

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 | sp ² , not sp ³ !! | sp ³ | An N or O next to a double bond becomes sp ² . An isolated N or O is sp ³ |
| 6 | Amines | sp ² | sp ³ | |
| 7 | Esters | sp ² | sp ³ | |
| 8 | Amides | sp ² | sp ³ | Very special, chapter 23, all of biochemistry, proteins, enzymes, etc. |
| 9 | Oxyanions (Carboxylates) | sp ² | sp ³ | Very special, chapter 21 |
| 10 | Carbanions (Enolates) | sp ² | sp ³ | Very special, chapter 22 |
| 11 | Aromatics | | | Very special, chapters 16 + 17 |

Conjugation: Anything that is or can be sp² hybridized is stabilized when next to π bonds.

- oxygen, nitrogen, cations, radicals, and anions

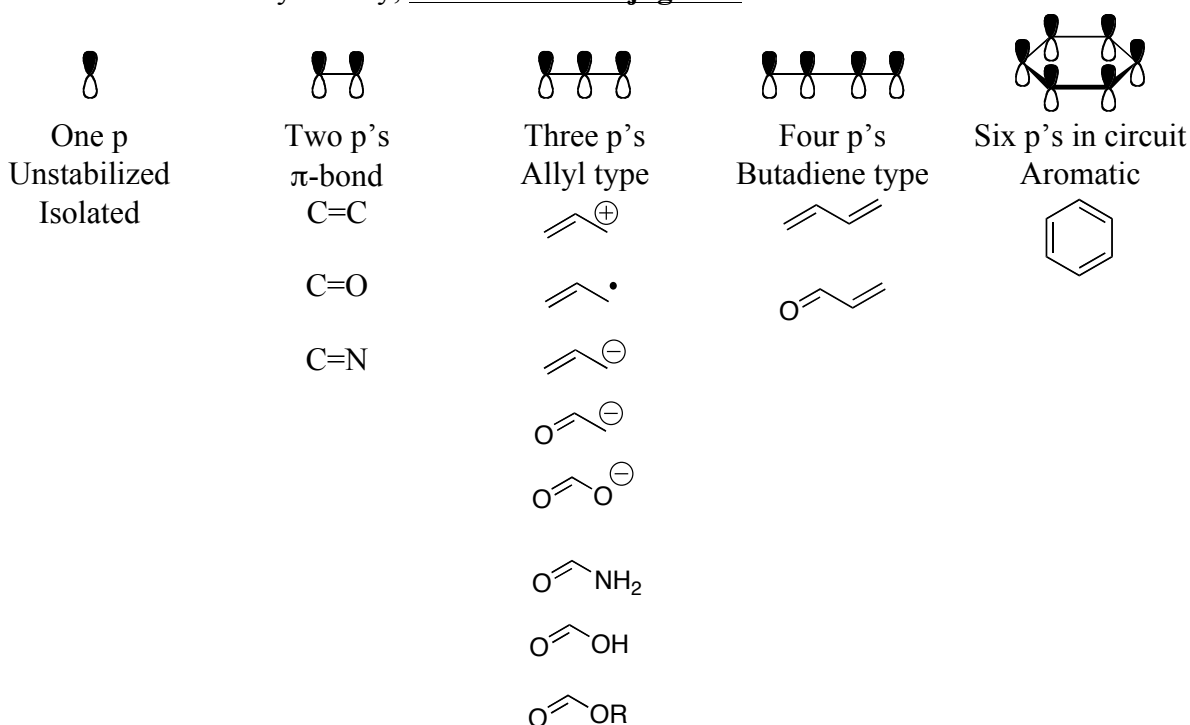
Notes:

- Any atom that can be sp² will be sp² when next to a double bond
- “Conjugation” is when sp² centers are joined in an uninterrupted series of 3 or more, such that an uninterrupted series of π-orbitals is possible
- Any sp² center has one p orbital

Impact of Conjugation

4. **Stability:** Conjugation is **stabilizing** because of π -orbital overlap (Sections 15.2, 4, 7)

- Note: In the allyl family, **resonance = conjugation**

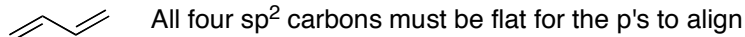


5. **Reactivity:** Conjugation-induced stability impacts **reactivity** (Sections 15.4-7)

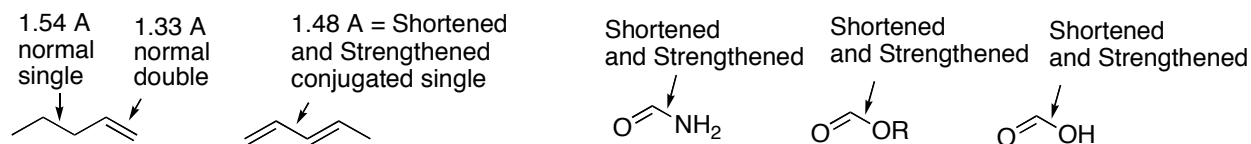
- If the **product** of a rate-determining step is stabilized, the reaction rate will go **faster** (product stability-reactivity principle)
 - Common when allylic cations, radicals, or carbanions are involved
- If the **reactant** in the rate-determining step is stabilized, the reaction rate will go **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 π -orbitals must be aligned in parallel for max overlap and max stability
- The sp^2 centers must be coplanar



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

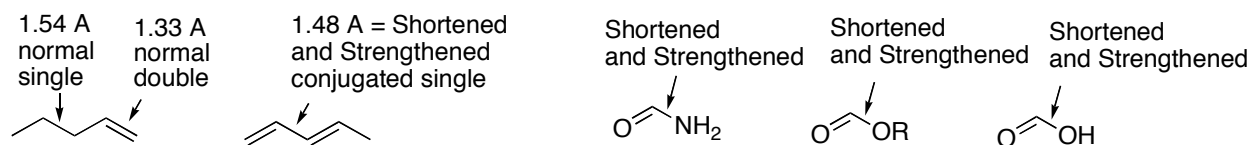


- In amides, esters, and acids, the bond between the carbonyl and the heteroatom is shortened

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

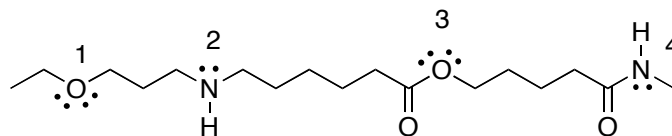
9. **Bond Rotation Barrier:** Bonds that look like singles but are actually between conjugated have much larger rotation barriers than ordinary single bonds

- Because in the process of rotating, the π -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, 109° bond angles
- **Conjugated nitrogens:** sp^2 atom hybridization, **p lone-pair hybridization (needed for conjugation)**, and 120° bond angles
- **Conjugated oxygens:** sp^2 atom hybridization, **one p lone-pair hybridization (needed for conjugation)**, **one sp^2 lone-pair**, and 120° bond angles



| <u>Atom</u> | <u>O-1</u> | <u>N-2</u> | <u>O-3</u> | <u>N-4</u> |
|---------------|------------|------------|------------|------------|
| Isolated vs. | | | | |
| Conjugated | | | | |
| Atom | | | | |
| Hybridization | | | | |
| Lone-Pair(s) | | | | |
| Hybridization | | | | |

Bond Angles

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

Q1: Rank the stability of the following dienes:

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

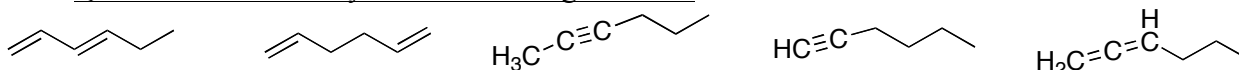
3. **Allenes** = "Cumulated Dienes": **Less stable than dienes or alkynes**
 - in allenes, the central carbon is sp rather than sp^2 hybridized



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:



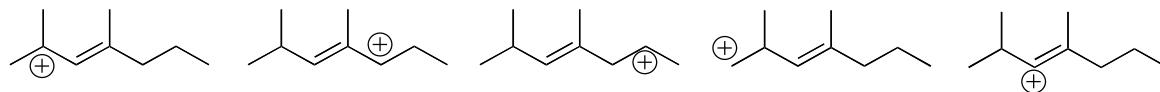
Q3: Rank the amount of heat produced if the isomers above were hydrogenated?
Burned?

15.4 Stability of Allylic/Benzylic (Conjugated) Cations

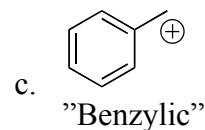
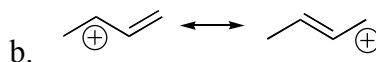
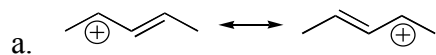
Stability Factors for Cations:

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)

Q1: Rank the stability of the following cations?



Q2: Rank the stability of the following alkene cations?

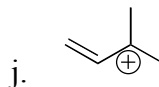
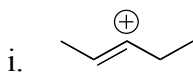
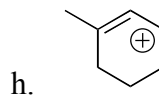
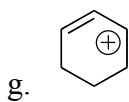
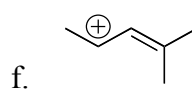
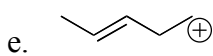
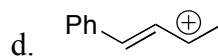
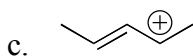
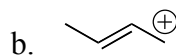
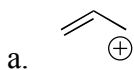
Allylic Cations, Resonance, and Allylic Symmetry/Asymmetry

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

Q3: For above cations, identify as symmetric or asymmetric.

Q4: For the following cations:

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

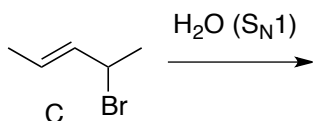
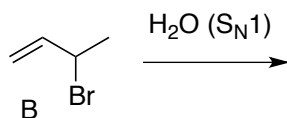
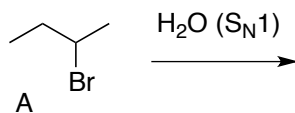


Impact of Allylic Cation Resonance on Reaction Rates and on Whether One or Two Products Form (S_N1 Reactions)

- Rates:** Resonance/conjugation stability enhances rates when cation formation is rate-determining
- One Product or Two?** Product mixtures result if an allylic cation is asymmetric.
 - two unequal resonance structures can lead to two products (structural isomers).
- Product Distribution**
 - When two isomeric products can form, consider two things:
 - Which product is more stable?
 - This will impact “product stability control” = “thermodynamic control” = “equilibrium control”
 - To assess product stability, focus on the alkene substitution
 - 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
- 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:

- Draw the cation intermediates.
- If an allylic cation is involved, recognize as symmetric or asymmetric.
- Rank the reactivity of the three bromides.
- Draw the product or products. Be clear to notice whether you’d get one isomer or two.
- If two products are possible, identify which is more stable (the “thermodynamic product”) based on product alkene stability.
- For the asymmetric allylic cation, identify which resonance structure makes a larger contribution to the resonance hybrid. Does this lead to the “thermodynamic” (more stable) product, or to the “kinetic” (less stable) product?



Impact of Allylic Cation Resonance on Addition of H-X to Conjugated Dienes.

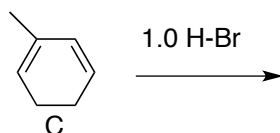
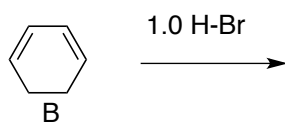
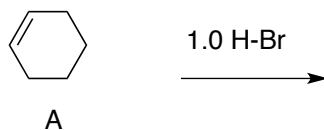
- Notes on predicting products when H-X adds to a diene.

Questions/Issues to Deal With When Predicting Product(s).

1. Always protonate first on an outside rather than inside carbon.
 - This will give an allylic rather than isolated cation
2. Is the diene symmetric or asymmetric?
 - If it's symmetric, it doesn't matter which outside carbon you add to first.
 - If it's asymmetric, then protonating at different ends will likely give allylic cations of unequal stability. Thus you should decide which protonation site will give the best allylic cation.
3. Is the allylic cation (once you have protonated) symmetric or asymmetric?
 - If it's symmetric, you'll get one structural isomer.
 - If it's asymmetric, you'll get two structural isomers.

Question 2: Key: Think about the cation! For the dienes A-C,

- a. Draw the cation intermediates.
- b. If an allylic cation is involved, recognize as symmetric or asymmetric.
- c. Rank the reactivity of the three bromides.
- d. Draw the product or products. Be clear to notice whether you'd get one isomer or two.
- e. If two products are possible, identify which is more stable (the "thermodynamic product") based on product alkene stability.
- f. For the asymmetric allylic cation, identify which resonance structure makes a larger contribution to the resonance hybrid. Does this lead to the "thermodynamic" (more stable) product, or to the "kinetic" (less stable) product?
- g. When two products form, classify each as a "1,2" or "1,4" product



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

1. “Thermodynamic Control” = “Product-Stability Control” = “Equilibrium Control”

- This is when **the most stable** of two possible **products** predominates.
 - **Use Alkene Stability to identify which product is more stable.**
 - The most stable product will be preferred if either:
 - The two products can equilibrate, or
 - The more stable product involves a more stable transition state

2. **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 reasons:
 - Charge distribution in an allylic cation or radical.
 - Proximity of reactants. In an H-X addition to a diene, often the halide anion is closer to the “2” carbon than to the “4” carbon of the allylic cation.
 - Steric factors. (Why bulky E2 base give less stable Hoffman alkenes.)

3. **Temperature Factor:** When allylic halides are produced, the “thermodynamic” product increases at higher temperature due to equilibration.

Example:



1,2- vs 1,4 Addition Product:

at -80°C

80% (major)

20% (minor)

at +40°C

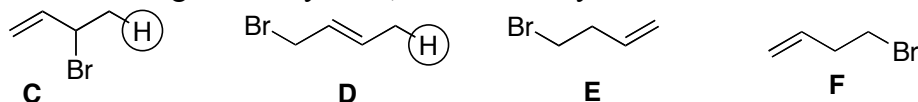
15% (minor)

85% (major)

More/Less stable:

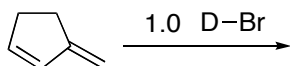
Mech (and why)

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



More H-X to Conjugated Dienes Practice

1. Draw the mechanism, including both resonance structures for the best allylic cation.
2. Predict the products for the following reaction.
3. Identify each product as 1,2 or 1,4 product.
4. Identify which product is the “thermodynamic” product, and which might be the “kinetic”.
5. 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.

**Review on predicting products when H-X adds to a diene.**

1. Always protonate first on an outside rather than inside carbon.
 - This will give an allylic rather than isolated cation
2. Is the diene symmetric or asymmetric?
 - If it's symmetric, it doesn't matter which outside carbon you add to first.
 - If it's asymmetric, then protonating at different ends will likely give allylic cations of unequal stability. Thus you should decide which protonation site will give the best allylic cation.
3. Is the allylic cation (once you have protonated) symmetric or asymmetric?
 - If it's symmetric, you'll get one structural isomer.
 - Is it's asymmetric, you'll get two structural isomers.

Mixtures of 1,2 and 1,4 addition also occur when dihalogens (Br₂, Cl₂) add to dienes

Q2: Draw the major products when the diene above reacts with Br₂. Which would you expect to be the “thermodynamic” product?

15.7 Allylic/Benzylic Radicals and Allylic HalogenationStability Factors for Radicals:

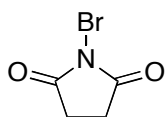
1. Isolated versus Conjugated/Allylic: Conjugation stabilizes
2. Substitution: More highly substituted are more stable.
 - Conjugation/allylic is more important than the substitution pattern

Impact of Radical Resonance on Reactivity and Product Formation: Allylic Radical Bromination is Fast!

1. **Rates:** Allylic bromination is fast.
2. **Position of Radical Formation: Allylic positions react.**
3. **Product Distribution A:** Unequal allylic positions can each lead to products.
4. **Product Distribution B:** Asymmetric allylic radicals product two bromide isomer.

Review on predicting products in allylic radical brominations.

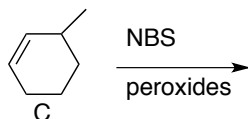
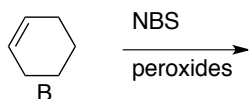
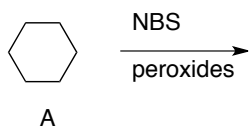
1. Is the alkene symmetric or asymmetric?
 - If it's symmetric, it doesn't matter which allylic carbon you convert to a radical.
 - If it's asymmetric, then you can remove a hydrogen from different allylic sites and make different allylic radicals, each of which can lead to products.
2. For each allylic radical, is it symmetric or asymmetric?
 - If it's symmetric, it will lead to one structural isomer bromide.
 - Is it's asymmetric, it will lead to two structural isomer bromides.



“**NBS**” = N-Bromosuccinimide = More commonly used than $\text{Br}_2/h\nu$ for allylic/benzylic radical brominations. Maintains dilute $[\text{Br}_2]$, 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.

Practice Problems

- a. Draw the radical intermediates, including resonance structures
- b. Ranks the reactivity of **A**, **B**, and **C**.
- c. Draw the product or products for the following reactions



Allylic Anions

1. Allylic anions are stabilized, just as are cations and radicals

2. Anion stability impacts acidity

- when something neutral functions as an acid, it releases H^+ and produces an anion

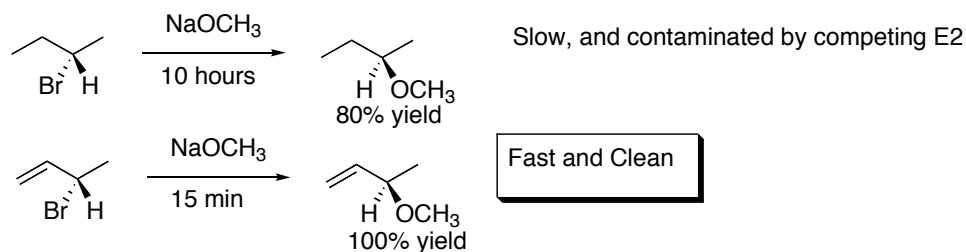
Question 1: Compare the acidity of cyclopentene to cyclopentane. One is a quintillion times more acidic than the other. Which is it, and why?

Question 2: Compare the acidity of acetone, 2-methylpropene, and 2-methylpropane

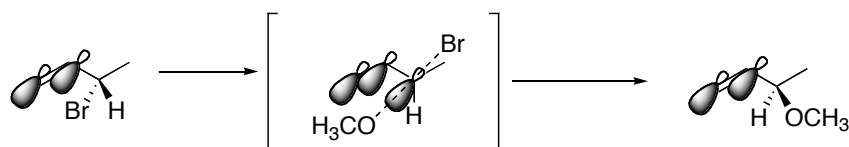


Section 15.10 **Allylic Halides and S_N2 Reactions. Allylic Systems Are Really Fast**

Ex.



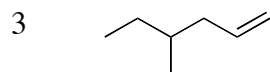
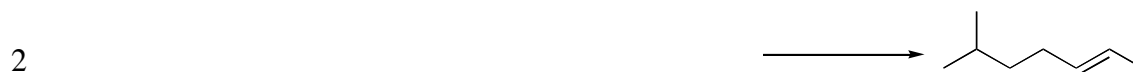
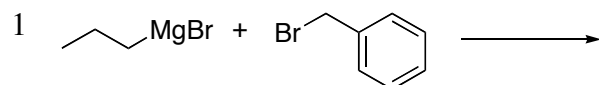
Why? Because the backside-attack transition-state is stabilized by conjugation!
(Transition state-stability-reactivity principle).



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 sp² hybridized
 - the nucleophile and the electrophile are essentially on opposite ends of a temporary p-orbital.
3. That transient sp² hybridization in the transition-state is stabilized by π-overlap with the adjacent 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

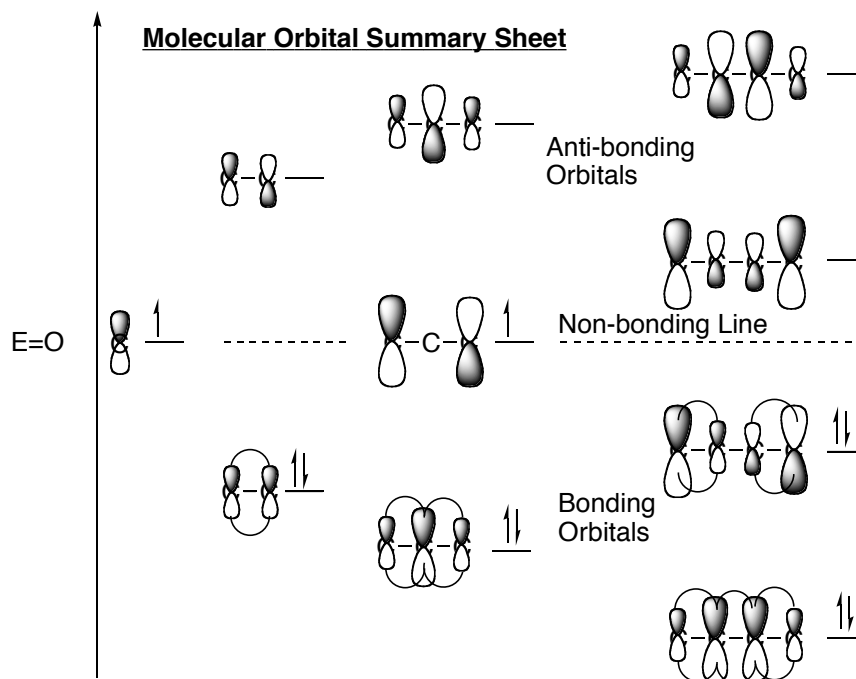
- RMgBr carbanionic nucleophiles can't do good S_N2's on normal 1° or 2° allylic bromides because of competing elimination and single-electron-transfer reactions.
- But they work well on allylic halides



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

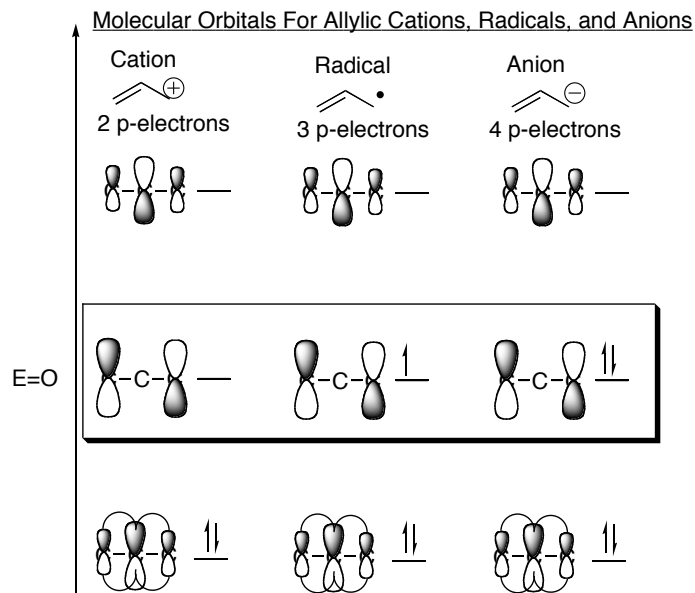
Note: When thinking backwards, identify the allylic carbon and the next carbon removed from the alkene. Those will be the two carbons that were linked.

Sections 15.3, 8, 9 Molecular Orbitals and Conjugation (not for test)

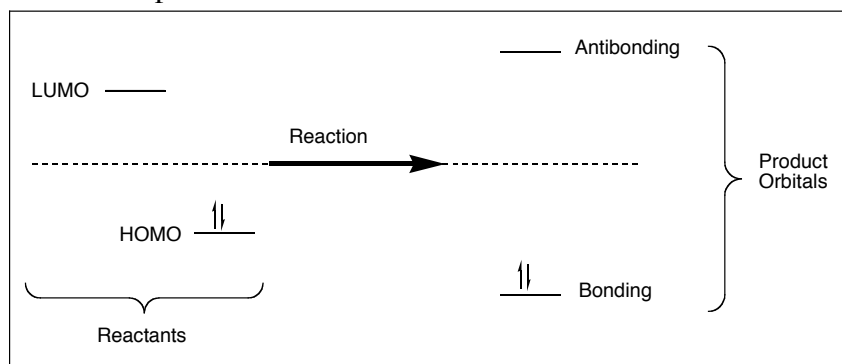


Observations:

1. Shown are 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 π -orbitals in the FMO's. When reactions happen, atoms with the big p-lobes are the ones that react.

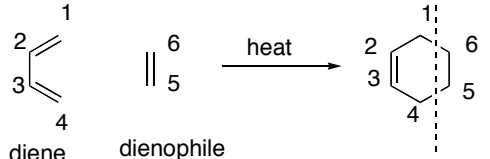
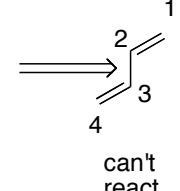
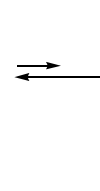
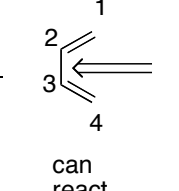
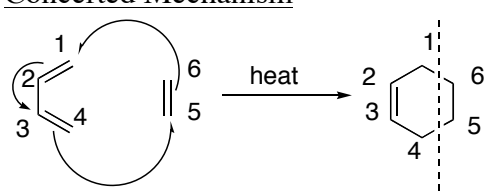
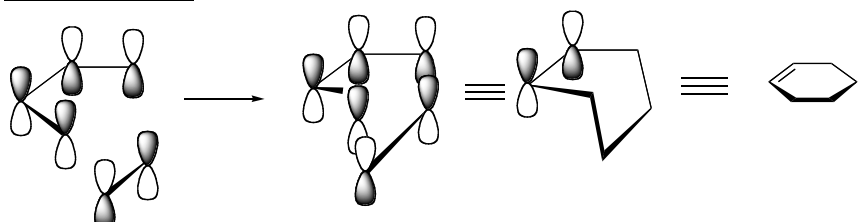


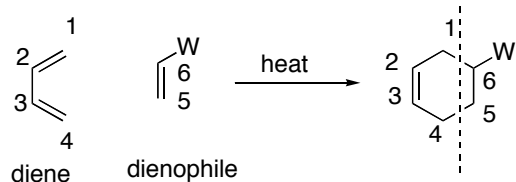
11. For allylic systems, notice that the energies and shapes of the MO's stay the same.
12. However, the occupancy does change. An allylic cation has two π -electrons, an allylic radical has three, and an allylic anion has four. Thus the key reactive middle MO goes from empty (strongly electrophilic) 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 $\text{CH}_2=\text{CH}^+ \longleftrightarrow ^+\text{CH}=\text{CH}_2$
14. Sometimes MO can explain things that the simpler resonance theory can't.
15. In an actual reaction, the HOMO and LUMO interact
- 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 15.11 The Diels-Alder Reaction. The Reaction of Conjugated Dienes (Dienes) with Electron-Poor Alkenes (Dienophiles) to make Cyclohexenes.

Quick Overview Summary

| | |
|----|--|
| 1. |  <p>diene dienophile</p> |
| 2. | <p><u>s-cis diene conformational requirement</u>: The diene must be locked or be able to single-bond rotate it's way into the "s-cis" conformation in order to react</p> <div style="display: flex; align-items: center;"> <div style="margin-right: 20px;"> <p>"transoid" or "s-trans" -relative to the <u>single bond</u></p>  <p>can't react</p> </div> <div style="margin-right: 20px;">  </div> <div style="margin-right: 20px;">  <p>can react</p> </div> <div style="border: 1px solid black; padding: 5px; margin-left: 20px;"> <p>"cisoid" or "s-cis" -meaning that it's "cis" relative to the <u>single bond</u> -even though the single bond is capable of rotation</p> </div> </div> |
| 3. | <p><u>Rate Factors</u></p> <ol style="list-style-type: none"> 1. Dienophile <ul style="list-style-type: none"> ▪ activated by electron withdrawing groups ("W" or "EWG") for electronic reasons 2. Diene: <ul style="list-style-type: none"> ▪ 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. | <p><u>Concerted Mechanism</u></p>  <p>All bond making and breaking happens at once: *3 π-bonds break *2 σ-bonds and 1 π-bond form</p> <p>The diene is really the "nucleophile" (HOMO) The dienophile is really the "electrophile" (LUMO)</p> |
| 5. | <p><u>Orbital Picture</u></p>  |
| 6. | <p><u>Product Prediction Highlights</u></p> <ul style="list-style-type: none"> ▪ Try to match up the 4 diene and 2 dienophile carbons with the product <ul style="list-style-type: none"> ○ 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 <ul style="list-style-type: none"> ○ Match δ^- end of nucleophilic diene with δ^+ end of electrophilic dienophile ▪ For disubstituted dienophiles: <ul style="list-style-type: none"> ○ cis-substituents end up cis, and trans-substituents end up trans |

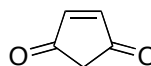
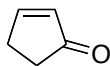
A. The General Diels-Alder Reaction

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

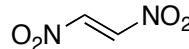
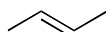
| Carbonyls | | | | Others | | | |
|------------|------------|------------|------------|----------------------------|-----------------|-------------------|-----------------|
| δ^- | δ^- | δ^- | δ^- | CN | NO ₂ | SO ₃ H | CF ₃ |
| | | | | $\delta^+ \delta^-$ C≡N | | | |

- 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

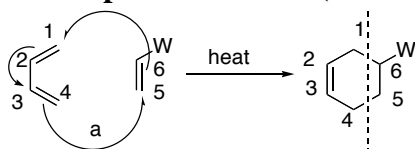
Q1/example: Rank the reactivity of the following alkenes as dienophiles. The actual relative reactivity ratios are 50,000 : 1,000 : 1. Huge differences.



Q2: Rank the reactivity of the following dienophiles:

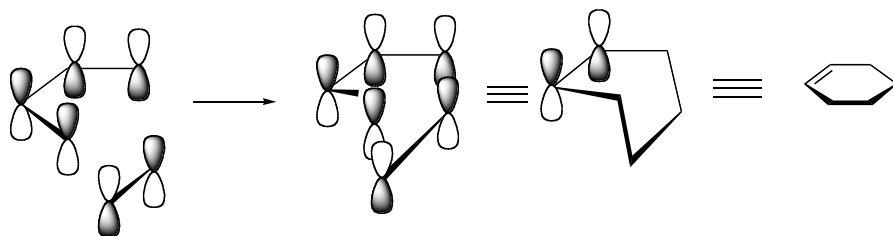
**3. Energetics:**

- 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

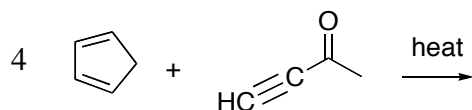
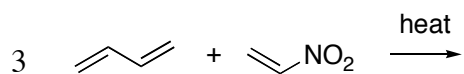
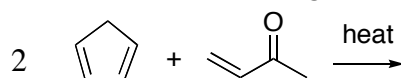
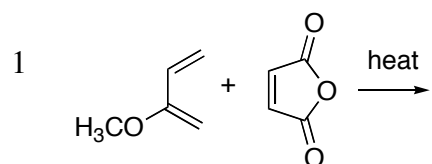
5. Orbital Picture



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

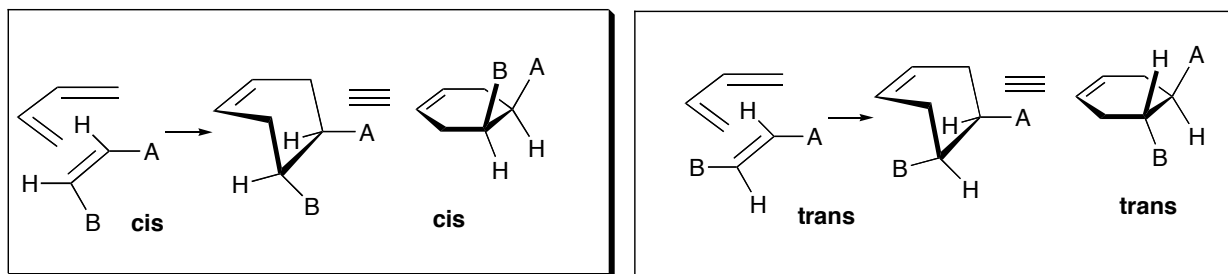
B. Predicting Products When the Diene or the Dienophile (or both) is Symmetric

- Always make a cyclohexene 6-ring product
- Number the diene from 1-4, and identify those four carbons in the product ring.
- A double bond in the product will always exist between carbons 2 and 3.
- 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 zigzag s-trans form, but could react following rotation into an s-cis form

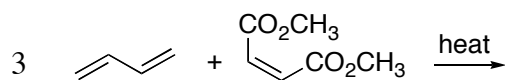
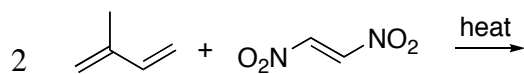
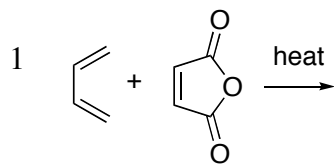
Noteworthy

C. Stereochemistry: For Cis- or Trans- Disubstituted Dienophiles

- Both carbons of a disubstituted dienophile usually turn into stereocenters.
- 1. **Cis in \rightarrow cis out:** If two substituents on the **dienophile** are cis to begin with, they will still have a cis relationship on the product cyclohexene
- 2. **Trans in \rightarrow trans out:** If two substituents on the **dienophile** are trans to begin with, they will still have a trans relationship on the product cyclohexene
- Note:** this is for the **dienophile only**. The diene alkenes may also have substitution such that one or both diene double bonds are cis or trans, but the “cis-in-cis-out” guideline does not apply to the diene.

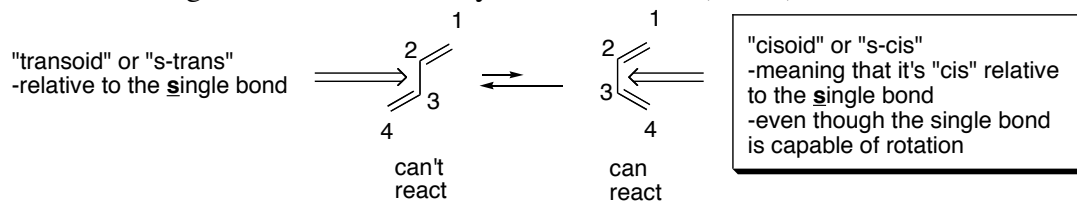


- Why:** Because of the concerted mechanism. The diene is basically doing a concerted “cis” addition to the dienophile. The attachments on the dienophile never have opportunity to change their position relative to each other.

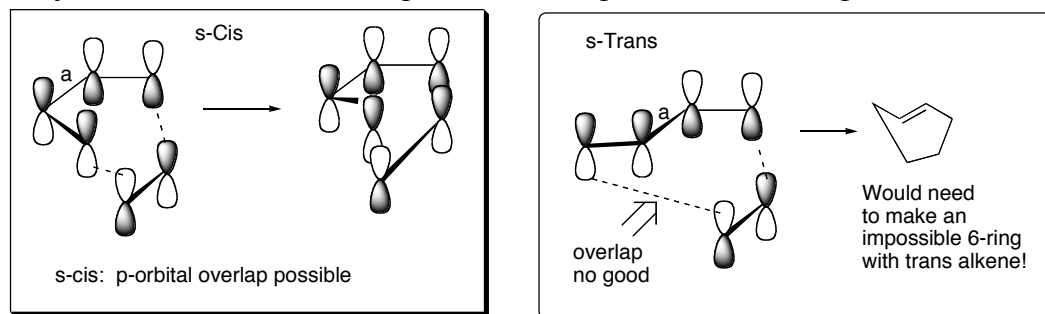


D. Structural Factors for Dienes

1. **s-cis (cisoid) diene conformational requirement:** 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



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



- Normally the s-cis conformation is less stable than the s-trans conformation (sterics).
- 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, reduces the equilibrium population of s-cis diene, and thus reduces Diels-Alder reactivity

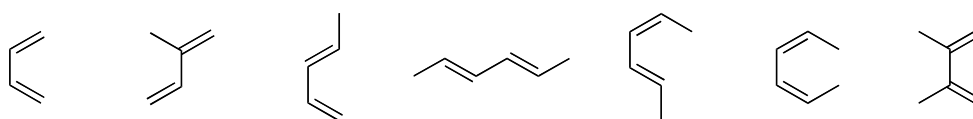
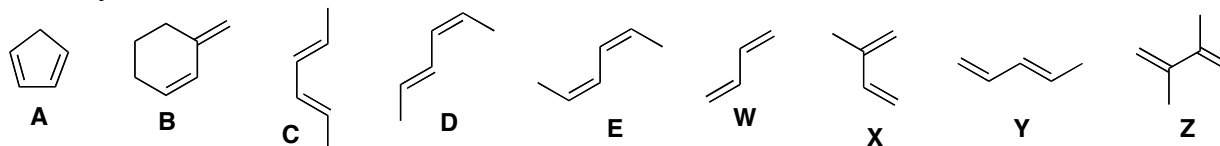
Q1: For the dienes **A-Z**, circle the letters for those that are in a reactive s-cis conformation.

Q2: For the acyclic dienes **C-Z**, identify any double bonds that are E or Z.

Q3: Match acyclic dienes **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%)

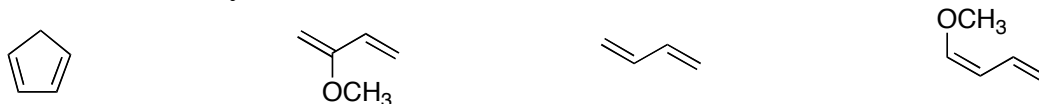
Q5: Try to redraw **D** and **E** into their s-cis forms



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

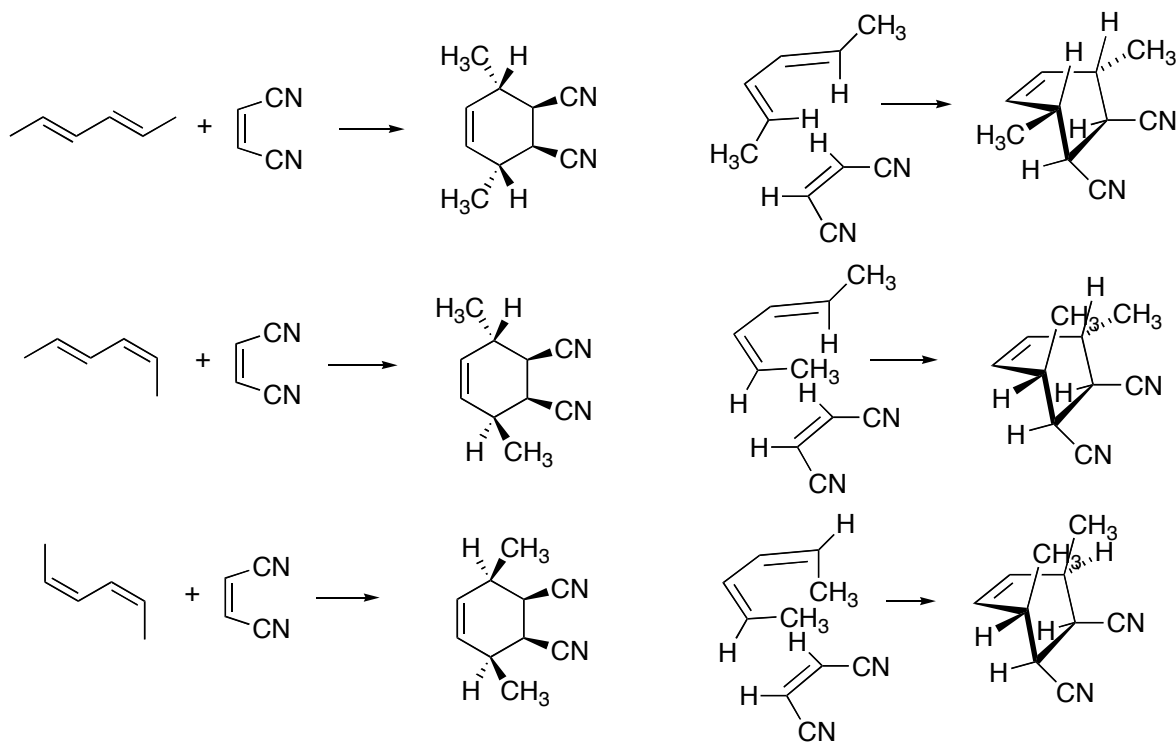
- OR, NR₂, R (memorize)
- Why: The diene functions as the nucleophile. A donor makes the diene more electron rich and thus more nucleophilic.

Rank the reactivity:



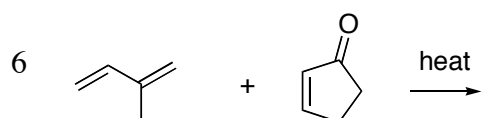
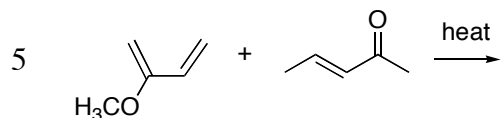
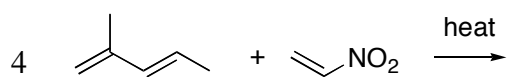
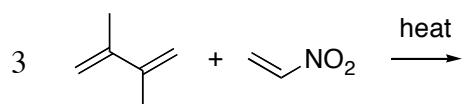
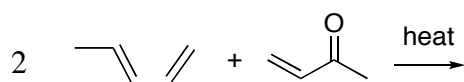
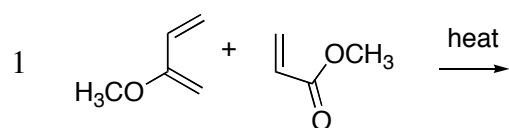
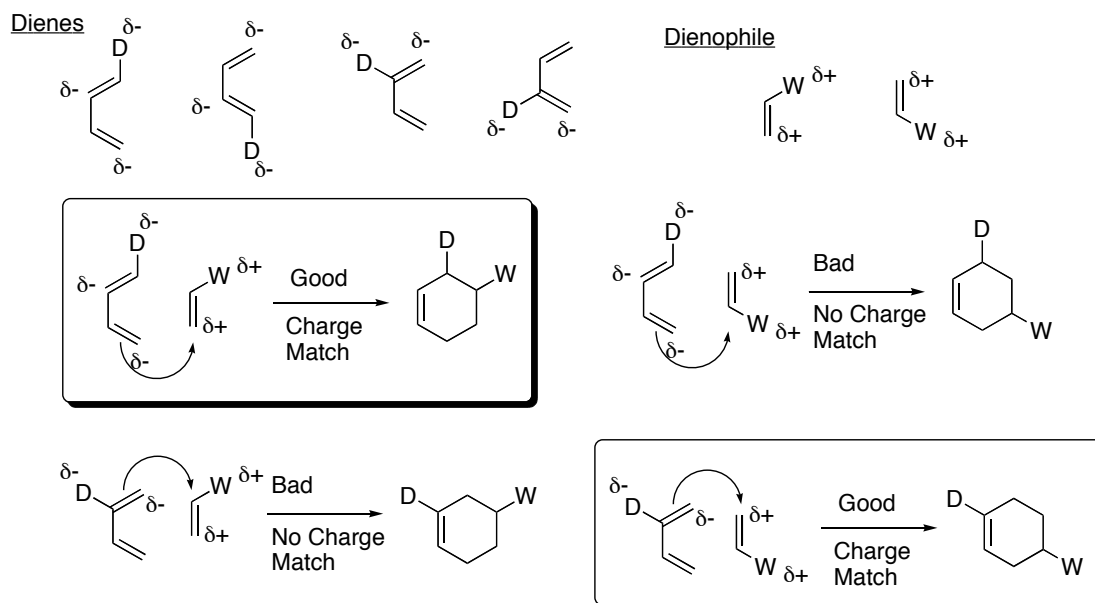
E. Stereochemistry: For **Dienophiles with Substituents on C1 and/or C4** (Not test responsible)

- 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

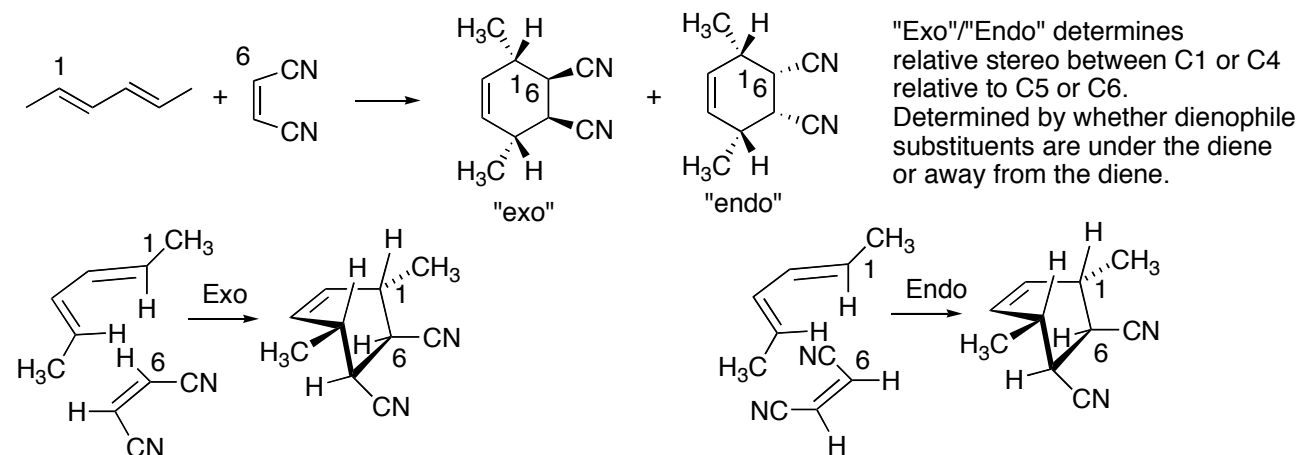


Explanation for Structural Isomer Selectivity in Addition of Asymmetric Dienes to Asymmetric Dienophiles: Electronics

- 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.



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)



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.)

