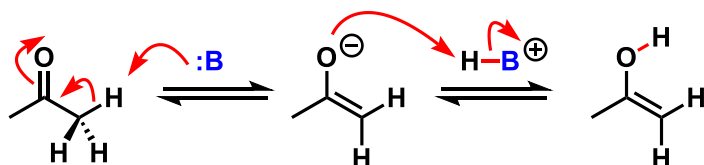
Thermal [1,3] hydrogen shifts do not occur despite the antarafacial migration being allowed by Woodward–Hoffmann rules. This antarafacial migration is **geometrically forbidden because it requires the reacting orbitals to completely unalign**

Relevance to intramolecular proton transfers

Keto–enol tautomerization

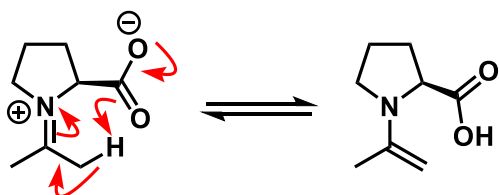


An intramolecular proton transfer, which represents a [1,3] H-shift, is thermally allowed but geometrically-forbidden due to poor orbital overlap.



Therefore, a base is necessary to mediate proton-transfers.

Unassisted, intramolecular proton transfers?



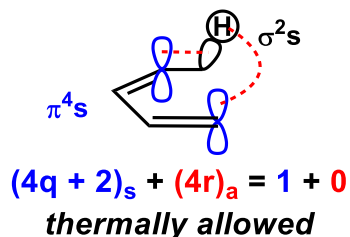
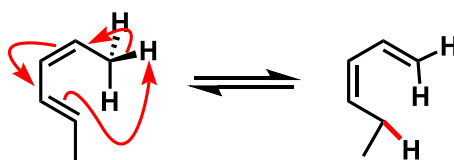
Not outside the realm of possibilities if the molecule can adopt a suitable conformation.

Higher likelihood if the solvent is not polar protic.

Woodward–Hoffmann Rules: Pericyclic Reactions

Sigmatropic Rearrangements (cont.)

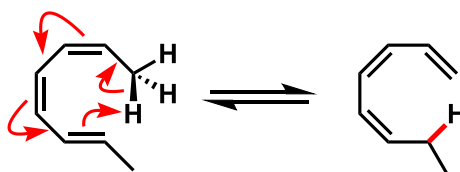
d) [1,5] hydrogen shift



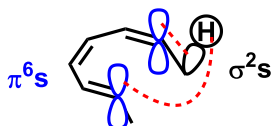
- *suprafacial migration*

- [1,5] H-shifts can compete with other reactions (e.g., [4 + 2] cycloadditions, especially with E, Z, dienes)

e) [1,7] hydrogen shift

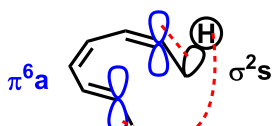


suprafacial migration
of hydrogen



thermally not allowed

antarafacial migration
of hydrogen

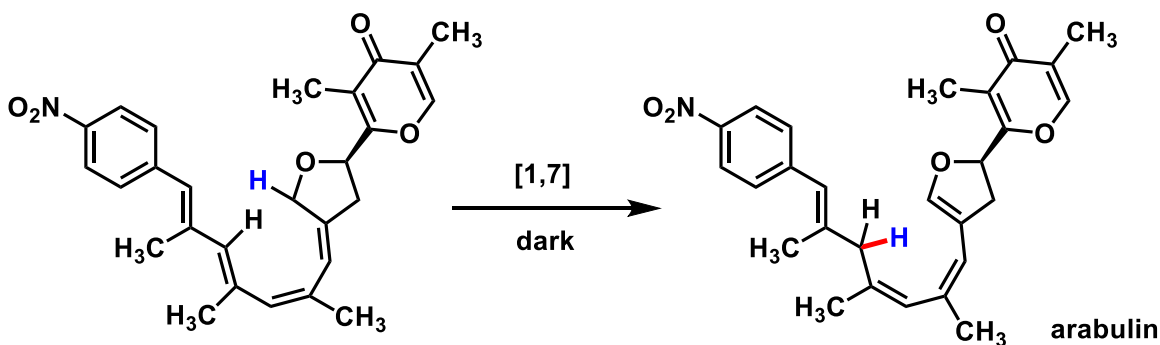


thermally allowed

- Unlike [1,3] H-shifts where antarafacial migration of hydrogen is geometrically forbidden, this 7 carbon chain is flexible enough to allow [1,7] H-shifts to occur without substantial disruption of the π -network;

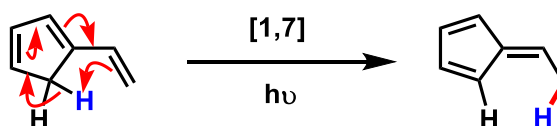
- Rigid structures will not undergo thermal [1,7] hydrogen shifts

- An antarafacial [1,7] hydrogen shift has been demonstrated in a biomimetic, natural product synthesis:



Parker: JACS 2011, 133, 20149.

- Thermally-forbidden, suprafacial [1,3] and [1,7] shifts may be promoted photochemically:

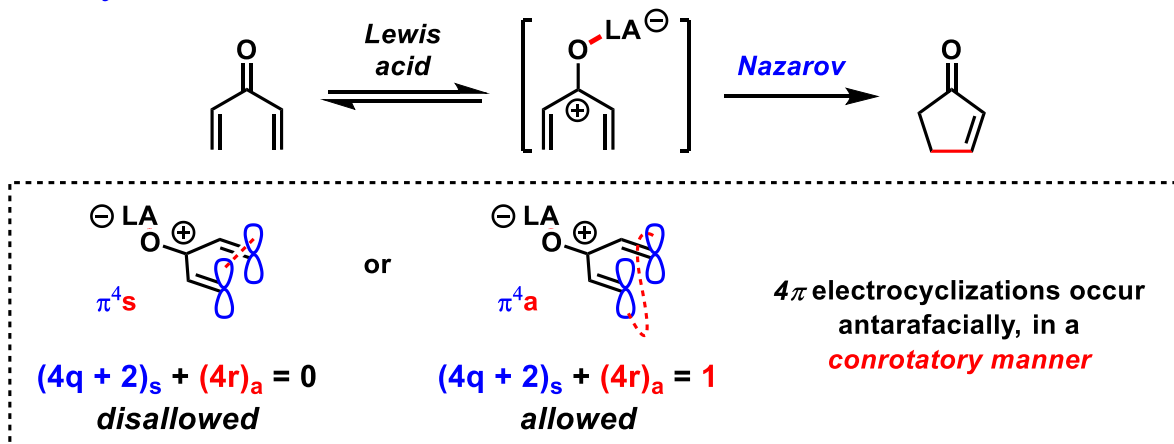


Woodward–Hoffmann Rules: Pericyclic Reactions

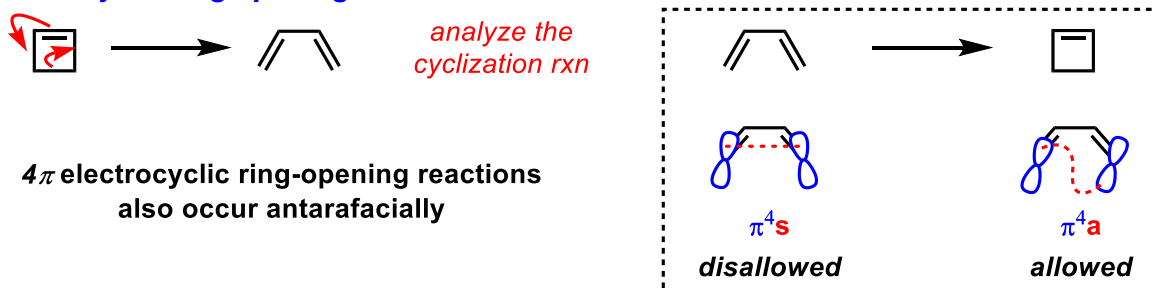
C) Electrocyclic Reactions

a) 4π electrocyclization or ring-opening

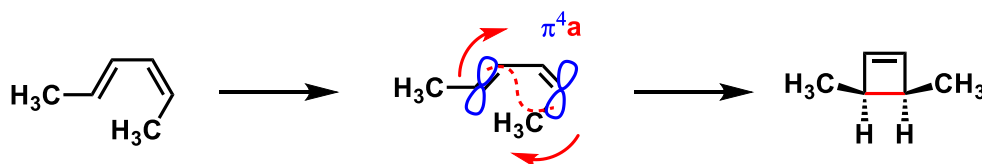
- Nazarov cyclization**



- 4π electrocyclic ring opening**

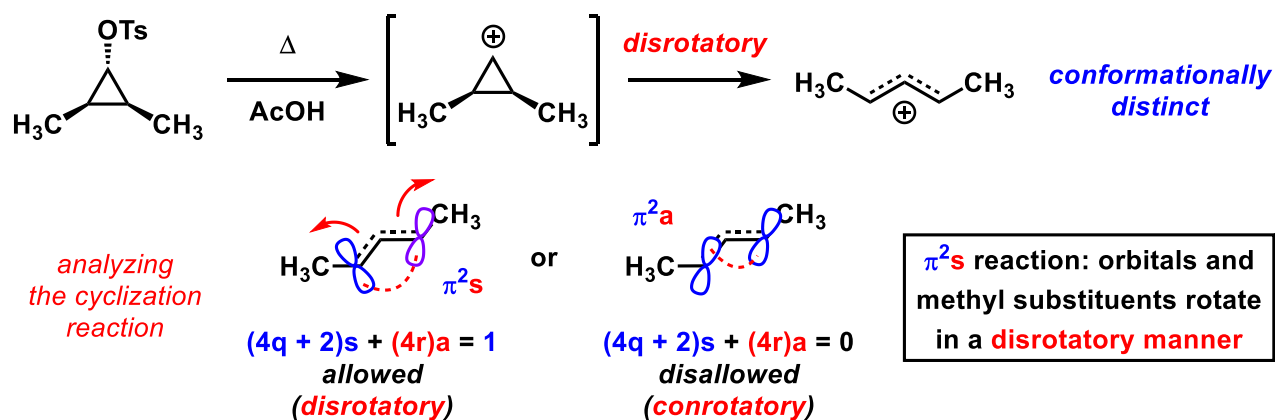


- Woodward–Hoffmann rules can rationalize stereoselectivity:



π^4_a reaction: the orbitals and methyl substituents rotate in a conrotatory manner

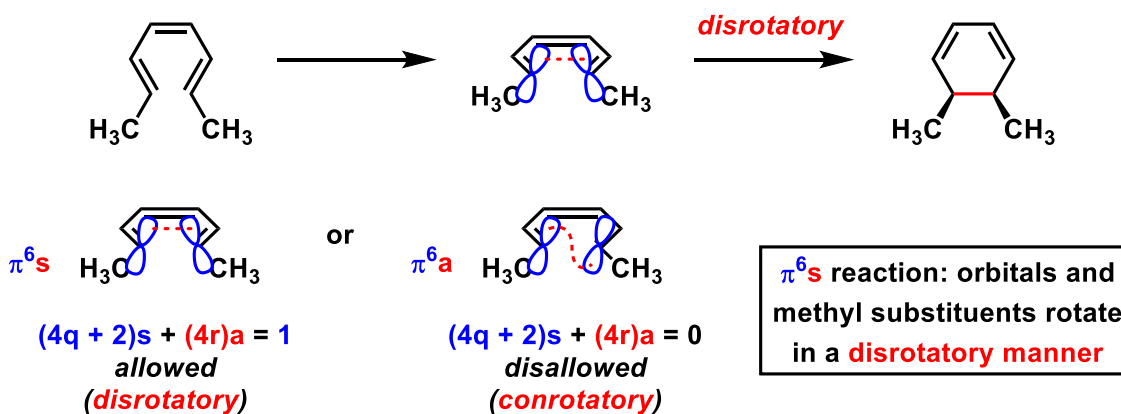
b) 2π electrocyclic ring opening



Woodward–Hoffmann Rules: Pericyclic Reactions

C) Electrocyclic Reactions

c) 6π electrocyclization



- Thermal electrocyclic reactions involving $(4n)\pi$ electrons **are conrotatory**
- Thermal electrocyclic reactions involving $(4n+2)\pi$ electrons **are disrotatory**

Pericyclic reactions are photochemically allowed when $(4q + 2)_s + (4r)_a = \text{even}$

- Those [1,3], [1,5], and [1,7] hydrogen shifts described in this Handout that are not thermally allowed are photochemically allowed
- Those electrocyclic reactions that are not thermally allowed are photochemically allowed