

# Organic Chemistry II

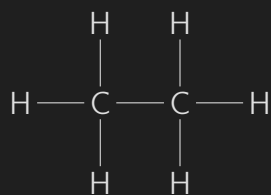
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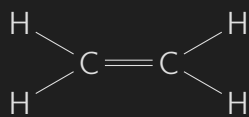
# 14: Alkenes

## Alkenes Basics/Review

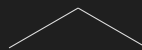
▷ Alkanes vs alkenes:



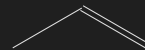
Saturated  
alkanes ethane



Unsaturated  
alkenes ethene



propane



propene

▷ We will fully investigate the nomenclature of alkenes ↗ later.

▷ Some relevant facts to start:

- **Alkene**: a hydrocarbon that contains a carbon-carbon double bond.
  - IUPAC recommends using alkene for only acyclic hydrocarbons with just one double bond; an **olefin** is a hydrocarbon with one or more double bonds.
- Generally prepared through beta elimination, which results in the formation of alkenes from alkanes.

## Types of Alkenes

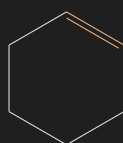
- Basic types of alkenes:



Terminal Alkene

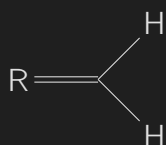


Internal Alkene

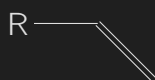


Cycloalkene

- Types of terminal alkenes:



Methylene



Vinyl

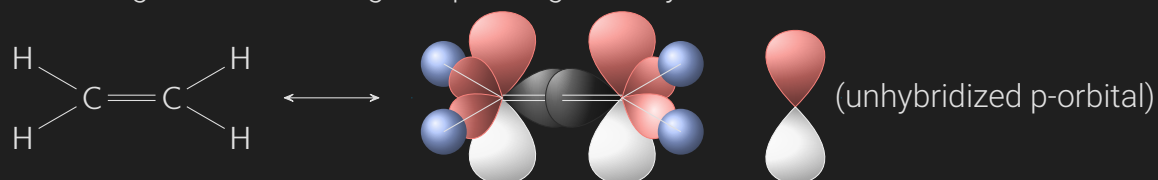


Allyl

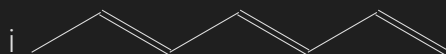
- "R" always tells you it's a carbon containing functional group, or hydrogen.
- "A" can be used to represent any functional group.

## Relevant Review

- **Electronegativity:** negative charges on atoms with lower hybridization result in greater stability due to proximity (overlap) to positive nucleus. More s character results in greater stability.
  - I.e.,  $sp$  (50% s) >  $sp^2$  (33% s) >  $sp^3$  (25% s)
  - E.g., ethene has two carbons that are both  $sp^2$  due to one unhybridized p-orbital. This gives ethene a trigonal planar geometry.



- **Hydrogen deficiency index (HDI):** the measure of degrees of unsaturation.
  - E.g., two degrees of unsaturation results in a HDI of 2.
  - Degrees of freedom help represent possible structures, indicating possible double bonds, triple bonds, rings, or various combinations of each.
  - Only helpful when molecular formula is known for certainty.
  - Formula:  $HDI = \frac{1}{2}(2C + 2 + N - H - X)$ 
    - X: halogen atoms.
- What is the HDI for the following molecules?

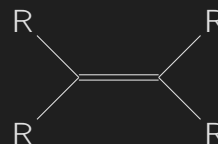


i  $\frac{1}{2}(2(7) + 2 + (0) - (3 + (5(1)) + 2) - 0) = 3$



ii  $\frac{1}{2}(2(6) + 2 + 0 - (6(1)) - 0) = 4$

- **Degree of substitution:** not a substitution reaction, but the number of groups connected to the double bond.



Monosubstituted

Disubstituted

Trisubstituted

Tetrasubstituted

## Common Patterns Between Formal Charge and Lone Pairs

- **Associated Patterns for Oxygen**
  - A negative ( $\ominus$ ) charge corresponds with 1 bond and 3 lone pairs.

- The absence of charge corresponds with 2 bonds and 2 lone pairs.
- A **positive** ( $\oplus$ ) charge corresponds with 3 bonds and 1 lone pair.
- **Associated Patterns for Nitrogen**
  - A **negative** charge corresponds with 2 bonds and 2 lone pairs.
  - The absence of charge corresponds with 3 bonds and 1 lone pair.
  - A **positive** charge corresponds with 4 bonds and 0 lone pairs.

## Chirality

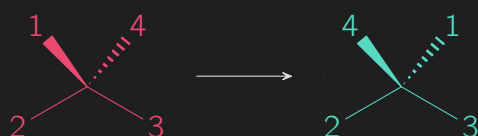
- **Achiral (nonsuperimposable)**: when an object's mirrored version is identical to the actual object.
- **Chiral**: objects that are not superimposable.
  - The most common source of molecular chirality is the presence of a **carbon bearing four different groups**.
- All three-dimensional objects can be classified as either chiral or achiral.
- **Enantiomer**: the nonsuperimposable mirror image of a chiral compound.
  - Can be used in speech the same way the word **twin** is used
  - The easiest way to draw enantiomers is to simply change wedges and dashes, but there are multiples ways to mirror a molecule, so it can be more complex.
- **Diastereomers**: non-identical stereoisomers (nonsuperimposable) that are **not mirror images** of one another.
  - Enantiomers have the same physical properties, while diastereomers have **different physical properties**.
  - Differences between enantiomers and diastereomers are especially relevant when comparing compounds with **more than one chiral center**.
  - **Maximum** (could be less) number of stereoisomers:  $2^n$ 
    - $n$ : number of chiral centers
    - $\frac{2^n}{2}$ : max pairs of enantiomers.

## Cahn-Ingold-Prelog System

- **Cahn-Ingold-Prelog system**: a system of nomenclature for identifying each enantiomer individually.
  1. Assign priorities to each of the four groups based on atomic number; the highest atomic number has the highest priority.
  2. Rotate the molecule so that the fourth priority group is on a dash (behind)

3. Determine the configuration, i.e., sequence of 1–2–3 groups;
  - clockwise (*R*, *rectus*, right) or counterclockwise (*S*, *sinister*, left).
- If there is a tie between the atoms connected, then continue outward until a difference is found.
  - Do not add the sum all atomic numbers attached to each atom, just the first in which the atoms differ.
  - Any multiple bonded atom, (2 or 3) is treated as if connected to multiple atoms equal to number of bonds.

- Switching any two groups on a chiral center will invert the configuration, e.g.,



- Switching twice results in a change without changing configuration, e.g.,



- **Configuration in IUPAC nomenclature:**

- The configuration of the chiral center is indicated at the beginning of the name, italicized, and surrounded by parentheses.
- When multiple centers are present, then each must be preceded by a locant.

## Rearrangements

- There are several kinds of rearrangements, but only those relating to carbocation rearrangements are focused here.
- **Hyperconjugation:** carbocations that can be stabilized by neighboring groups due to molecular orbitals that slightly overlap with empty *p* orbitals, placing some of its electron density there.
  - **Primary (1°), secondary (2°), and tertiary (3°):** refers to the number of groups directly attached to the carbocation.
  - Tertiary are the most stable (more slight overlap) and primary are the least (less overlap)
- **Hydride shift:** involves the migration of a  $\text{H}^-$ .
  - Involves the rearrangement of the carbocation to a more stable variant due to change migration of the  $\text{H}^-$ .

- **Methyl shift:** similar to a hydride, except a whole methyl group is migrated instead.
  - The methyl group must be attached to the carbon atom that is adjacent to the carbocation for this to occur.

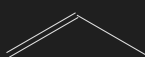
## Nomenclature of Alkenes

### Basic Alkene Nomenclature Rules

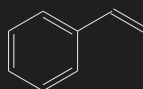
- Alkenes are named using the same four steps in the previously used nomenclature, though the suffix of "ane" is replaced with "ene."
- When choosing the parent chain, choose the parent chain that **includes** the double bond.
- When numbering the parent chain, the double bond should receive the **lowest** number possible.
  - Define the location  $k$  of the double bond as being the number of its first carbon.
  - The locant ( $k$ ) of the double bond should be placed right before the suffix of "ene," though, it was previously recommended before the parent (both are acceptable), e.g., 2-pentene = pent-2-ene
- Name and the side groups (other than hydrogen) according to the appropriate rules.
- Define the position of each side group as the number of the chain carbon it is attached to.
- E-Z notation:** recommended instead of *cis* and *trans* in order to account for cases that has more than two different groups attached to the double bond by first determining the **CIP priority** ↗.
  - E**, *entgegen*, "opposite".
  - Z**, *zusammen*, "together"; "on ze same side."
- Commonly recognized alternative names:



Ethylene



Propylene



Styrene

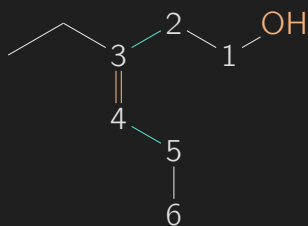
- Groups containing C=C have common names as well, which can be found under **types of alkenes** ↗.

### Alkenes Containing an Alcohol

- If there is **more than 1** functional group, then the **alcohol** has the **higher priority** over alkenes.
- There are more rules depending on functional groups, but for now the distinction between alcohol and alkenes are all that is needed.
- I.e., find the longest chain and number in a way that the carbon **containing the OH** gets the **lowest** possible number while still including both the OH and alkene.



- An example with alcohol:

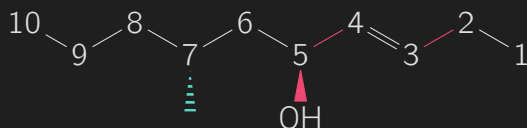


(3Z)-3-propyl-hex-3-en-1-ol

or

(3Z)-3-propyl-3-hexen-1-ol

- An example with OH still being lowest (name still ends with -ol), but alkene happens to be lower:



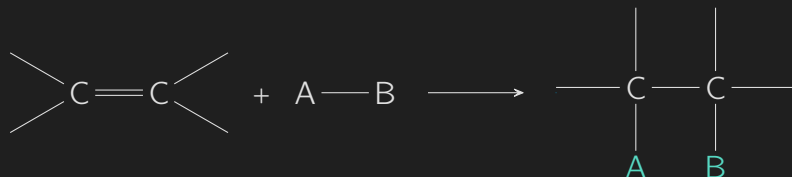
(3E,5S,7R)-4-methyl-3-en-5-ol

- Note: if planar geometry was not given, R and S could not be determined. Check out the [Cahn-Ingold-Prelog System](#) for review.

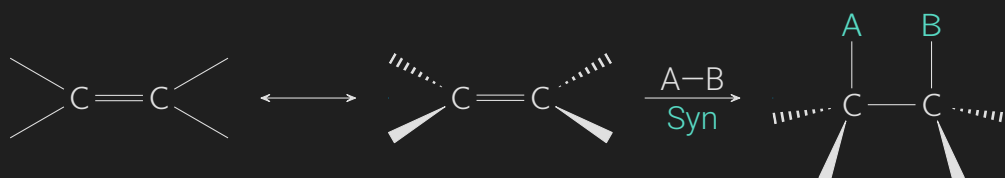
## Addition Reactions of Alkenes

### Syn Addition

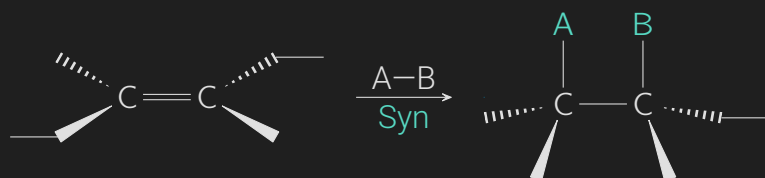
- Syn addition means that both components (A & B) came in from the same side.



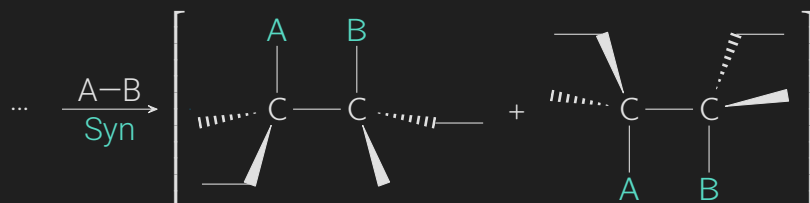
- When there is mixture of products, then the stereochemistry is important—A & B could come from different directions.
- Switching to a 3D perspective, with groups pointing towards and away from the viewer, rather than a flat view:



- The final product above results in no chiral compounds (no carbons contain four different groups). If a product does have chiral compounds, you must show the other possible products.

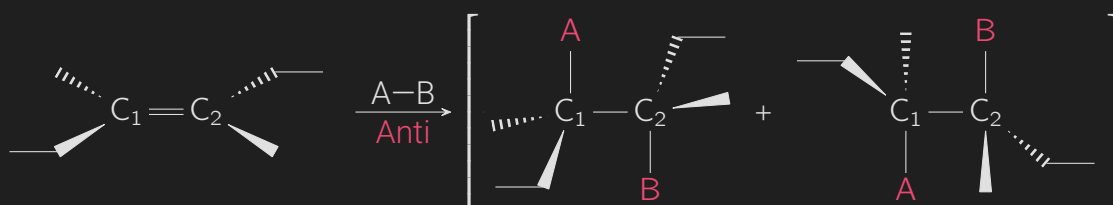


- The product in this case has **chiral centers**, so enantiomers must be considered.



### Anti Addition

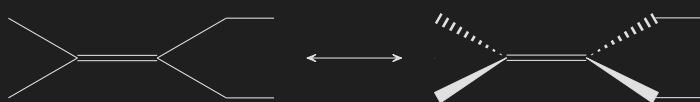
- Anti addition means that the added components come in from different sides.



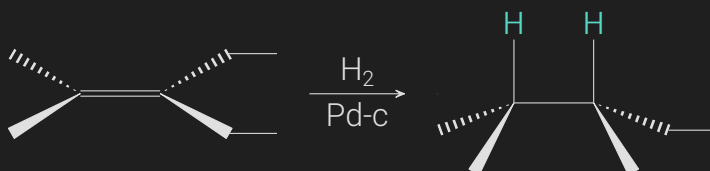
## Hydrogenation

- **Hydrogenation:** a chemical reaction between molecular hydrogen  $H_2$  and another compound or element, usually in the presence of a catalyst such as nickel, palladium (typically  $Pd$ , due to cost) or platinum.
  - Commonly employed to **reduce** ( $\pi$  bonds) or **saturate** (add hydrogens) organic compounds.
  - Usually constitutes the addition of pairs of hydrogen atoms to a molecule, often an alkene.
  - Catalysts are required for the reaction to be usable; non-catalytic hydrogenation takes place only at very high temperatures.
  - Always occurs with **syn addition**, with hydrogen entering from the least hindered side.
- Hydrogenation of 2-methyl-3-ethyl-2-pentene:

- First convert to 3D view:

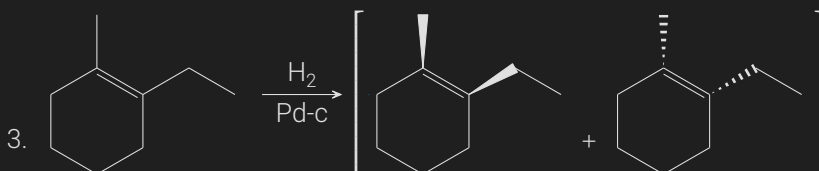
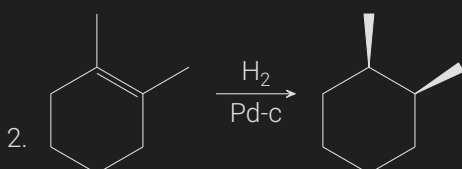
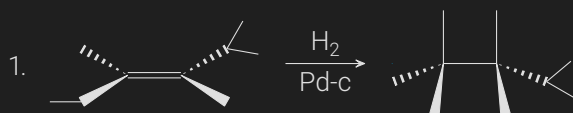


- Then apply  $H_2$  with catalyst to trigger syn addition:



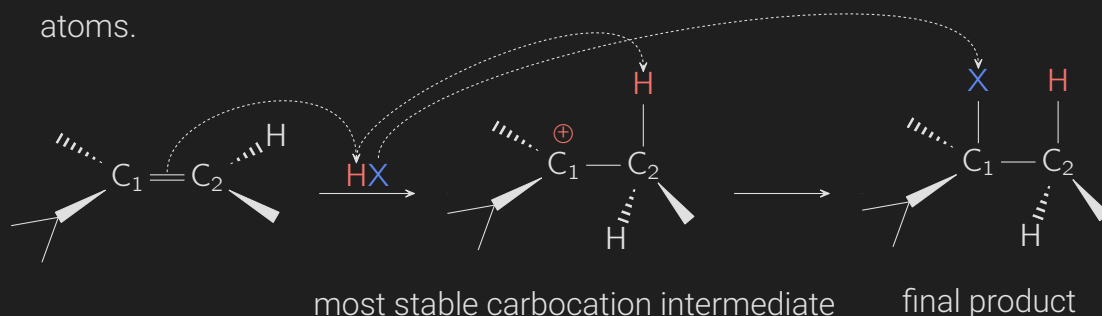
- Product is achiral; no enantiomers. Bottom would attack just flips the orientation; not a different product.

## Hydrogenation Practice Problems

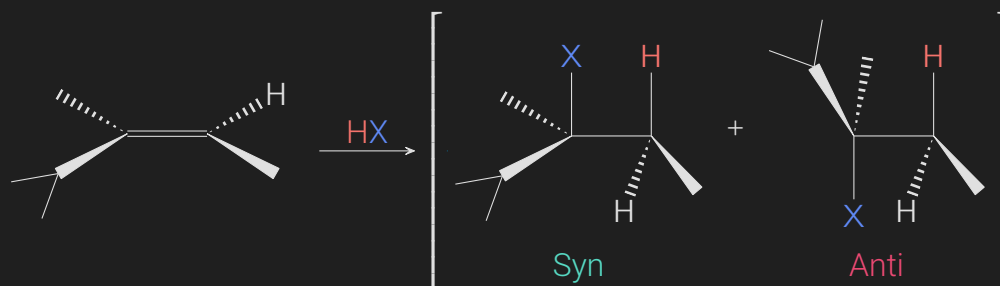


## Hydrohalogenation

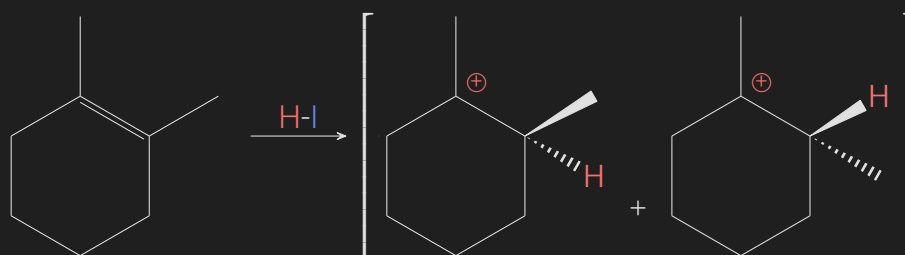
- **Hydrohalogenation:** the electrophilic addition ( $\pi \rightarrow 2\sigma$  bonds) of hydrohalic acids (HX, e.g., HCl or HBr) to alkenes to yield the corresponding haloalkanes.
- **Markovnikov's Rule:** an addition of a protic acid (HX) or other polar reagent to an asymmetric alkene results in the **electropositive part (usually H)** gets attached to the carbon with **more hydrogen substituents**, and the **electronegative part (usually the halide)** attaches to the carbon with **more alkyl substituents**.
  - Alternatively:  $H^+$  is added to the carbon with the **greatest** number of hydrogen atoms while the  $X^-$  component is added to the carbon with the **fewest** hydrogen atoms.



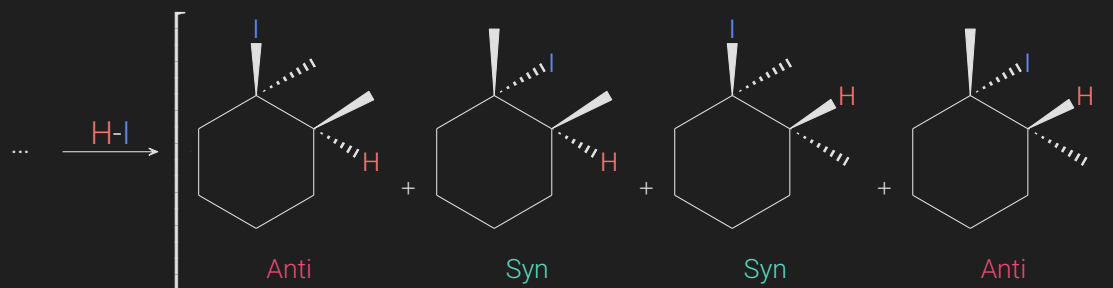
- However, we have a chiral carbon, so we have to take enantiomers into account:



- The previous example is an example of a regioselective reaction, i.e., it's a chemical reaction where one reaction site is preferred over another.
  - Markovnikov additions are common examples of regioselective reactions since there is a specific region in where the hydrogen is supposed to go.
- Another example that contains multiple products:

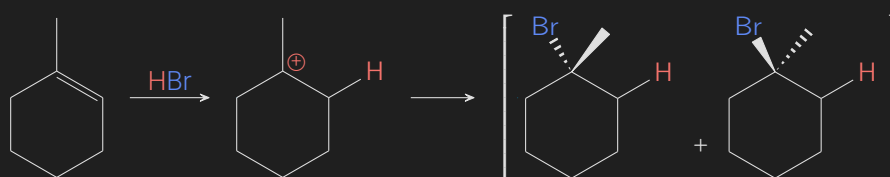


- Again, this first step shows the most stable carbocation intermediate, which helps determine where the  $H^+$  will attach to. In this case either location works, so four products are formed, each with syn and anti enantiomers.



- The above products are all **stereoisomers** of each other. Note: not all chemical reactions produce all possible stereoisomers.

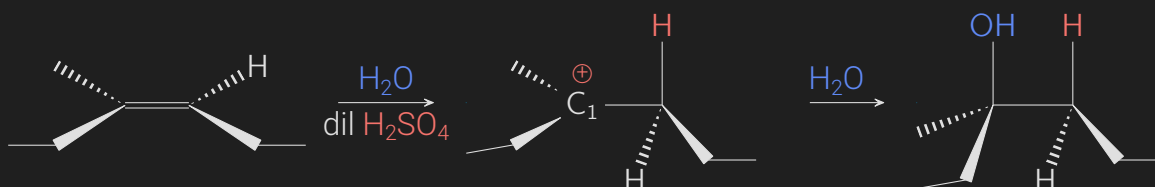
### Hydrohalogenation Practice Examples



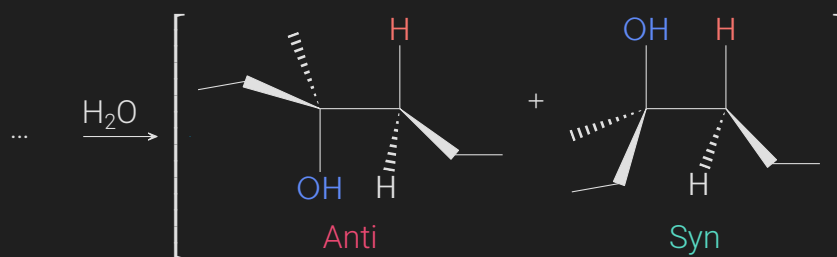
### Addition of Water or Alcohol

**Addition of Water or Alcohol (ROH):** analogous to that of hydrohalogenation (HX); both of which involve a carbocation intermediate, syn/anti stereochemistry, and Markovnikov regioselectivity.

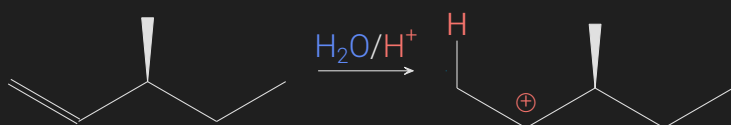
- Note: the hydronium ion ( $\text{H}_3\text{O}^+$ ) forms via the reaction of  $\text{H}_2\text{SO}_4$  with  $\text{H}_2\text{O}$ , and is the source of the proton that reacts with the starting alkene.
- $\text{H}-\text{OH}$  and  $\text{RO}-\text{H}$  helps to visualize where the proton is coming from. What ever works with water also works with alcohol and vice versa.
- An example that is very similar to the example from **hydrohalogenation**  $\nearrow$ :



- Note:  $\text{H}_2\text{SO}_4$  is a **strong acid** and can be generalized to  $\text{H}^+$  or  $\text{HA}$ .
- Note: I occasionally use **red** for **cations**, **acids**, and  $\text{E}^+$  (electrophile). I also use **blue** for **anions**, **bases**, and  $\text{nu}^-$  (nucleophile) to help easily keep track of things. This is an arbitrary color choice, but it holds weight in these notes. However, not all bases/acids are nucleophile/electrophiles, so keep that in mind.
- Again, this reaction is stereoselective, so there is actually more than one product:

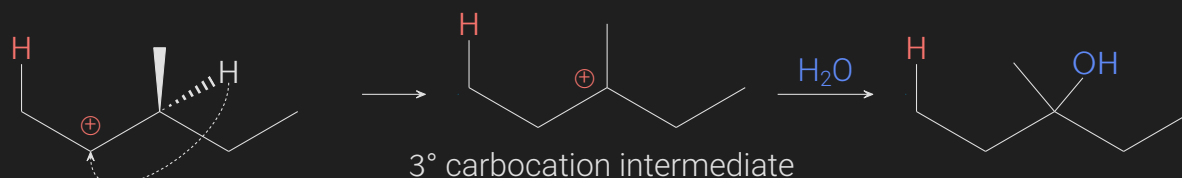


- Example 2:

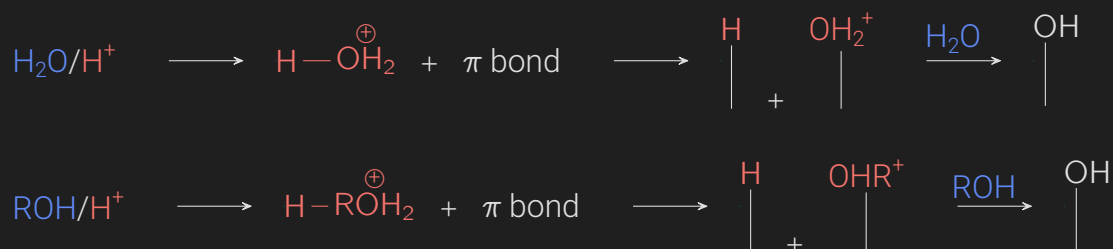


- **Rearrangement**  $\rightarrow$  is always a possibility to be considered when cation are generated. In this case, a 2° carbocation was generated, but we can do better:

- Note: showing H is not necessary, but useful to visualize the hydride shift and avoid the urge to move the methyl. "Why move a sofa when you can move a chair?"



- Note: the carbocation intermediate changes planar geometry due to change in hybridization ( $sp^3 \rightarrow sp^2$ ).
- Top and bottom attacks do not need to be considered in this case, as there are chiral centers; no enantiomers.
- Reminder,  $\text{H}_2\text{O}$  and alcohols ( $\text{ROH}$ ) behave very similarly; the reduction of the  $\pi$  bond generates 2  $\sigma$  bonds, one of which that takes a **hydrogen**, and the other (with possible carbocation rearrangement first) which first takes up the **cation** generated in the medium, then interacts with **base**, removing an **H** and leaving **OH**.
- Note: the OH is not actually negatively charged on the end, I just keep the blue there to help show where it's coming from; it helps determine syn/anti if needed.



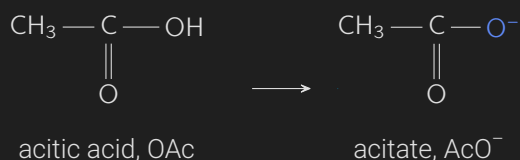
- **Problems of going through carbocation intermediate:**

- Carbocations are  $sp^2$ , which makes them trigonal planar, so  $\text{nu}^-$  can attack from top or bottom.

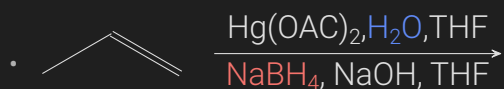
- $C^+$  can cause rearrangements leading to **multiple products**.

## Oxymercuration-Demercuration

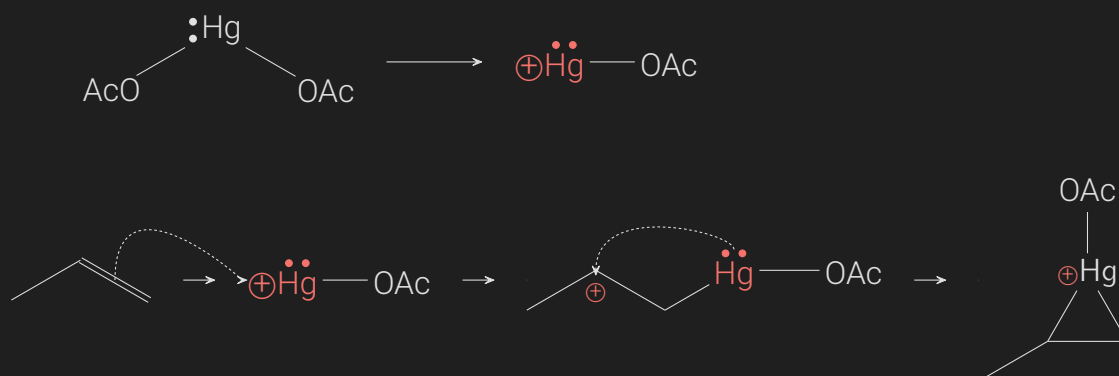
- **Oxymercuration-Demercuration** is another electrophilic addition organic reaction that transforms an alkene into a neutral alcohol.
- Reacts with mercuric acetate ( $AcO-Hg-OAc$ ) in aqueous solution to yield the addition of an acetoxymcury ( $HgOAc$ ) group and a hydroxy ( $OH$ ) group across the double bond.



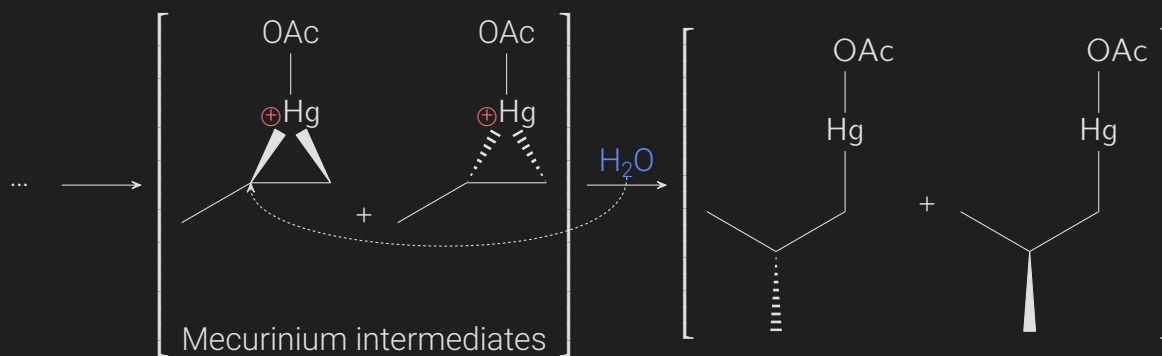
- Carbocations are not formed in this process and thus rearrangements are not observed.
- The reaction follows **Markovnikov's rule**.
- The reaction is stereospecific—it is always an **anti addition**.
- Example using propylene:



- $H_2O$  is  $nu^-$ ; ROH can be used instead.
- THF has no function directly; it is the solvent.
- $NaBH_4$  is the reducing agent.

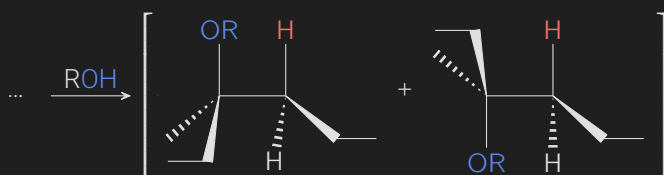
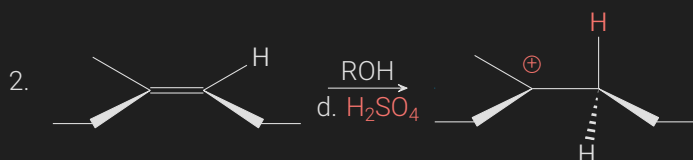
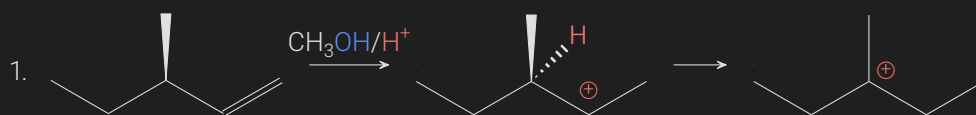


- Note: the above is a concerted (one step) process, but drawn out for illustration.
- Also, we are not done, we have a chiral center that forms, plus it is just an intermediate step, a nucleophilic attack will occur on the strained (highly reactive) epoxide:

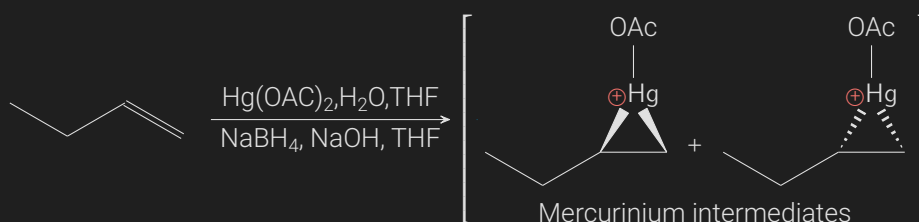


- Notice the nucleophile attack the carbon with the greater flow of electrons (more substituted), since there was a positive charge on mercury. Epoxides with no charge are attacked on the side with less steric hindrance.
- Also, the nucleophilic attack occurs on the opposite side of the plane since there is less hindrance on that side.

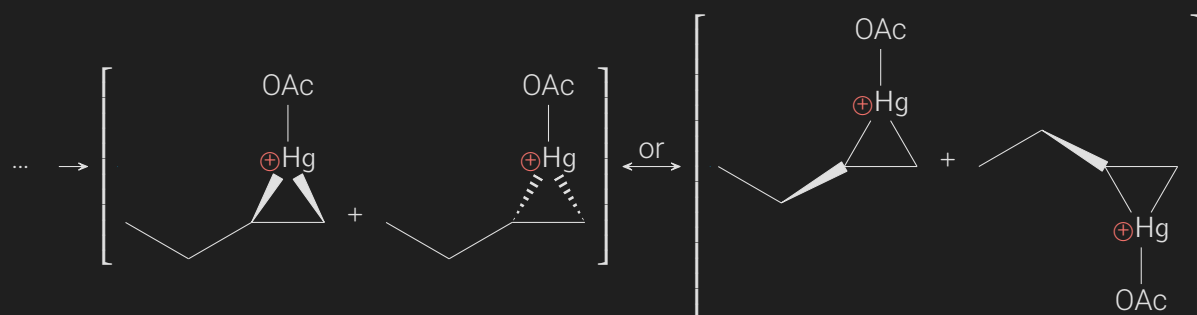
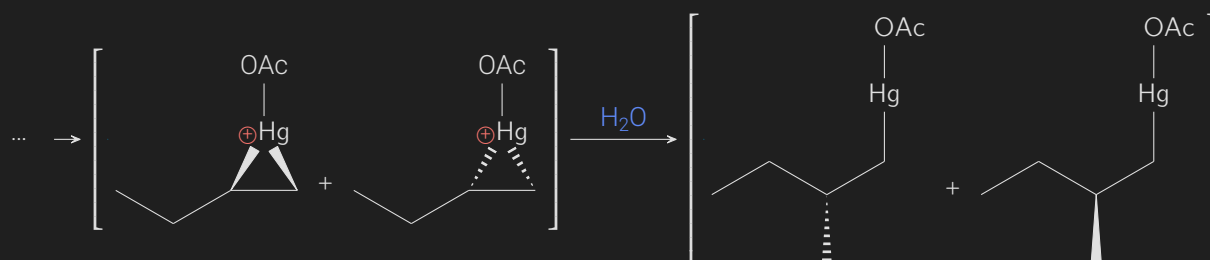
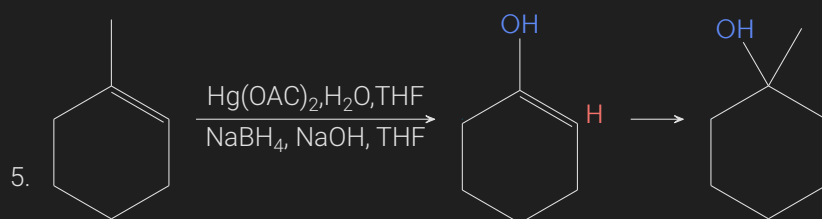
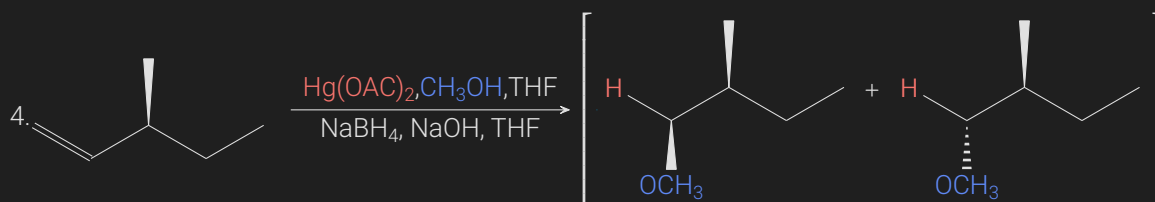
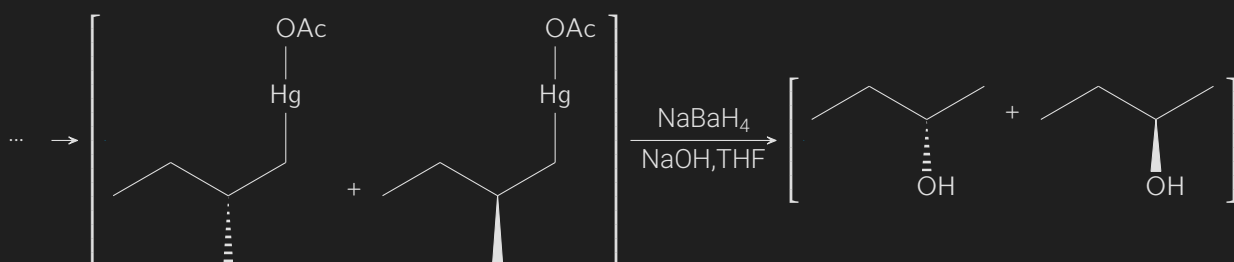
### Related Practice Problems



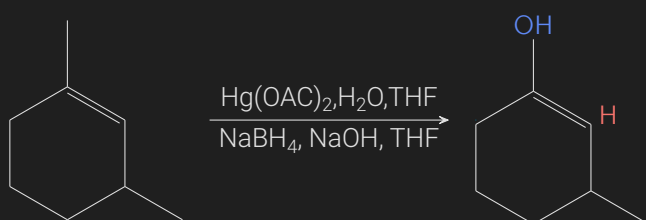
3. + Alternate ways of drawing rings (was done in lecture):



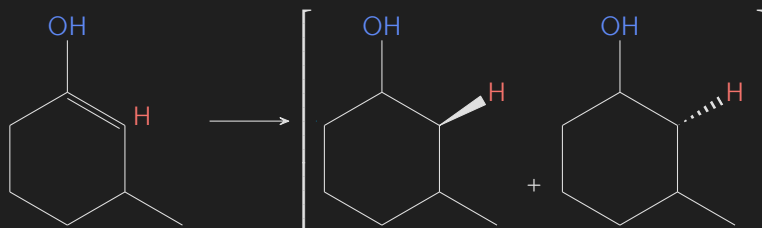


**Oxymercuration:****Demercuration:**

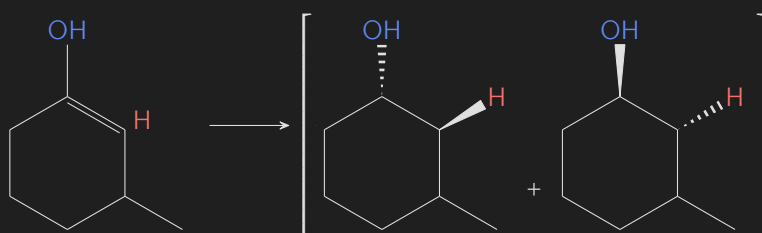
6. (was done in lecture)



- We know these are the locations of the H and OH, so we can start by labeling them.



- The methyl will be the same no matter what, so we can ignore that.
- H has two options, which gives us the above.
- Since oxymercuration-demercuration is always an **anti addition**, then we know OH must be **anti** to the hydrogen in both of the products:

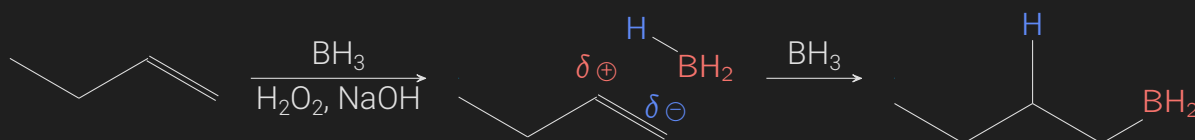


## Hydroboration-Oxidation

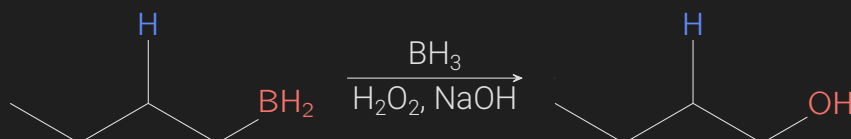
- Hydroboration-Oxidation:** a two-step hydration reaction that converts an alkene into an alcohol.
  - Results in the **syn addition** of a hydrogen and a hydroxyl group where the double bond had been.
  - An **anti-Markovnikov reaction**—the hydroxyl group attaches to the less-substituted carbon.
  - Provides a more stereospecific and complementary regiochemical alternative to other hydration reactions such as acid-catalyzed addition (stereoselective) and oxymercuration-demercuration (stereospecific for anti).
  - Usually  $\text{BH}_3$ ,  $\text{B}_2\text{H}_6$ ,  $\text{R}_2\text{BH}$  are used. The presence of Boron is key.
- Like  $\text{H}_2\text{O}$  and  $\text{ROH}$ , it's useful to think of them in the following way:



- Unlike water/alcohol, the hydrogen is now the partial negative component and the boron is the positive.



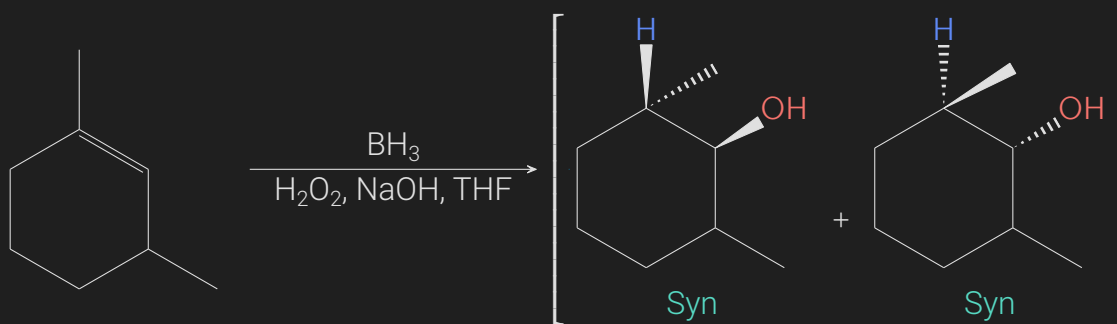
- There are no chiral centers, but there is still one more step—the oxidation:



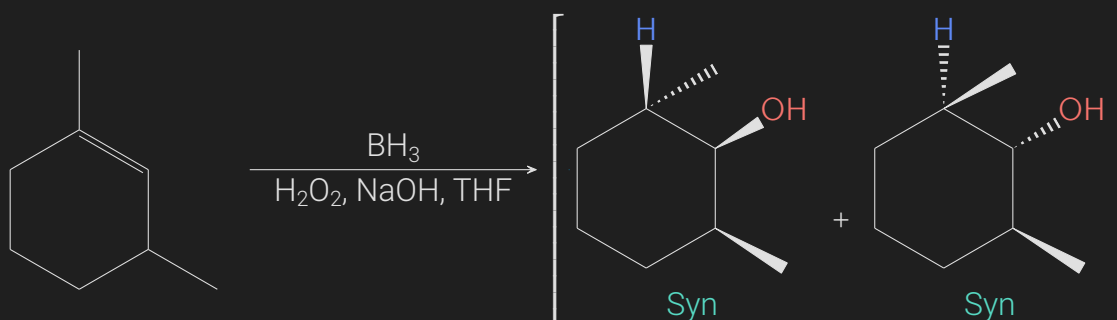
- If we had used  $\text{Hg}(\text{OAc})_2$ , then the above reaction would be different; partial charges change the possible final products:  $\overset{\delta^-}{\text{H}}-\overset{\delta^+}{\text{BH}_2}$  vs.  $\overset{\delta^+}{\text{H}}-\overset{\delta^-}{\text{OH}_2}$ :



- Revisiting a practice example, using different reagents:

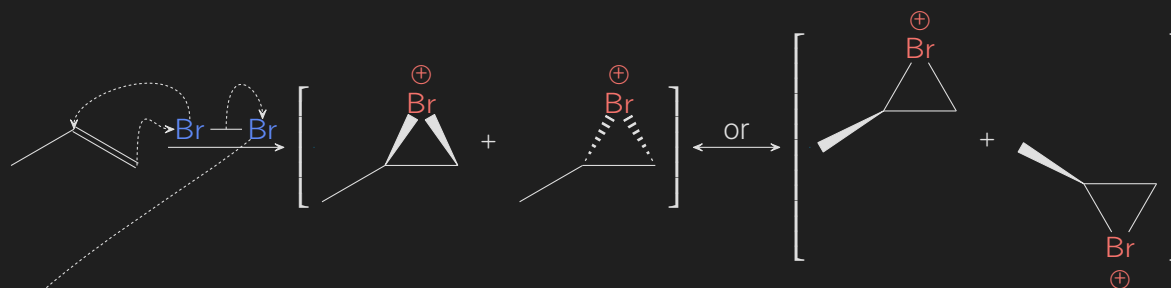


- If the untouched methyl happened to be above or below the plane initially, then you would keep that the same, e.g:

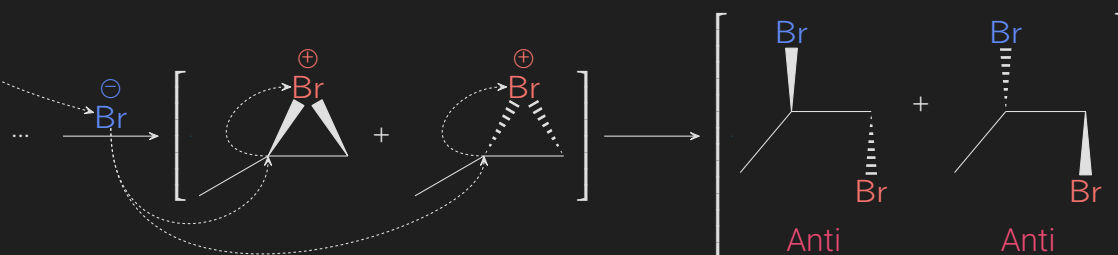


## Halogenation

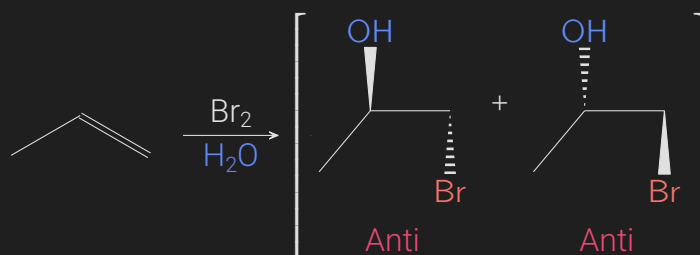
- Halogenation:** a reaction that involves the addition of one or more halogens to a compound or material.
  - The addition of halogens to alkenes proceeds via intermediate halonium ions.
  - Halonium ion:** any onium ion containing a halogen atom carrying a positive charge. This cation has the general structure:  $\text{R}-\text{X}^+-\text{R}'$
  - Onium ion:** a cation formally obtained by the protonation of mononuclear parent hydride of a pnictogen (group 15 of the periodic table), chalcogen (group 16), or halogen (group 17).



- In the above example we see a cyclic bromonium ion intermediate being formed. Next, one bromine is now left to act as the  $nu^\ominus$ :



- Alternatively, if you did the reaction in  $H_2O$ , then water would become the dominant  $nu^\ominus$ , leaving OH.



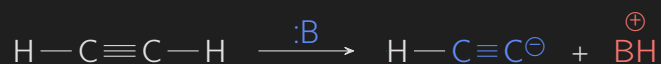
# 15: Alkynes

## Alkynes Basics/Review

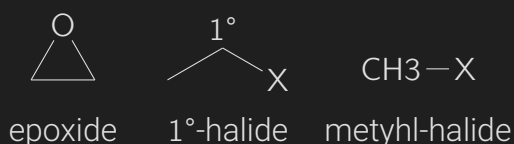
- ▷ **Alkynes**: an unsaturated hydrocarbon containing at least one carbon—carbon triple bond.
    - Contains two unhybridized p-orbitals (sp) on each carbon.
- $$\begin{array}{ccccccc} \delta+ & \delta- & \delta- & \delta+ \\ \text{H} & -\text{C} & \equiv & \text{C}-\text{H} \end{array}$$
- Large amount of s character (sp: 50% s) makes the hydrogens very acidic and the carbons very basic.
  - 1 mole of base takes off 1 hydrogen (1 equivalent, equiv, eq), which can be done twice to take off both (2 equivalent).
  - Traditionally known as acetylenes, though acetylene refers specifically to C<sub>2</sub>H<sub>2</sub> (ethyne)

## Acetylides

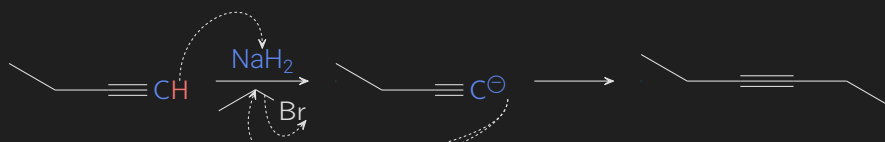
- ▷ **Acetylide**: an alkyne with a negatively charged carbon on one end, e.g.,



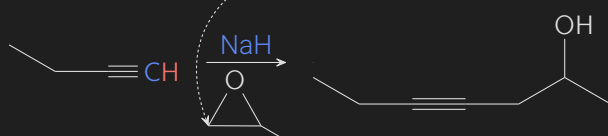
- :B is a name of generic base, typical bases used:
  - NaNH<sub>2</sub> → sodamide, or NaH → sodium hydride.
- Acetylide acts as a **nucleophile** when it reacts with an epoxide, 1°-halide, or a methyl-halide.



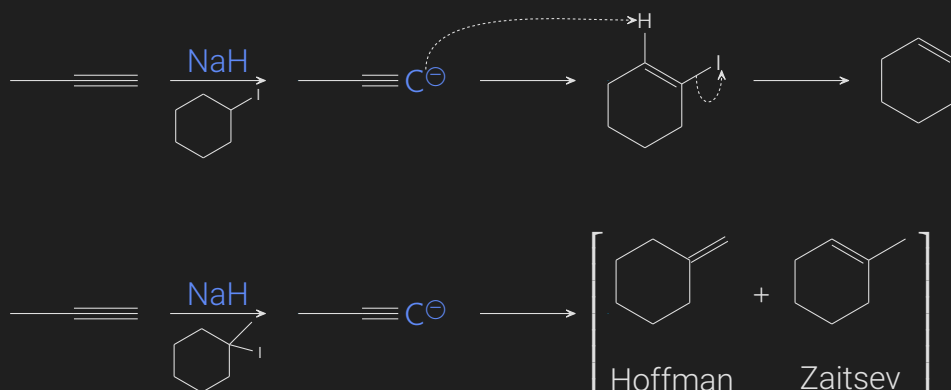
- Is a S<sub>N</sub>2 reaction.
- Can be used for chain extension, e.g.,



- Example two:



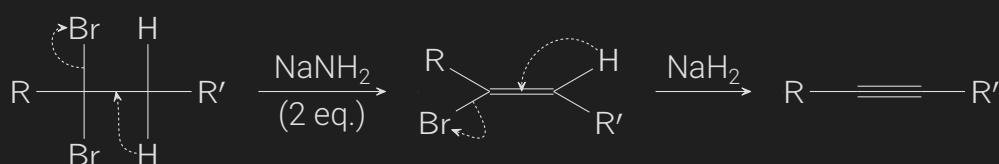
- Acetylide acts as a **base** when it reacts with 2°-halide or a 3°-halide due to steric crowding.
  - Is an E2 reaction.



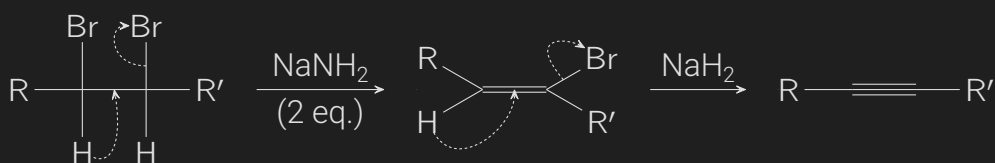
- The Zaitsev product is more likely to be the major product due to the thermodynamics (more energetically stable) than the Hofmann product; a bulkier base would likely increase the Hofmann product.

## Preparation of Alkynes

- Introductory example of a geminal dihalide going through two E2 reactions to generate an alkyne:



- Related example with a vicinal dihalide (halide on adjacent carbons):



## Regioselectivity and Stereospecificity of E2 Reactions

- **Regiochemistry**: when a chemical reaction is said to produce two different regiochemical outcomes.
  - **Regiochemical**: preference of chemical bonding or breaking **direction**.
- **Regioselective**: when there is a preference in products of a regiochemical reaction.
- **Zaitsev product**: name of the **more substituted** alkene that is generally observed to be the major product.
- **Hofmann product**: name of the **less substituted** alkene.

- There ratio between the Zaitsev and Hofmann product is dependent on a number of factors and often difficult to predict.
  - Steric hindrance of the base often plays a major role, often increasing the Hofmann product.
  - The outcome of E2 reactions can often be carefully **controlled by choosing the base**, despite difficulty in overall prediction.
- **Stereospecific**: when the stereoisomeric product of the E2 process depends on the configuration of the starting stereoisomeric substrate.
  - The stereospecificity is only relevant when the  **$\beta$  position has only one proton**.
- **Stereoselective**: when the substrate itself is not necessarily stereoisomeric, but can yield two stereoisomeric products, one of which that often has a higher yield.
  - Occurs when there are **more than one proton in the  $\beta$  position**.
- **Coplanar**: when the proton in the  $\beta$  position, the leaving group, and the two carbons atoms that form a double bond lie on the same plane.
  - Often leads only one stereoisomer product being formed, thus more often stereospecific.
    - If it stereoselective, then usually *trans* conformation is favored.
  - **Periplanar**: when the proton and leaving group are **nearly coplanar**; often is used in place of coplanar to incorporate both situations.
- **Syn-coplanar**: when the proton and the leaving group are **eclipsed** in a coplanar conformation.
  - Elimination in this state involves a higher energy transition state due to eclipsed geometry, and is **slower** than anti-coplanar arrangement.
- **Anti-coplanar**: when the proton and the leaving group are **staggered** in a coplanar conformation.
  - Elimination in this state involves a lower energy transition state due to staggered geometry, leading to a **faster** reaction relative to syn-coplanar.

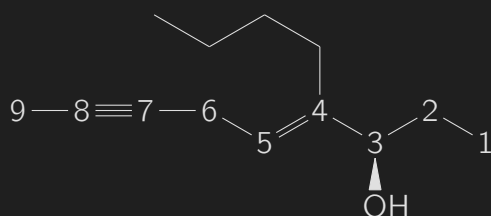
## Alkyne Nomenclature

### Basic Alkyne Nomenclature

- All other basic IUPAC rules still apply; the suffix is "yne".
- Find the longest carbon chain that includes both carbons of the triple bond.
- Number the longest chain starting at the end closest to the triple bond.
- Compounds with > 1 triple bond are called diynes, triynes, etc.
- Enynes are compounds that contain both double and triple bonds, and enynols also contain an alcohol.
- The functional groups have their assigned carbon numbers written directly before their name.

### Priority Rules

- More functional groups will change the as we get introduced to more, but for now we only need to know the following (somewhat follows electronegativity):
  1. Alcohol
  2. Alkenes
  3. Alkynes
  4. Alkyls
  5. Halogens
- Preference for naming order if multiple functional groups are present in the same chain: OH + DB + TB > OH + DB > OH + TB.
- When alkynes are substituents, then they are named as *k*-alkynyl. (*k* = locant)
- Example containing all three:



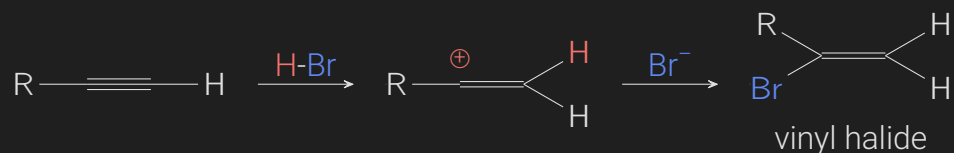
(3R,4E)-butylnon-4-en-7-yn-3-ol



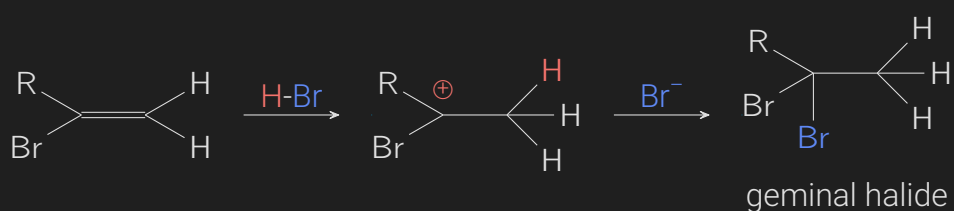
## Addition Reactions of Alkynes

### Hydrohalogenation of Alkynes

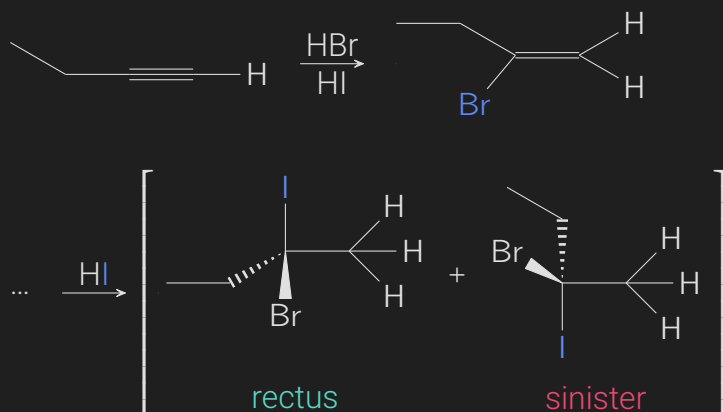
- Introductory example:



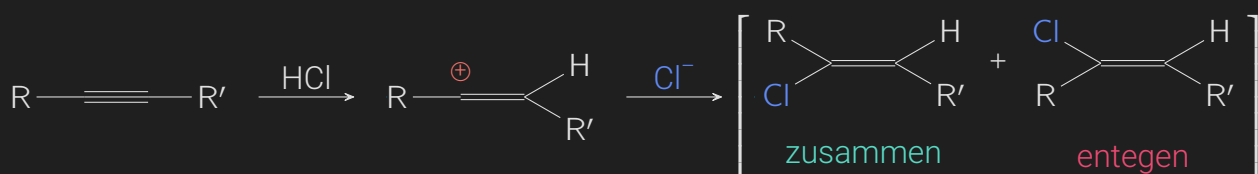
- Is **Regioselective** ↗
- Follows **Markovnikov's Rule** ↗
- This reaction can be done again (2 equiv):



- Geminal halide: a carbon that contains two halides.
- Related practice problem that generates chiral carbon due to use of different reagents for each equivalence (needs to be verified still, I might be wrong):

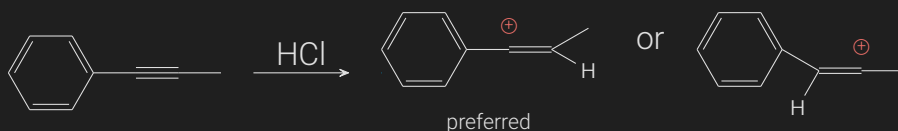


- Example with an internal alkyne; either side can be chosen if the R groups are not specified:

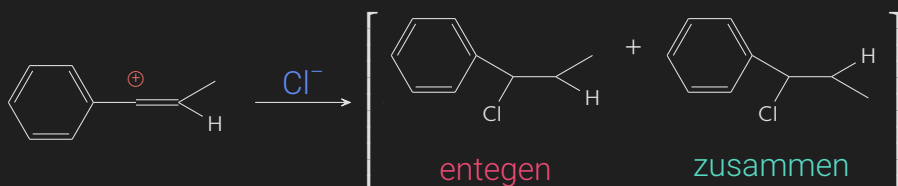


- Cl is higher priority than any carbon containing group (R), and any R' is higher than H, so both top and bottom attacks are possible.

- Related practice problem:

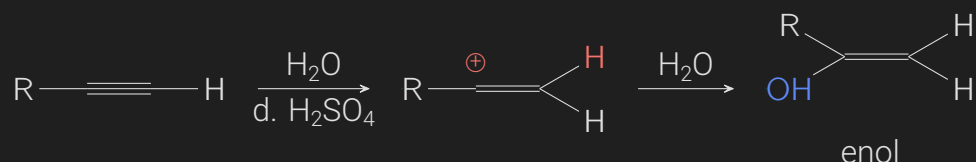


- The former carbocation intermediate is preferred due to resonance of the benzene ring, which does a better job stabilizing the carbocation.
- Continuing the reaction:

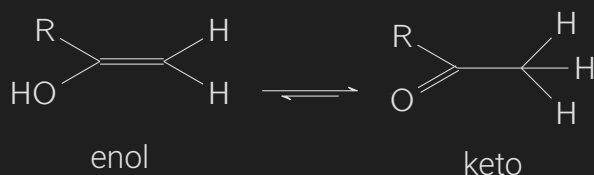


## Hydration of Alkynes

- Introductory example:



- Follows Markonikov's Rule ↗
- However, enols readily interconvert with more stable form:



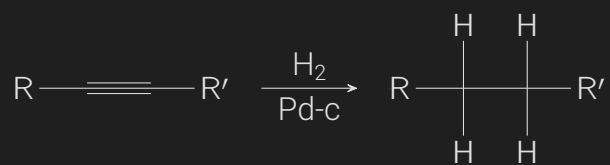
- **Tautomers:** a class of structural isomers (constitutional isomers) that readily interconvert, commonly due to the relocation of a proton (protonation-deprotonation) across a  $\pi$  bond.
  - The chemical reaction is called tautomerization; the concept is referred to tautomerism, which is sometimes desmotropism.
- Keto-enol tautomerism major product is the keto form, which does not allow for a second addition reaction.
- $\text{HgSO}_4$  is frequently used instead of d.  $\text{H}_2\text{SO}_4$ , due to the mercurinium intermediate vs. the carbocation intermediate, which is both faster and a means to reduce the probability of byproducts.

- Example of an alkyne in a hydroboration-oxidation reaction ↗:

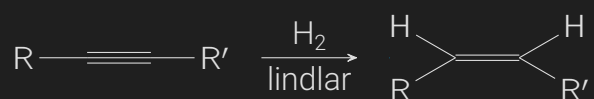
- **Aldehyde:** generally created by removing a hydrogen from an alcohol; in our case it is generated by the **anti-Markovnikov** reaction that results in a terminal enol, which then undergoes tautomerization and produces the aldehyde as the major product.

## Hydrogenation of Alkynes

- Complete hydrogenation of an alkyne:



- Alkyne  $\rightarrow$  cis-alkene; use of lindlar catalyst (Pd-c poisoned with lead) limits further reduction by controlling hydrogens available:

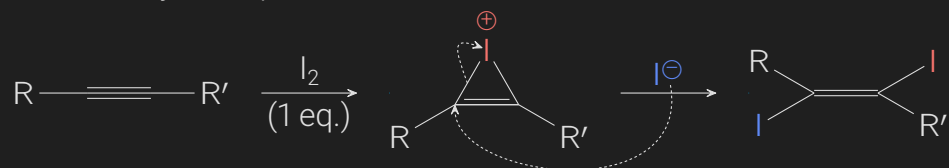


- Alkyne → **trans**-alkene; using generation of free radicals (•, single electron) that pair up with another electron generated by the dissociation of  $\text{Na} \rightarrow \text{Na}^+ + \text{e}^-$  to create a free pair of electrons that then receive a hydrogen from  $\text{NH}_3$ :

- Note, in lecture the added hydrogens were drawn separately; I am unsure, but I assume they happen near-simultaneously.

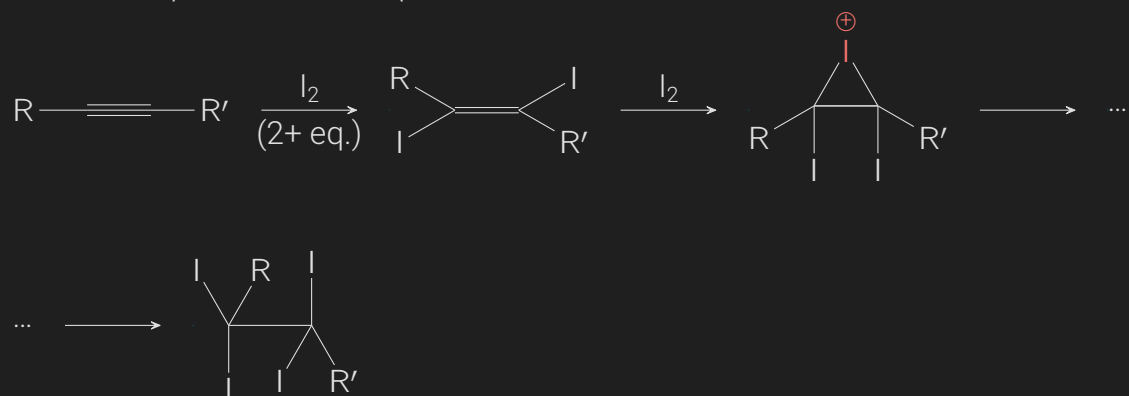
## Halogenation of Alkynes

- Introductory example:



- The 3-membered cationic ring with a double bond is not very stable, so it does not form readily with a rate that is  $10^3$ – $10^7$  times slower than that on an alkene.

- Same example, but with 2 equivalent or excess:

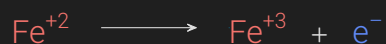


- Note: if you had controlled the second addition and added a different halide, then stereochemistry would have been important to consider since the products would have had chiral carbons.

# 16: Oxidation and Reduction

## Redox Basics/Review

- ▷ **Oxidation:** is the **loss of electrons** or an **increase in the oxidation state** of an atom, an ion, or of certain atoms in a molecule.



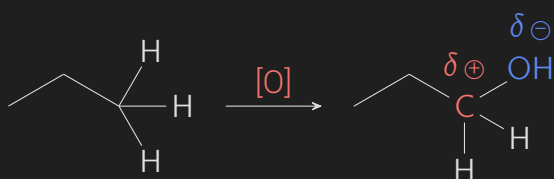
- ▷ **Reduction:** is the **gain of electrons** or a **decrease in the oxidation state** of an atom, an ion, or of certain atoms in a molecule (a reduction in oxidation state).



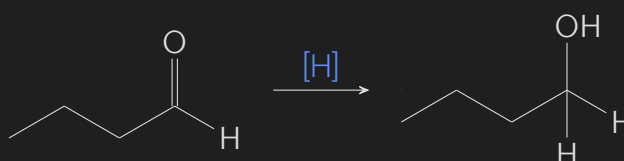
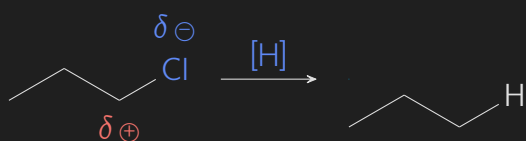
- ▷ **Redox (reduction-oxidation):** a type of chemical reaction in which the oxidation states of atoms are changed.
- Characterized by the actual or formal transfer of electrons between chemical species.
  - Most often one species (**the reducing agent**) undergoing **oxidation** while another species (**the oxidizing agent**) undergoes **reduction**.
- ▷ Many reactions in organic chemistry are redox reactions due to changes in oxidation states but without distinct electron transfer; rather changes in **electron density**.
- **Oxidation [O]:** going from a C–H → C– $\delta^{\ominus}$  bond; pulls **electron density away** from the carbon.
  - **Reduction [H]:** going from a C– $\delta^{\ominus}$  → C–H bond; pulls **electron density towards** the carbon.

## Redox Practice Examples

- Examples of oxidation reactions:



- Examples of reduction reactions:



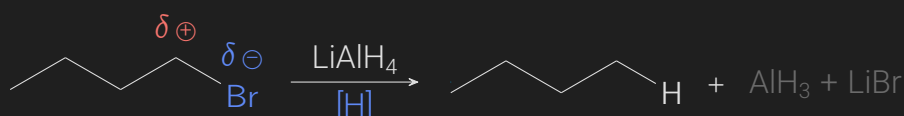
## Reduction Reactions

### Reduction Agents

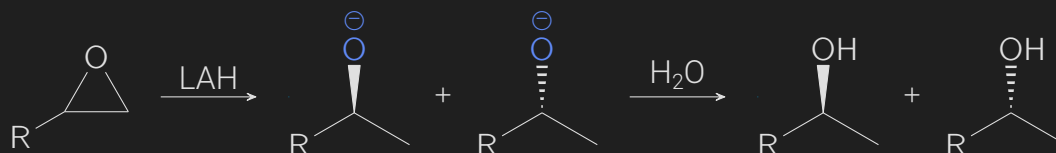
- **Hydride:**  $\text{H}^-$ , a negatively charged hydrogen ion (anion); commonly used as a **strong base** that react with **weak acids**, releasing  $\text{H}_2$ .
- $\text{NaBH}_4$ : sodium borohydride.
- $\text{LiAlH}_4$  (LAH): lithium aluminum hydride.
- Both  $\text{NaBH}_4$  and  $\text{LiAlH}_4$  are **hydride donors**; they give up a hydride to become neutral.
  - Boron < aluminum in terms of size; electrons are attracted to boron to a greater degree, making it harder to remove the hydride for boron vs. aluminum. Thus:
    - $\text{LiAlH}_4$  is a **stronger** reducing agent.
    - $\text{NaBH}_4$  is a **weaker** reducing agent.

### Reduction with $\text{LiAlH}_4$

- Example with an alkyl halide:



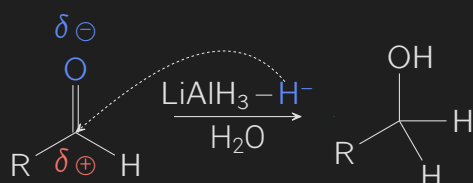
- Example with an epoxide:



- Remember: epoxide rings **no positive charge** will have the **less sterically hindered** side attacked.
- **Quenching:** deactivation of any unreacted reagents (adding a hydrogen source using  $\text{H}_2\text{O}$  for the negatively charged oxygen in this case).

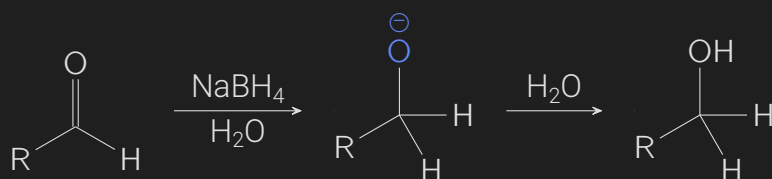
### Reduction of Aldehydes

- Example of reduction to 1° alcohol:



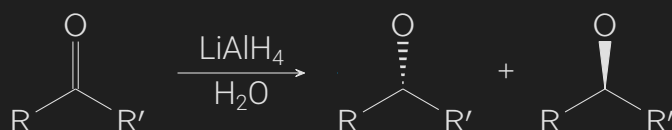
- Note: the reaction is done in two steps, but the addition of water was omitted here.

- The partial charge on the carbon double bonded to oxygen gives a slight **electrophilic** center for the **hydride** to attack due to the **inductive effect**.
- Same example as above, but with  $\text{NaBH}_4$  and showing the intermediate step:



## Reduction of Ketones

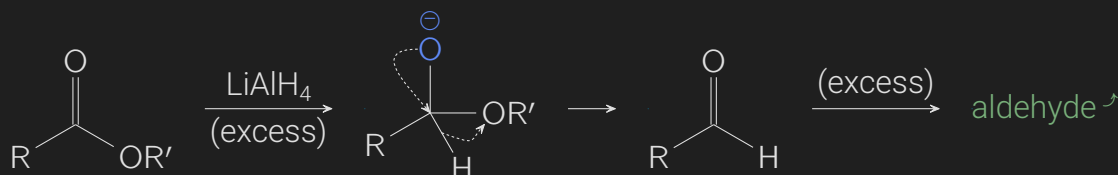
- Examples of generating racemic mixtures of 2° alcohols:



- Note: the above can be done with  $\text{NaBH}_4$ , it's just slower.
- The inductive effect is slightly increased vs. aldehydes, since there are now two alkyl groups pushing electron density.

## Reduction of Esters

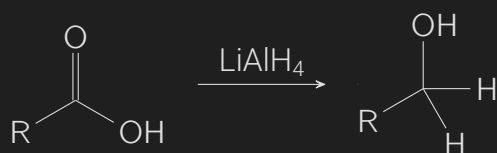
- First the ester is reduced to an aldehyde, then in presence of excess it will be further reduced from an aldehyde to a 1° alcohol.



- Resonance (shared electron density due to delocalization of electrons between either oxygen) is stronger than inductive effect, so **only reduction using  $\text{LiAlH}_4$**  works.

## Reduction of Carboxylic Acids

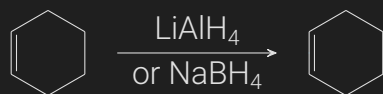
- Very similar to Esters, which ends up producing a 1° alcohol:



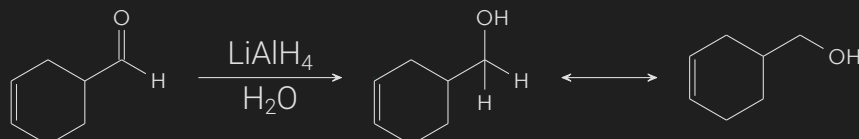
- Again, the presence of resonance will only allow the use of  $\text{LiAlH}_4$ ; the first step will not occur if  $\text{NaBH}_4$  is used as it is too weak to be a reagent.

## Reduction Practice Problems

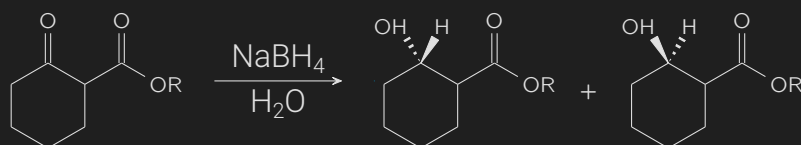
1. No reaction, needs carbonyl (C=O) functional group to proceed:



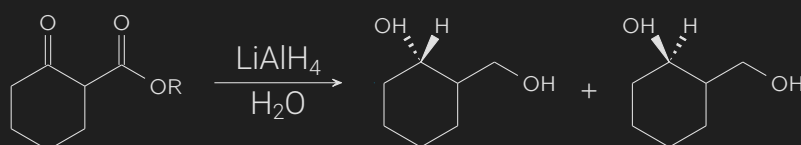
2. Example that contains a carbonyl group:



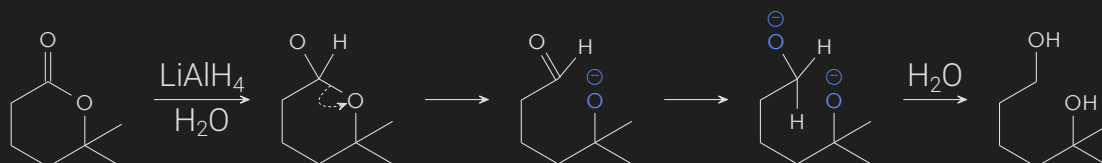
3. Example with a ketone and an acyclic ester:



- 3b. Same example as above but with LiAlH<sub>4</sub> (assuming excess):



4. Example with a cyclic ester (assuming excess):

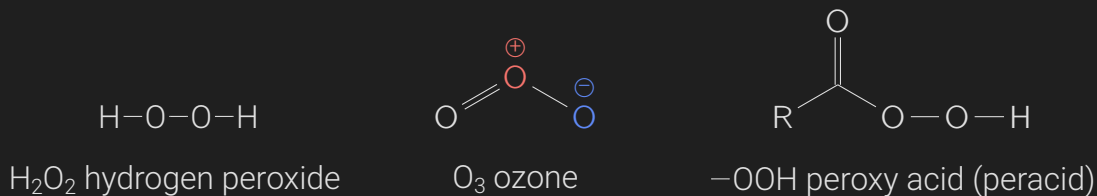




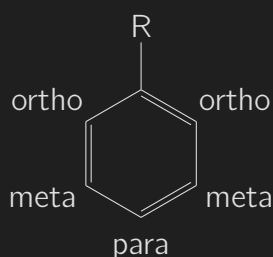
## Oxidation Reactions

### Oxidizing Agents

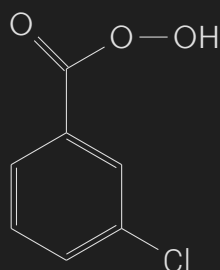
- **Peroxide reagents:** reagents that contain O—O linkage of some kind:



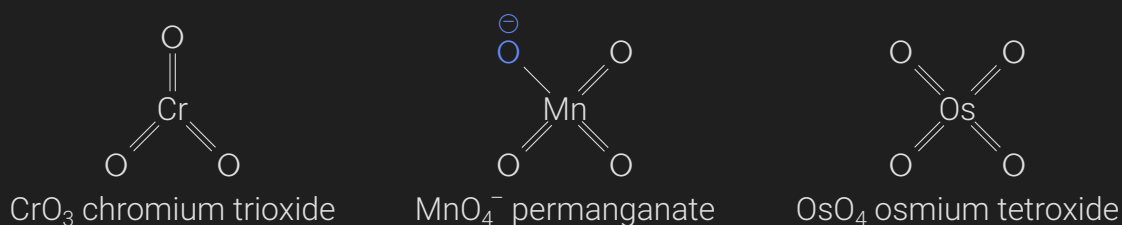
- **Arene substitution patterns:** IUPAC nomenclature for naming substituents other than hydrogen in relation to each other on an aromatic hydrocarbon:



- **meta-Chloroperoxybenzoic acid (mCPBA):** a strong and widely used oxidant in organic synthesis due to relative ease of handling.

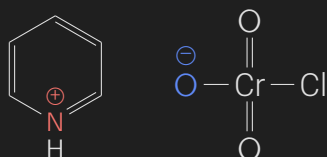


### Metal Based Oxidizing Agents



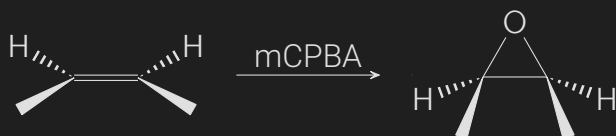
- $\text{KMnO}_4$  is **inexpensive**, but a very **strong oxidizing** agent and is **not soluble** in organic solvents.
  - $\text{MnO}_4^-$  comes as  $\text{KMnO}_4$ ; the anion must be created in order to be used as a reagent.
  - Keeping  $\text{KMnO}_4$  cold can help reduce activation energy, leading a reduction of the more oxidized byproduct.

- $\text{OsO}_4$  is **very expensive**, but a **mild oxidizing** agent that is **soluble** in organic solvents.
  - N-methylmorpholine N-oxide (NMO): used with  $\text{OsO}_4$  to reduce cost; it oxidizes the byproduct ( $\text{Os}^{+6}$ ) back to  $\text{OsO}_4$  in solution, allowing for reuse.
- $\text{CrO}_3$  is a **strong oxidizing** agent that is **not soluble** in most organic solvents; it tends to explode in the presence of organic compounds and solvents.
  - In water it forms chromic acid and anhydrides, from which salts such as sodium dichromate ( $\text{Na}_2\text{Cr}_2\text{O}_7$ ) and PCC.
  - Other chromium based oxidizing reagents:
    - $\text{NaCrO}_4$ : sodium chromate.
    - $\text{K}_2\text{Cr}_2\text{O}_7$ : potassium dichromate.
- **Pyridinium chlorochromate (PCC)**:  $[\text{C}_5\text{H}_5\text{NH}]^+[\text{CrO}_3\text{Cl}]^-$  — a **mild** oxidizing reagent primarily used for **selective oxidation** of alcohols to **aldehyde or ketones** rather than carboxylic acid.

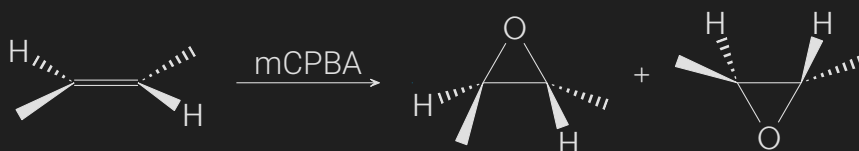


## Epoxidation

- Example of oxidizing a *cis*-alkene to a *cis*-epoxide:



- Note: epoxide rings are always (commonly?) made when using mCPBA.
- The epoxide ring is an example of a **meso compound**, where there are chiral centers, but there is a plane of symmetry making it **superimposable on its mirror image**, so no other products are made.
- Similar to example of above, but with a *trans*-alkene to a *trans*-epoxide:



- The *trans*-epoxide ring is no longer a meso compound, so you must show both products; one when the ring forms on the top and one where the ring forms on the bottom.

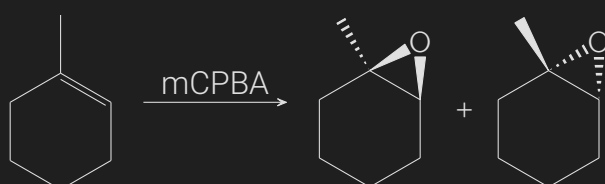
- These examples show that epoxidation reactions are **concerted** reactions, since there is no mixture of products between cis and trans products; it's dependent on the starting compound.

### Epoxidation Practice Problems

1.

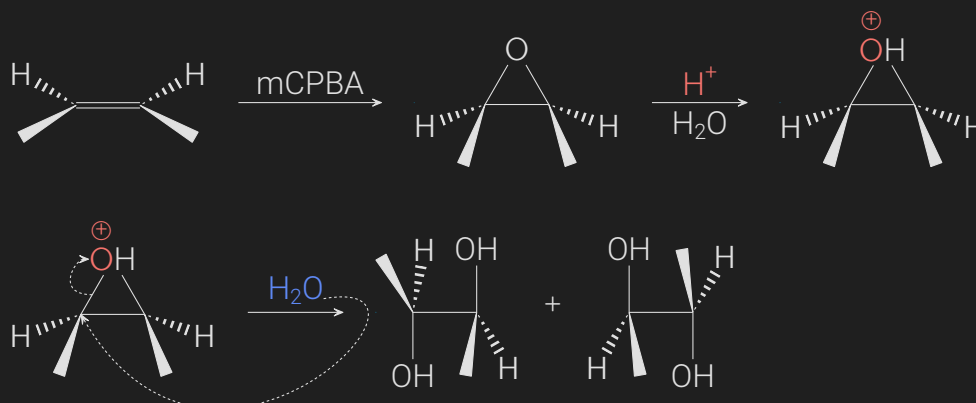


2.



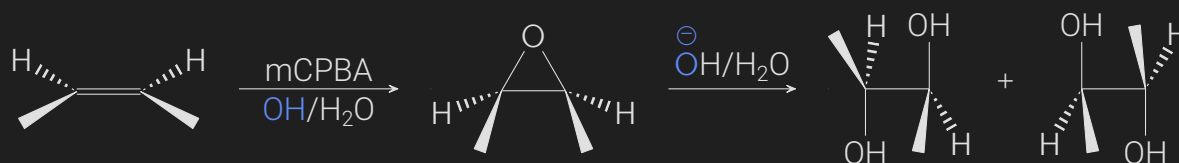
### Trans Dihydroxylation

- Acid catalyzed:



- If both carbon centers in a product have the same configuration (S–S, R–R), then means it must have as corresponding enantiomer; R–S would be meso.
- Our first product is S–S, so we must show the second product, where OH comes from the top vs. the bottom.

- Base catalyzed:

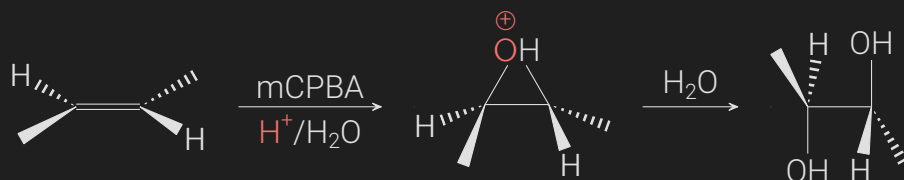


- Note: the result is the same as acid catalyzed conditions when both sides of the alkene are equally substituted.

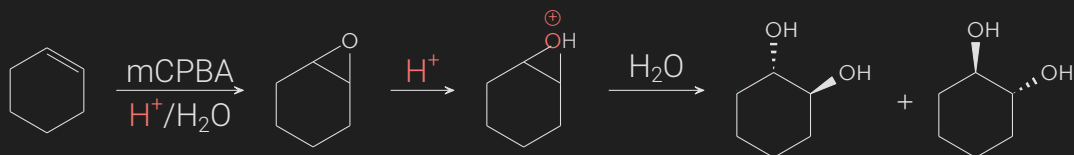
- However, under **acidic conditions** then the **more substituted** side will get attacked, while under **basic conditions** then the **less substituted** side will get attacked.

### Trans Hydroxylation Practice Problems

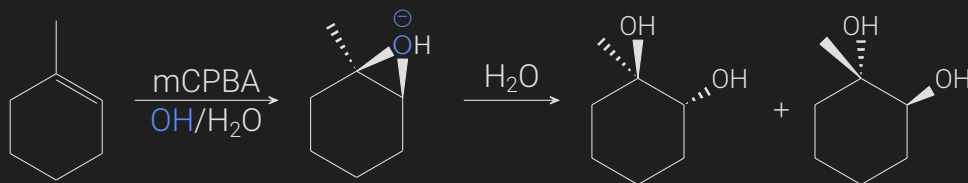
- *Trans*-alkene reactant (**acid catalyzed** in this case, but a **base catalyzed** would produce same product):



- Cyclohexene reactant:

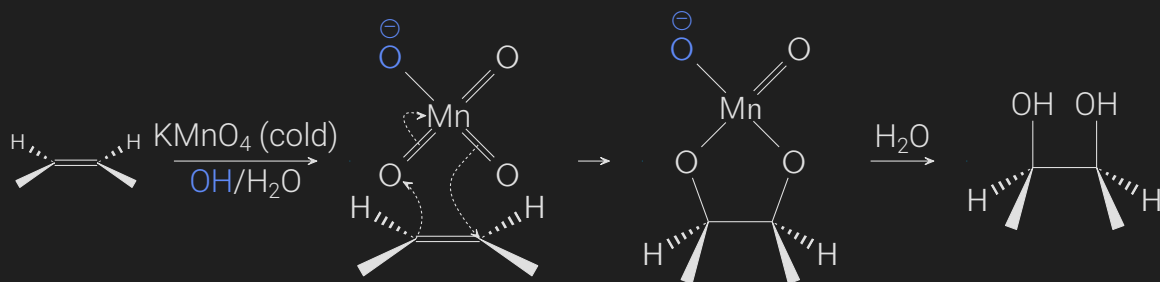


- 1-methylcyclohexene reactant:

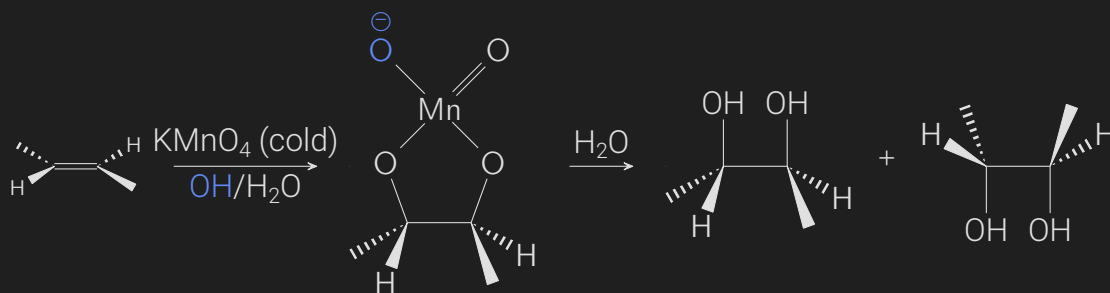


### Syn Dihydroxylation

- Using potassium permanganate on a *cis*-alkene:



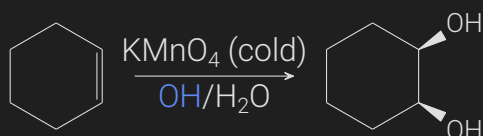
- The addition of  $\text{MnO}_4^-$  is a **concerted** reaction, which is then replaced by hydroxyl groups due to addition of water to create a syn product.
- The product is a meso compound, so it is achiral, making it have no enantiomers.
- Same reaction, but on a *trans*-alkene:



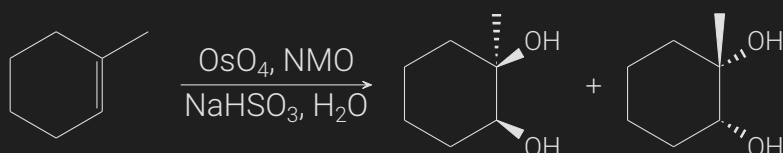
- The product is no longer chiral, giving us different products depending on which side  $\text{MnO}_4^-$  attached to.

### Syn Dihydroxylation Practice Problems

- Cyclohexene with cold potassium permanganate:

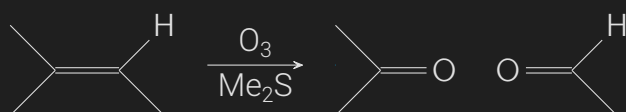


- 1-methylcyclohexene with osmium tetroxide:

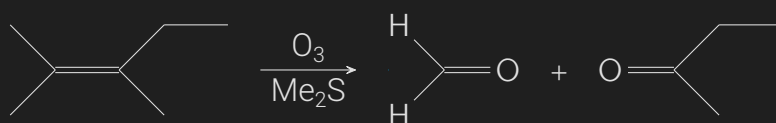


### Ozonolysis

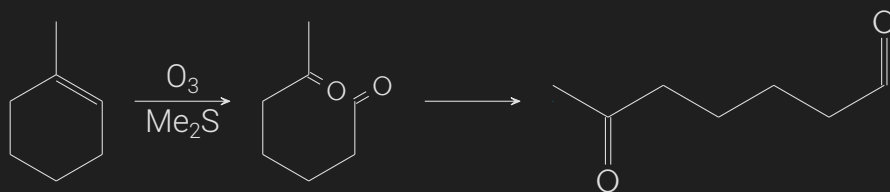
- Ozonolysis:** when the unsaturated bonds of alkenes, alkynes, or azo compounds (azo compounds not important for this class) are **cleaved** with ozone.
- Basic example demonstrating bond cleavage:



- $\text{Me}_2\text{S}$ : dimethyl sulfide; used as reducing agent that decomposes the intermediate (ozonide), making dimethyl sulfoxide (DMSO).
- Alkenes can be oxidized with ozone to form alcohols, aldehydes or ketones (depends on substituents), or carboxylic acids.
- Example of ozonolysis on an alkene, generating both an aldehyde and a ketone due to difference in substituents:



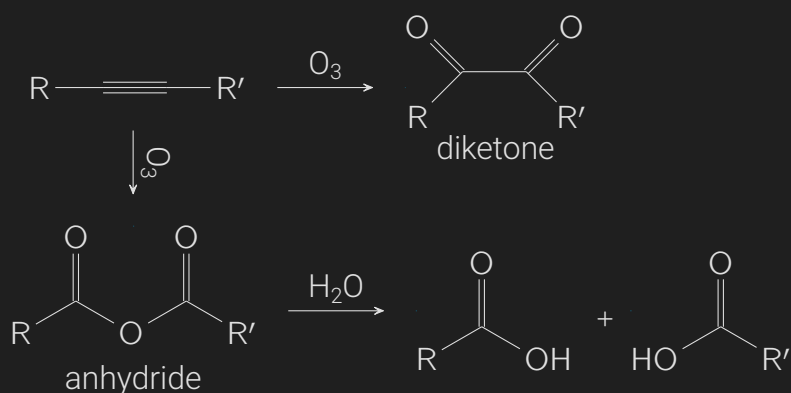
- Example with 1-methylcyclohexene:



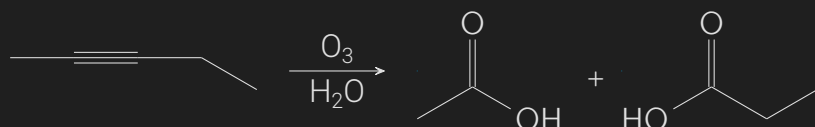
- Ozonolysis of alkynes generally gives an acid anhydride or diketone product, unlike the complete fragmentation in alkenes.

- If the reaction is performed in the presence of water, then the anhydride hydrolyzes to give two carboxylic acids.

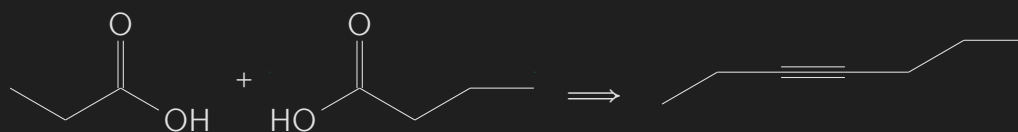
- Example of ozonolysis on alkynes:



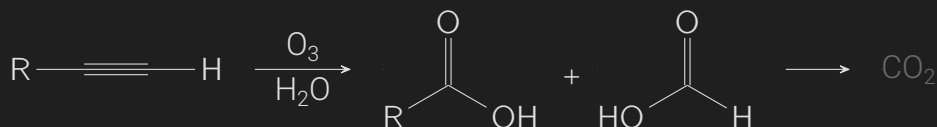
- Example of alkyne with different substituents:



- Retro synthesis (products → reactants) example:



- Example with a terminal alkyne:



- Terminal alkynes generate a carboxylic acid and a formic acid; formic acid will break down to CO<sub>2</sub>.