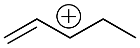
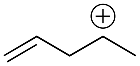
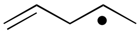
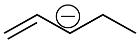
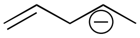
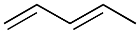
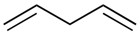
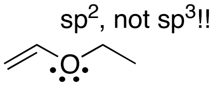
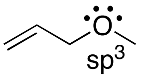
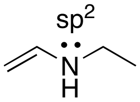
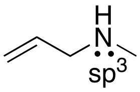
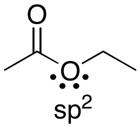
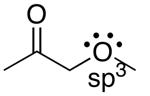
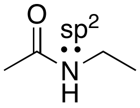
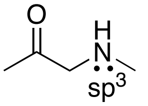
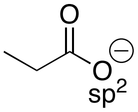
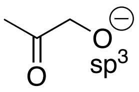
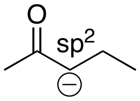
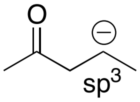
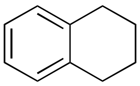
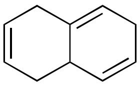
Ch. 15 Conjugated Systems

The General Stabilization Effect of Conjugation (Section 15.1, 2, 3, 8, 9)

		Conjugated (more stable)	Isolated (less stable)	Notes:
1	Cations			
2	Radicals			
3	Anions			
4	Dienes			
5	Ethers			An N or O next to a double bond becomes sp^2. An isolated N or O is sp^3
6	Amines			
7	Esters			
8	Amides			Very special, chapter 23, all of biochemistry, proteins, enzymes, etc.
9	Oxyanions (Carboxylates)			Very special, chapter 21
10	Carbanions (Enolates)			Very special, chapter 22
11	Aromatics			Very special, chapters 16 + 17

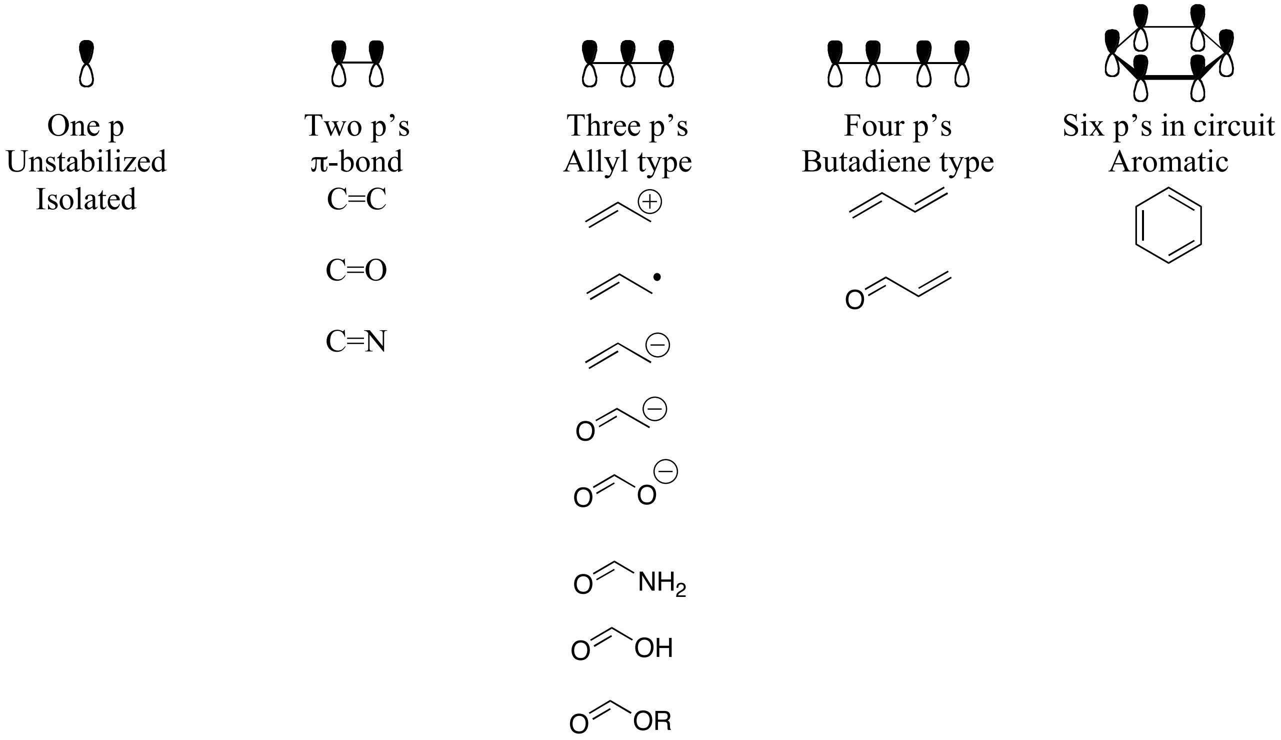
Conjugation: Anything that is or can be sp^2 hybridized is stabilized when next to π bonds.
- oxygens, nitrogens, cations, radicals, and anions

Notes:

1. Any atom that can be sp^2 will be sp^2 when next to a double bond
2. "Conjugation" is when sp^2 centers are joined in an uninterrupted series of 3 or more, such that an uninterrupted series of p-orbitals is possible
3. Any sp^2 center has one p orbital

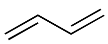
Impact of Conjugation

4. **Stability:** Conjugation is **stabilizing** because of p-orbital overlap (Sections 15.2, 4, 7)
   - Note: In the allyl family, **resonance = conjugation**

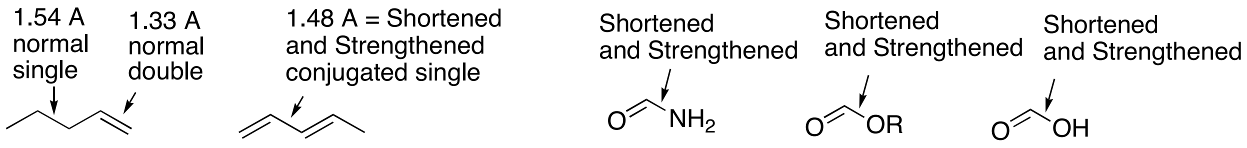


5. **Reactivity:** Conjugation-induced stability impacts **reactivity** (Sections 15.4-7)
   - If the **product** of a rate-determining step is stabilized, the reaction rate will go **faster** (product stability-reactivity principle)
     - Common when allylic cations, radicals, or carbanions are involved
   - If the **reactant** in the rate-determining step is stabilized, the reaction rate will go **slower** (reactant stability-reactivity principle)
     - Why aromatics are so much less reactive
     - Why ester, amide, and acid carbonyls are less electrophilic than aldehydes or ketones

6. **Molecular shape** (Sections 15.3, 8, 9)
   - The p-orbitals must be aligned in parallel for max overlap and max stability
   - The sp^2 centers must be coplanar


All four sp^2 carbons must be flat for the p's to align

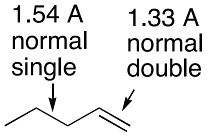
7. **Bond Length:** Bonds that look like singles but are actually between conjugated sp^2 centers are **shorter** than ordinary single bonds

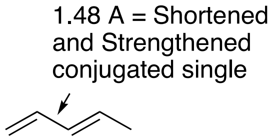


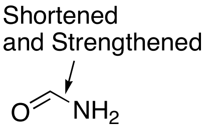
   - In amides, esters, and acids, the bond between the carbonyl and the heteroatom is shortened
   -

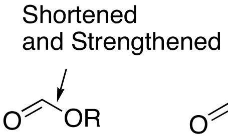
8. **Bond Strength:** Bonds that look like singles but are actually between conjugated sp^2 centers are **stronger** than ordinary single bonds

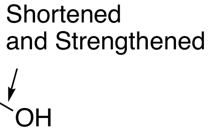
9. **Bond Rotation Barrier:** Bonds that look like singles but are actually between conjugated have much larger rotation barriers than ordinary single bonds
   - Because in the process of rotating, the p-overlap and its associated stability would be temporarily lost



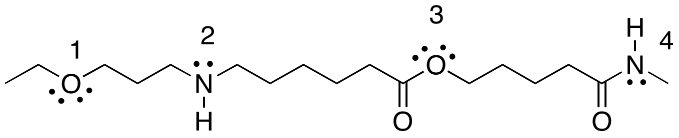








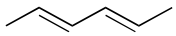
10. **Hybridization:** Conjugated sp^2 atoms have both sp^2 and p orbitals. You should always be able to classify the hybridization of **lone pairs on nitrogen and oxygen**.
   - **Isolated** oxygens or nitrogens: sp^3 atom hybridization, sp^3 lone-pair hybridization, and tetrahedral, 109º bond angles
   - **Conjugated nitrogens**: sp^2 atom hybridization, **p lone-pair hybridization (needed for conjugation)**, and 120º bond angles
   - **Conjugated oxygens**: sp^2 atom hybridization, **one p lone-pair hybridization** (needed for conjugation), **one sp^2 lone-pair**, and 120º bond angles

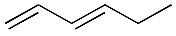


Atom	O-1	N-2	O-3	N-4
Isolated vs Conjugated	isolated	isolated	conjugated	conjugated
Atom Hybridization	sp^3	sp^3	sp^2	sp^2
Lone-Pair(s) Hybridization	sp^3	sp^3	p, sp^2	p
Bond Angles	109	109	120	120

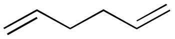
15.2 Diene Stability and the Stability of other Acyclic Systems with 2 Elements of Unsaturation

Q1: Rank the stability of the following dienes:


1


2

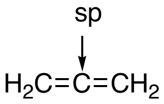

3


4

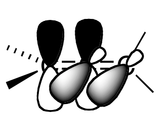
Stability Factors for Simple Dienes:
1. Isolated versus Conjugated: Conjugation stabilizes
2. Substitution: More highly substituted are more stable.

Stability Patterns for Regular Dienes versus Other Systems with 2 elements of unsaturation

3. **Allenes** = "Cumulated Dienes": **Less stable than dienes or alkynes**
   - in allenes, the central carbon is sp rather than sp^2 hybridized



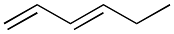
$H_2C=\overset{\overset{sp}{\downarrow}}{C}=CH_2$



4. **Alkynes**: **Less stable than dienes, but more stable than allenes**.

As for alkenes and dienes, more substituted alkynes are more stable less substituted alkynes

Q2: Rank the stability of the following isomers: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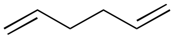
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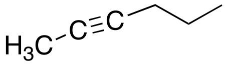
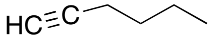


3



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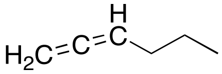


5

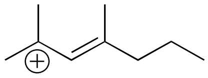
Q3: Rank the amount of heat produced if the isomers above were hydrogenated? Burned?

5	4	3	2	1
5	4	3	2	1

15.4 Stability of Allylic/Benzylic (Conjugated) Cations

Stability Factors for Cations:
1. Isolated versus Conjugated/Allylic: Conjugation stabilizes
2. Substitution: More highly substituted are more stable.
   - Conjugation/allylic is more important than the substitution pattern of an isolated cation (i.e. 1° allylic > 3° isolated)

Q4: Rank the stability of the following cations?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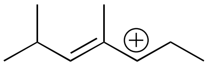
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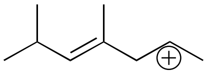
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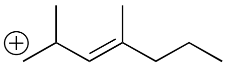
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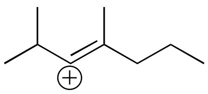
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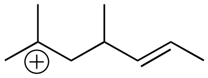
Q5: Rank the stability of the following alkene cations?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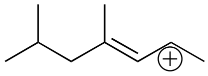
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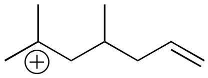
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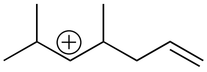
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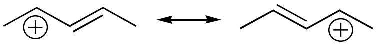
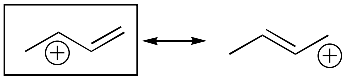
Allylic Cations, Resonance, Charge Delocalization, and Allylic Symmetry/Asymmetry

a.



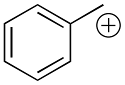
symmetric

b.



asymmetric

c.



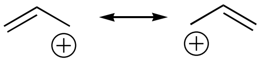
"Benzylic"

1. Two resonance structures each (at least)
2. Charge is delocalized, shared
3. Allylic cations can be symmetric or asymmetric
4. When an allylic cation is asymmetric, it's helpful to evaluate which form would make a larger contribution to the actual hybrid
   - Cation substitution is more important than alkene substitution

Q1: For above cations, identify as symmetric or asymmetric.
Q2: For any asymmetric cations shown above, identify the larger contributor to the hybrid.

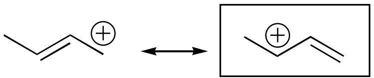
Q3: For the following cations:
   a. identify which are allylic (would have a resonance structure).
   b. For those that are allylic, identify which are symmetric vs asymmetric?
   c. For any asymmetric allylic cations, draw the resonance structure
   d. For any asymmetric allylic cations, identify which resonance structure would make the larger contribution to the actual resonance hybrid

a.



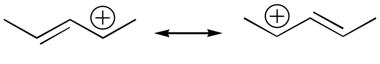
symmetric

b.



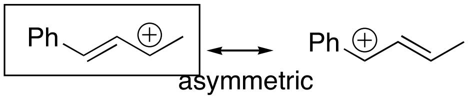
asymmetric

c.



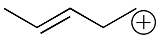
sym

d.



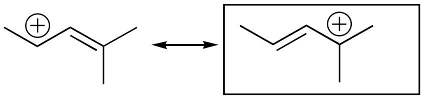
asymmetric

e.



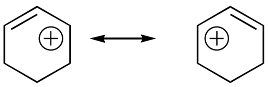
isolated

f.



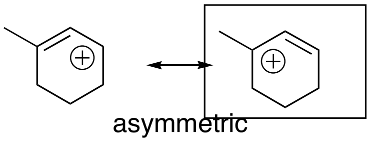
asymmetric

g.



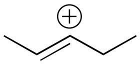
symmetric

h.



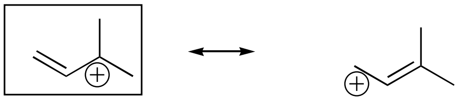
asymmetric

i.



vinyl

j.

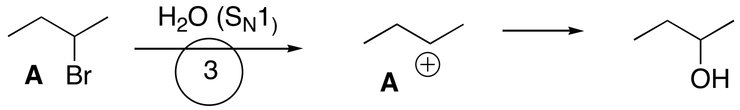


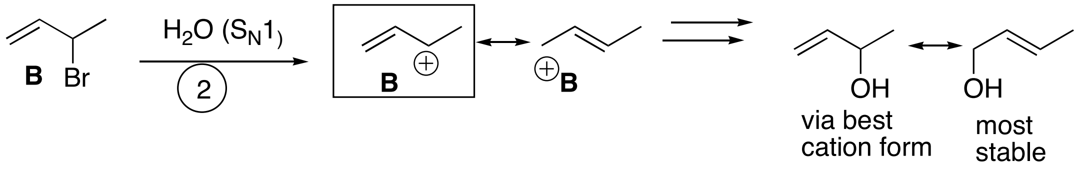
asymmetric

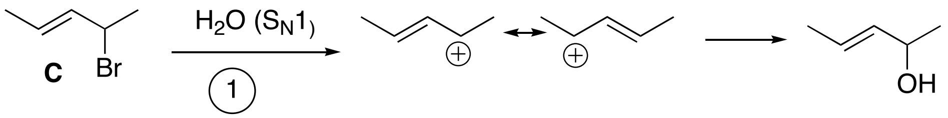
Impact of Allylic Cation Resonance on Reactivity and Product Formation

1. **Rates**: Resonance/conjugation stability enhances rates when cation formation is rate-determining
2. **Product Distribution:** Product mixtures often result if an allylic cation is asymmetric.
   - The two different resonance structures can lead to different products.
   - When two isomeric products can form from an allylic cation, consider two things:
     1. Which product is more stable?
        - This will impact "product stability control" = "thermodynamic control" = "equilibrium control"
        - To assess product stability, focus on the alkene substitution
     2. Which resonance form of the cation would have made a larger contribution?
        - This will often favor "kinetic control", in which a product which may not ultimately be the most stable forms preferentially
3. **Position of Cation Formation**: When a conjugated diene is protonated, consider which site of protonation would give the best allylic cation.

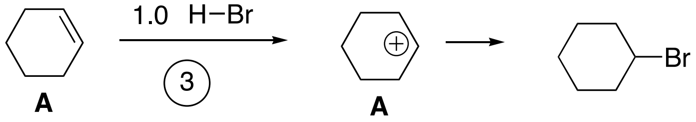
Q1: Key: Think about the cation! For the bromides A-C, a) draw the product or products, and b) rank the three bromides in terms of relative reaction speed. C) For any that give structural isomers, identify which product is more stable, and which might derive from the better resonance contributor.

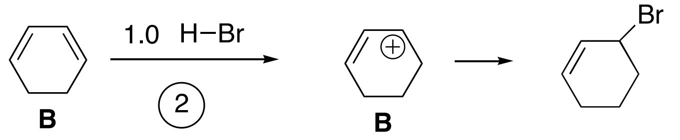


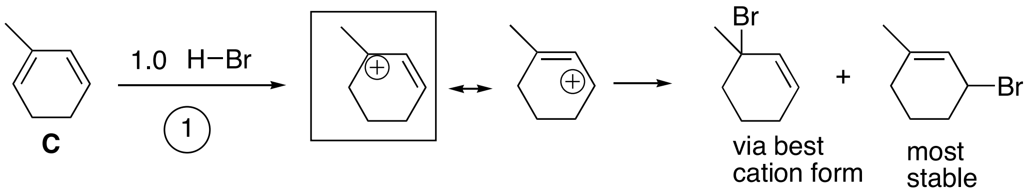




Q2: Key: Think about the cation! For the dienes A-C, a) draw the product or products, and b) rank the three dienes in terms of relative reaction speed. C) For any that give structural isomers, identify which product is more stable, and which might derive from the better resonance contributor.







Sections 15.5,6 1,2 vs 1,4 Addition to Conjugated Dienes: "Kinetic" vs "Thermodynamic" Control

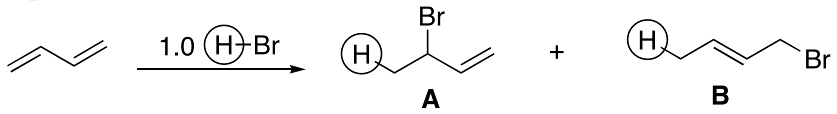
Note: "Thermodynamic Control" = "Product-Stability Control" = "Equilibrium Control"

- This is when **the most stable** of two possible **products** predominates. Either of two factors can cause this:
  - **Transition State:** The most stable product is formed fastest via the most stable transition state (normally true, but not always)
  - **Equilibrium**: Even if the most stable product is not formed fastest, if the two products can equilibrate, then **equlibrium** will favor the most stable product

Kinetic Control: If **the less stable** of two possible products predominates.

- This will always require that for some reason the less stable product forms via a better transition state (transition-state stability/reactivity principle). Common factors:
  - Charge distribution in an allylic cation or radical. The position of charge in the major resonance contributor may lead to one product, even though it may not give the most stable product.
  - Proximity of reactants. In an H-X addition to a diene, often the halide anion is closer to one end of the allylic cation than the other, resulting in "1,2 addition" over "1,4 addition".
  - Steric factors. With a bulky E2 base, for example, the transition state leading to what would be the more stable Zaytsev alkene has steric problems, so it gives the Hoffman alkene instead.

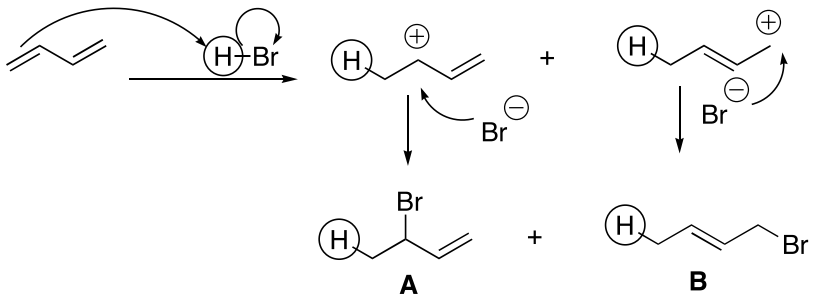
Example:



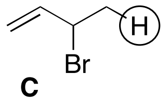
Kinetic vs Thermodynamic Control Conditions

1,2- vs 1,4 Addition Product:			
at -80°C	80% (major)	20% (minor)	Kinetic
at +40°C	15% (minor)	85% (major)	Thermodynamic
More/Less stable:	Less	More	

Mech (and why)

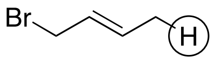


What about the following? Do they form, and if not why not?



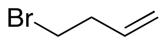
C

same as A



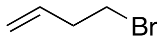
D

same as B



E

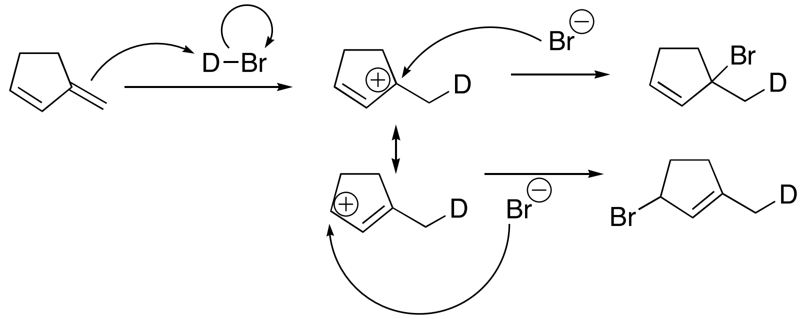
via an isolated cation



F

via an isolated cation

Q1: Predict the products for the following reaction. Draw the mechanism. One product **X** is the major product at low temp, but the other product **Y** is major at higher temperatures. Assign "**X**" and "**Y**" to the appropriate products.



15.7 Allylic/Benzylic Radicals

Stability Factors for Radicals:

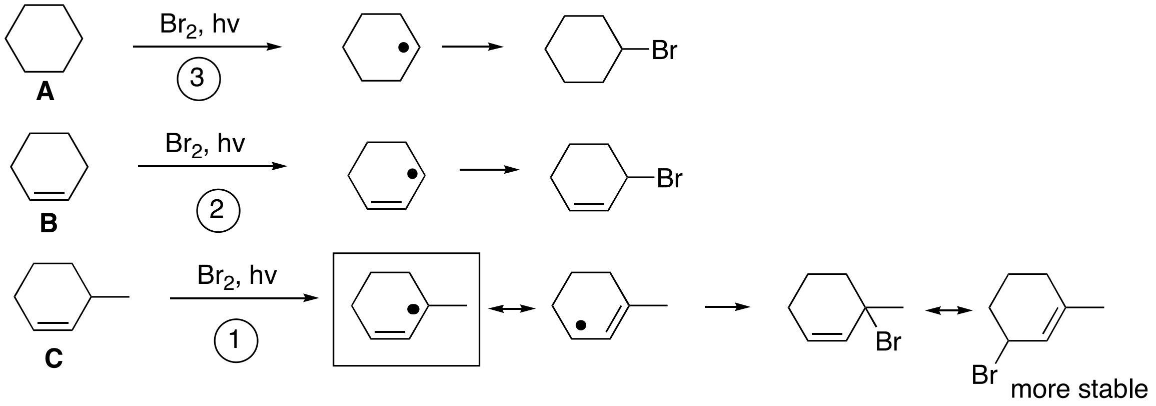
1. Isolated versus Conjugated/Allylic: Conjugation stabilizes
2. Substitution: More highly substituted are more stable.
    - Conjugation/allylic is more important than the substitution pattern of an isolated cation

Impact of Radical Resonance on Reactivity and Product Formation

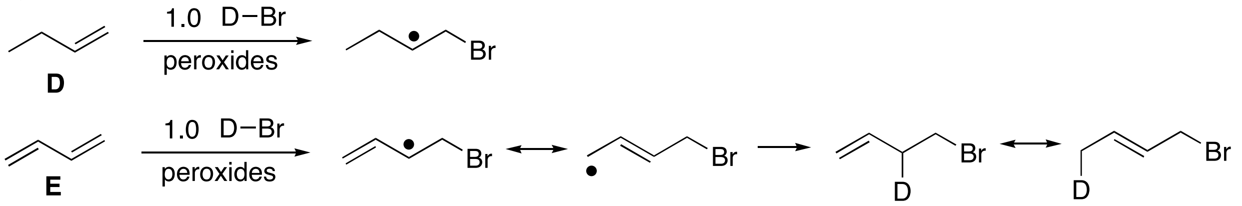
1. **Rates**:
2. **Product Distribution:** Product mixtures often result if an allylic radical is asymmetric.
3. **Position of Radical Formation**

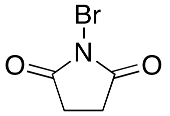
Question 2

a. Ranks the reactivity of **A**, **B**, and **C**.
b. Draw the major products for the following reactions
c. If more than one major product it likely to form, evaluate the relative stability.



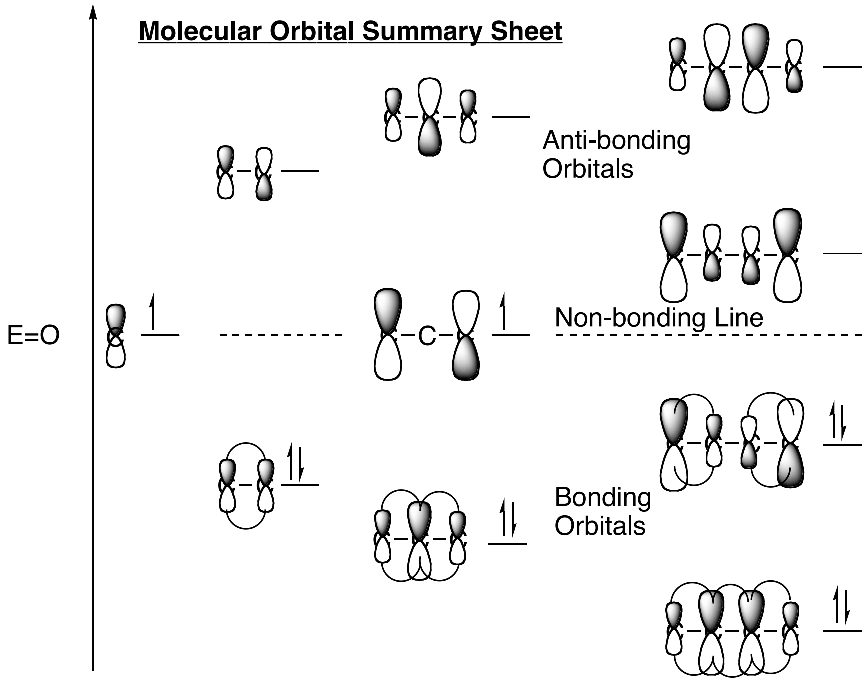
Question 3





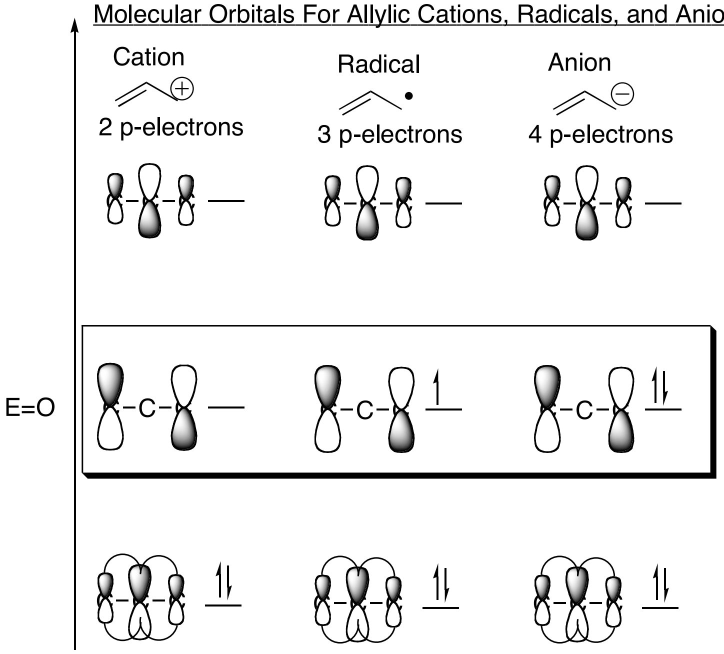
"**NBS**" = N-Bromosuccinimide = Actually more commonly used than Br_2/hv for allylic/benzylic radical brominations. Maintains dilute [Br_2], absorbs HBr. Prevents Br_2 or HBr from undergoing ionic addition to alkenes. More convenient to weigh out (solid). Some mechanistic complexity. Often higher yields.

Sections 15.3, 8, 9 Molecular Orbitals and Conjugation



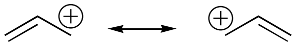
Observations:

1. Shown is an isolated radical, a double bond, an allyl radical, and butadiene.
2. "**MO**" = "**M**olecular **O**rbital"
3. MO's lower/stabler in energy than the non-bonding line are referred to as "bonding MO's", while those that are higher (less stable) in energy are called "antibonding MO's"
4. The number of π MO's equals the number of contributed π (p) orbitals. (One p in gives one MO. Two p's in gives two MO's. Three p's in gives three MO's. Four p's in gives four MO's. Etc.)
5. Any bonding MO is mirrored by an antibonding MO, whose energy is as high above nonbonding as the bonding MO is above it.
6. Thus the sum energies of the MO's (ignoring electron occupancy) equals 0.
7. However, not all MO's are occupied by electrons. Electron occupancy proceeds from the lowest MO's up. And it's the energies of the electrons that determine the molecular energy. Thus explains why it's energetically profitable for a molecule to be conjugated. CONJUGATING THE P ORBITALS LOWERS THE ENERGIES OF THE ELECTRONS AND THUS IS STABILIZING.
8. The **h**ighest **o**ccupied **m**olecular **o**rbital is called the "**HOMO**", and the **l**owest **u**noccupied **m**olecular **o**rbital is called the "**LUMO**". These are also referred to as the Frontier Molecular Orbitals (**FMO**'s). The frontier molecular orbitals are the orbitals involved as nucleophiles or electrophiles in reactions. If electrons are donated (nucleophile), they will come from the HOMO. If electrons are accepted (electrophile), they will go to the LUMO. Thus the energies and shapes of the HOMO/LUMO are really important.
9. The lowest MO keeps getting lower and lower (more and more stable). But, the energy level of the HOMO does **not** get progressively lower. Notice that the diene HOMO is higher than the simple alkene HOMO.
10. Notice that not all atoms have the same sized p-orbitals in the FMO's. When reactions happen, atoms with the big p-lobes are the ones that react.



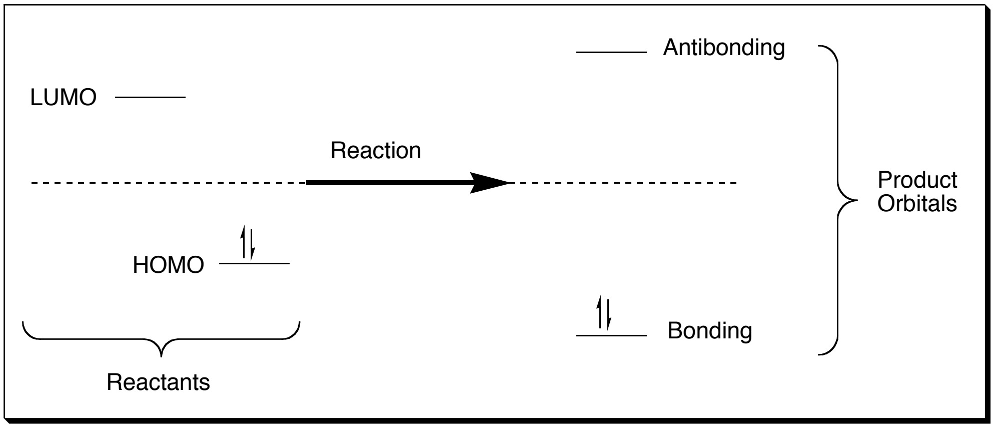
11. For allylic systems, notice that the energies and shapes of the MO's stay the same.

12. However, the occupancy does change. An allylic cation has two π-electrons, an allylic radical has three, and an allylic anion has four. Thus the key reactive middle MO goes from empty (strongly electrophilic) to full (strongly nucleophilic) across the series.

13. The MO picture tells the same story that resonance pictures show: there is no reactivity on the central carbon, but the outside carbons are the ones that react, whether in an allylic cation, radical, or anion.
    - MO theory explains this with the orbital lobes
    - Resonance theory explains this with 

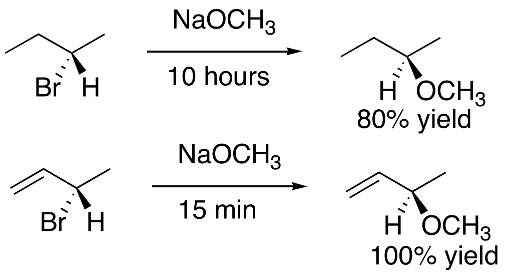
14. Sometimes MO can explain things that the simpler resonance theory can't.

15. In an actual reaction, the HOMO and LUMO intereact
    - As usual two orbitals in produce two new orbitals (molecular orbitals) out.
    - The electrons end up lower in energy: more stable
    - MO fact: the closer the HOMO and LUMO are to each other in energy, the more favorable and profitable the reaction will be



Section 15.10 S_N2 on Allylic, Benzylic Systems Are Really Fast

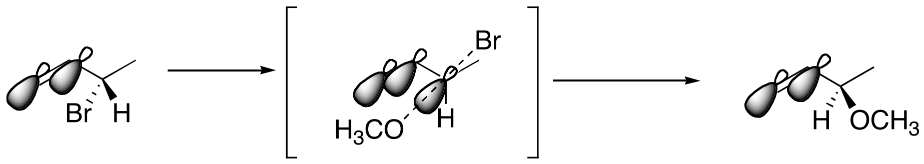
Ex.



Slow, and contaminated by competing E2

Fast and Clean

Why? Because the backside-attack transition-state is stabilized by conjugation!
(Transition state-stability-reactivity principle).

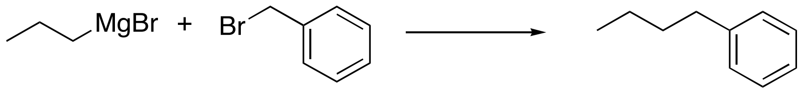


1. Neither the product nor the reactant has conjugation, so it's hard to see why conjugation should apply
2. However, in the 5-coordinate T-state the reactive carbon is sp^2 hybridized
- the nucleophile and the electrophile are essentially on opposite ends of a temporary p-orbital.
3. That transient sp^2 hybridization in the transition-state is stabilized by π-overlap with the adjacenty p-bond.
4. This stabilization of the transition-state lowers the activation barrier and greatly accelerates reaction

Key Application: RMgBr can do Clean S_N2 Reactions on 1° Allylic Bromides or Tosylates

- RMgBr can't do good S_N2's on normal 1° or 2° allylic bromides because of competing elimination and single-electron-transfer reactions.

1



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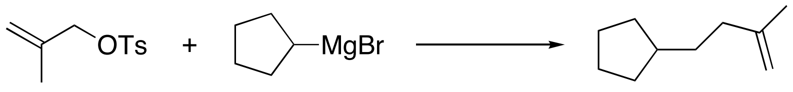

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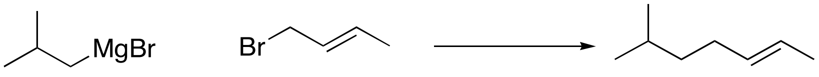

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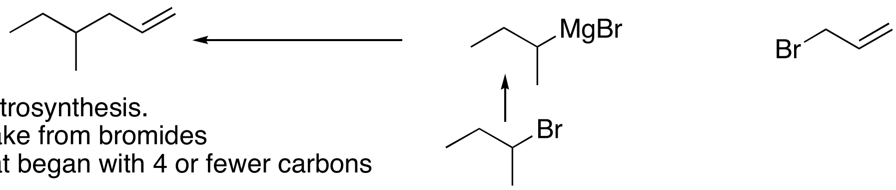
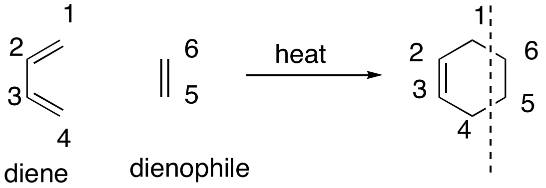
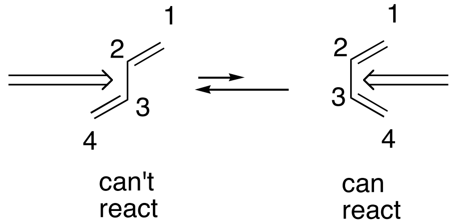
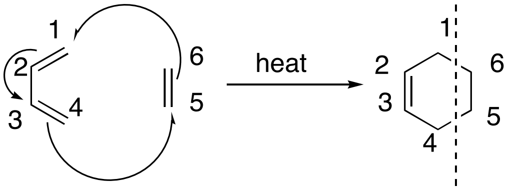
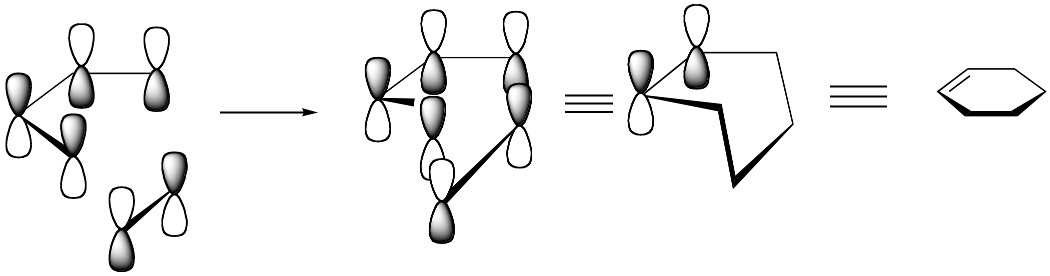


Retrosynthesis.
Make from bromides
that began with 4 or fewer carbons

Note: When thinking backwards, identify the allylic carbon and the next carbon removed from the alkene. Those will be the two carbons that were linked.

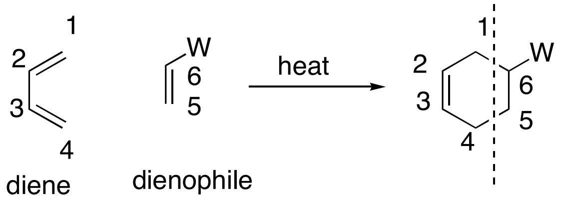
Section 15.11 The Diels-Alder Reaction. The Reaction of Conjugated Dienes (Dienes) with Electron-Poor Alkenes (Dienophiles) to make Cyclohexenes.

Quick Overview Summary

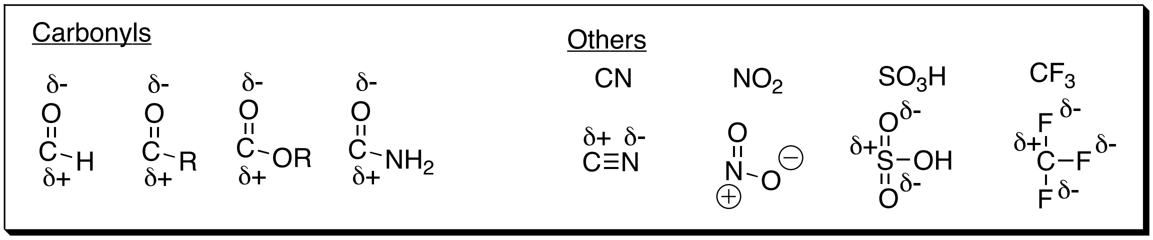
1.	
2.	s-cis diene conformational requirement: The diene must be locked or be able to single-bond rotate it's way into the "s-cis" conformation in order to react "transoid" or "s-trans" -relative to the **s**ingle bond  "cisoid" or "s-cis" -meaning that it's "cis" relative to the **s**ingle bond -even though the single bond is capable of rotation
3.	Rate Factors 1. Dienophile - activated by electron withdrawing groups ("W" or "EWG") for electronic reasons 2. Diene: - Deactivated by substituents that make it harder or less stable to exist in the s-cis conformation. This is true when a diene alkene has a Z-substituent. - Steric factors equal, activated somewhat by electron donating groups ("D" or "EDG")
4.	Concerted Mechanism  All bond making and breaking happens at once: *3 π-bonds break *2 σ-bonds and 1π-bond form The diene is really the "nucleophile" (HOMO) The dienophile is really the "electrophile" (LUMO)
5.	Orbital Picture 

6.	Product Prediction Highlights
	- Try to match up the 4 diene and 2 dienophile carbons with the product product
	  o The product double bond will be between C2 and C3 of the diene
	- Substituents are spectators
	- 1,4/1,2 Rule: when asymmetric dienes react with asymmetric dienophiles
	  o Match δ- end of nucleophilic diene with δ+ end of electrophilic dienophile
	- For disubstituted dienophiles:
	  o cis-substituents end up cis, and trans-substituents end up trans

A. The General Diels-Alder Reaction

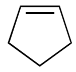


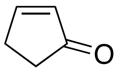
1. **Electronics**: The diene HOMO reacts with the dienophile LUMO
   - Effectively the diene is the nucleophile and the dienophile functions as the electrophile
2. The **dienophile** usually **needs an electron-withdrawing attachment** ("W") (at least one)
   - This makes the dienophile more electrophilic
   - Electron Withdrawing Groups to Memorize:

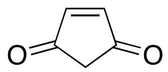


   - Keys:
     - The atom that is connected to the alkene has δ+ charge
     - Anything with a double-bond to a heteroatom tends to have this
       - C=O, C≡N, N=O, S=O

Q1/example: Rank the reactivity of the following alkenes as dienophiles. The actual relative reactivity ratios are 50,000 : 1,000 : 1. Huge differences.


1


1000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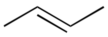
Q2: Rank the reactivity of the following dienophiles: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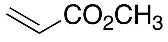

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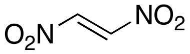
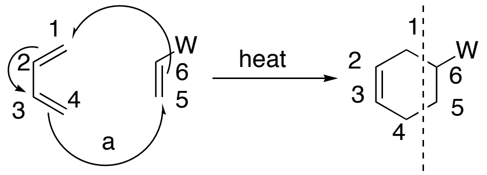


1

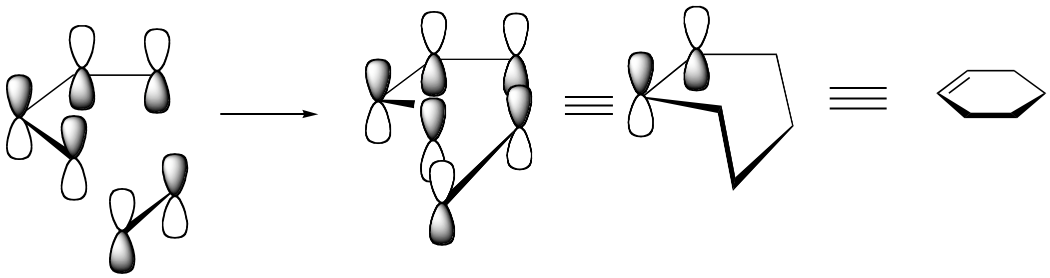
3. **Energetics**:
   - **Bonds broken**: 3 π bonds
   - **Bonds made**: 2 σ bonds, 1 π bond
   - **Enthalpy:** The net replacement of 2 π bonds (weaker) with 2 σ bonds is normally **strongly enthalpy favored**
   - **Entropy:** The high required organization of the concerted transition state makes the reaction **entropy disfavored**.
   - Heat normally required to overcome entropy

4. **Simple Mechanism (Good enough for test)**



Concerted: All bond making and breaking happens at once
-three arrows show each of the three p-bonds breaking and the three new bonds forming
-the arrow "a" from the diene to the dienophile is really key

5. **Orbital Picture**



a. the p orbitals on the dienophile overlap with the p-orbitals on C1 and C4 of the diene
b. the overlapped p orbitals from the diene and dienophile end up being σ bonds in product
c. the leftover p orbitals on C2 and C3 end up overlapping to give the π bond in product
d. the diene must be in the s-cis conformation; in the zig-zag s-trans layout, can't react
e. Not tested: perfect HOMO/LUMO orbital symmetry match (Section 15.12)

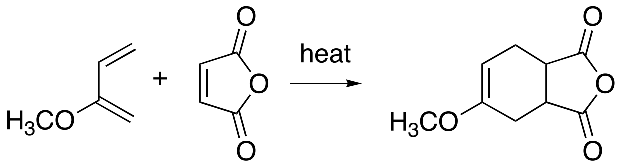
B. Predicting Products When the Diene or the Dienophile (or both) is Symmetric

1. Always make a cyclohexene 6-ring product
2. Number the diene from 1-4, and identify those four carbons in the product ring.
3. A double bond in the product will always exist between carbons 2 and 3.
4. Any substituents on the diene or dienophile are spectators: they will be attached to the same carbons at the end.

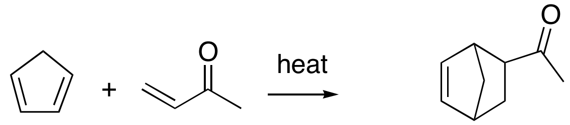
- Beware of cyclic dienes
- Beware of dienes that are drawn in their zig-zag s-trans form, but could react following rotation into an s-cis form

Noteworthy

1



2



Cyclic diene

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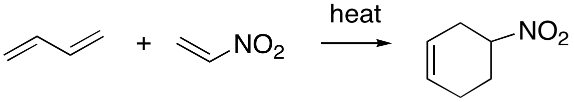

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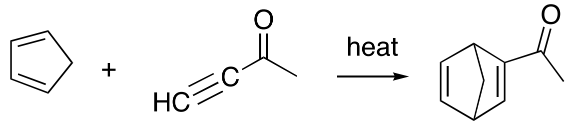

Alkyne

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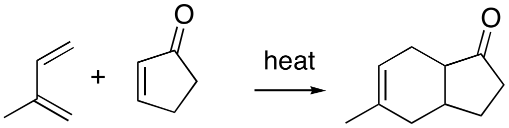

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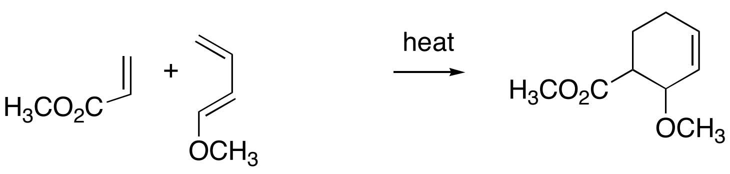
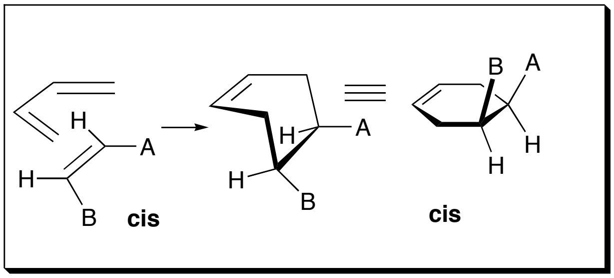


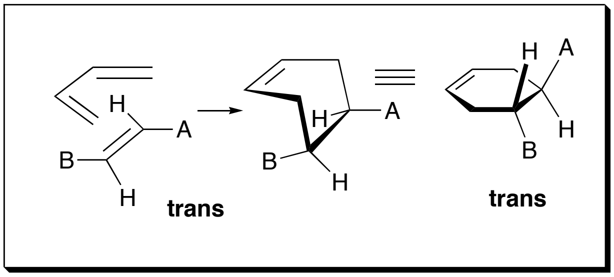
C. <u>Stereochemistry</u>: For Cis- or Trans- **<u>Disubstituted Dienophiles</u>**

- Both carbons of a disubstituted dienophile usually turn into stereocenters.

1. **Cis in → cis out**: If two substituents on the **<u>dienophile</u>** are cis to begin with, they will still have a cis relationship on the product cyclohexene
2. **Trans in → trans out**: If two substituents on the **<u>dienophile</u>** are cis to begin with, they will still have a cis relationship on the product cyclohexene

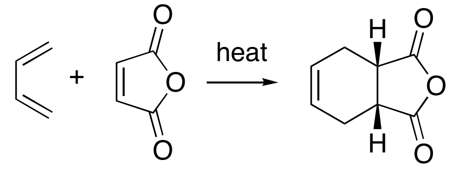
- **Note**: this is for the **<u>dienophile only</u>**. The diene alkenes may also have substitution such that one or both diene double bonds is cis or trans, but the "cis-in-cis-out" guideline does not apply to the diene.





- **<u>Why</u>**: Because of the concerted mechanism. The diene is basically doing a concerted "cis" addition to the dienophile. The attachments on the dienophile never have opportunity to change their position relative to each other.

1



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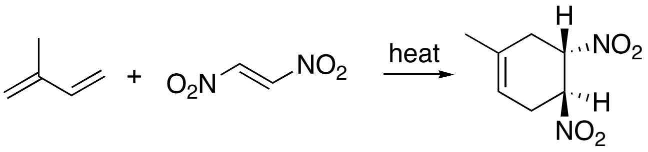

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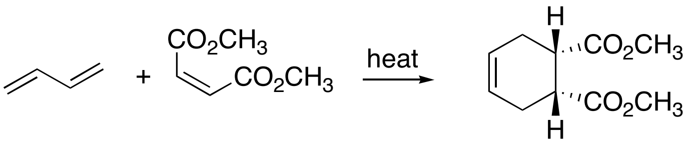

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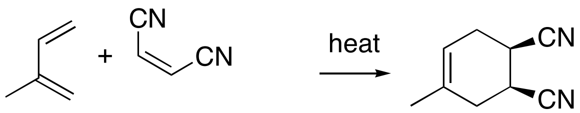

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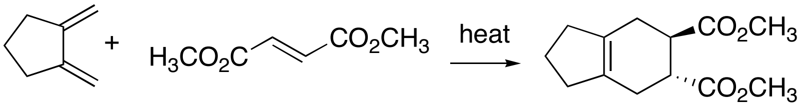
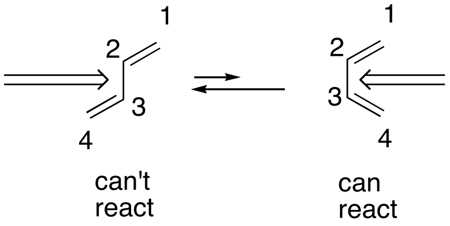


D. Structural Factors for **Dienes**

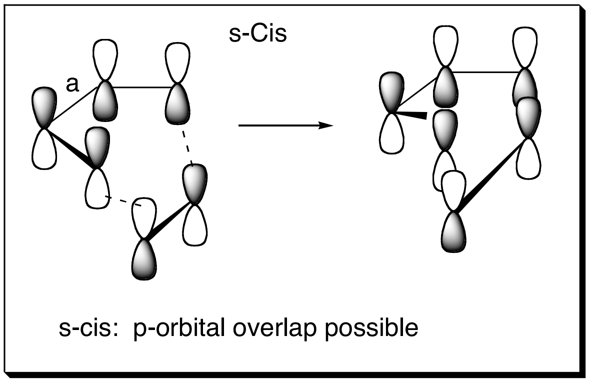
1. s-cis (cisoid) diene conformational requirement (p 682): The diene must be locked "s-cis" or be able to single-bond rotate it's way into the "s-cis" (cisoid) conformation in order to react

"transoid" or "s-trans"
-relative to the **s**ingle bond

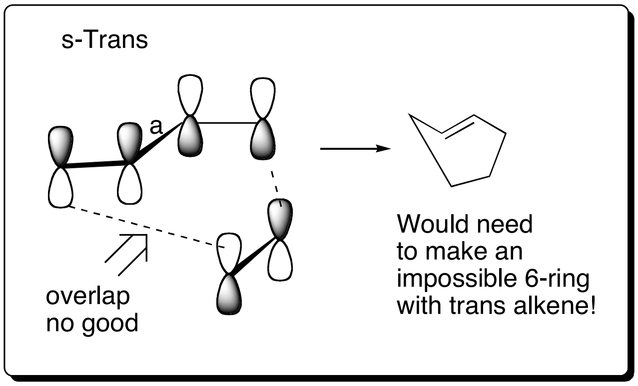


"cisoid" or "s-cis"
-meaning that it's "cis" relative to the **s**ingle bond
-even though the single bond is capable of rotation

Why? Because the concerted, p-orbital overlap mechanism is impossible from s-trans.



s-cis: p-orbital overlap possible

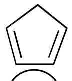


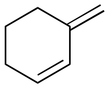
Would need to make an impossible 6-ring with trans alkene!

- Normally the s-cis conformation is less stable than the s-trans conformation for steric reasons.
- Only the minor fraction of a diene in the s-cis conformation is able to react
- The larger the equilibrium population in the s-cis conformation, the greater the reactivity

2. For an acyclic diene, a "Z" substituent on either (or both) of the diene alkenes causes major steric problems for the s-cis conformation, makes it's equilibrium population really small, and thus greatly reduces Diels-Alder reactivity

Q1: For the dienes **A-Z**, circle the letters for those that are in a reactive s-cis conformation.
Q2: For the acyclic dienes **C-Z**, identify any double bonds the are E or Z.
Q3: Match acyclic dienez **C-Z** with the alternate s-cis/s-trans form shown below.
Q4: For the dienes **A-E**, try to rank their probable Diels-Alder reactivity based on the probable relative population of their s-cis conformations. (or match: 100%, 3%, 001%, 0.000001%, 0%)
Q5: Try to redraw **D**, **E**, and the s-trans version of **C** from the bottom row into their s-cis forms


[✓ **A**]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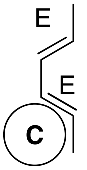
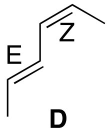


[✓ **C**]



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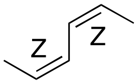

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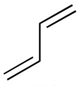
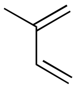
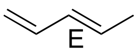

W


[✓ **X**]



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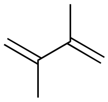
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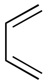
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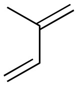
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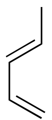
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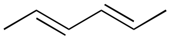
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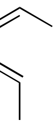
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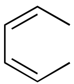
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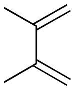
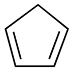

Z

3. When steric factors are not a problem (in other words, when not in a "Z" position), electron donating groups ("D" or "EDG") have a mild activating effect
   - OR, NR_2, R (memorize)
   - Why: The diene functions as the nucleophile. A donor makes the diene more electron rich and thus more nucleophilic.

Rank the reactivity: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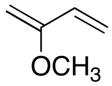

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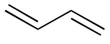
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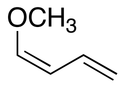
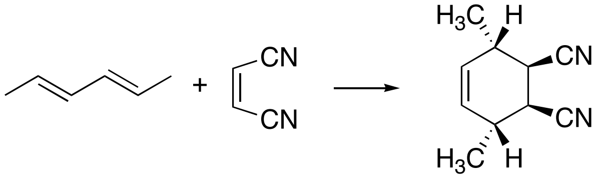
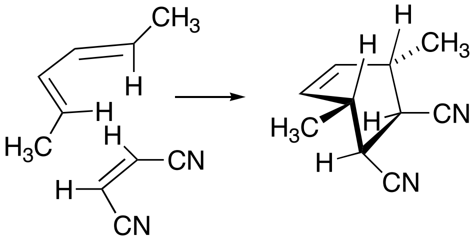


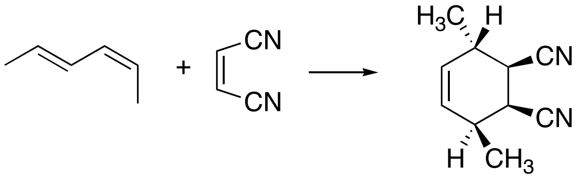
4

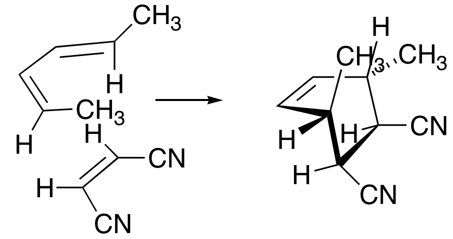
E. <u>Stereochemistry</u>: For **<u>Dienophiles with Substituents on C1 and/or C4</u>** (Not test responsible)

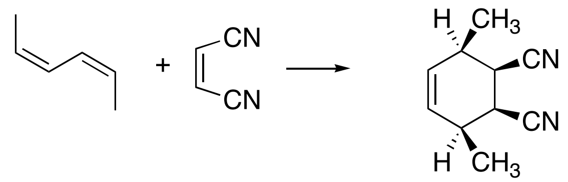
- Need to convert diene into s-cis conformation, then envision the transition state
- The "inside" (Z) substituents on C1/C4 end up "up" (cis); the "outside" (E) substituents on C1/C4 end up "down" (and cis to each other); inside/outside attachments on C1/C4 end up trans

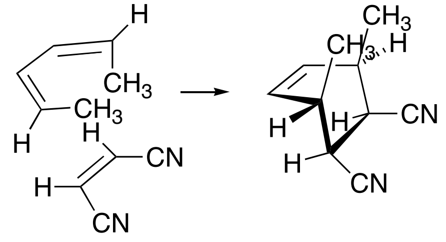






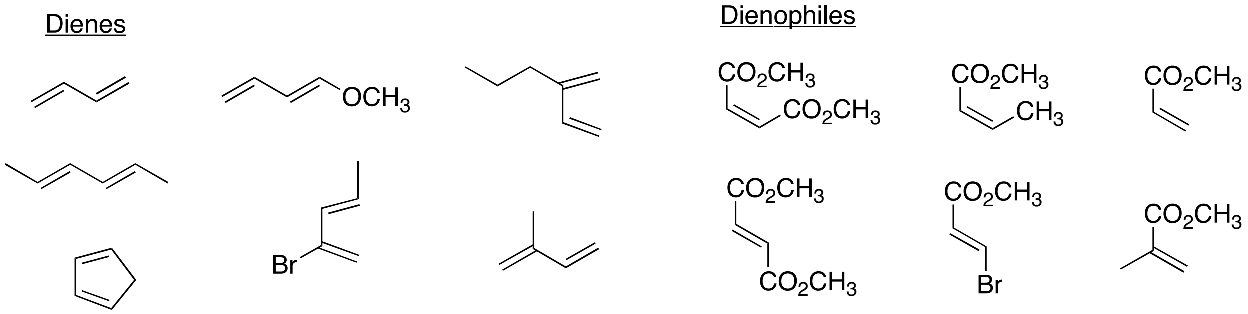






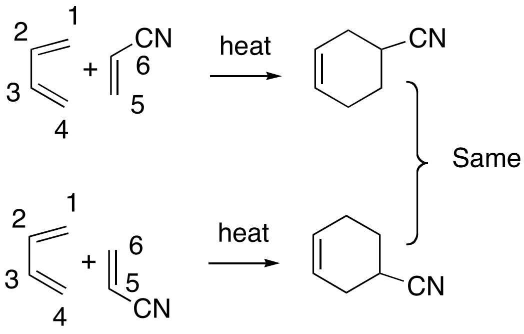
F. Predicting Products When **Both Diene and Dienophile are Asymmetric** (****) (15-11B)

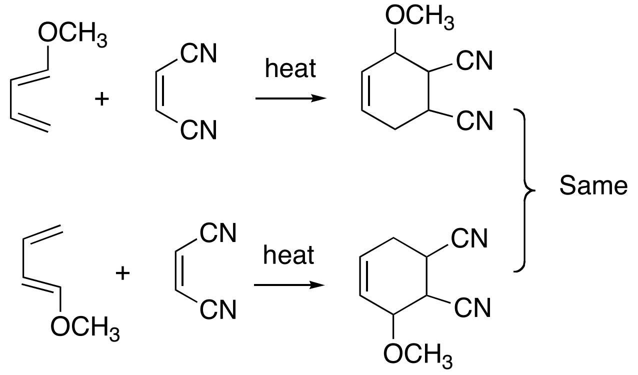
Q. Circle the symmetric dienes or dienophiles



- Any monosubstituted diene or monosubstituted dienophile is asymmetric
- You can be trans and still symmetric
- Symmetry requires equal attachments on: C1+C4, C2+C3 (dienes), C5+C6 (dienophile)

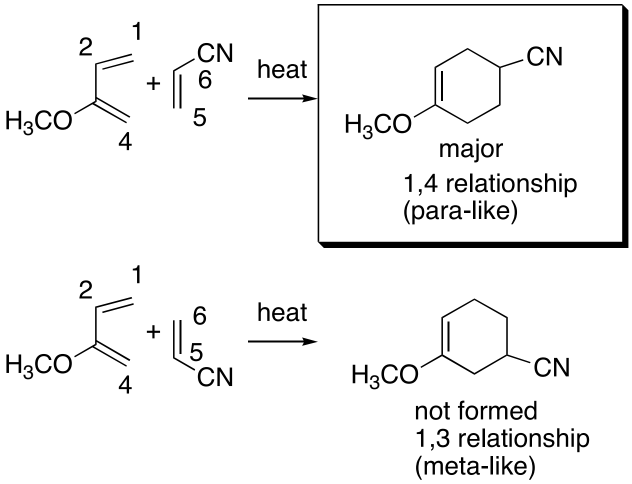
If either component is symmetric, you don't have structural isomer issues.

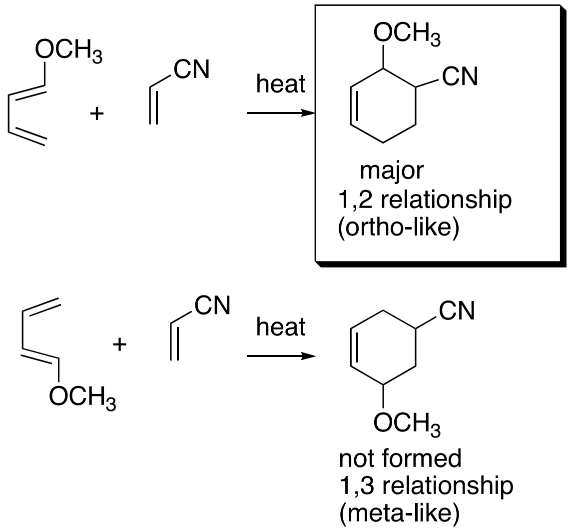




- If both ends of diene are the same, it doesn't matter which adds to which end of dienophile
- If both ends of dienophile are the same, it doesn't matter which adds to which end of diene

If both components are asymmetric: two structural isomers are possible; one dominates.



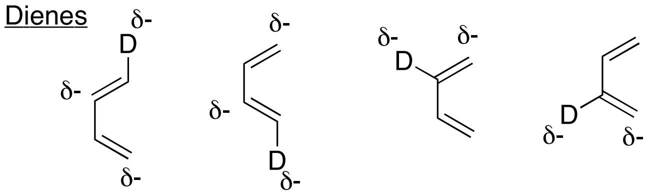


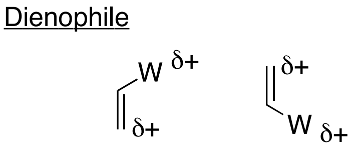
****** **A 1,2 or 1,4 relationship is always preferred over a 1,3 relationship, if possible** *****

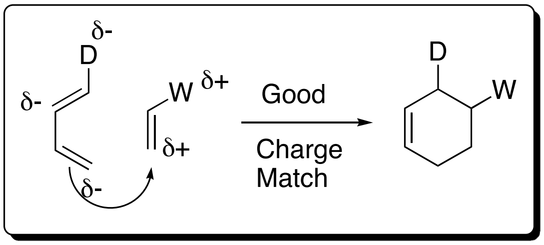
- Although ortho/meta/para terms don't really correctly apply to cyclohexenes, many students remember this is an "**ortho/para preferred**" rule, to avoid number confusion

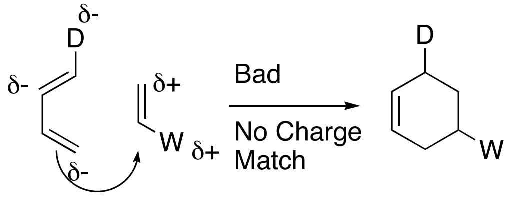
Explanation for Structural Isomer Selectivity in Addition of Asymmetric Dienes to Asymmetric Dienophiles: Electronics

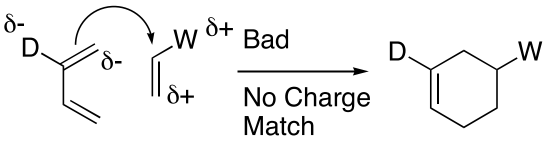
- Donors function as electron rich (δ-); withdrawers function as electron poor (δ+)
- δ- or δ+ partial charges are shared on **alternating atoms** (ala allylic) over π-systems
- For an asymmetric diene, one of the two terminal carbons ends up δ- and nucleophilic
- For an asymmetric dienophile, one of the alkene carbons ends up δ+ and electrophilic.
- Matching the δ- diene terminus with the δ+ dienophile carbon gives major structural isomer.

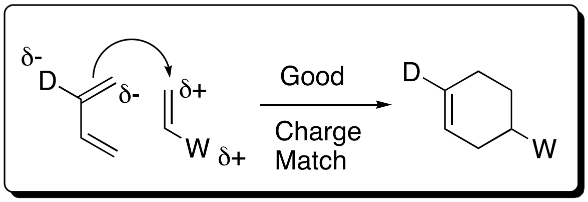












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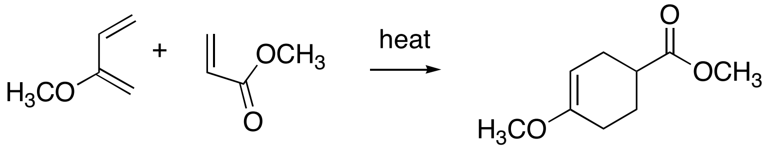

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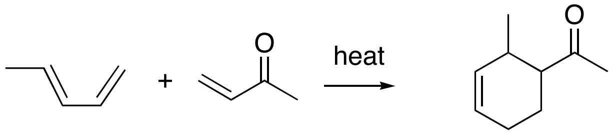

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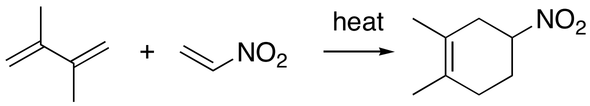

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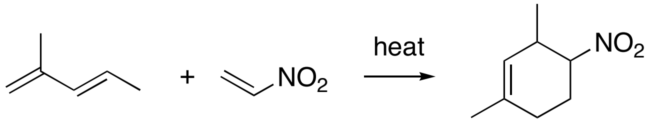

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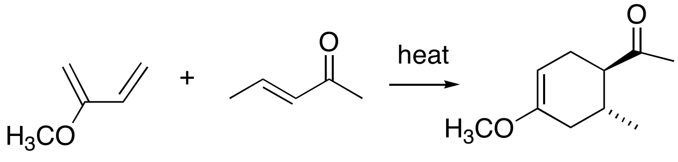

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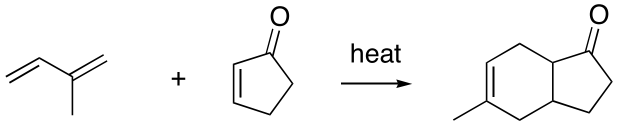
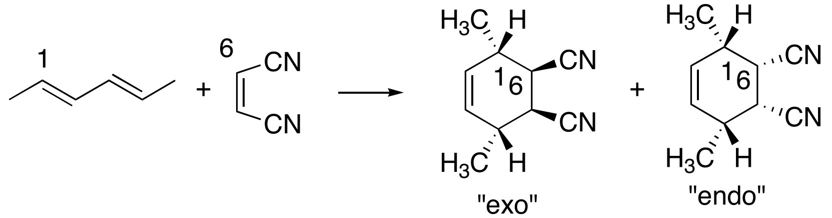
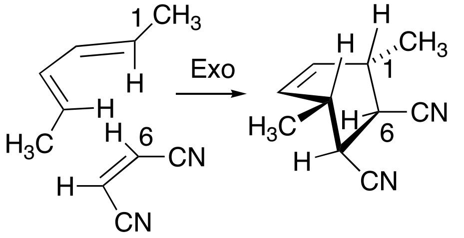
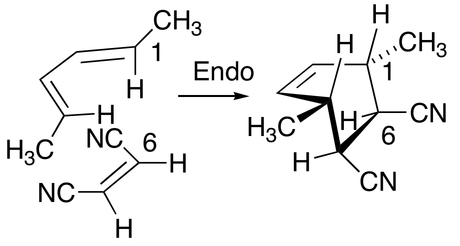


G. Endo/Exo Stereochemistry: Relative stereochemistry when both diene and dienophile generate stereocenters. (This will involve **Dienophiles with Substituents on C1 and/or C4)** (p 684. Not test responsible)



"Exo"/"Endo" determines relative stereo between C1 or C4 relative to C5 or C6. Determined by whether dienophile substituents are under the diene or away from the diene.





1. In the exo product, the relative stereochemistry at C1-C6 is trans.
2. In the endo product, the relative stereochemistry at C1-C6 is cis.
3. The difference results from how the dienophile lays out under the diene.
   - In the exo case, the dienophile substituent extends away from the diene, while the dienophile hydrogens extend underneath the diene. (Sterically preferable)
   - In the endo case, the dienophile substituent extends under the diene, while the dienophile hydrogens extend away from the diene. (Some electronic advantage.)