Ch. 7 Structure and Synthesis of Alkenes

7.1,2 Review

Bond Strength	
C-C σ Bond	83 kcal/mol
C=C π Bond	63 kcal/mol

- π Bonds are much weaker
- π Bonds are thus more breakable and more reactive

Double Bonds can't rotate

7.3 Elements of Unsaturation ("EU")

- **"Saturated Alkane"**: C_NH_{2N+2}
- **Unsaturated** Formula: Has less than the maximum 2N+2 number of hydrogens

1. "**Element of Unsaturation**": Something that reduces the hydrogen count by two
   a. Double bond
   b. Ring

2. Each element of unsaturation reduces the hydrogen count by two
3. A molecule may well have several elements of unsaturation, each one progressively reducing it's hydrogen count by two.

4. Knowing how many elements of unsaturation are present helps to classify, and helps in isomer problems.

5. Calculating EU

General Concept

$$\boxed{EU = \frac{\text{Theory \# H's - Actual \# H's}}{2}}$$

For Formulas With Nothing Other than C, H, or O

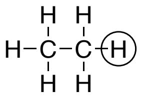
$$\boxed{EU = \frac{(2C + 2) - H}{2}}$$

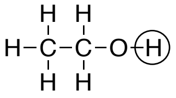
For Formulas That May Include Nitrogen or Halogens

$$\boxed{EU = \frac{(2C + 2 + N) - (H + X)}{2}}$$

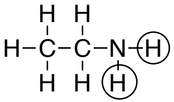
C = # C's
H = # H's
N = # N's
X - # halogens

6. Heteroatom Effect:
   - Oxygens: No effect
   - Nitrogen: each nitrogen increases the theory # H's by 1
   - Halogen: each halogen takes the place of a hydrogen and reduces the theory # H's by 1.

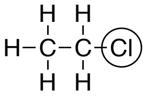




Oxygen: no impact



Nitrogen: adds one



Halogen: replaces one

Calculate how many elements of unsaturation are in the following formulas:

2. C_5H_{12}

3. C_4H_8

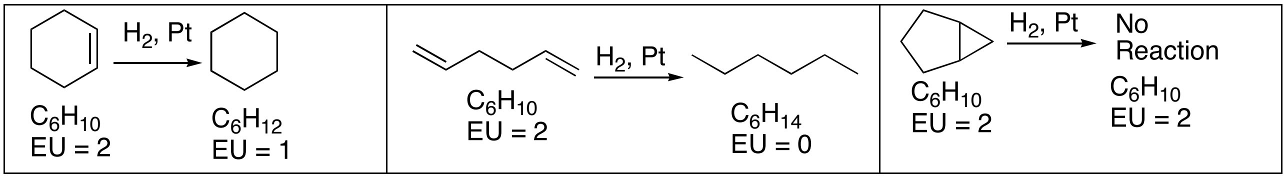
4. C_3H_4O

5. C_5H_9Cl

6. $C_4H_{11}N$

Distinguishing Rings from Double Bonds by H_2/Pt Hydrogenation

a. H_2/Pt will "saturate" **all** C=C double bonds by adding H_2 across each one.
b. However, rings will not add hydrogen upon treatment with H_2/Pt
c. Thus you can count how many of your EU's are rings versus double bonds
d. Note: 2H's add per 1 double bond



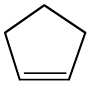
7. For C_4H_8 , draw all possible structures for isomer A and isomer B, given the following:

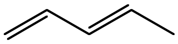
a. $C_4H_8\ (A) \xrightarrow{H_2,\ Pt} C_4H_{10}$

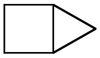
b. $C_4H_8\ (B) \xrightarrow{H_2,\ Pt}$ No reaction

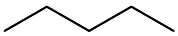
8. Which of the following is possible for structure C?

$C_5H_8\ (C) \xrightarrow{H_2,\ Pt} C_5H_{10}$









7.4,5 Nomenclature

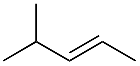
A. When the Alkene is in the Core Name (the priority functional group)

1. Number the longest continuous alkene-containing C-chain from the end nearest the alkene → core name = "x-…..ene"
2. Designate the position of the alkene by using the lower-numbered of the two alkene carbons
3. Attach and number substituents
4. When alkene stereoisomer issues apply:
   - Designate stereochemistry as "E" or "Z" if the alkene is tri- or tetrasubstituted
   - If the alkene is di-substituted, you can use either E/Z or cis/trans to designate stereochemistry.

Give formal names for the following alkenes

Simple Acyclics

1.



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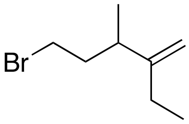
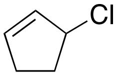


Rings

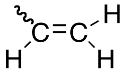
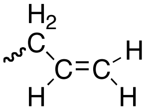
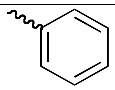
3.



B. Alkenes as Substitutents

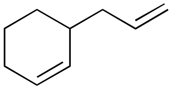
- Many functional groups have higher priority than alkenes, so that alkenes may need to be named as substituents rather than in the core name

Four to Memorize:

 Vinyl	 Allyl	$=CH_2$ Methylene	 Phenyl = "Ph"

Name the following:

1.



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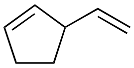

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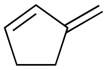

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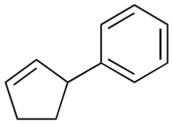
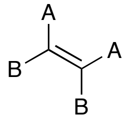


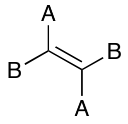
C. **E-Z Nomenclature for Alkene Stereochemistry** (7-5)

- Each carbon of an alkene has two attachments.

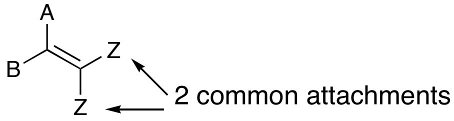
1. Check whether E/Z stereochemistry is relevant. If so:
2. Identify which of the two attachments on the left alkene carbon has higher priority.
   - Use the same priority rules as were used in R/S chirality context
3. Then identify which attachment on the right alkene carbon has higher priority.
4. Assign "E" or "Z" based on whether the two priority attachments are on same or opposite side
   - "Z" ("zusammen" = "together"): the priority attachments are cis
   - "E" ("entgegan = "opposite"): the priority attachments are trans



Z ("together")



E (opposite)

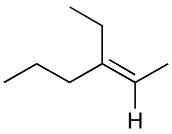


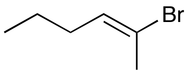
no Stereo

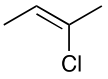
When does E/Z apply?

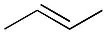
1. If either alkene carbon has two common attachments, than stereo doesn't apply
2. For tri- or tetrasubstituted alkenes (3 or 4 non-hydrogen attachments), E/Z must be used if there is stereochemistry
3. For di-substituted alkenes (one H on each alkene carbon), either E/Z or cis/trans designation can be used

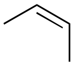
Assign as Z or E

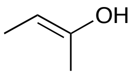
1. 

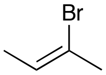
2. 

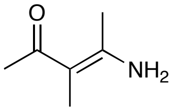
3. 

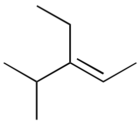
4. 

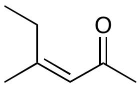
5. 

6. 

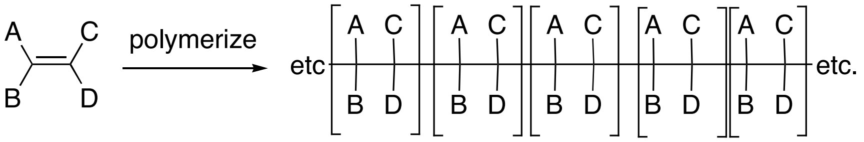
7. 

8. 

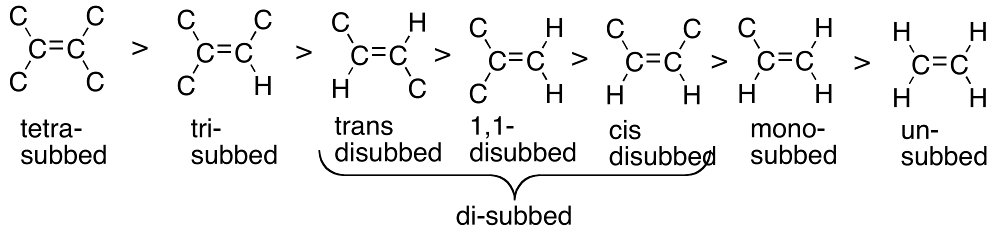
9. 

10. 

7.6 Alkenes and Polymers



7.7 Alkene Stability Pattern



1. Increasing Substitution (# of non-hydrogens directly attached to alkene carbons) → Increased Stability
   - Why? Electronic Reasons.

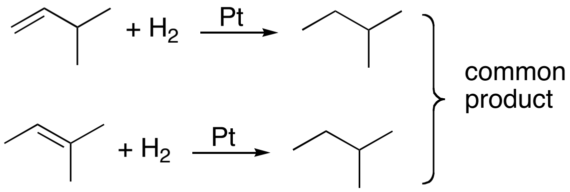
   a. Alkene carbons are somewhat electron poor due to the inferior overlap of pi bonds. (One carbon doesn't really "get" as much of the other carbon's electron as is the case in a nice sigma bond).

   b. Since alkyl groups are electron donors, they stabilize electron-deficient alkene carbons.

   c. Analogous to why electron-donating alkyls give the 3° > 2° > 1° stability pattern for cations and radicals

2. Trans is more stable than cis for 1,2-disubstituted alkenes
   - Why? Steric Reasons

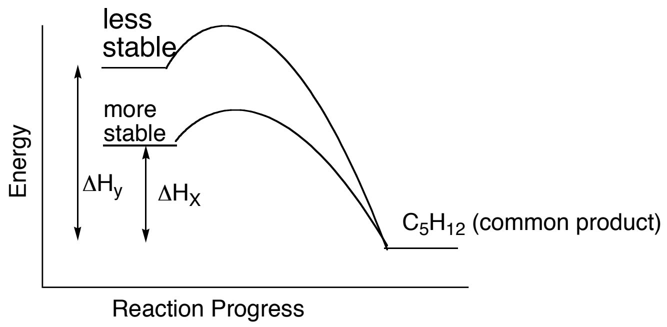
3. Measuring Relative Stability of Isomers by Heats of Hydrogenation or Heats of Combustion (6.2)



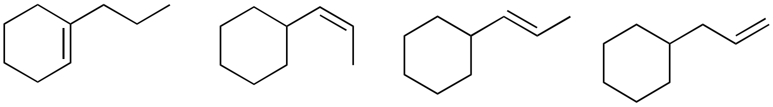
ΔH = -30.3 kcal/mol
More exo, more energy released

ΔH = -26.9 kcal/mol
Less exo, less energy released

- When 2 isomers can be converted to a common product, the relative magnitude of ΔH tells which isomer is more stable
- The more heat released, the less stable the isomer. The less heat released, the more stable.
- Heat of combustion works the same way (converts products to common CO_2 and H_2O)



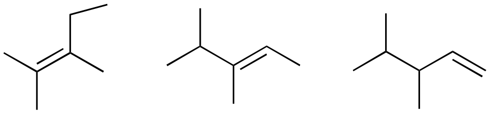
1. List the number of non-hydrogen substitutents on each alkene; rank the relative stability; rank by heat of hydrogenation, from 1 (most) to 4 (least)



Stability:

Heat:

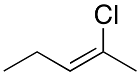
2. List the number of non-hydrogen substitutents on each alkene; rank the relative stability; When the following are burned, rank from the largest heat of combustion (1) to the smallest.



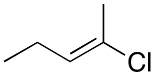
Stability:

Heat:

3. Which isomer is more stable, given the indicated heats of hydrogenation?



80 kcal/mol

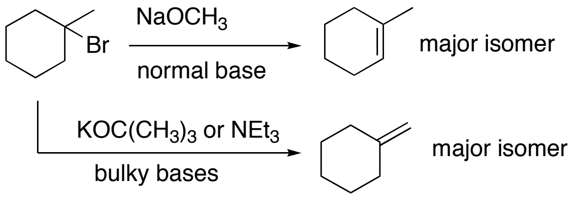


74 kcal/mol

7.8 Physical Properties of Alkenes
- Nonpolar
- No hydrogen bonding
  - low boiling
  - Hydrophilic

- 7.9 Synthesis of Alkenes by E2 Elimination of Alkyl Halides (7.9A)

1



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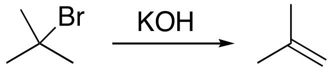

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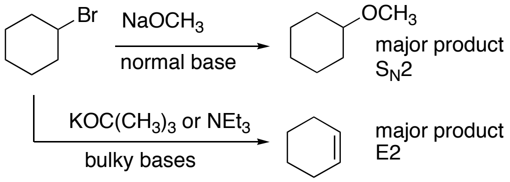

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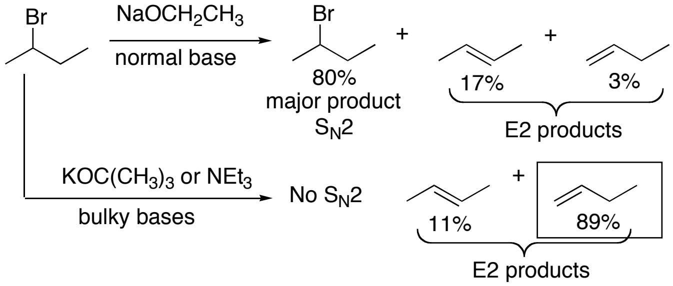
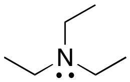
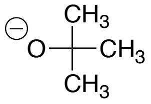


Factors to Consider

1. **3° R-X or 2° R-X**
   a. 3° R-X gives E2 with any base
   b. 2° R-X gives largely SN2 with normal anions.
   c. 2° R-X gives largely E2 with a **bulky base**. E2 prevails over S_N2
      - Because SN2 backside attack is so sterically sensitive, bulky bases have problems doing SN2. Get E2 instead.
2. **Base Size: Bulky Base versus Normal Base**
   a. Normal anions:
      - 3° R-X give E2 only, no S_N2
      - 2° R-X give predominantly S_N2 rather than E2
      - E2 elimiantions proceed with Zaytsev orientation: more-subbed alkene predominates

   b. Bulky base.
      - 3° R-X gives E2 only, no SN2 .
      - 2° R-X gives E2 only, no SN2 .
3. **E2's proceed via Hofmann orientation: less-subbed alkene predominates**
   - For steric reasons: base goes after less sterically hindered neighbor hydrogen
4. **2 Bulky Bases to Memorize:**
   - NEt3 (Triethylamine)
   - KOC(CH3)3 potassium t-butoxide

Bulky Bases: 2 to remember	Normal Bases
NEt$_3$ =  Neutral but amines are basic anyway "triethylamine" KOC(CH$_3$)$_3$ = KOCMe$_3$ =  $^{\ominus}O-C(CH_3)_3$ "potassium t-butoxide"	NaOH, KOH, LiOH NaOCH$_3$, NaOCH$_2$CH$_3$, NaOCH$_2$CH$_2$CH$_3$ KOCH$_3$, KOCH$_2$CH$_3$, KOCH$_2$CH$_2$CH$_3$ etc.
Bulky bases are: 1. Good S$_N$2 nucleophiles only for 1° R-X 2. Do clean E2 with both 3° R-X and 2° R-X 3. Give Hofmann elimination (less substitued alkene major)	Normal bases are: 1. Anionic 2. Not especially bulky 3. Good S$_N$2 nucleophiles for 1° or 2° R-X 4. Only do clean E2 with 3° R-X 5. Give Zaitsev elimination (more substitued alkene preferred)

5. **Alkene Orientation: Zaytsev versus Hofmann Elimination**
   a. Zaytsev: most subbed alkene
      - The major E2 product involves removal of a hydrogen from the most substituted neighbor carbon
      - This results in a maximally substituted, maximally stable alkene (product stability)
      - Normal-sized bases give predominantly Zaytsev elimination

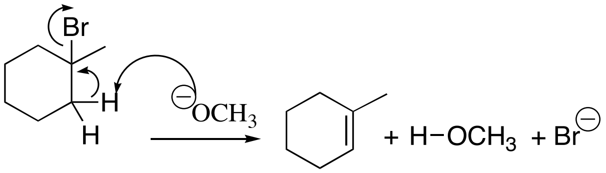
   b. Hofmann: least subbed alkene
      - The major E2 product involves removal of a hydrogen from the least substituted neighbor carbon
      - This results in a less substituted, less stable alkene
      - Bulky bases give predominantly Hofmann elimination

   c. Why: Steric reasons. A bulky base ends up having an easier time reaching a hydrogen on a less substituted carbon than on a more substituted carbon (transition-state stability-reactivity principle)

6. **Stereochemistry: A trans-hydrogen is required.**

7. **Mechanism: Concerted.**

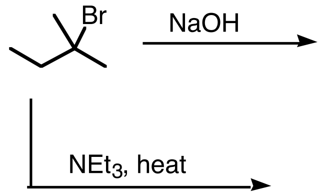
Mech:



Predicting E2 Eliminations:
1. Is the base normal or bulky?
2. Is the R-X 3°, 2°, or 1°?
3. Will E2 or S$_N$2 occur predominantly?
4. Will you get Zaitsev or Hoffman elimination?
5. Is there a trans hydrogen available?

Draw the major Product for each of the following Reactions.

1.



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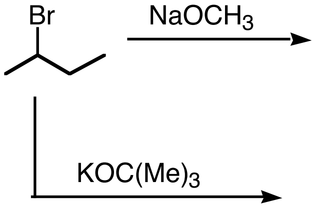

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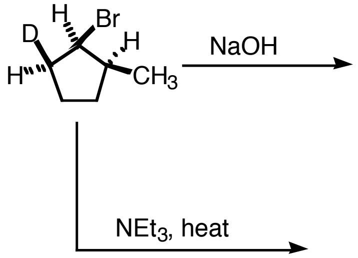
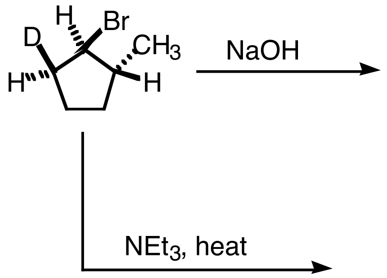


4.



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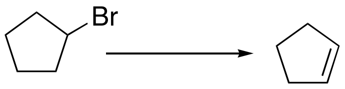
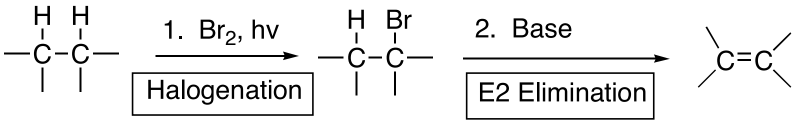
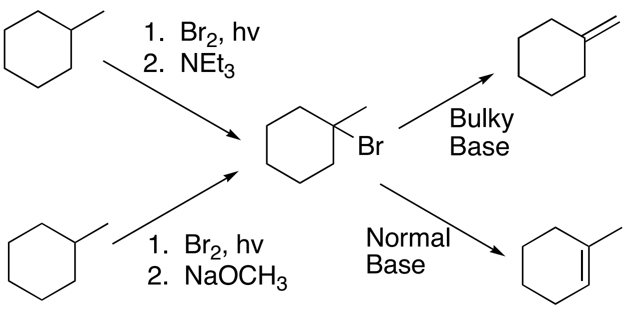


Indirect Route to Alkenes from Alkanes

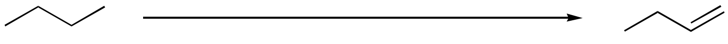
Via 2 Reactions:

1. **Bromination (reaction 1) followed by**
2. **Elimination (reaction 2)**





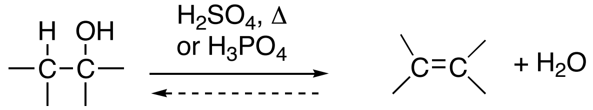
Provide Recipe:

1. 

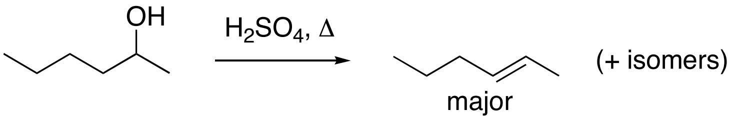
2. 

Synthesis of Alkenes from Alcohol

General:



1



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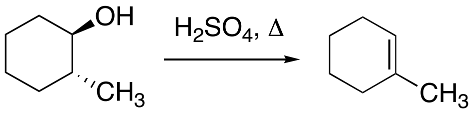

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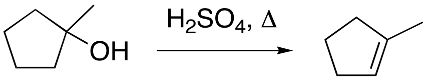
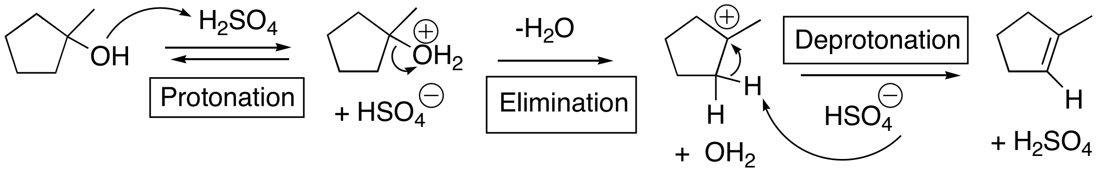


Observations:

1. Zaitsev, not Hoffman elimination.
2. No requirement for a trans hydrogen.
3. Acidic conditions, need an acidic mechanism.

Mechanism (Memorize)



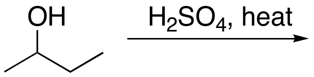
3 steps: Protonation – Elimination – Deprotonation

1. Protonation converts OH, a bad leaving group, into a very good leaving group (neutral water)
2. Carbocation formation is slow step (like E1 mechanism)
   - Cation stability dictates reactivity
   - Reactivity: allylic > 3º R-OH > 2º R-OH >>> 1º R-OH > vinyl, aryl
   - Allylic, 3º, and 2º work; 1º, vinyl, and aryl do not.
3. C-H cleavage comes last.

4. Mechanism typical for acid-catalyzed processes: protonate-react-deprotonate.
   - Protonation and deprotonation sandwich the key step.
5. Strong acidic conditions → intermediates should be positive, not negative
6. Because the cation is flat, and forgets original stereochemistry, there is no trans-H requirement.
7. The reaction is actually reversible, an equilibrium
8. Get complete E1, not S_N1, because the water that falls off in step 2 is converted to hydronium H_3O^+
9. Often the equilibrium is driven by distilling the alkene off as it forms (if it's low boiling due to loss of weight and being non-polar) or phase separating out from the acid layer.

Draw Products

1.



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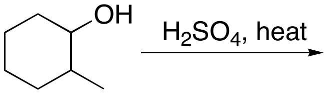

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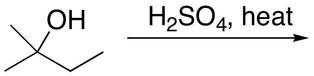

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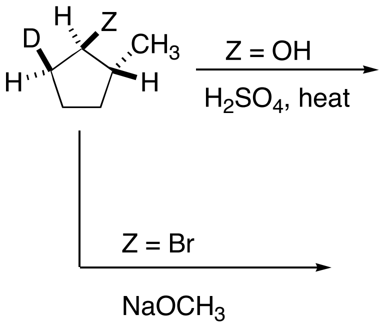
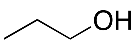
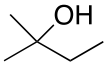
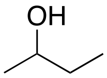
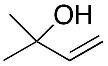


5. Rank the reactivity of the following toward H_2SO_4-catalyzed elimination (1 most). Why?









Key Issue:

Reactivity:

Reaction Mechanisms (Summary and Practice, see p. 310)

A. Recognizing/Classifying as Radical, Cationic, or Anionic

1. Radical
    - initiation requires both energy (either hv or Δ) and a weak, breakable heteroatom-heteroatom bond
        - Cl-Cl, Br-Br, O-O (peroxide), N-Br, etc..

> 2 Guides for That are Usually Reliable:
> hv → radical mechanism
> peroxides → radical mechanism

2. Anionic
    a. **a strong anion/base appears in the recipe**
    b. no strong acids should appear in the recipe
    c. mechanisms should involve anionic intermediates and reactants, not strongly cationic ones
        - (except for do-nothing spectators like metal cations)
    d. The first step in the mechanism will involve the strong anion/base that appears in the recipe

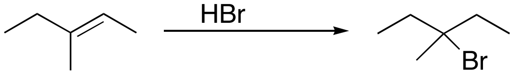
3. Cationic
    a. **a strong acid/electrophile appears in the recipe**
    b. no strong anion/base should appear in the recipe
    c. mechanisms should involve cationic intermediates and reactants, not strongly anionic ones
        - (except for do-nothing spectators like halide or hydrogen sulfate anions)
    d. The first step in the mechanism will involve the acid that appears in the recipe. The last step will often involve a deprotonation step. Often the main step occurs in between the proton-on and proton-off steps

B. Miscellaneous Mechanism Tips

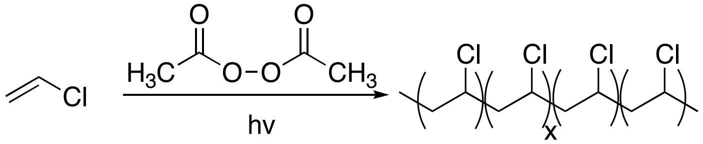
1. Keep track of hydrogens on reacting carbons
2. **Each step in a mechanism must balance**
3. The types of intermediates involved (cation, anion, or radical) should be consistent with the reaction classification above
    a. **If the reaction is cationic, don't show anionic intermediates**
    b. **If the reaction is anionic, don't show cationic intermediates**
4. Usually conditions are ionic.
5. **Use a reactive species, whether strong anion or an acid, to start the first step**
    a. **If acidic, first step will involve protonation of the organic**
    b. **If anionic, the first step will involve the anion attacking the organic.**
6. While it isn't always easy to figure out what is a good mechanism, you should often be able to eliminate an unreasonable mechanism.

1. Classify each mechanism as radical, cationic, or anionic.

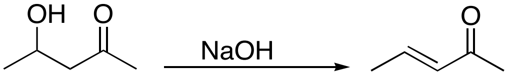
a.



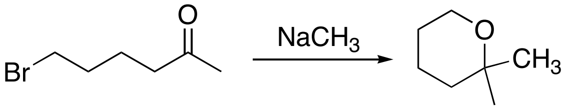
b.



c.



d.



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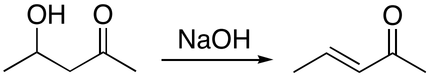
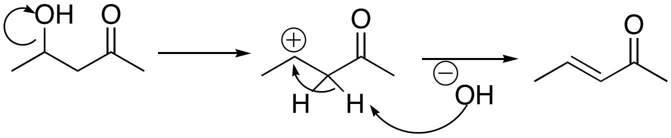
2. Which of the following mechanisms is reasonable or unreasonable for the transformation shown. <u>Identify recognition keys for things wrong with those that aren't right.</u>



<u>Problems</u>

1.



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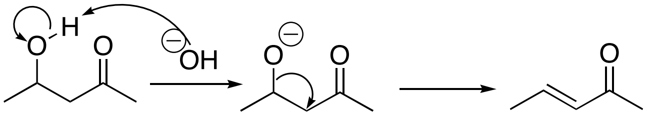

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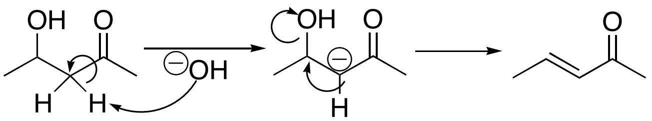
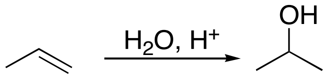


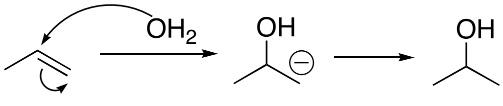
Q: Which of the following mechanisms is reasonable or unreasonable for the transformation shown:



Identify recognition keys for things wrong with those that aren't right.

Problems

4.



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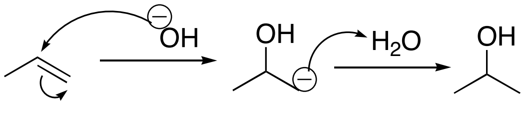

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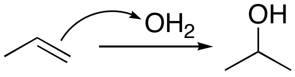

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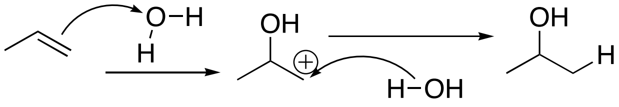

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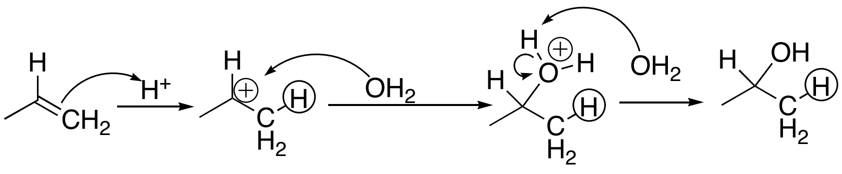
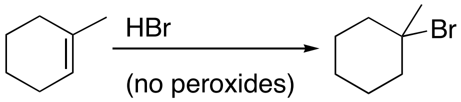
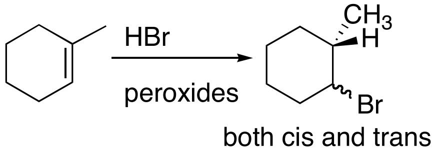
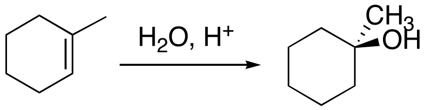
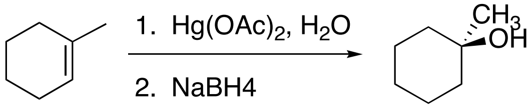
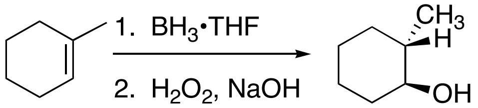
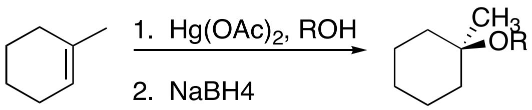
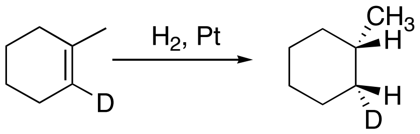
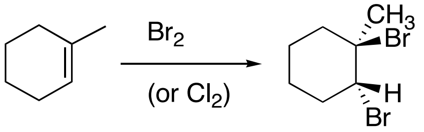
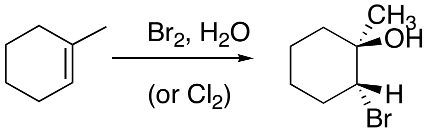
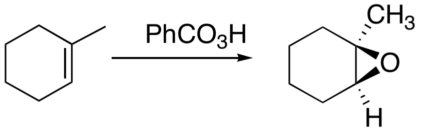
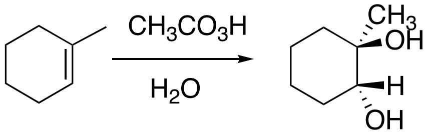
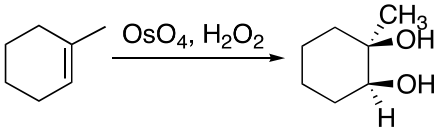
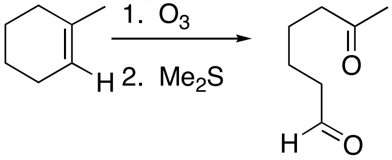
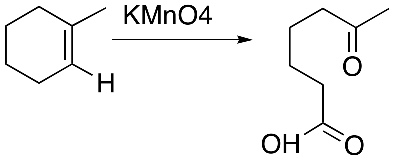


Summary of Alkene Reactions, Ch. 8.
Memorize Reaction, Orientation where Appropriate, Stereochemistry where Appropriate, and Mechanism where Appropriate.

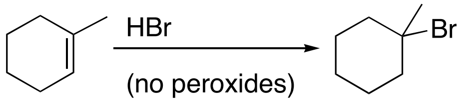
-all are drawn using 1-methylcyclohexene as a prototype alkene, because both orientation and stereochemistry effects are readily apparent.

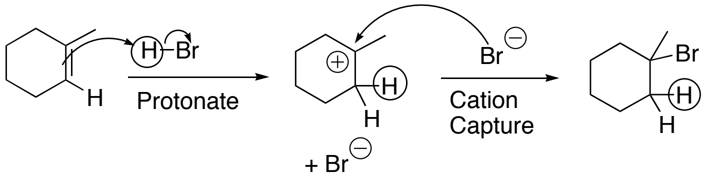
		Orientation	Stereo	Mechanism
1		Markovnikov	None	**Be able to draw completely**
2		Anti-Markovnikov	**Nonselective. Both cis and trans**	**Be able to draw propagation steps.**
3		Markovnikov	None	**Be able to draw completely**
4		Markovnikov	None	Not responsible
5		Anti-Markovnikov	**Cis**	Not responsible
6		Markovnikov	None	Not responsible
7		None	**Cis**	Not responsible

		Orientation	Stereo	Mechanism
8		None	**Trans**	**Be able to draw completely**
9		Markovnikov	**Trans**	**Be able to draw completely**
10		None	**Cis**	Not responsible
11		None	**Trans**	**Be able to draw acid-catalyzed epoxide hydrolysis**
12	 • t-butyl hydroperoxide often used instead of hydrogen peroxide	None	**Cis**	Not responsible
13	 Note: H-bearing alkene carbon ends up as aldehyde. • Zn common option to $(CH_3)_2S$ in step 2	None	None	Not responsible
14	 H-bearing alkene carbon ends as carboxylic acid	None	None	Not responsible

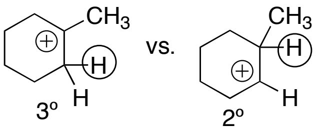
Summary of Mechanisms, Ch. 7 + 8. Alkene Synthesis and Reactions.

1



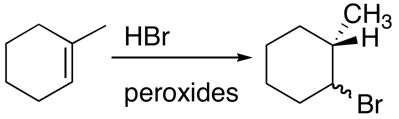


Note: For unsymmetrical alkenes, protonation occurs at the less substituted alkene carbon so that the more stable cation forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle

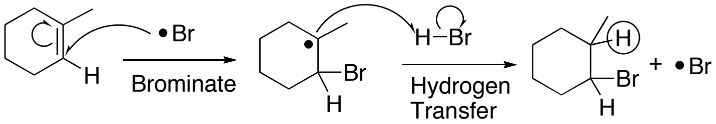


Test Responsible

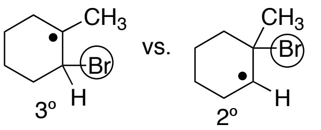
2



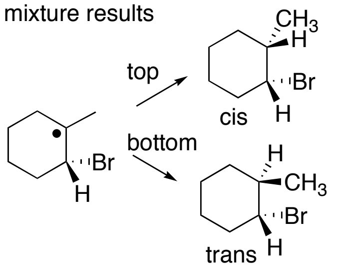
both cis and trans



Note 1: For unsymmetrical alkenes, bromination occurs at the less substituted alkene carbon so that the more stable radical forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle

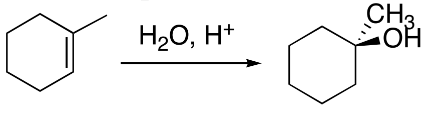


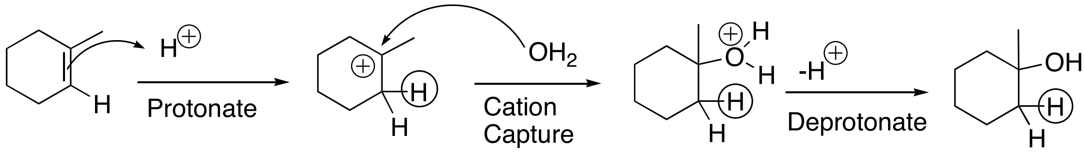
Note 2: Hydrogenation of the radical comes from either face, thus cis/trans mixture results



Not test responsible

3

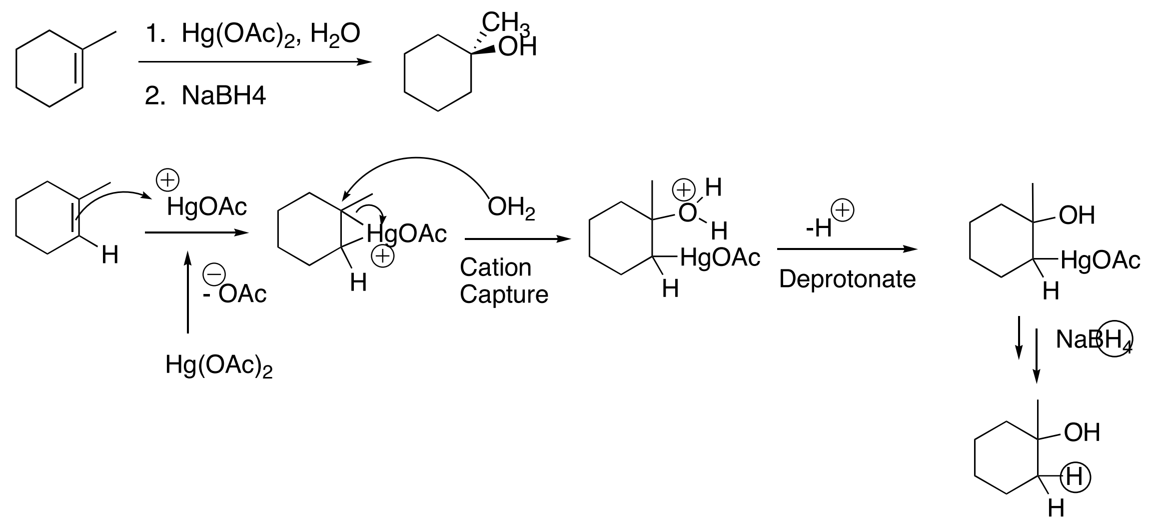




Note: For unsymmetrical alkenes, protonation again occurs at the less substituted end alkene, in order to produce the more stable radical intermediate (3° > 2° > 1°)

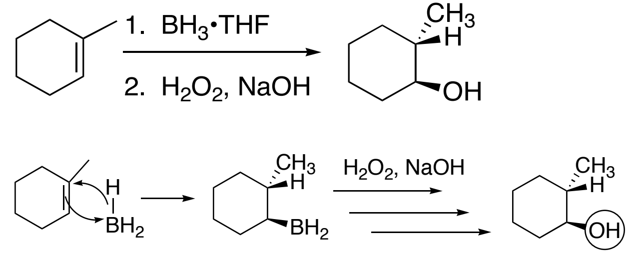
Test Responsible

4



Not test responsible

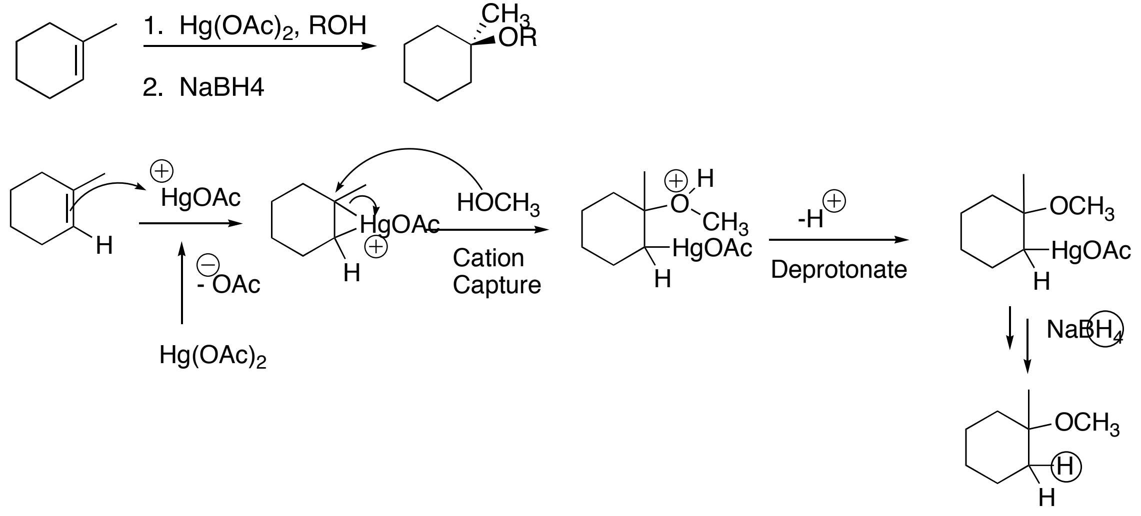
5



Notes
a. concerted addition of B-H across C=C
-explains the cis stereochemistry
b. the B-H addition is Markovnikov; the B is $\delta+$, the H is $\delta-$
c. The H_2O_2, NaOH process is complex, but replaces the B with OH with complete retention of stereochem
-the explains why the cis stereochemistry established in step one is preserved in step 2.

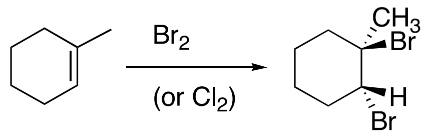
Not test responsible

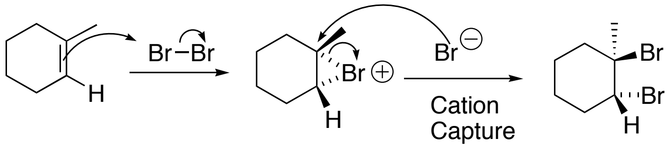
6



Not test responsible

8

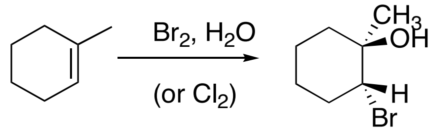


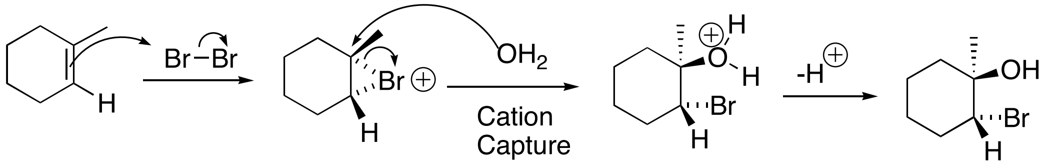


3 Notes
1. Cation intermediate is cyclic bromonium (or chloronium) ion
2. The nucleophile captures the bromonium ion via backside attack
-this leads to the trans stereochemistry
3. The nucleophile attacks the bromonium ion at the *more* substituted carbon

Test Responsible

9





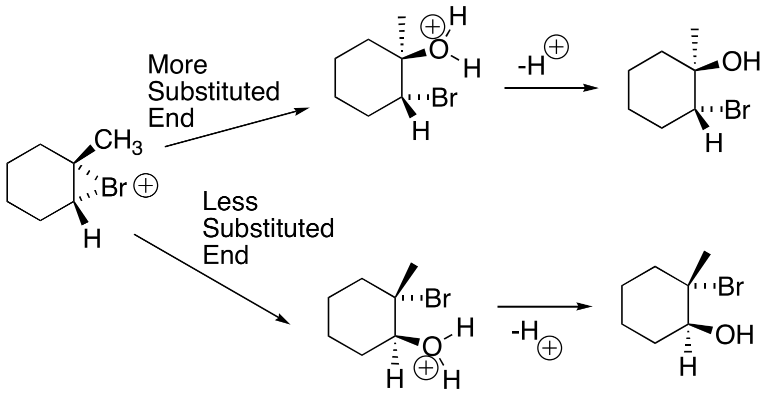
4 Notes

1. Cation intermediate is cyclic bromonium (or chloronium) ion

2. The nucleophile captures the bromonium ion via backside attack (ala SN2)
-this leads to the trans stereochemistry

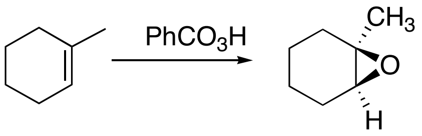
3. The nucleophile attacks the bromonium ion at the *more* substituted carbon
-this explains the orientation (Markovnikov)

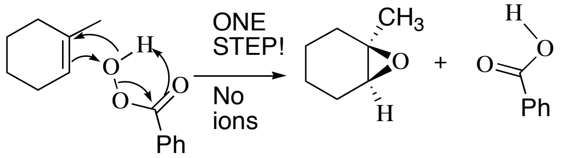
- There is more + charge at the more substituted carbon
- The Br-C bond to the more substituted carbon is a lot weaker

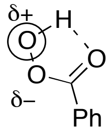


4. Alcohols can function in the same way that water does, resulting in an ether OR rather than alcohol OH.
Test Responsible

10







Carbonyl-hydrogen
Hydrogen-bonded reactant

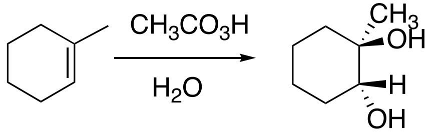
Notes

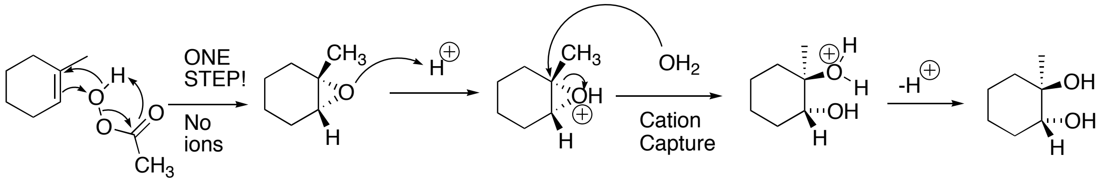
1. Complex arrow pushing
2. No ions required
3. The carbonyl oxygen picks up the hydrogen, leading directly to a neutral carboxylic acid

-The peracid is already pre-organized for this' via internal H-bonding between carbonyl and H

Not Test Responsible

11





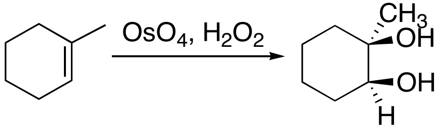
Notes:

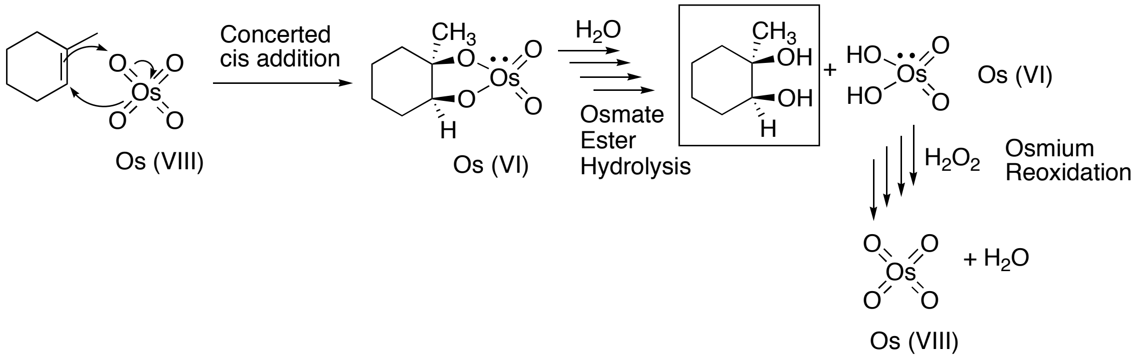
a. The nucleophile (water) attacks from the more substituted end of the protonated epoxide
   - More δ+ charge there
   - The C-O bond to the more substituted end is much weaker

b. The nucleophile adds via S$_N$2-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.

Test Responsible for Epoxide Opening

12

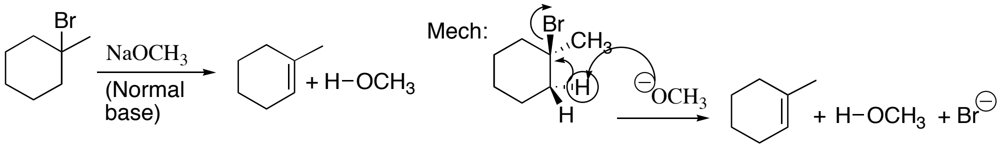




Not Test Responsible

Chapter 7 Reactions and Mechanisms, Review

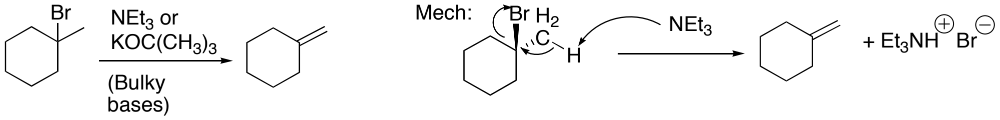
E2
On
R-X,
Normal
Base



Notes
1. Trans hydrogen required for E2
2. Zaytsev elimination with normal bases
3. For 3° R-X, E2 only. But with 2° R-X, S_N2 competes (and usually prevails)
4. Lots of "normal base" anions.

Test Responsible

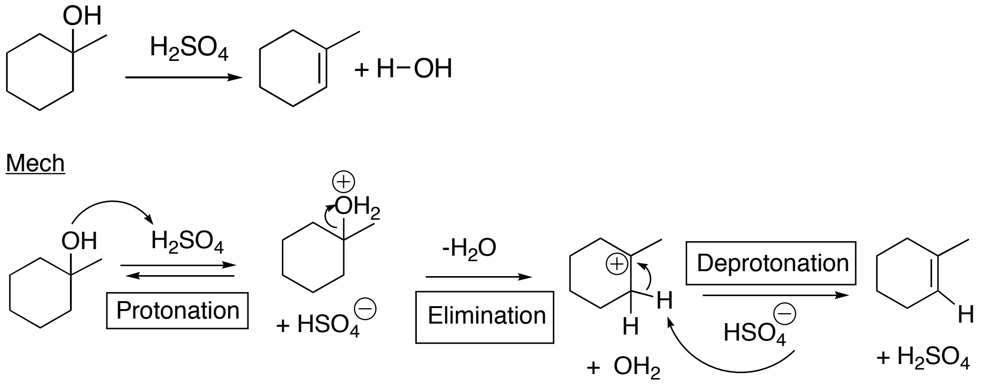
E2,
On
R-X, Bulky
Base



Notes:
1. Hoffman elimination with Bulky Bases
2. E2 dominates over S_N2 for not only 3° R-X but also 2° R-X
3. Memorize NEt_3 and $KOC(CH_3)_3$ as bulky bases.

Test Responsible

Acid-
Catalyzed
E1-
Elimination
Of
Alcohols

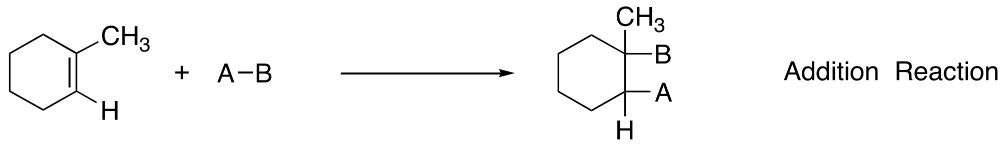


Notes:
1. Zaytsev elimination
2. Cationic intermediate means 3° > 2° > 1°
3. 3-Step mechanism

Test Responsible

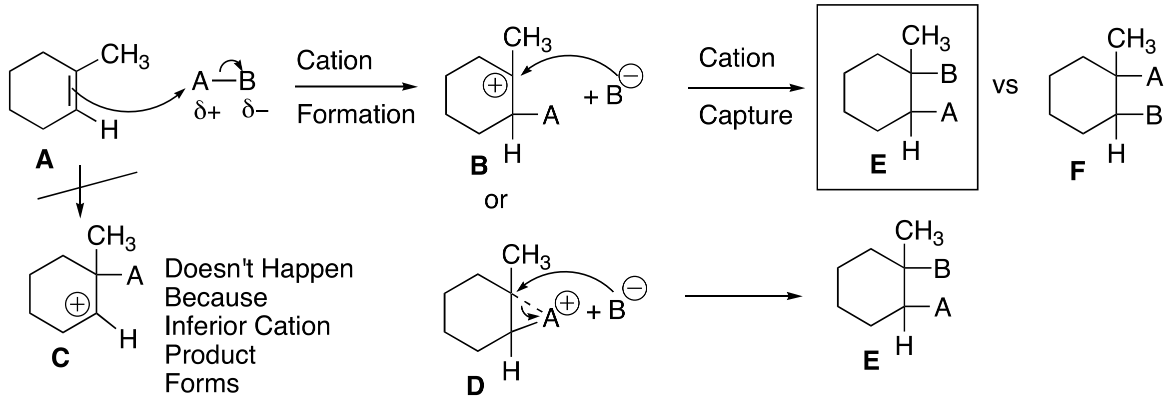
Ch. 8 Reactions of Alkenes

8-1,2 Introduction



1. Thermodynamics: Usually exothermic
   - 1 π + 1 σ → 2 σ bonds
2. Kinetics: π bond is exposed and accessible

Generic Electrophilic Addition Mechanism



2 Steps: Cation formation and cation capture

- Cation formation is the slow step
  - Cation stability will routinely determine the orientation in the first step
    - Which is preferred, **A → B** or **A → C?**
- Often the cation is a normal cation **B**. Sometimes 3-membered ring cations **D** will be involved.
- In some cases, the cation will be captured by a neutral species (like water), in which case an extra deprotonation step will be involved

4 Aspects to Watch For

1. Orientation
   - Matters only if both of two things are true:
     a. The alkene is unsymmetrical, and
     b. The electrophile is unsymmetrical

2. Relative Stereochemistry
   - Matters only if both the first and the second alkene carbons are transformed into chiral centers

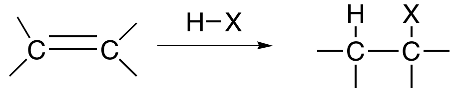
3. Mechanism

4. Relative Reactivity of Different Alkenes
   - Stability of cation formed is key

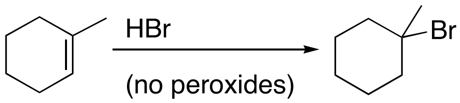
8.3 H-X Hydrogen Halide Addition: Ionic/Cationic Addition in the Absence of Peroxides

(Reaction 1)

General:



1



Orientation	Stereo	Mechanism
Markovnikov	None	**Be able to draw completely**

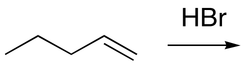
Markovnikov's Rule (For Predicting Products): When H-X (or any unsymmetrical species $A^{\delta+}B^{\delta-}$) adds to an unsymmetrical alkene:

- the H^+ (or $A^{\delta+}$) adds to the less substituted carbon (the one with more H's)
- the X^- (or $B^{\delta-}$) adds to the more substituted carbon (the one with more non-H's).
- Note: Markovnikov's rule does not apply if either the alkene or the atoms that are adding are symmetrical

Examples, Predict the Products.

Does Markovnikov's Rule matter?

1



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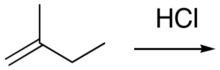

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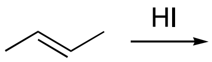

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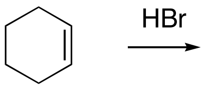

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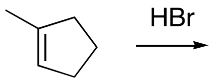

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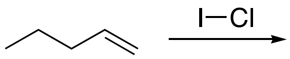
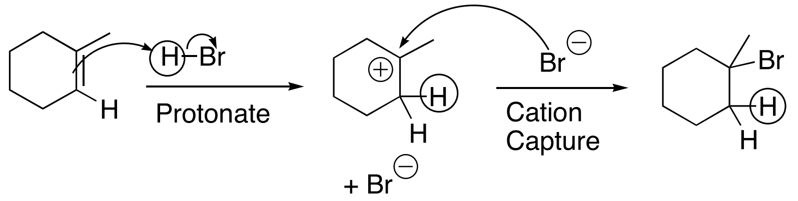
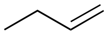


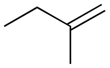
Mechanism

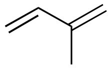


- Protonate first
- Capture cation second
- Cation formaton (step 1) is the slow step

Rank the Reactivity of the following toward HBr addition.



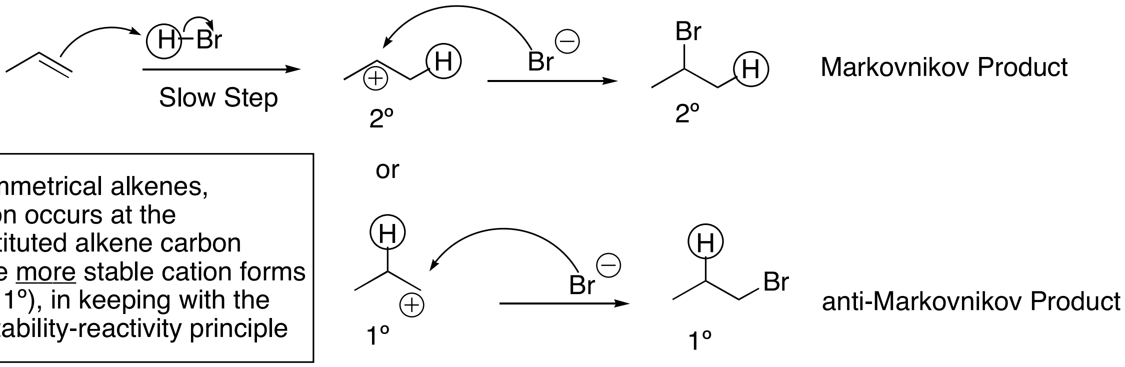




Issue:

Why Does Markovnikov's Rule Apply? Product/Stability Reactivity Rule.

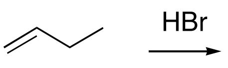
- Formation of the most stable carbocation results in Markovnikov orientation



For unsymmetrical alkenes, protonation occurs at the <u>less</u> substituted alkene carbon so that the <u>more</u> stable cation forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle

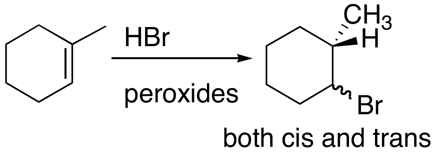
- This same logic applies anytime something adds to an alkene.
- You want to make the best possible intermediate in the rate-determining step.

Draw the mechanis for the following reaction:



8.3B Free Radical Addition of HBr with Peroxide Initiator: Anti-Markovnikov Addition (Rxn 2)

2



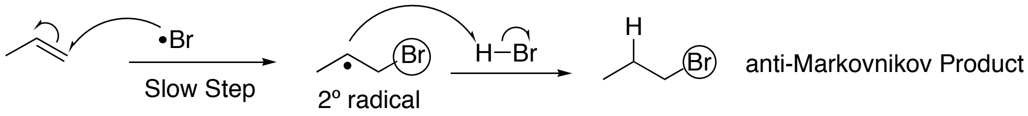
Anti-Markovnikov

Nonselective. Both cis and trans

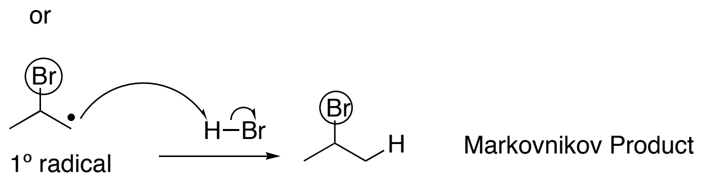
Not test responsible.

1. Peroxides are radical initiators, and cause the mechanism to shift to a radical mechanism
2. With peroxides, the orientation is reversed to anti-Markovnikov: now the Br adds to the less substituted end and the H adds to the more substituted end of an unsymmetrical alkene
    a. No peroxides: Br goes to more substituted end
    b. With peroxides: Br goes to less substituted end
3. The anti-Markovnikov radical process works only with HBr, not HCl or HI
4. The radical process is faster, and wins when peroxides make it possible. In the absence of peroxides, the slower cationic process happens.

Mechanism, and Reason for AntiMarkovnikov Orientation



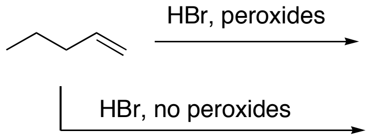
For unsymmetrical alkenes, **bromination** occurs at the less substituted alkene carbon so that the more stable **radical** forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle



Examples, Predict the Products.

Does Markovnikov's Rule matter?

1



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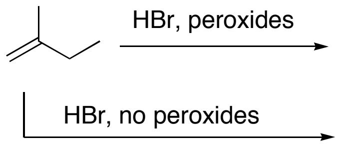

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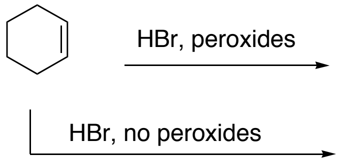
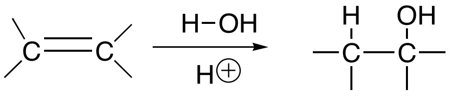


8.4 Addition of H-OH. Direct acid-catalyzed addition. (Reaction 3)

General:



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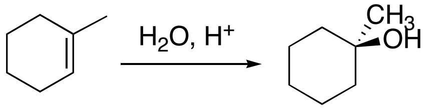


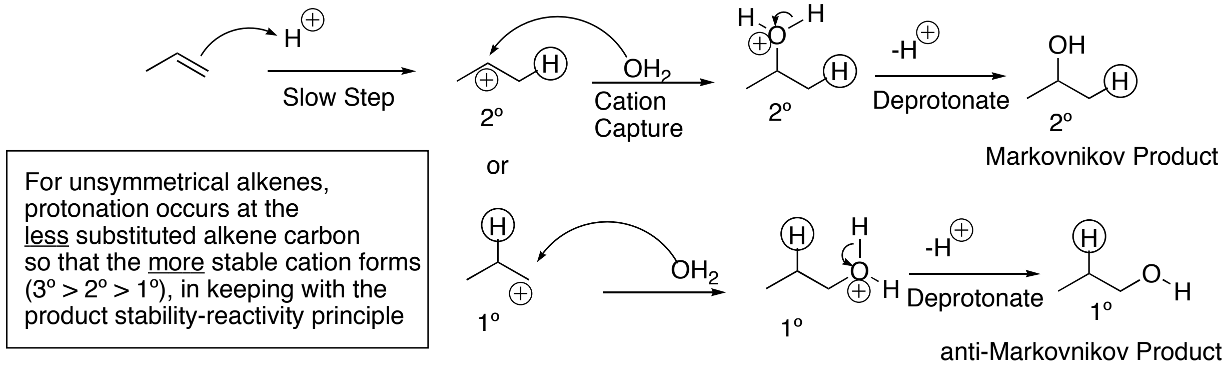
Markovnikov None **Be able to draw completely**

Markovnikov: $H\delta^+OH\delta^-$ → H adds to the less substituted end of the alkene, OH adds to the more substituted end

- **OH ends up on more substituted end of the alkene**

Mechanism: 3 Steps.

1. **Protonation**
2. **Cation Capture**
3. **Deprotonation**



For unsymmetrical alkenes, protonation occurs at the less substituted alkene carbon so that the more stable cation forms (3° > 2° > 1°), in keeping with the product stability-reactivity principle

Notes

1. The sequence in which key step (cation capture in this case) is sandwiched by proton on-proton off protonation-deprotonation is super common for acid-catalyzed reactions.
   - **Whenever you see an acid-catalyzed process, expect to use H^+ in first step and to deprotonate in the last step**

2. Cation stability dictates reactivity

3. Cation stability explains why the Markovnikov orientation occurs. This involves the more substituted, more stable carbocation product in the rate-determining step.

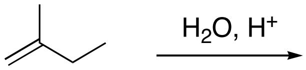
4. The actual reaction is an equilibrium.
   - The reverse of alcohol dehydration to make alkenes!
   - A key drive is to have excess water. That pushes the equilibrium to the alcohol side.
   - Under alcohol → alkene conditions, the equilibrium is often driven to the alkene side by having no water, or by distilling off the lower-boiling alkene as it forms.

Examples, Predict the Products.

Does Markovnikov's Rule matter?

1

2



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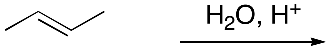

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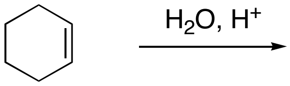

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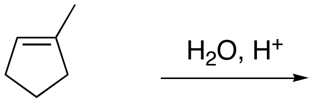
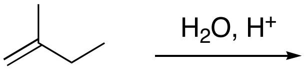


Problems with Acid-Catalyzed Addition of Water to Alkenes

1. Alkenes with poor water solubility often don't add very well.
   - Can't drive the equilibrium strongly to the alcohol side in that case
   - Solvent mixtures can often help, but not always good enough
2. Alcohol/Alkene equilibrium sometimes poor
3. Carbocation rearrangements can be a problem
4. The degree of Markovnikov selectivity isn't always satisfactory
   - 99:1 isomer selectivity is a lot nicer than 90:10…
   - Especially if you have to purify!
5. Obviously you can't get the reverse, anti-Markovnikov alcohol products.

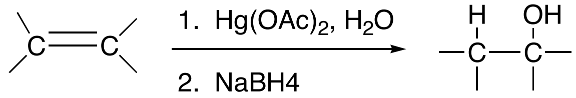
Each of these limitations, when they are a problem, can be solved by alternative recipes that indirectly add H-OH.

Draw the mechanism for the following reaction:



8.5 Indirect Markovnikov Addition of H-OH via Oxymercuration/Demercuration. Reaction 4.

General:



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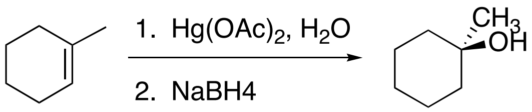


Markovnikov

Stereo: None

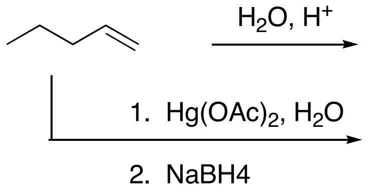
Mech: Not responsible

Notes:

5. Often higher yields, cleaner, faster, and easier
6. No restrictions
7. No cation rearrangements
8. **Very strong**, often superior **Markovnikov selectivity**
   - OH adds to the more substituted end, H to the less substituted end

Does Markovnikov's Rule matter?

1



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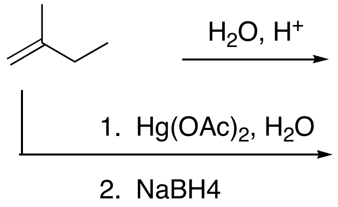
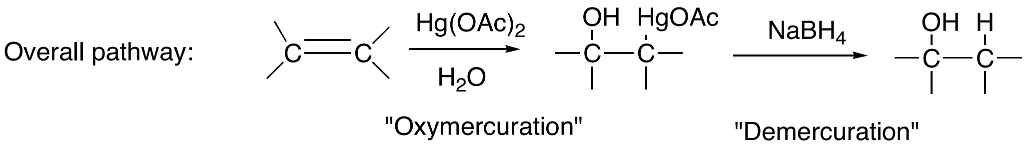


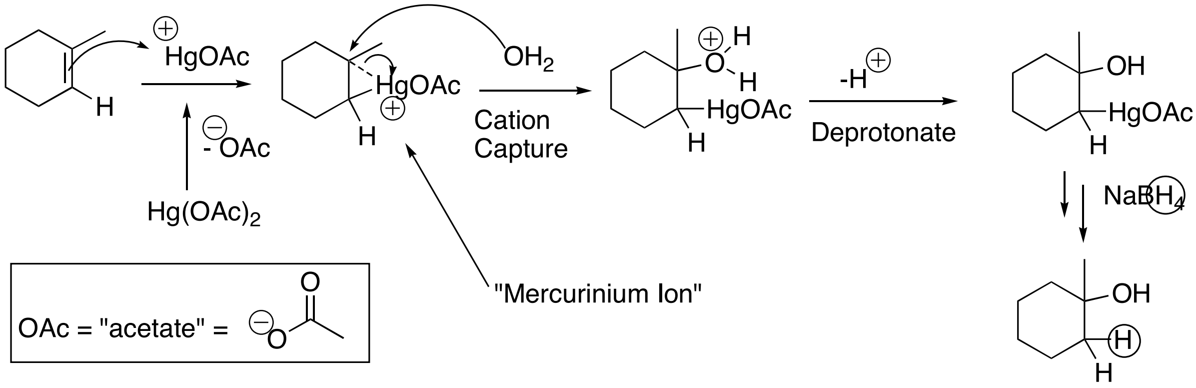
H_2O/H^+ vs Oxymercuration/Demercuration: Which should I use?

1. Both normally give same product
2. For predict-the-product problems, be able to handle either recipe
3. **For provide-the-right-recipe problems, I will accept either answer.**
   - H_2O/H^+ is easier to write!
4. In the real lab, the choice is decided on a case-by-case basis.
   - Default to H_2O/H^+
   - Go to oxymercuration/demercuration when direct acid-catalyzed hydration doesn't work as well as you'd like

Mechanism (For interest sake. Not for memorization, not for test.)



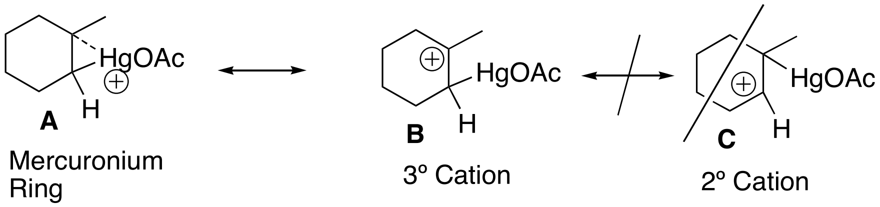
More Details for the Oxymercuration Phase



Notes:

1. "demercuration" with NaBH4 replaces the mercury with a hydrogen
2. The initial "oxymercuration" essentially adds $(HgOAc)^{\delta+}(OH)^{\delta-}$, and follows Markov.'s rule
3. The interesting new thing here is the "mercuronium" ion
4. This is normally drawn as a 3-ring, but can also be viewed as a resonance structure of a hybrid

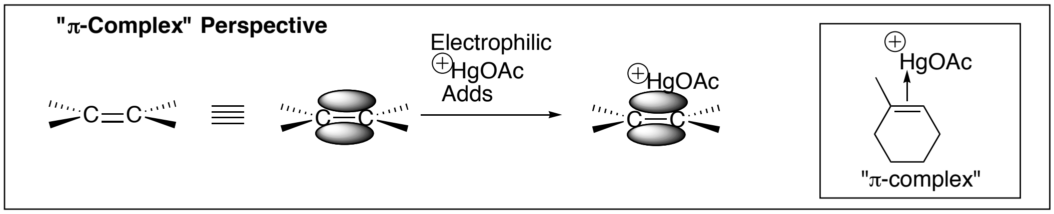
Mercuronium Ion



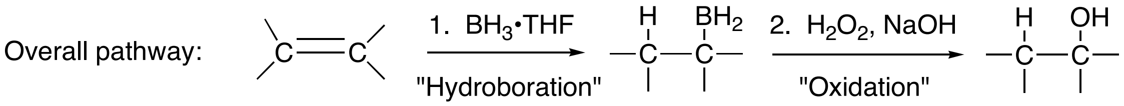
Both participation from structures **A** and **B** are required to explain everything

- **A** explains why you don't get cation rearrangments, ever: you don't have a free carbocation
- **A** also explains structure studies, which show that the mercury is weakly bonded to the more substituted carbon
- **B** helps to explain why water adds to the more substituted carbon, which has extensive positive charge
- **C** doesn't contribute, isn't really involved

In the real thing, there is a long, very weak and super breakable bond between mercury and the more substituted carbon. The bond to the less substituted carbon is much shorter and stronger.



8.7 Indirect anti-Markovnikov Addition of H-OH via Hydroboration/Oxidation. Reaction 5.



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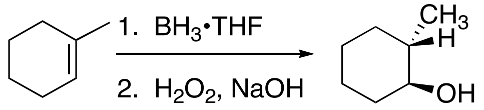
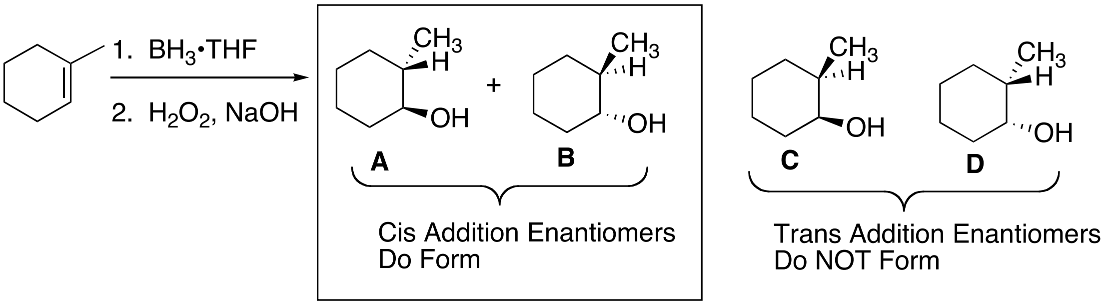


Anti-Markovnikov   **<u>Cis</u>**   Not responsible

plus enantiomer

Notes:

1. **<u>Anti-Markovnikov orientation</u>**: the **<u>OH ends up on the less substituted end</u>** of an unsymmetrical alkene; the H adds to the more substituted end
2. **<u>Cis addition. Both the H and the OH add from the same side</u>**.
3. When does cis/trans addition stereochemistry matter?
   - Only <u>when both alkene carbons turn into chiral centers</u> in the product.
   - If one does but not both, then the relative stereochemistry doesn't matter
   - For Markovnikov additions involving H-Br or H-OH, the H usually adds to a carbon that already has an H, so that in the product it is not a stereocenter.
   - In anti-Markovnikov additions, much more common for both carbons to become chiral carbons
4. **<u>Chiral products are Racemic (two enantiomers form) but not optically active</u>**
   - When only one chiral center forms (often in the Markovnikov additions), any chiral product will always be racemic
   - When two chiral centers form, as in the example above, of the four possible stereoisomers, you get only two of them, in racemic mixture.

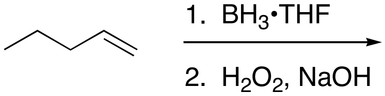


Cis Addition Enantiomers Do Form

Trans Addition Enantiomers Do NOT Form

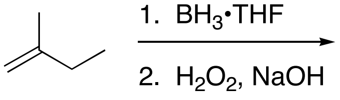
Examples, Predict the Products.

	Does Markov. Matter?	Does Stereo Matter?
1		



Does Markov. Matter?

Does Stereo Matter?

2


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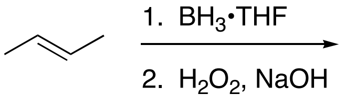

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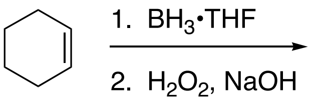

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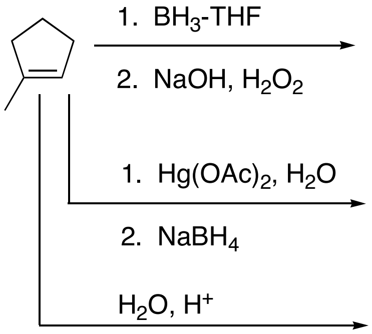
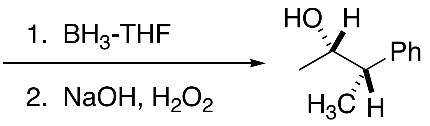
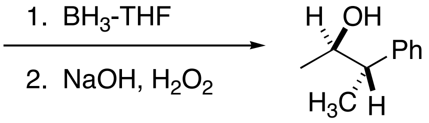


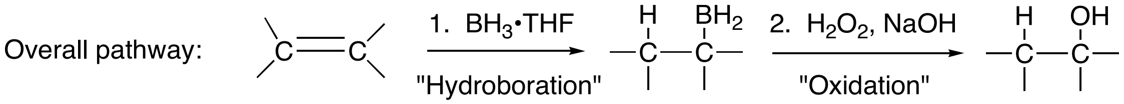
1. Which starting alkenes would produce the following products following hydroboration-oxidation? Factor in the stereochemistry of the products in considering what starting materials would work.





2. Fill in recipes for converting 1-butene into the three derivatives shown.

Mechanism (For interest sake. Not for memorization, not for test.)



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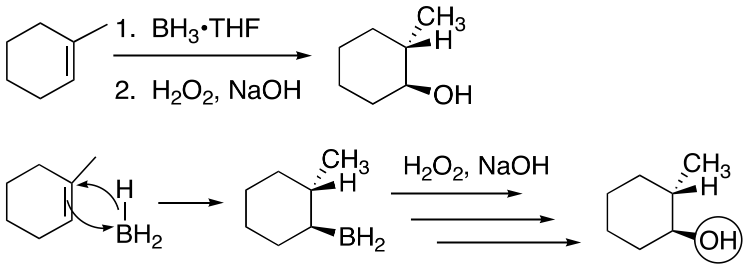
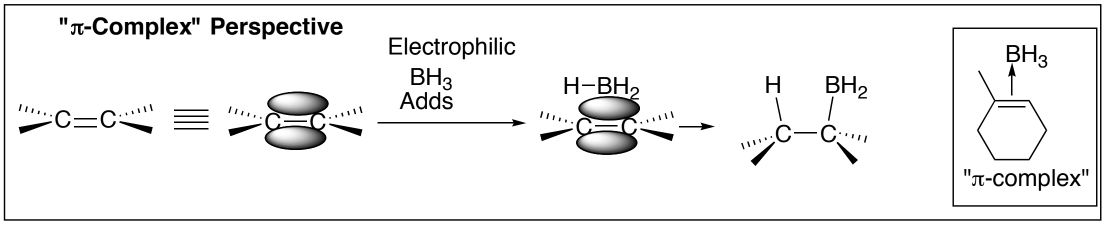
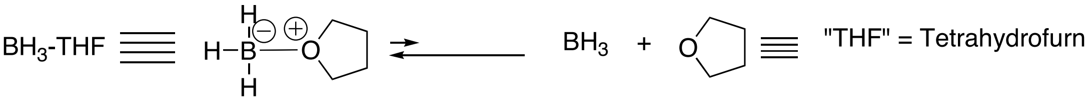




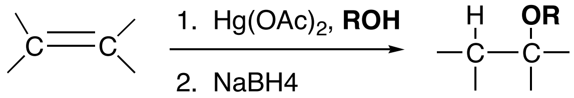


Notes

1. Other recipes (B_2H_6, etc. are common)
2. BH_3-THF is a convenient complex in which the oxygen provides the extra electron pair. But the weak complex provides a small equilibrium amount of free, reactive BH_3
3. Free BH_3 is actually the electrophile
4. Because BH_3 does not have octet rule, the boron is very electrophilic
5. The electrophilic boron originally makes a π-complex, but then you get actual hydroboration via a 4-centered ring
6. The key is that both the boron and the hydrogen enter from the same side of the alkene
   - **concerted addition of B-H across C=C**
   - **cis addition**
7. Why do you get the orientation?
   - the B-H addition actually does follow Markovnikov's rule
     - $H_2B\delta+H\delta-$
     - The B is δ+, the H is δ-, because boron is a semi-metal and less electronegative than hydrogen! The only case this chapter where the hydrogen is δ- rather than δ+
   - Sterics: The Boron end is pretty big, so it prefers to go to the less substituted, less hindered end of the alkene for steric as well as electronic reasons.
8. The NaOH/H2O2 workup is complex and beyond our scope, but replaces the B with OH with complete retention of stereochem
   - the cis stereochemistry established in the hydroboration
   - the oxygen stereo is preserved in the oxidation.

8.6 **Alkoxymercuration-Demercuration**: Markovnikov Addition of H-OR (Reaction 6)

General:



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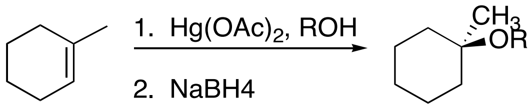
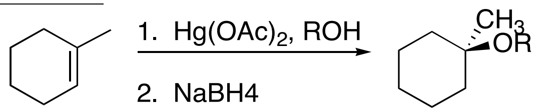


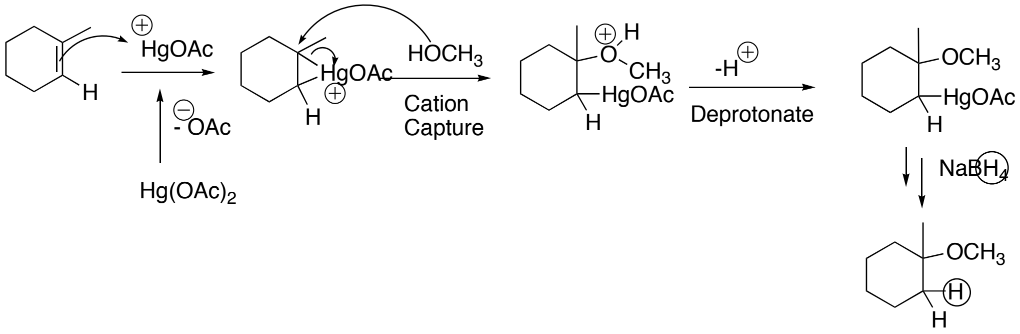
Markovnikov

Stereo:
None

Mech:
Not
responsible

Mechanism
6





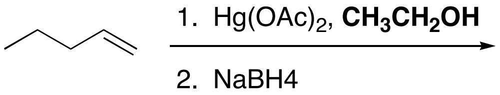
Notes:

1. Everything is the **same as with oxymercuration-demercuration to form an alcohol, except you use an alcohol instead of water**
2. This results in an oxygen with it's spectator carbon chain adding rather than an OH
3. Strong Markovnikov orientation
    - The OR adds to the more substituted end of the alkene
    - The Hydrogen ends up on the less substituted end of the alkene
4. The mechanisms are analogous.

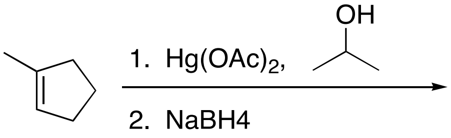
Examples, Predict the Products.

	Does Mark's Rule matter?	Does Stereo?

1



2



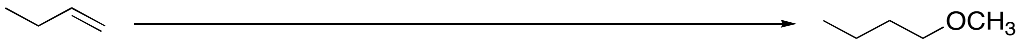
Ether Synthesis: Two Routes

1. From Alkene and Alcohol: By Oxymercuration/Demercuration
2. From R-Br and Alkoxide Anion: By S_N2

Multistep Synthetic Design: Design Reactants for the Following Conversions

1. Note: It is often most strategic to think backward from product to precursor.
2. Then think back how you could access the precursor from the starting material.
3. There may sometimes be more than one suitable route.
4. There will be problems of this style/format on the next test.

1.



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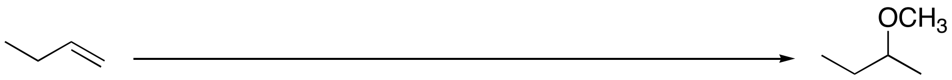

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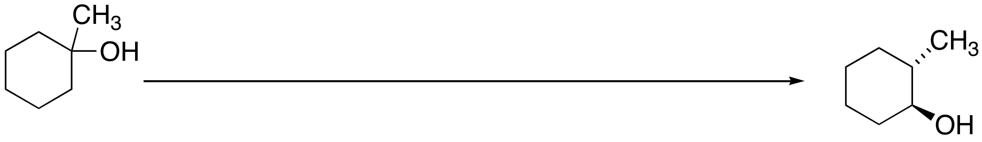

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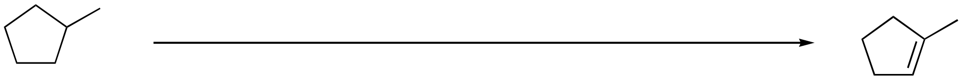

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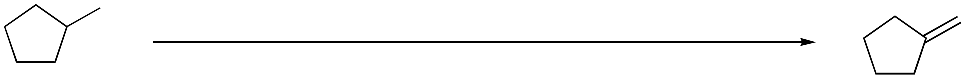
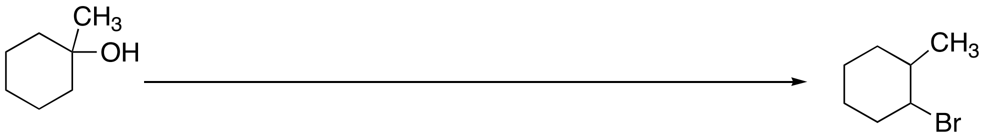


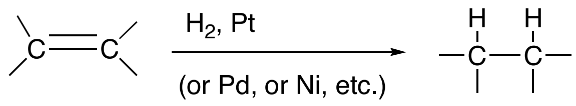
6.

7.



8-10. H-H addition. Catalytic Hydrogenation (Reaction 7)

General:



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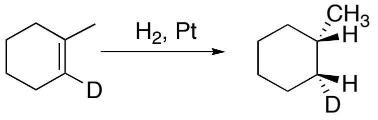


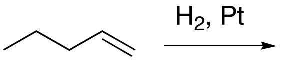
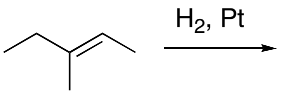
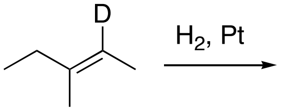
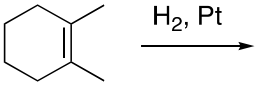
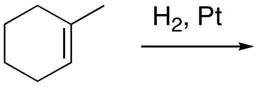
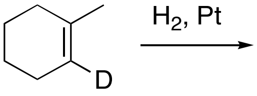
plus enantiomer

Orientation:	Stereo:	Mech:
None	**Cis**	Not responsible

Notes:

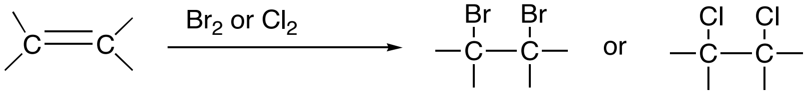
1. Since both atoms adding are the same (H), Markovnikov orientation issues don't apply
   - You're adding a hydrogen to both the more and less substituted alkene carbon!
2. Stereochemistry isn't often relevant, but when it is it's **cis**
   - Rarely relevant because if either alkene carbon has even one hydrogen attached, addition of an additional hydrogen will result in an achiral carbon.
3. The reaction is substantially exothermic
4. But some kind of transition-metal catalyst is required to active the otherwise strong H-H bonds.

Examples, Predict the Products.

	Does Mark's Rule matter?	Does Stereo?
1 		
2 		
3 		
4 		
5 		
6 		

8.8 X-X Dihalogen Addition: Trans Addition (Reaction 8)

General:



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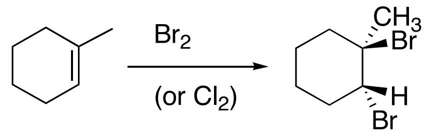


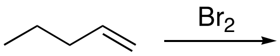
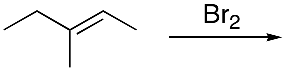
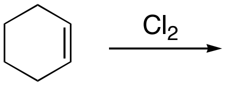
plus enantiomer

Orientation	Stereo	Mechanism
None	**Trans**	**Be able to draw completely**

Notes:

1. **Orientation: Non-issue**, since you're adding the same atom to each alkene carbon
2. **Trans addition**
3. **Solvent** matters: to get X-X addition, you need a solvent other than water or alcohol.
   - With water or alcohol, you get different products, see reaction 9

Examples, Predict the Products.

	Does Mark. matter?	Does Stereo?	Chiral?
1 			
2 			
3 			
4 			
5 			
6 			

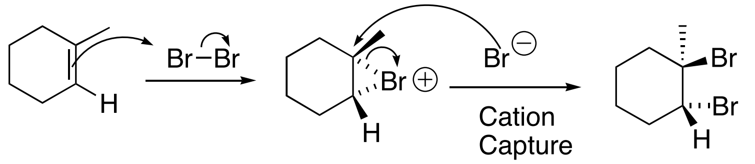
Notes:

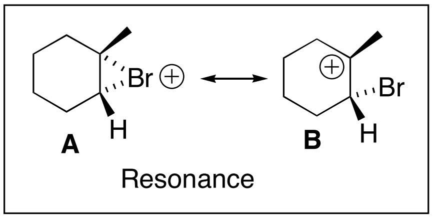
1. Cis and trans reactants give different products!
2. For any product (in this and other reactions), be able to identify whether it is chiral or not

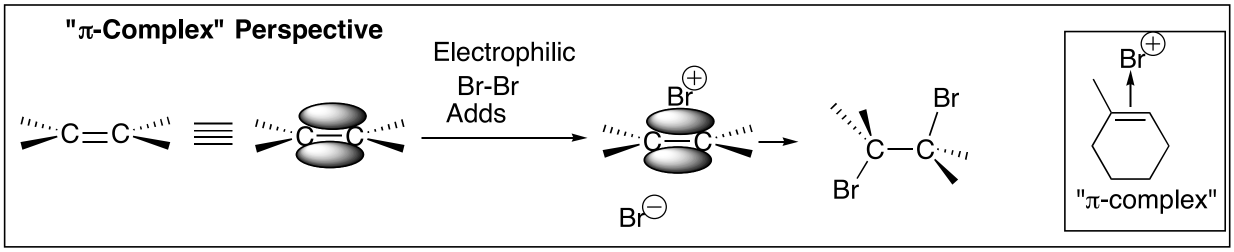
Chemical Test for Alkenes**:** Br_2 in CCl_4 solvent is reddish/brown color. Add a few drops to an unknown organic:

a. If the color stays reddish/brown → the unknown does not contain any alkenes
b. If the reddish/brown color goes away → the unknown did have an alkene that is reacting with the bromine

Mechanism (Very important) (6.16)





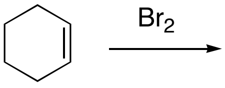


Notes

1. **Cation Formation: Step 1**
2. **Cation capture: Step 2**
3. Br_2 and Cl_2 are exceptionally good electrophiles
4. **The cation that forms is a 3-membered ring**
    - "Bromonium ion"
    - "Chloronium ion"
5. Or, it can be viewed as a π-complex, with a halogen cation sitting on a p-bond
6. When the nucleophile captures the cation, it must come in from the opposite face
    - **Backside attack, ala S_N2**
    - **Trans addition results**
7. **The nucleophile actually attacks at the more substituted carbon!**
    - This is contrary to S_N2 expectations!
8. Resonance pictures **A** and **B** help to explain things
    a. The cyclic form **A** explains stereochemistry
    - If acyclic form **B** was all there was, you wouldn't need backside attack and you wouldn't get trans stereochemistry
    b. Form **B** helps explains why the nucleophile attacks the more substituted carbon.
    - Of the two carbons, the more substituted one has the positive charge and is thus more electrophilic, in spite of steric issues.

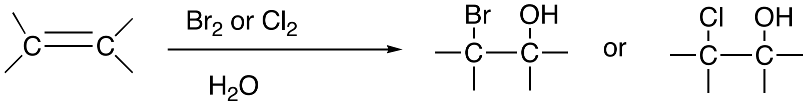
Solvent Limitation: Solvents that are nucleophilic (water or alcohols…) successfully compete with bromide or chloride in the cation capture step.

Draw the mechanism for:

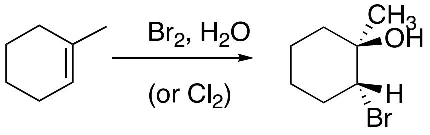


8-9. Br-OH or Cl-OH Addition. Markovnikov Addition, Trans Addition, to form "Halohydrins" (reaction 9)

General:



9



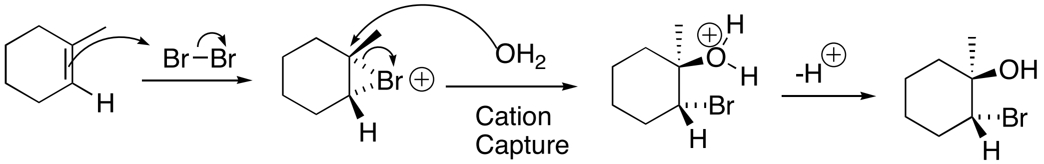
plus enantiomer

Orientation	Stereo	Mechanism
Markovnikov	**Trans**	**Be able to draw completely**

Notes:

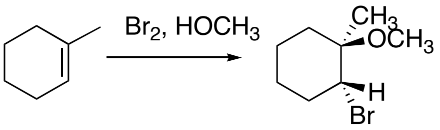
1. **Markovnikov Orientation**
   - OH adds to more substituted alkene carbon
   - Br or Cl adds to less substituted alkene carbon
   - This literally follows Markovnikov's Rule, since the relative electronegativity makes for BrOH (or ClOH) is Brδ+(OH)δ-
2. **Trans addition**
3. **Solvent** matters: whenever you see Br_2 or Cl_2 recipes, check whether there is a water (or alcohol) solvent

Mechanism

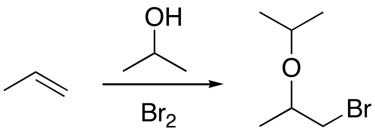


1. 3 Steps:
   - bromonium formation (cation formation)
   - cation capture/nucleophile addition
   - deprotonation (since the nucleophile was neutral)
2. The mechanism is closely analogous to the Br_2 or Cl_2 additions
3. Water is a better bromonium (chloronium) capture nucleophile than bromide (or chloride) anion
   - The large population of water molecules in the solvent give it a statistical advantage
   - When the bromide anion forms in step one, it is initially formed on the wrong side of the bromonium. It needs to swim around to the opposite side in order to attack. Usually water has already captured the cation before then.
   - Water really is inherently a better electron donor than bromide anion. This is why in water a proton goes onto water to make hydronium ion rather than going onto bromide to make covalent HBr
4. Notice that the water attacks the **more substituted** carbon of the bromonium (chloronium) ion

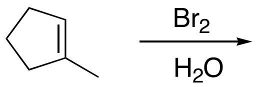
Alcohol Reactions



Alcohols
Give
Haloethers



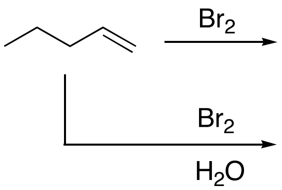
Draw the mechanism for the following reaction:



Examples, Predict the Products.

Does Mark. matter?	Does Stereo?	Chiral?

1



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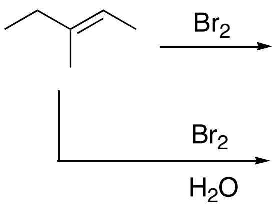

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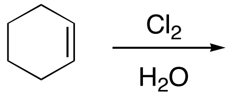

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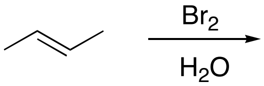

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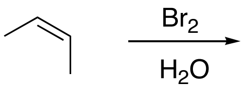
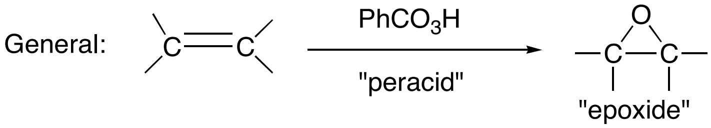
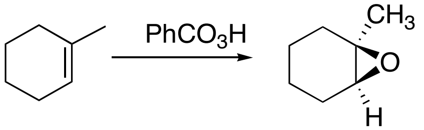


8-12 Epoxidation. Addition of one Oxygen (Reaction



10 

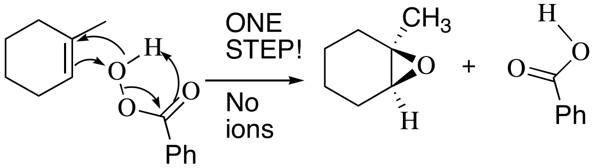
plus enantiomer

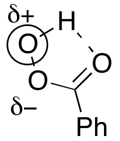
None **Cis** Not responsible

Notes:

1. No orientation issues, since the same oxygen atom connects to both bonds
2. Cis addition: both oxygen bonds come from the same direction

Mechanism: No test Responsibility



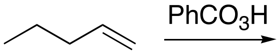


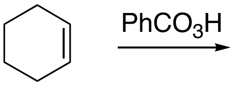
Carbonyl-hydrogen
Hydrogen-bonded reactant

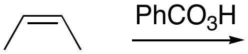
a. Any peracid with formula RCO_3H has an extra oxygen relative to a carboxylic acid.
b. Any peracid can deposit the extra oxygen onto the p-bond to make the epoxide
c. No ions are actually involved, because the leaving group is the neutral carboxylic acid

Examples, Predict the Products.

Does Mark. matter?	Does Stereo?	Chiral?

1 

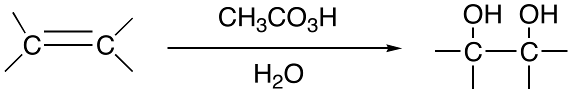
2 

3 

4 

8-13 Trans OH-OH addition. Epoxidation in water. The initially formed epoxide undergoes Acid-Catalyzed Ring Opening. Reaction 11.

General:



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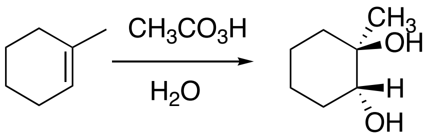


plus enantiomer

None

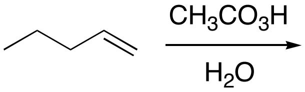
Trans

Be able to draw acid-catalyzed epoxide hydrolysis

Examples, Predict the Products.

Does Mark. matter?	Does Stereo?	Chiral?

1



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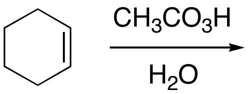

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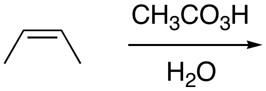

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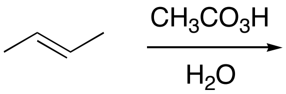
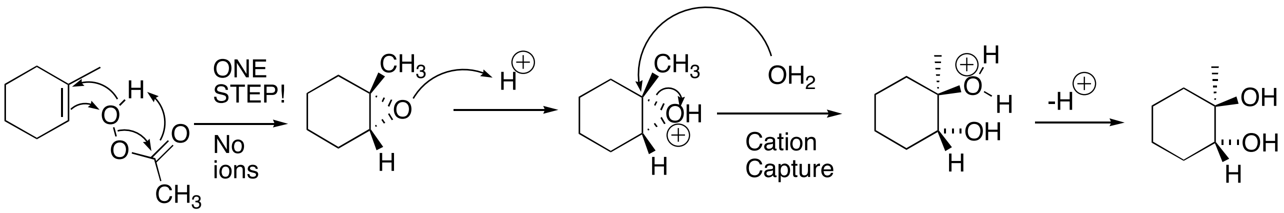


Mech

11



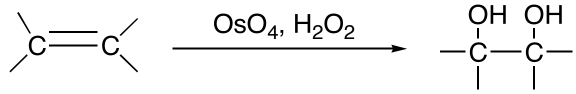
Notes:

a. The nucleophile (water) attacks from the more substituted end of the protonated epoxide
   - More δ+ charge there
   - The C-O bond to the more substituted end is much weaker

b. The nucleophile adds via S_N2-like backside attack. Inversion at the top stereocenter, but not the bottom, explains the trans stereochemistry.

8-14 Cis OH-OH addition. Catalytic Osmylation. Reaction 12.

General:



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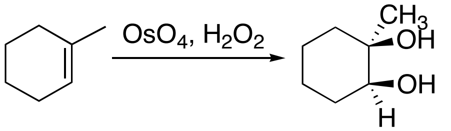


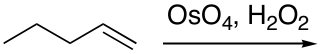
plus enantiomer

None **Cis** Not responsible

Examples, Predict the Products.

Does Mark. matter? Does Stereo? Chiral?

1



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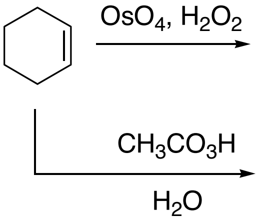

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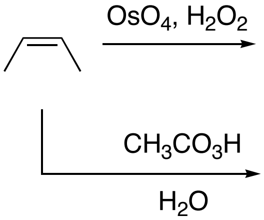

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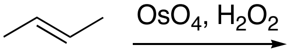
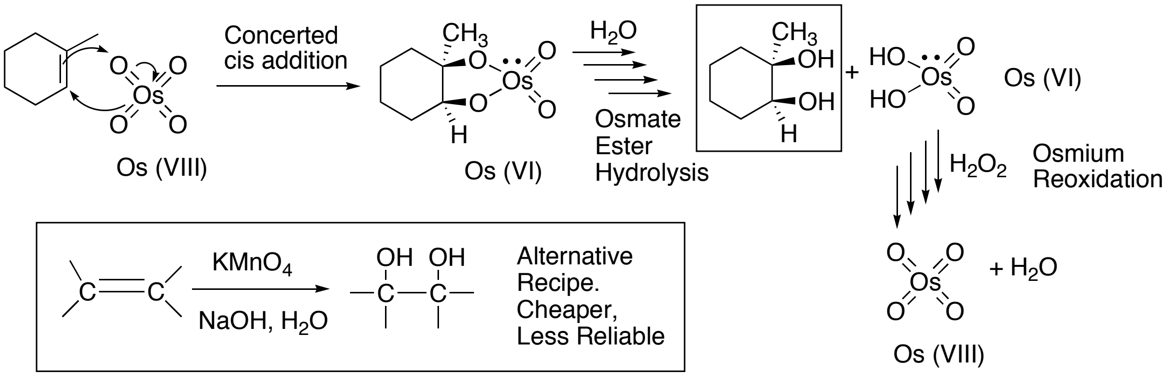


Mech: (Not required)

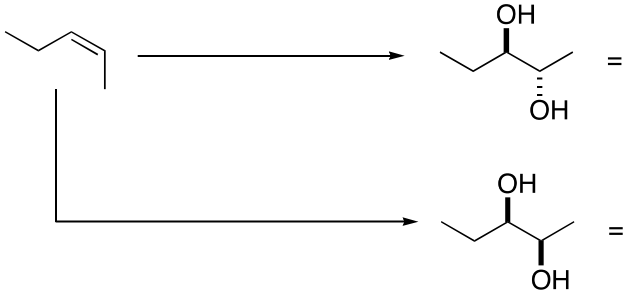
12



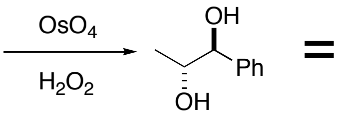
Stereochemically complementary methods

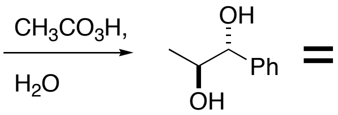
		Skills:
CH_3CO_3H/H_2O	trans	3. Given starting material and product, provide reagent
OsO_4/H_2O_2	cis	4. Given product and reagent, what was the starting material?

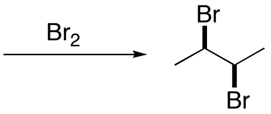
1. Given starting material and product, provide reagent. Consider stereo.

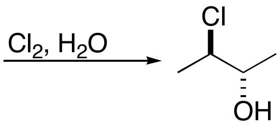


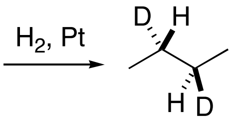
2. Stereochemistry Problems. Given product + reagent, what was the starting alkene?

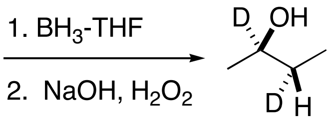


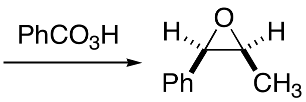






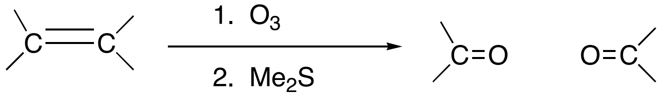






8.15-B Ozonolysis. Cleavage of Alkenes. Reaction 13

General:



13

Note: H-bearing alkene carbon ends up as aldehyde.

None

None

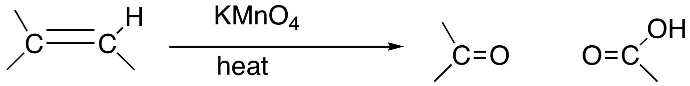
Not responsible

Notes

1. Double bond gets sliced in half, gives two corresponding carbonyls per alkene
2. Alkene bonds and nothing else are oxidized.
3. **Get ketones and/or aldehydes and/or formaldehyde**
4. **Zn often used in workup step two instead of dimethylsulfide**

Oxidative Cleavage of Alkenes by Permanganate. Reaction 14

General:



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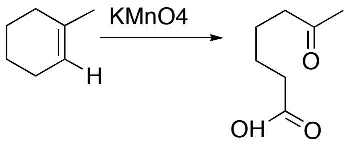


H-bearing alkene carbon ends as carboxylic acid

None

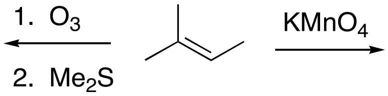
None

Not responsible

Notes

1. Double bond gets sliced in half, gives two carbonyls per alkene
2. Alkene C-H bonds are also oxidized to C-OH bonds.
3. **Get ketones and/or carboxylic acids and/or carbonic acid.**

1



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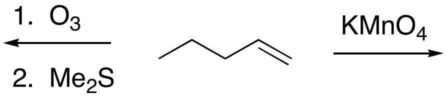

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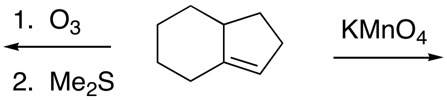
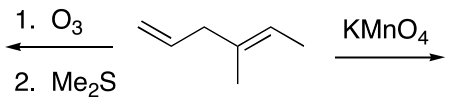
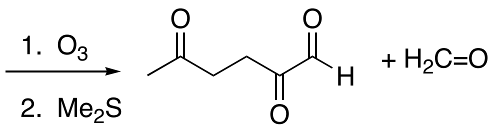
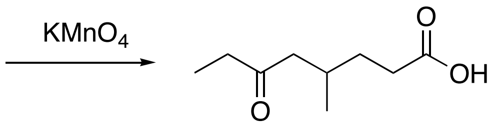


4.

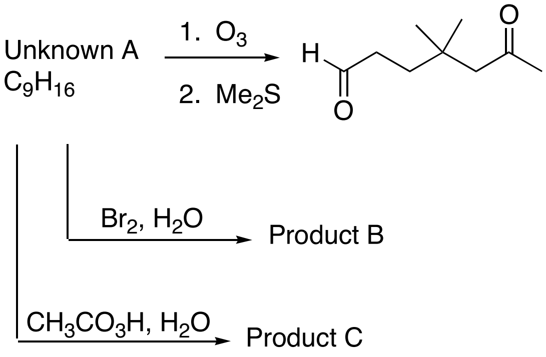


1. Identify reactants.



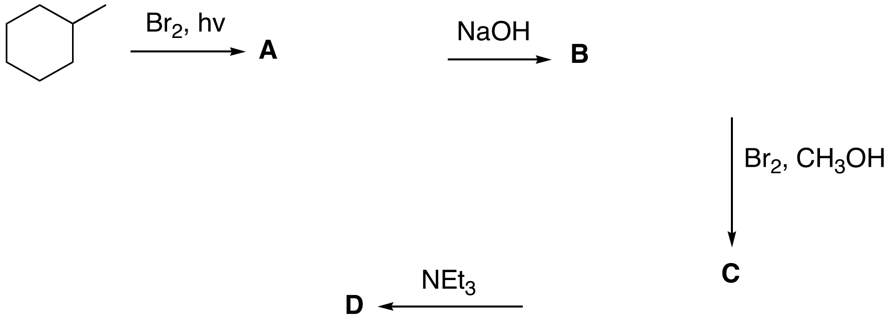


2. Identify A, B, and C.



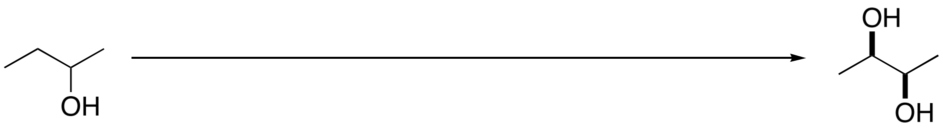
Review Problems.

3. "Roadmap format". Identify products **A-D**.

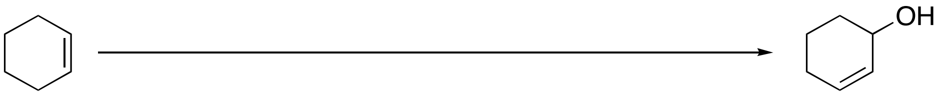


4. Design a synthetic plan for the following conversions. (Several on test)

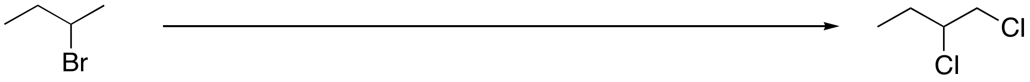
a.



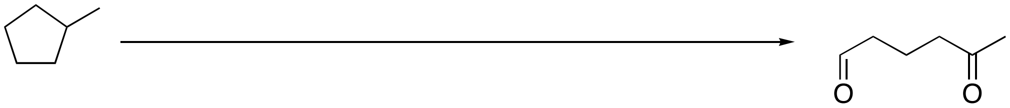
b.



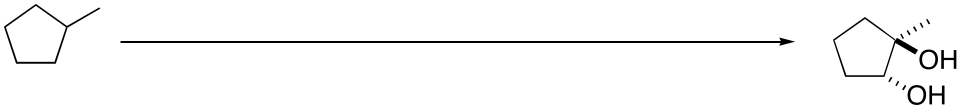
c.



d.



e.



f.

5. What is a structure for C_3H_6, if it reacts with Br_2?

Elements of Unsaturation Problems

6. What is a structure for $C_5H_{10}O$, if it does not react with H_2/Pt, but does react with H_2SO_4 to give 2 different isomeric alkenes C_5H_8?

7. What is a possible structure for C_5H_8, if it reacts with H_2/Pt to give C_5H_{10}?

8. Identify products **A-C**.