CFQ & PP: Pericyclic Reactions

Reading

Brown and Foote: Sections 23.3 and 23.4

Suggested Text Exercises

Brown and Foote Chapter 23: 4 – 8, 21 – 34, 38 - 43

Optional Web Site Reading

- 1950 Nobel Prize in Chemistry (http://www.nobel.se/chemistry/laureates/1950)
- 1981 Nobel Prize in Chemistry (http://www.nobel.se/chemistry/laureates/1981/)

Optional Interactive Organic Chemistry CD and Workbook

Claisen Rearrangement (p. 23)

Concept Focus Questions

1. Define the following terms.
   (a) Cheletropic reaction
   (b) Concerted reaction
   (c) Cycloaddition reaction
   (d) Electrocyclic reaction
   (e) HOMO
   (f) LUMO
   (g) Pericyclic reaction
   (h) Sigmatropic reaction
   (i) Woodward-Hoffmann rules

2. Provide general examples of the following reactions, including curved arrows and transition states. Provide a brief written description outlining the key features of each reaction.
   (a) Claisen rearrangement
   (b) Cope rearrangement
   (c) Decarboxylation by 1,5-H shift
   (d) Diels-Alder reaction
   (e) Vinyl cyclopropane rearrangement

3. What stabilizing structural feature is common to the transition states of the Diels-Alder reaction, Claisen rearrangement and Cope rearrangement?

4. Very briefly explain the fundamental concept of the Woodward-Hoffmann rules.

5. Why is a $[4\pi + 2\pi]$ cycloaddition thermally allowed and photochemically forbidden, whereas a $[2\pi + 2\pi]$ cycloaddition is photochemically allowed and thermally forbidden?

Concept Focus Questions Solutions

1. (a) <u>Cheletropic reaction</u>: A retrocycloaddition in which a small molecule such as CO or SO_2 is lost.

   (b) <u>Concerted reaction</u>: Any reaction in which all bond breaking and bond making occurs in a single step.

(c) Cycloaddition reaction: Any addition reaction that results in the formation of a new ring.

(d) Electrocyclic reaction: An intramolecular reaction of a single conjugated π electron system in which a ring is formed or broken.

(e) HOMO: **H**ighest **O**ccupied **M**olecular **O**rbital. The highest energy molecular orbital that bears an electron pair.

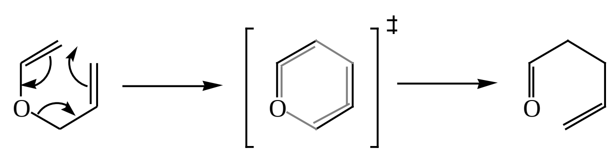
(f) LUMO: **L**owest (energy) **U**noccupied **M**olecular **O**rbital.

(g) Pericyclic reaction: Any reaction that occurs by a concerted shift of electrons in a cyclic transition state.

(h) Sigmatropic reaction: Any pericyclic reaction in which the σ bond at one end of the molecule is broken while a new σ bond is formed at the other end.

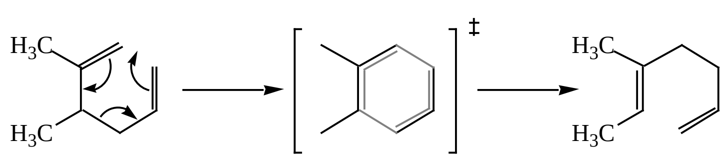
(i) Woodward-Hoffmann rules: Orbital combination rules that define the number of atoms and orbitals involved in pericyclic reactions.

2. (a) Claisen rearrangement: An allyl vinyl ether rearranges to a γ,δ-unsaturated carbonyl compound.

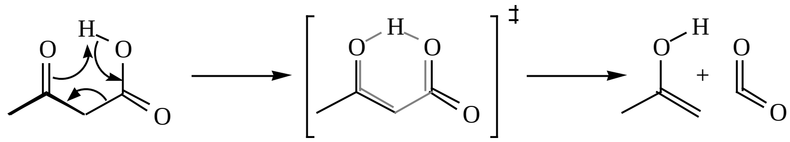


The curved arrows can "flow" clockwise or counterclockwise. Either is acceptable as the reaction has no nucleophile and electrophile, and both directions give the same product.

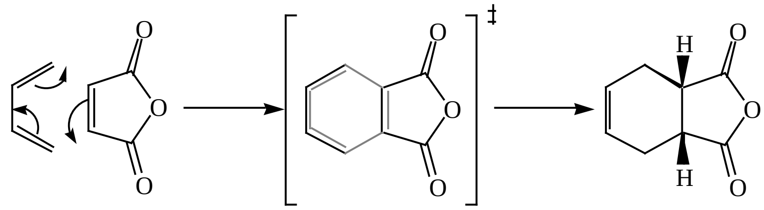
(b) Cope rearrangement: A 1,5-diene rearranges to another 1,5-diene.



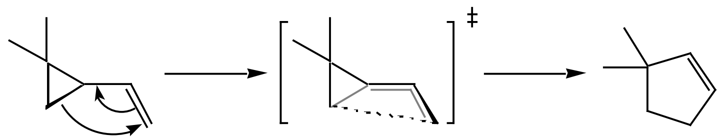
(c) Decarboxylation by 1,5-H shift: A molecule bearing a carbonyl group β to a carboxylic acid loses CO_2 through a 1,5-H shift.



(d) Diels-Alder reaction: A concerted cycloaddition reaction between an *s*-cis 1,3-diene and another π bond (termed the dienophile) to afford a new six-membered ring.



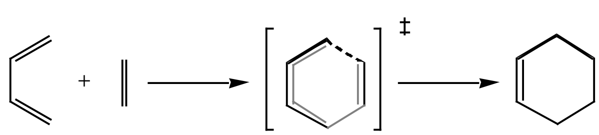
(e) Vinyl cyclopropane rearrangement: A vinylcyclopropane undergoes a 1,3-shift to give a new five-membered ring.



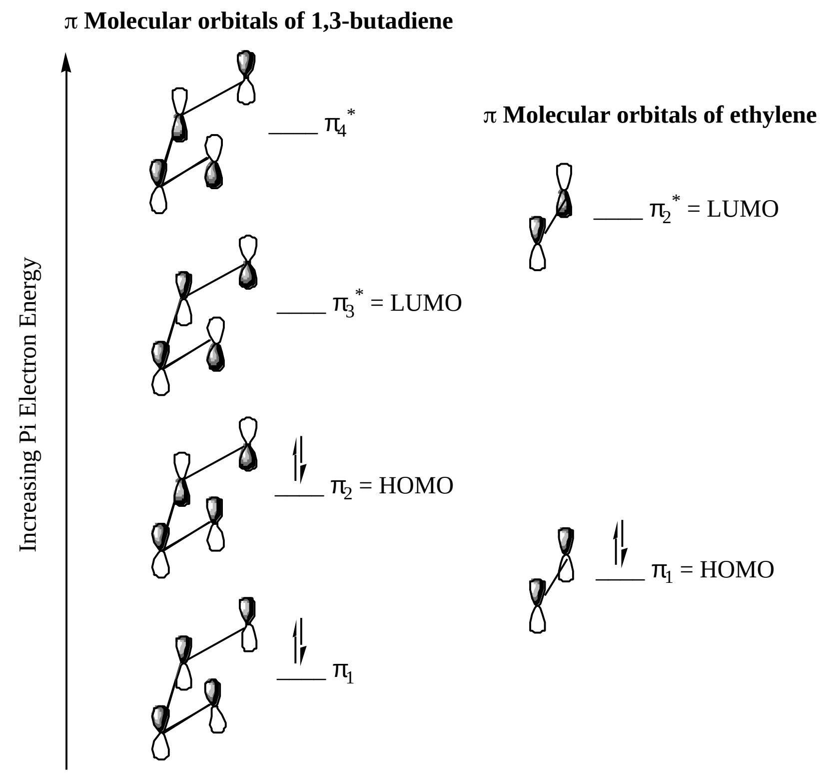
3. Each features a six-membered ring in which six electrons occupy p orbitals, giving the transition state some aromatic character. This aromatic character is a stabilizing feature that lowers the energy of activation and thus assists the reaction.

4. The Woodward-Hoffmann rules describe pericyclic reactions as thermally or photochemically forbidden or allowed, based upon the symmetry of the HOMO and/or LUMO of the reactant(s). The HOMO and/or LUMO lobes that are forming new bonds in the transition state must overlap in phase.

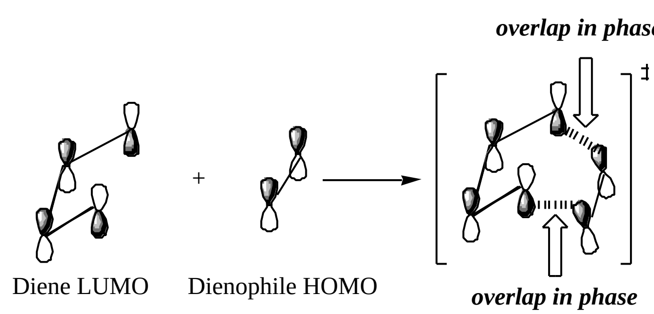
5. In a cycloaddition reaction, the ends of the two reactants must meet in the transition state so that the orbitals that form the new bonds overlap in phase. One of the reactants uses its HOMO and the other the LUMO. For this example, we consider the simplest Diels-Alder reaction between 1,3-butadiene and ethylene.



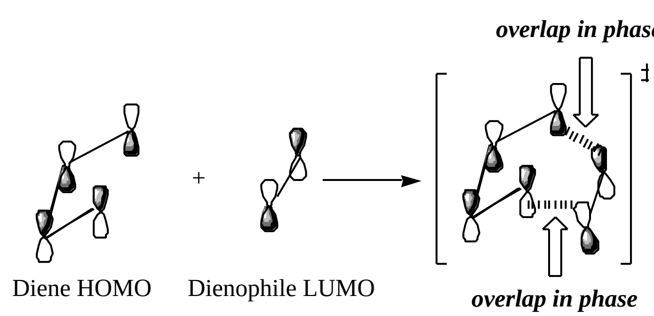
The HOMO and LUMO of the reactants are determined from a molecular orbital diagram. (Compare the diagram below with the molecular orbital diagrams in the Conjugation and Molecular Orbital Theory CFQ & PP.)



The orbital overlap in the Diels-Alder transition state is now considered. It may involve the LUMO of the diene and HOMO of the dienophile. (Hydrogen atoms have been omitted for clarity.)



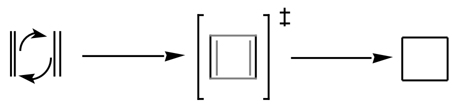
Alternately, it may involve the HOMO of the diene and the LUMO of the dienophile.



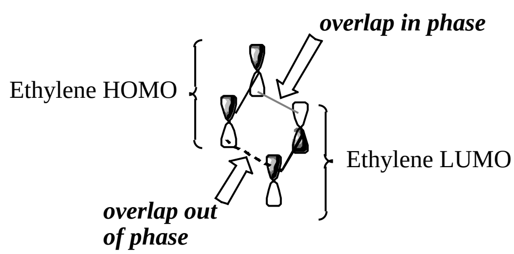
In either case, the HOMO/LUMO orbital overlap requirement is met using the ground state electronic configurations of the reactants, so the reaction is said to be thermally allowed. ("Thermally allowed" does not mean the reaction needs to be heated, but rather that the reaction proceeds through a concerted mechanism without photochemical excitation.)

Photochemical excitation of either the diene or dienophile promotes an electron to a higher energy orbital, thus changing which orbitals are the HOMO and LUMO. The orbital phase overlap requirement cannot be met in this case, so the reaction does not proceed. It is said to be photochemically forbidden.

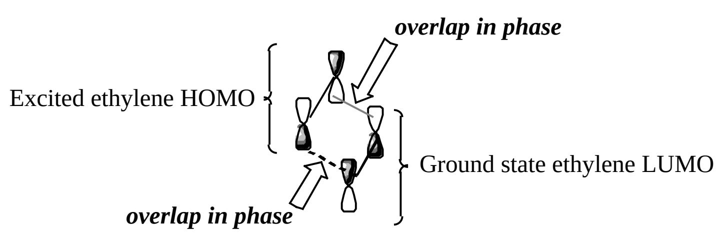
The [2π + 2π] case is analyzed the same way.



The ground state HOMO and LUMO of ethylene cannot combine with the appropriate orbital lobe phases, so the reaction is thermally forbidden.



Photochemical excitation of one ethylene molecule promotes an electron from π_1 to π_2, so π_2 becomes the HOMO for the excited molecule. Now the HOMO of the excited ethylene molecule and the LUMO of a ground state ethylene can overlap in phase, and the cycloaddition occurs. (The excited molecule does not have a π LUMO to consider.)



Thus the [2π + 2π] reaction of two ethylene molecules is thermally forbidden and photochemically allowed. (Reactions that are thermally forbidden to proceed through a concerted mechanism may instead proceed through a stepwise mechanism in the absence of photochemical excitation.)

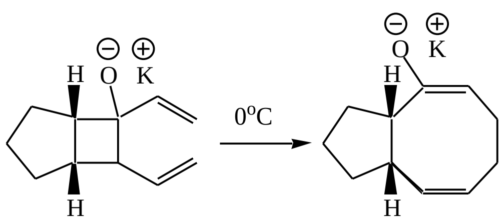
In summary, whether a reaction is thermally or photochemically allowed or forbidden is controlled by the phase of the orbitals that overlap in the transition state to form new σ bonds. In general, six-electron processes like the Diels-Alder reaction, Cope rearrangement and Claisen rearrangement are thermally allowed and photochemically forbidden. Four-electron processes as thermally forbidden and photochemically allowed.

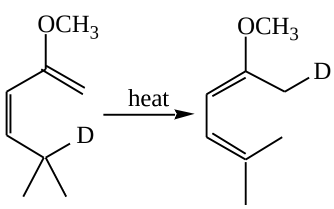
Practice Problems

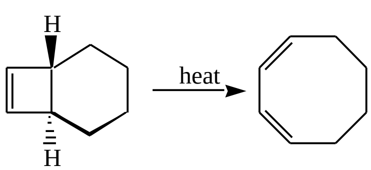
1. Give an example of each reaction type, including curved arrows.

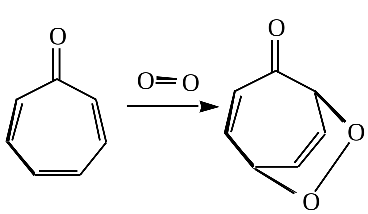
   (a) Cycloaddition reaction. (b) Electrocyclic reaction. (c) Sigmatropic reaction.

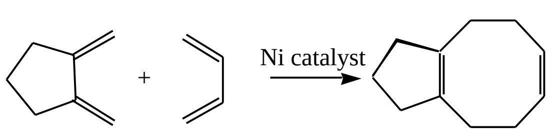
2. For each reaction draw a curved arrow mechanism. Assume each step is concerted. Classify each reaction as a cycloaddition, electrocyclic reaction or sigmatropic reaction. Further classify cycloadditions as [xπ + yπ] processes, and sigmatropic reactions as [x,y] shifts.

(a) 

(b) 

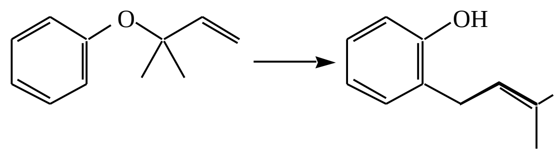
(c) 

(d) 

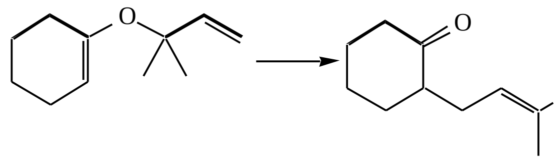
(e) 

3. Draw a curved arrow mechanism for reaction **A**. With this mechanism in mind, rank reactions **A – C** in order of rate. Briefly explain your reasoning.

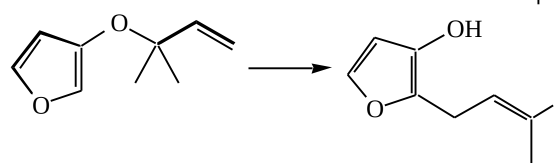
A:



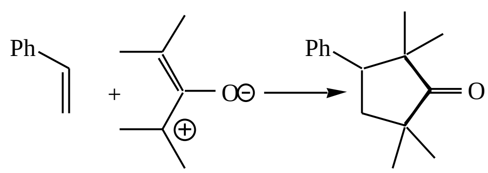
B:



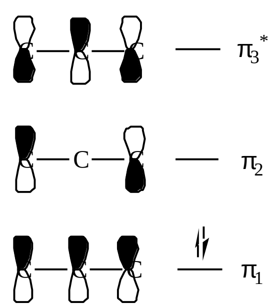
C:



4. Consider the concerted cycloaddition reaction of an allyl cation with an alkene.

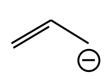


An allyl cation is constructed from three p_z carbon orbitals, so it has three π molecular orbitals.



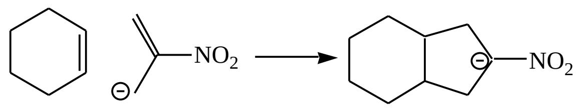
(a) Is this cycloaddition reaction allowed thermally or photochemically? Suggest a mechanism. The oxygen lone pairs may participate in this reaction, but because they are not part of the cyclic electron flow in the transition state, they are ignored when applying the Woodward-Hoffmann rules.

(b) An allyl anion has two more π electrons than an allyl cation. Draw a molecular orbital diagram for an allyl anion.



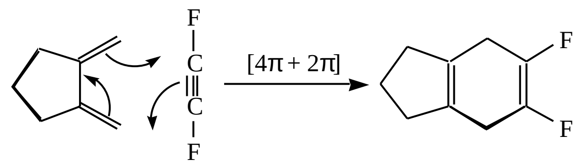
Allyl anion

(c) Is the reaction shown below allowed thermally or photochemically? Suggest a mechanism and briefly explain.

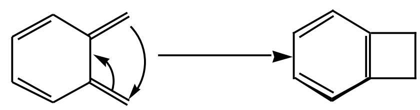


Practice Problems Solutions

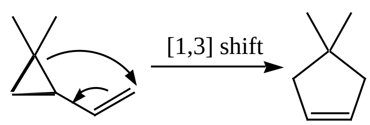
1. (a) Cycloaddition reaction:



(b) Electrocyclic reaction:

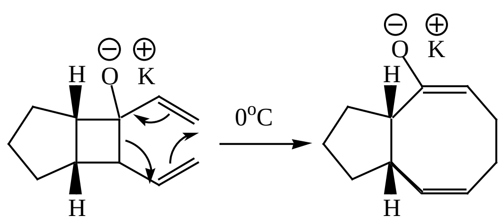


(c) Sigmatropic reaction:



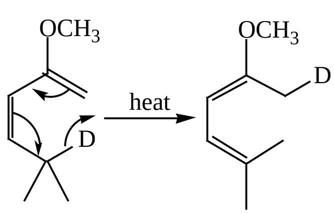
2. It does not matter if the arrow flow is clockwise or counterclockwise.

(a)



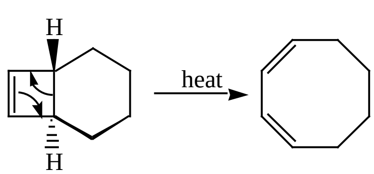
sigmatropic [3,3] shift
Cope rearrangement

(b)



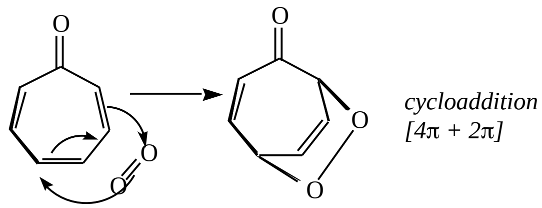
sigmatropic
[1,5] D shift

(c)

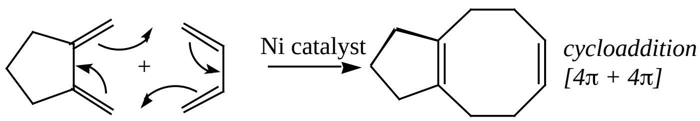


electrocyclic

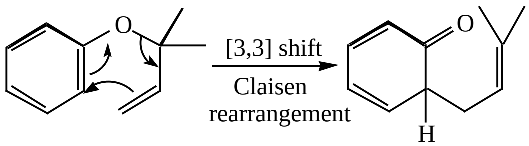
(d)



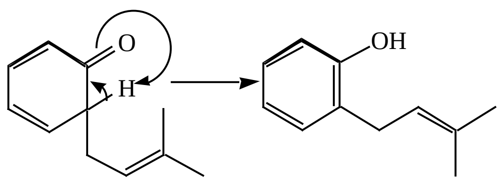
(e)



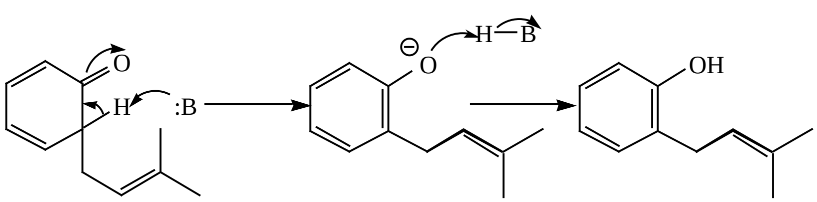
3. (a)



We might be tempted at this point to finish the mechanism by a [1,3] H shift:

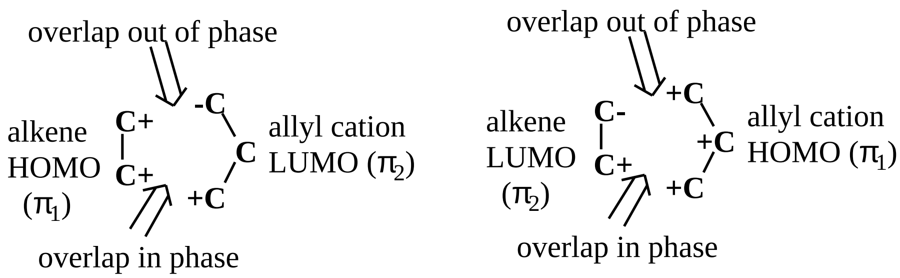


Such [1,3] shift are uncommon, for reasons beyond the scope of our discussion. The normal keto-enol tautomerization mechanism operates instead. The actual proton shuttle might be the intermediate ketone, or a trace of water; both of these are represented as "B:". In the lab, we add a tertiary amine such as N,N-methyl-aniline to the reaction to serve as the proton shuttle for enolization (thus accelerating the shift of the equilibrium towards products) and to remove traces of acid which might cause side reactions at high temperatures.

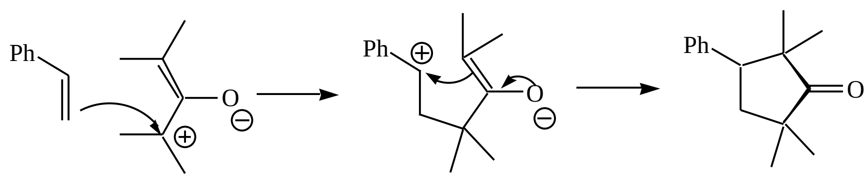


To rank the reactions by rate, we need to see that the first step of the Claisen rearrangement is the rate-determining step, as aromaticity is lost. Steps 2 and 3 are proton transfers and therefore probably fast. In reaction **B**, no aromaticity is lost, so we predict this to be faster than reaction **A**. A furan ring is less aromatic than a benzene ring, so interruption of furan aromaticity will be easier than interruption of benzene aromaticity, and reaction **C** will be faster than **A** but slower than **B**. Thus, the predicted reaction rates are: **A** (slowest) < **C** < **B** (fastest).

4. (a) Concerted cycloaddition reaction proceeds by in-phase overlap of frontier molecular orbitals (HOMO and LUMO).



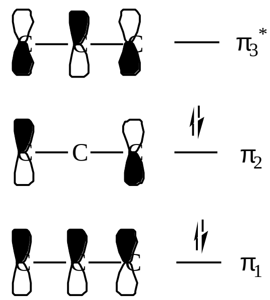
If all the orbital overlaps are not in phase, these orbitals cannot mix and become new bonds. Since both of the thermal modes of this [2π + 2π] process cannot happen, this is a thermally forbidden reaction. This does not mean the reaction cannot occur, but rather just that it cannot occur by a concerted pathway. A stepwise mechanism is possible:

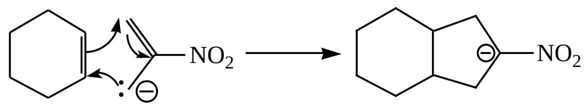


When the reaction is stimulated by light, an electron is promoted from the HOMO to the LUMO. Whether the alkene or the allyl cation is excited will depend upon the wavelength of light used. Repeating the HOMO-LUMO analysis using either the excited state of the alkene with the ground state of the allyl cation or the ground state of the alkene with the excited state of the allyl cation reveals the reaction is photochemically allowed.

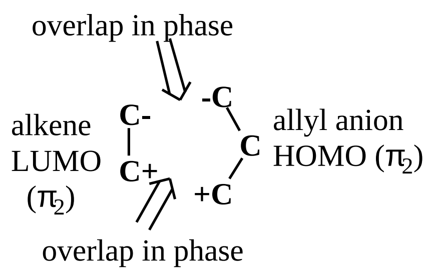
In reality, the reaction proceeds without photochemical excitation by a two-step alkene electrophilic addition mechanism

(b) The orbitals are the same for the allyl anion as for the allyl cation. The allyl anion has two more π electrons than the allyl cation, so these extra electrons will change the electronic configuration.



(c) Mechanism: 

Considering the interaction of the alkene LUMO and the allyl anion HOMO shows the process to be thermally allowed.



By now, you're may have noticed that concerted cycloaddition reactions involving $4n + 2$ π electrons (usually 6) are thermally allowed and photochemically forbidden, whereas those involving $4n$ π electrons (most commonly 4) are thermally forbidden and photochemically allowed.