

Organic Chemistry II

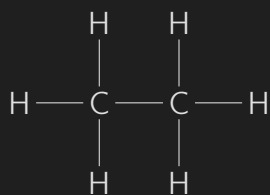
14: Alkenes	3
Alkenes Basics/Review	3
Types of Alkenes.....	3
Relevant Review	4
Common Patterns Between Formal Charge and Lone Pairs.....	4
Chirality	5
Cahn-Ingold-Prelog System	5
Rearrangements	6
Nomenclature of Alkenes	8
Basic Alkene Nomenclature Rules	8
Alkenes Containing an Alcohol.....	8
Addition Reactions of Alkenes	10
Syn Addition	10
Anti Addition	10
Hydrogenation	11
Hydrogenation Practice Problems	11
Hydrohalogenation	12
Hydrohalogenation Practice Examples	13
Addition of Water or Alcohol	13
Oxymercuration-Demercuration.....	15
Related Practice Problems	16
Hydroboration-Oxidation.....	18
Halogenation	19
15: Alkynes	21
Alkynes Basics/Review	21
Acetylides.....	21
Preparation of Alkynes	22
Regioselectivity and Stereospecificity of E2 Reactions	22
Alkyne Nomenclature	24
Basic Alkyne Nomenclature.....	24
Priority Rules.....	24
Addition Reactions of Alkynes	25
Hydrohalogenation of Alkynes	25
Hydration of Alkynes.....	26
Hydrogenation of Alkynes.....	27
Halogenation of Alkynes	28
16: Oxidation and Reduction	29
Redox Basics/Review	29
Redox Practice Examples	29

Reduction Reactions	30
Reduction Agents	30
Reduction with LiAlH_4	30
Reduction of Aldehydes	30
Reduction of Ketones	31
Reduction of Esters	31
Reduction of Carboxylic Acids	31
Reduction Practice Problems	32
Oxidation Reactions	33
Oxidizing Agents	33
Metal Based Oxidizing Agents	33
Epoxidation	34
Epoxidation Practice Problems	34
Trans Dihydroxylation	35
Trans Hydroxylation Practice Problems	35
Syn Dihydroxylation	36

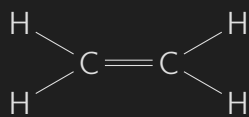
14: Alkenes

Alkenes Basics/Review

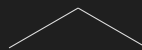
▷ Alkanes vs alkenes:



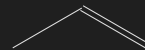
Saturated
alkanes ethane



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

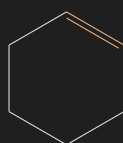
- Basic types of alkenes:



Terminal Alkene

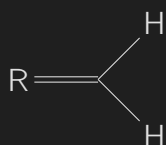


Internal Alkene

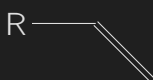


Cycloalkene

- Types of terminal alkenes:



Methylene



Vinyl

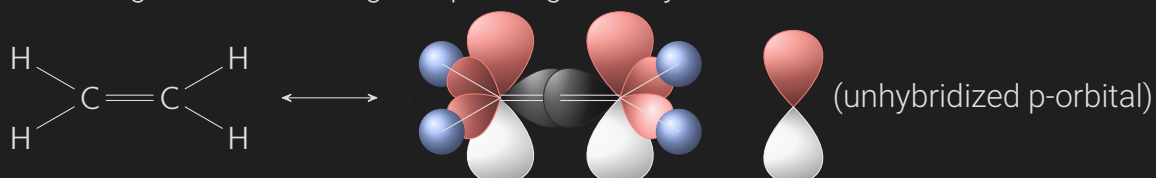


Allyl

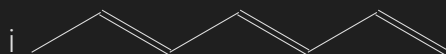
- "R" always tells you it's a carbon containing functional group, or hydrogen.
- "A" can be used to represent any functional group.

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?

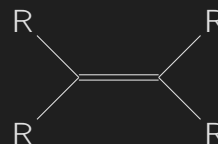


i $\frac{1}{2}(2(7) + 2 + (0) - (3 + (5(1)) + 2) - 0) = 3$



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

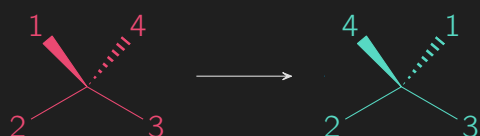
- **Achiral (nonsuperimposable)**: when an object's mirrored version is identical to the actual object.
- **Chiral**: objects that are not superimposable.
 - The most common source of molecular chirality is the presence of a **carbon bearing four different groups**.
- All three-dimensional objects can 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 H^- .
 - Involves the rearrangement of the carbocation to a more stable variant due to change migration of the 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.

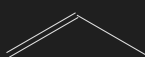
Nomenclature of Alkenes

Basic Alkene Nomenclature Rules

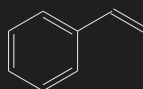
- Alkenes are named using the same four steps in the previously used nomenclature, though the suffix of "ane" is replaced with "ene."
- When choosing the parent chain, choose the parent chain that **includes** the double bond.
- When numbering the parent chain, the double bond should receive the **lowest** 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



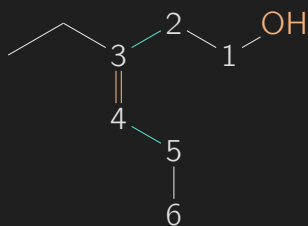
Styrene

- 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:

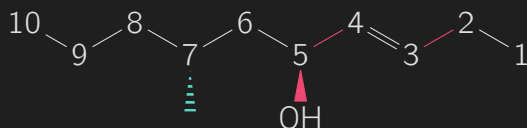


(3Z)-3-propyl-hex-3-en-1-ol

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:



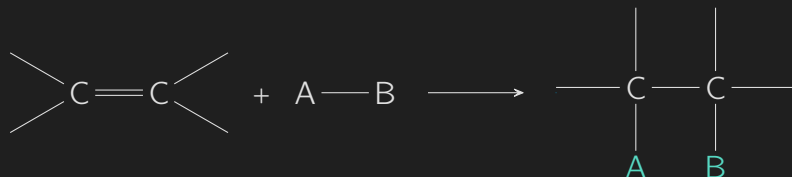
(3E,5S,7R)-4-methyl-3-en-5-ol

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

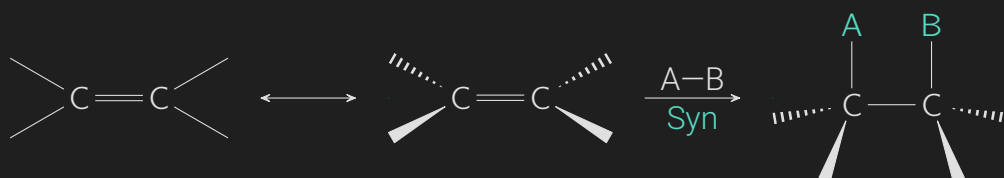
Addition Reactions of Alkenes

Syn Addition

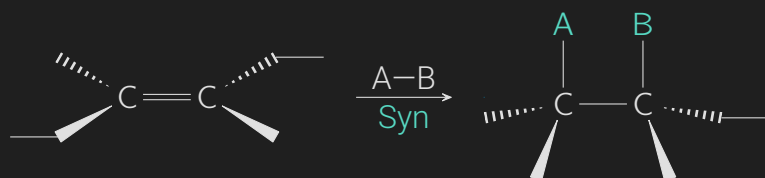
- Syn addition means that both components (A & B) came in from the same side.



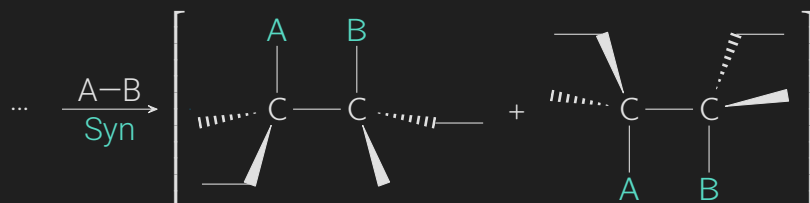
- When there is mixture of products, then the stereochemistry is important—A & B could come from different directions.
- Switching to a 3D perspective, with groups pointing towards and away from the viewer, rather than a flat view:



- 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.

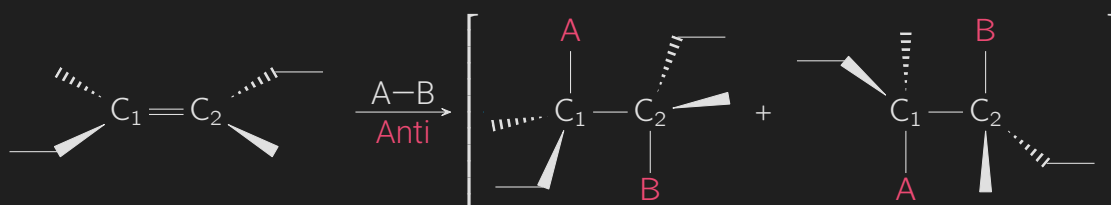


- The product in this case has **chiral centers**, so enantiomers must be considered.



Anti Addition

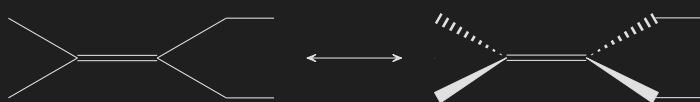
- Anti addition means that the added components come in from different sides.



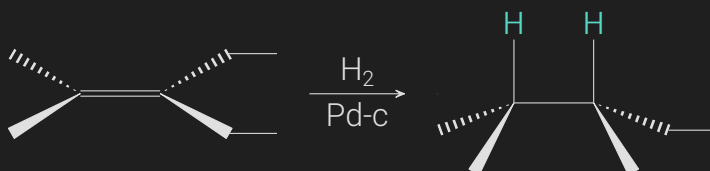
Hydrogenation

- **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** (π 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:

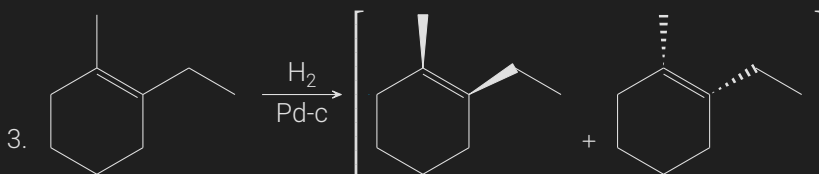
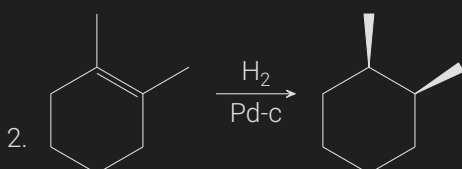
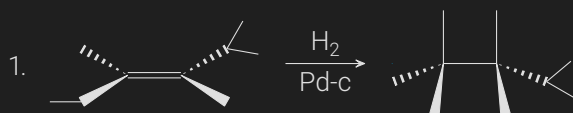


- Then apply H_2 with catalyst to trigger syn addition:



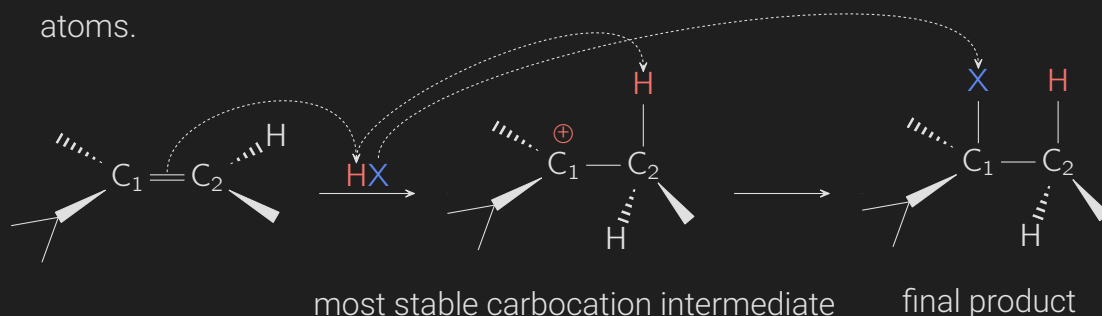
- Product is achiral; no enantiomers. Bottom would attack just flips the orientation; not a different product.

Hydrogenation Practice Problems

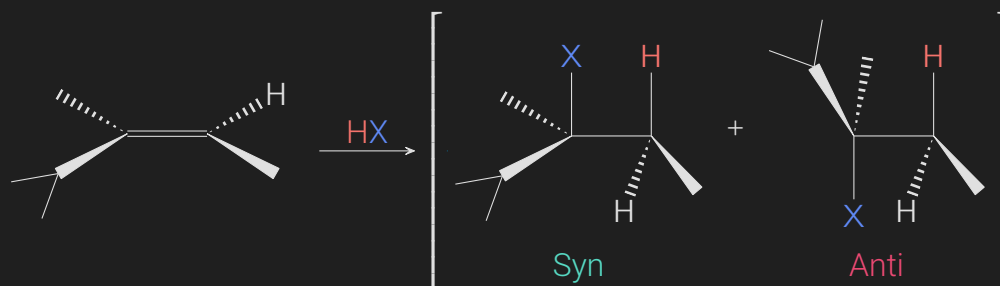


Hydrohalogenation

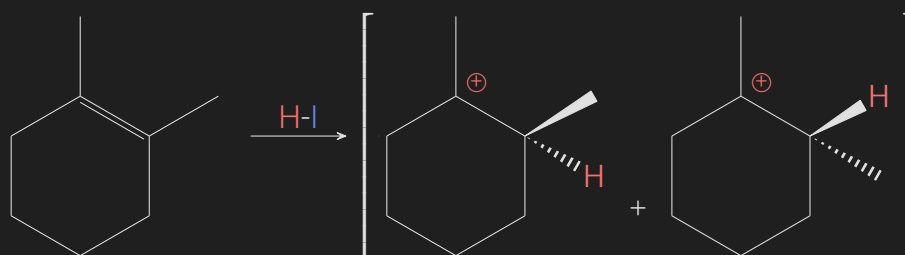
- **Hydrohalogenation:** the electrophilic addition ($\pi \rightarrow 2\sigma$ bonds) of hydrohalic acids (HX, e.g., HCl or HBr) to alkenes to yield the corresponding haloalkanes.
- **Markovnikov's Rule:** an addition of a protic acid (HX) or other polar reagent to an asymmetric alkene results in the **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.



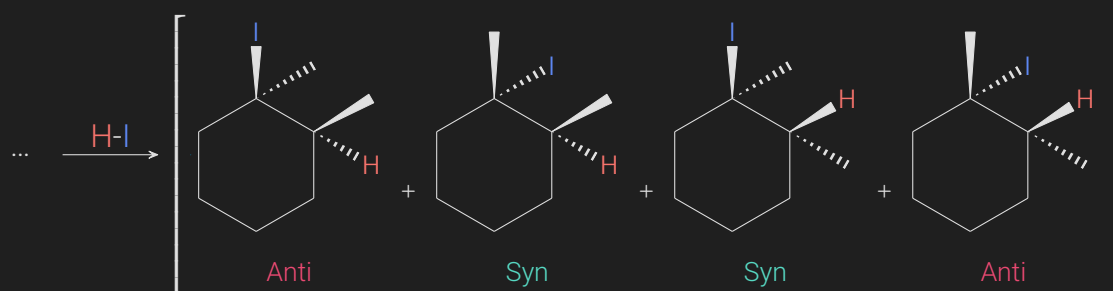
- However, we have a chiral carbon, so we have to take enantiomers into account:



- 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:

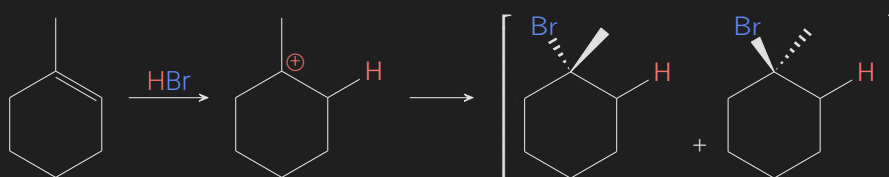


- Again, this first step shows the most stable carbocation intermediate, which helps determine where the H^+ will attach to. In this case either location works, so four products are formed, each with syn and anti enantiomers.



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

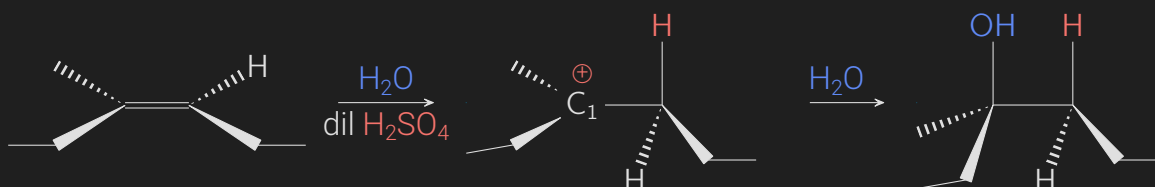
Hydrohalogenation Practice Examples



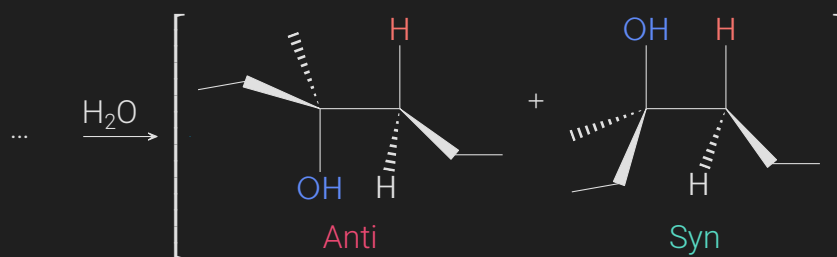
Addition of Water or Alcohol

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.

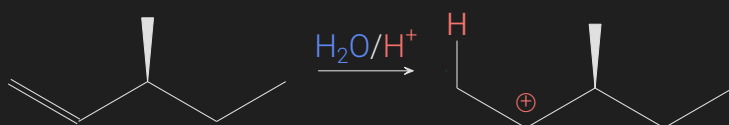
- Note: the hydronium ion (H_3O^+) forms via the reaction of H_2SO_4 with H_2O , and is the source of the proton that reacts with the starting alkene.
- H–OH and RO–H helps to visualize where the proton is coming from. What ever works with water also works with alcohol and vice versa.
- An example that is very similar to the example from **hydrohalogenation** ↗:



- Note: H_2SO_4 is a **strong acid** and can be generalized to H^+ or HA.
- Note: I occasionally use **red** for **cations**, **acids**, and E^+ (electrophile). I also use **blue** for **anions**, **bases**, and 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:

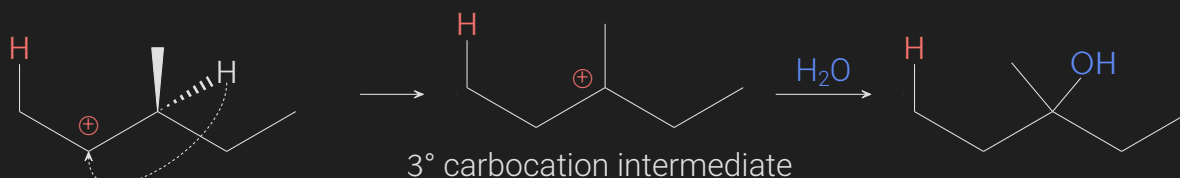


- Example 2:

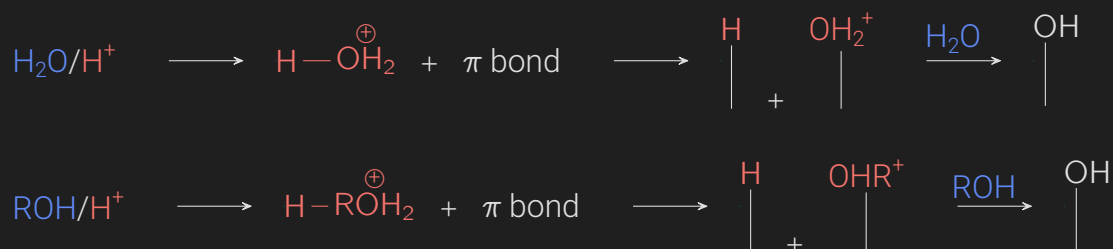


- **Rearrangement** \rightarrow is always a possibility to be considered when cation are generated. In this case, a 2° carbocation was generated, but we can do better:

- 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, H_2O and alcohols (ROH) behave very similarly; the reduction of the π bond generates 2 σ 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.



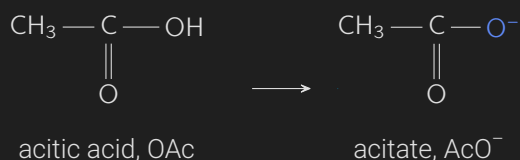
- **Problems of going through carbocation intermediate:**

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

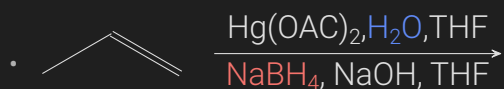
- C^+ can cause rearrangements leading to **multiple products**.

Oxymercuration-Demercuration

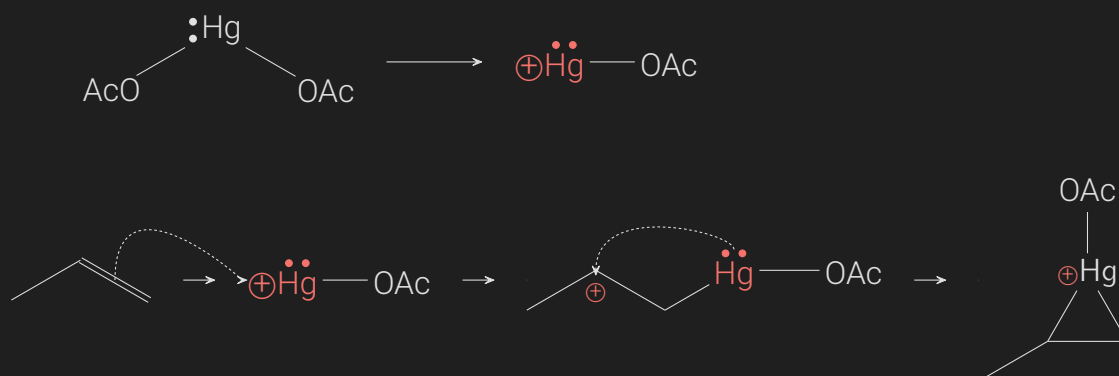
- **Oxymercuration-Demercuration** is another electrophilic addition organic reaction that transforms an alkene into a neutral alcohol.
- Reacts with mercuric acetate ($AcO-Hg-OAc$) in aqueous solution to yield the addition of an acetoxymcury ($HgOAc$) group and a hydroxy (OH) group across the double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



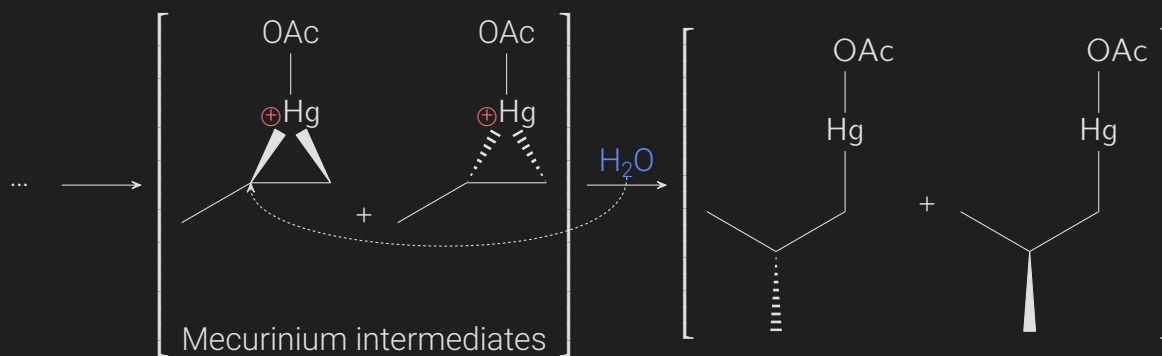
- Carbocations are not formed in this process and thus rearrangements are not observed.
- The reaction follows **Markovnikov's rule**.
- The reaction is stereospecific—it is always an **anti addition**.
- Example using propylene:



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

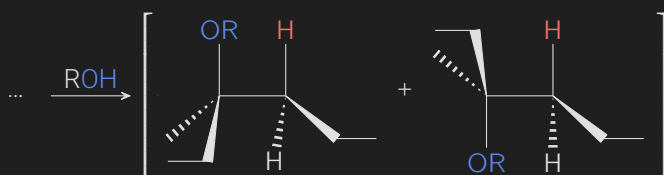
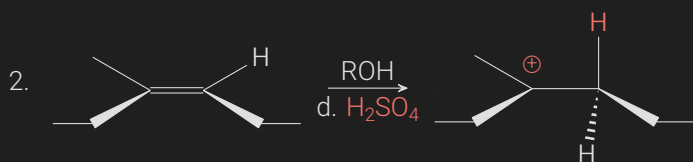
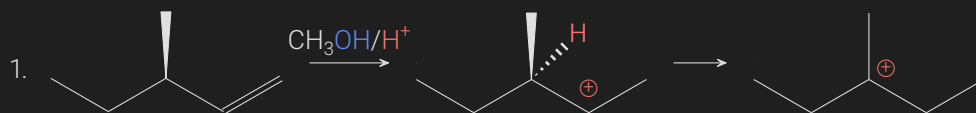


- Note: the above is a concerted (one step) process, but drawn out for illustration.
- Also, we are not done, we have a chiral center that forms, plus it is just an intermediate step, a nucleophilic attack will occur on the strained (highly reactive) epoxide:

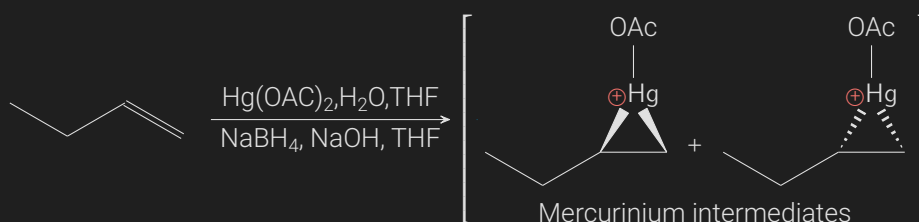


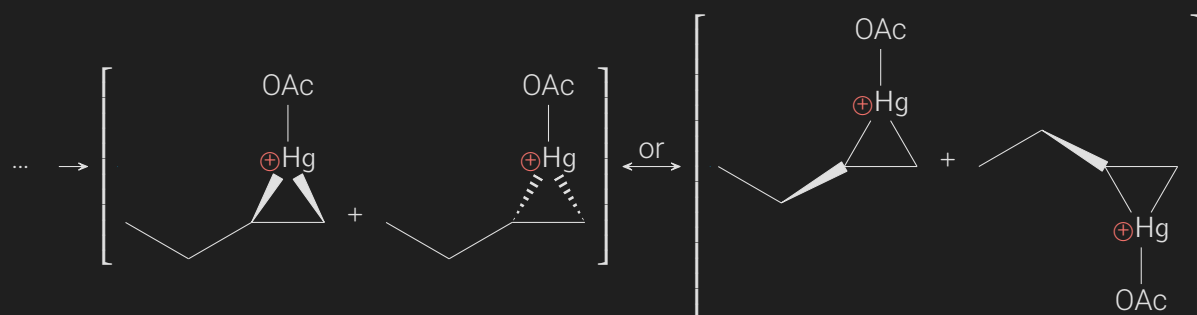
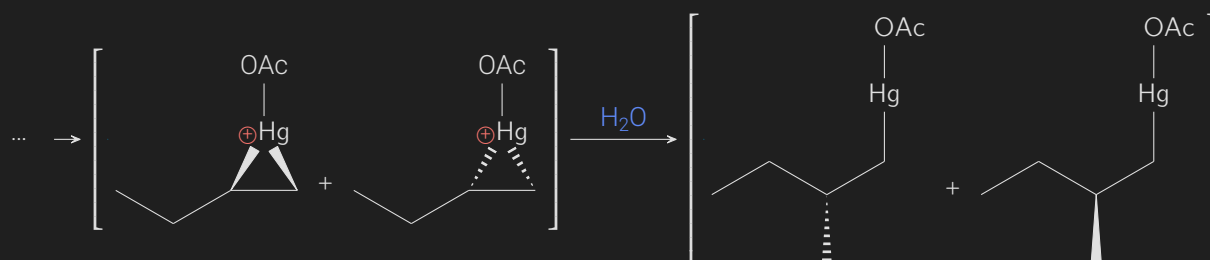
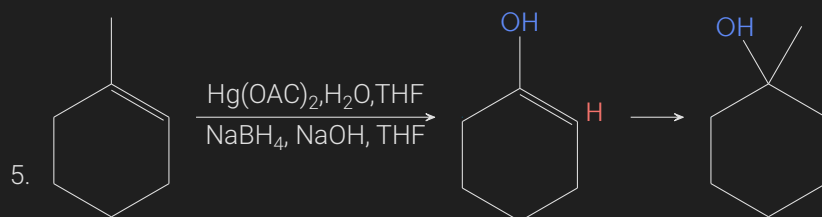
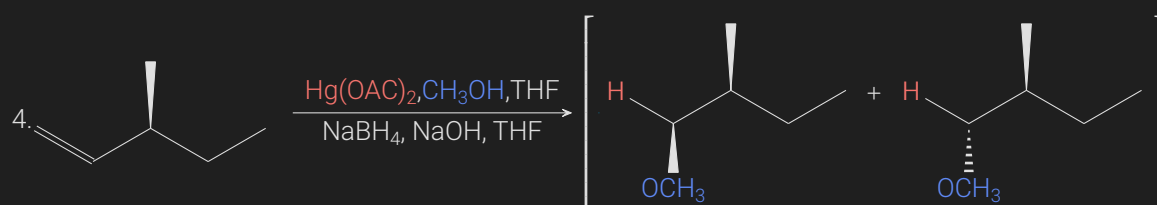
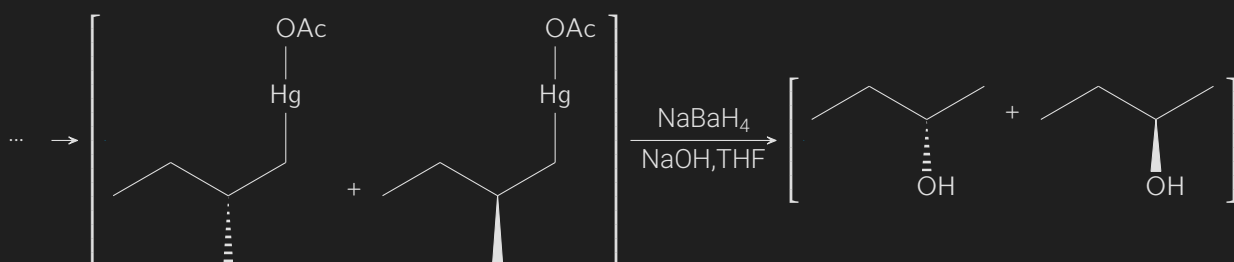
- Notice the nucleophile attack the carbon with the greater flow of electrons (more substituted), since there was a positive charge on mercury. Epoxides with no charge are attacked on the side with less steric hindrance.
- Also, the nucleophilic attack occurs on the opposite side of the plane since there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

Related Practice Problems

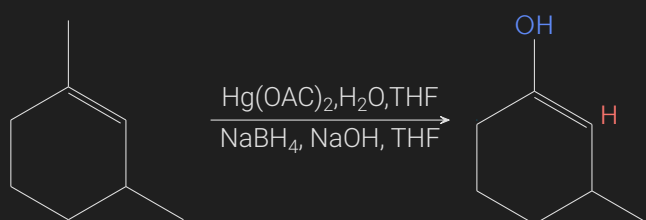


3. + Alternate ways of drawing rings (was done in lecture):

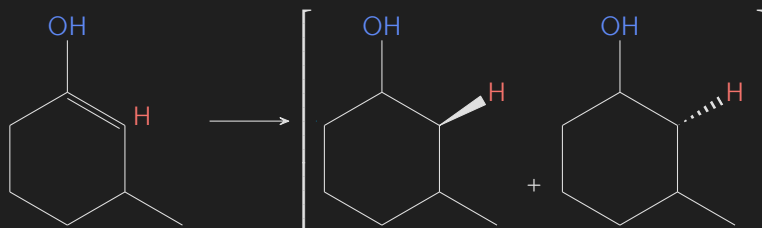


**Oxymercuration:****Demercuration:**

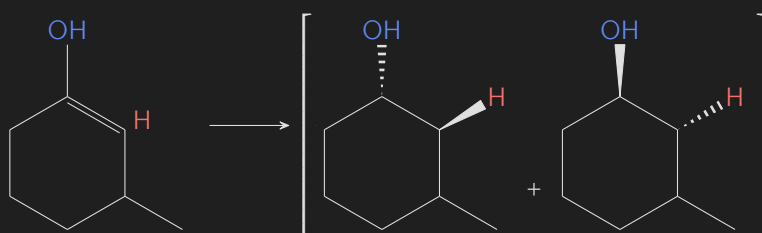
6. (was done in lecture)



- 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:

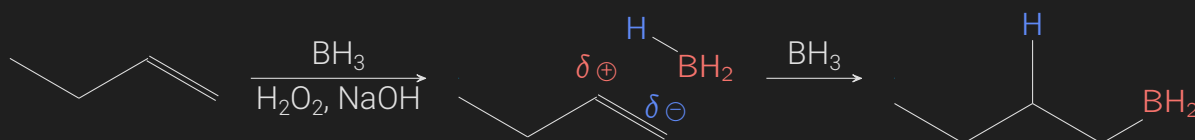


Hydroboration-Oxidation

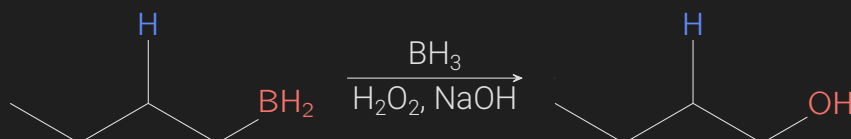
- Hydroboration-Oxidation:** a two-step hydration reaction that converts an alkene into an alcohol.
 - Results in the **syn addition** of a hydrogen and a hydroxyl group where the double bond had been.
 - An **anti-Markovnikov reaction**—the hydroxyl group attaches to the less-substituted carbon.
 - 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 BH_3 , B_2H_6 , R_2BH are used. The presence of Boron is key.
- Like H_2O and 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.



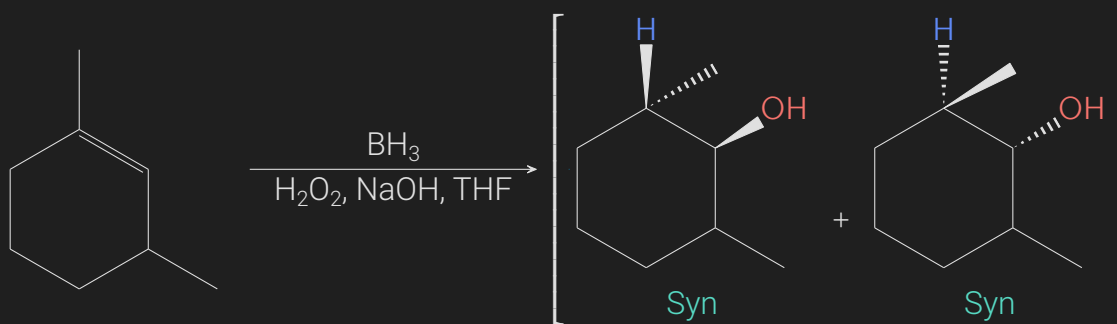
- There are no chiral centers, but there is still one more step—the oxidation:



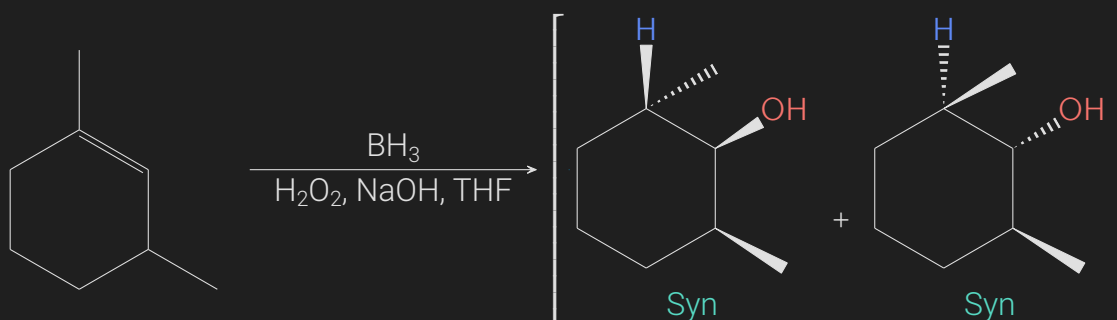
- If we had used $\text{Hg}(\text{OAc})_2$, then the above reaction would be different; partial charges change the possible final products: $\overset{\delta^-}{\text{H}}-\overset{\delta^+}{\text{BH}_2}$ vs. $\overset{\delta^+}{\text{H}}-\overset{\delta^-}{\text{OH}_2}$:



- Revisiting a practice example, using different reagents:

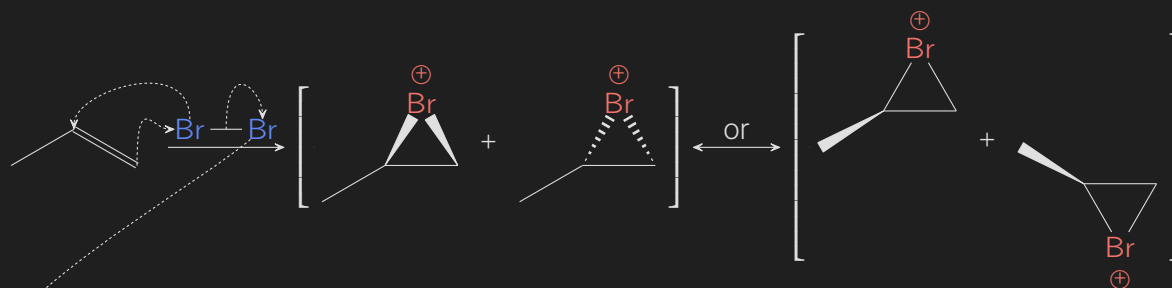


- If the untouched methyl happened to be above or below the plane initially, then you would keep that the same, e.g:

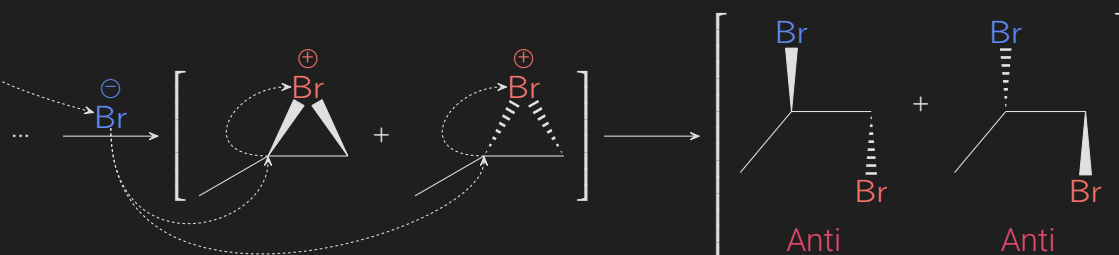


Halogenation

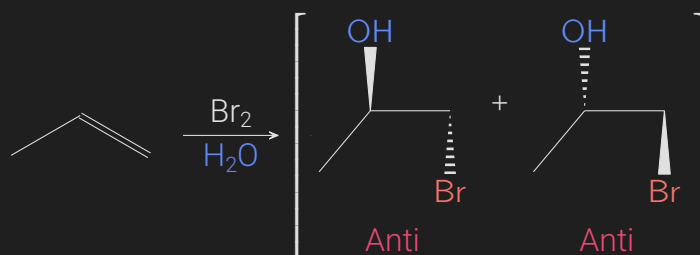
- Halogenation:** a reaction that involves the addition of one or more halogens to a compound or material.
 - The addition of halogens to alkenes proceeds via intermediate halonium ions.
 - Halonium ion:** any onium ion containing a halogen atom carrying a positive charge. This cation has the general 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.



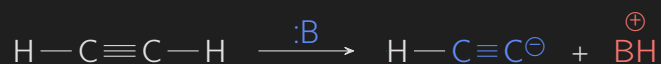
15: Alkynes

Alkynes Basics/Review

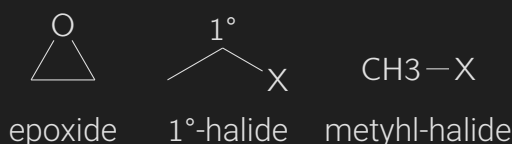
- ▷ **Alkynes**: an unsaturated hydrocarbon containing at least one carbon—carbon triple bond.
 - Contains two unhybridized p-orbitals (sp) on each carbon.
 - $\delta^+ \quad \delta^- \quad \delta^- \quad \delta^+$
 $\text{H} - \text{C} \equiv \text{C} - \text{H}$
 - Large amount of s character (sp: 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_2H_2 (ethyne)

Acetylides

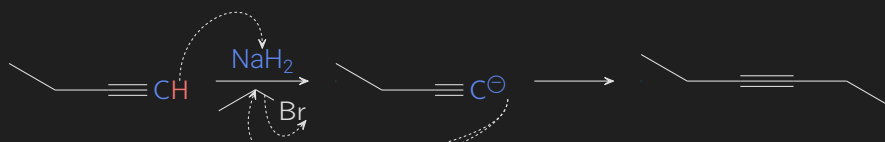
- ▷ **Acetylide**: an alkyne with a negatively charged carbon on one end, e.g.,



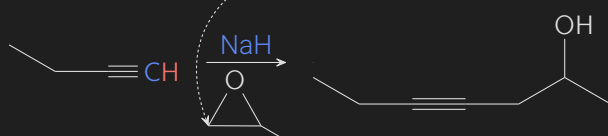
- :B is a name of generic base, typical bases used:
 - $\text{NaNH}_2 \rightarrow$ sodamide, or $\text{NaH} \rightarrow$ sodium hydride.
- Acetylide acts as a **nucleophile** when it reacts with an epoxide, 1°-halide, or a methyl-halide.



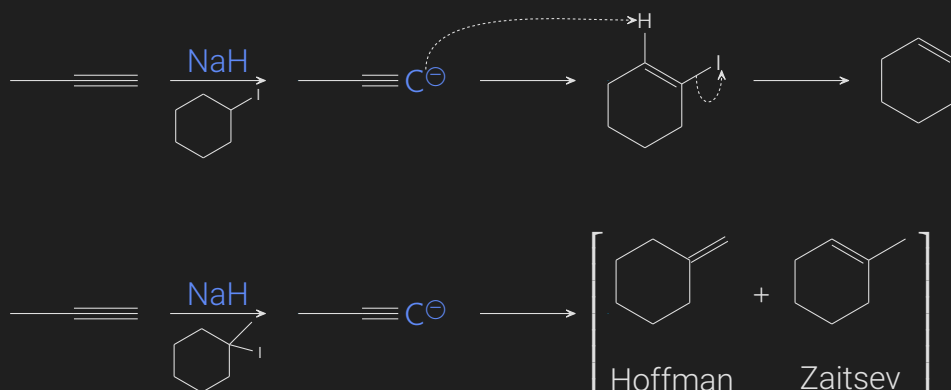
- Is a $\text{S}_{\text{N}}2$ reaction.
- Can be used for chain extension, e.g.,



- Example two:



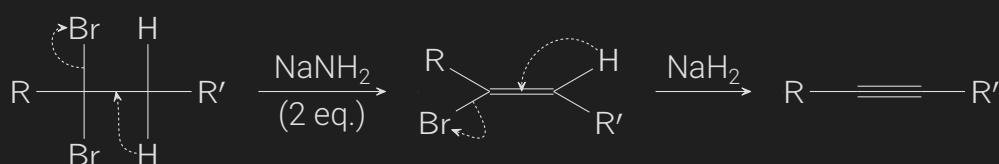
- Acetylide acts as a **base** when it reacts with 2°-halide or a 3°-halide due to steric crowding.
 - Is an E2 reaction.



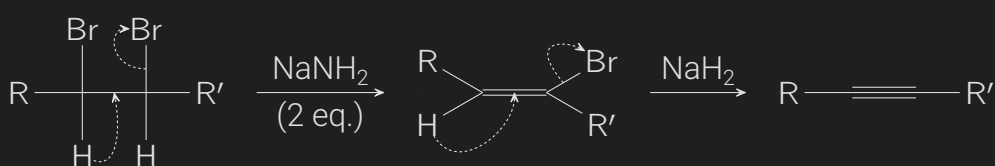
- The Zaitsev product is more likely to be the major product due to the thermodynamics (more energetically stable) than the Hofmann product; a bulkier base would likely increase the Hofmann product.

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 **β 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 β position**.
- **Coplanar**: when the proton in the β 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.

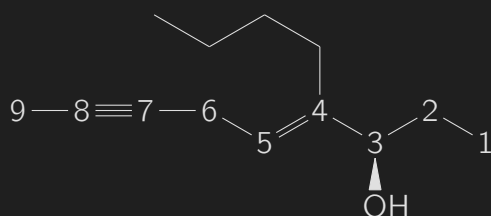
Alkyne Nomenclature

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:

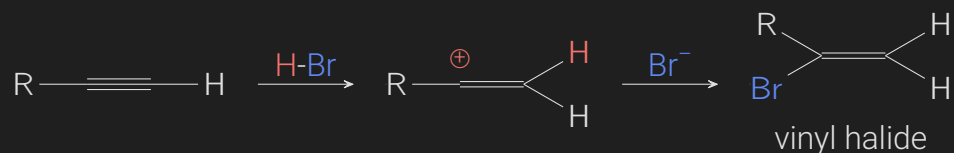


(3R,4E)-butylnon-4-en-7-yn-3-ol

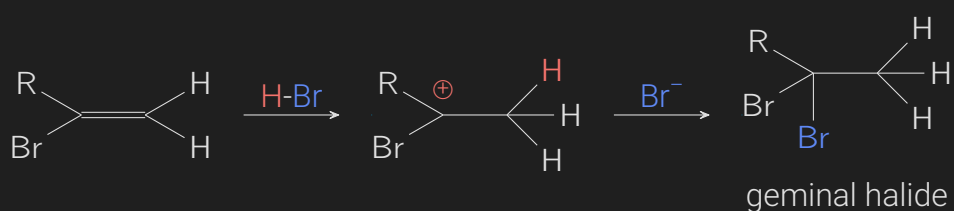
Addition Reactions of Alkynes

Hydrohalogenation of Alkynes

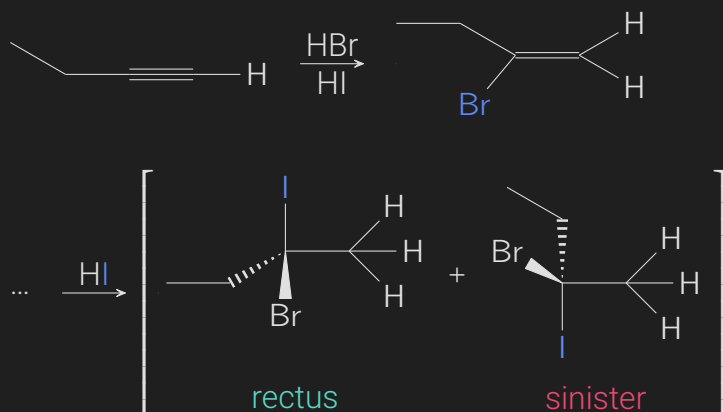
- Introductory example:



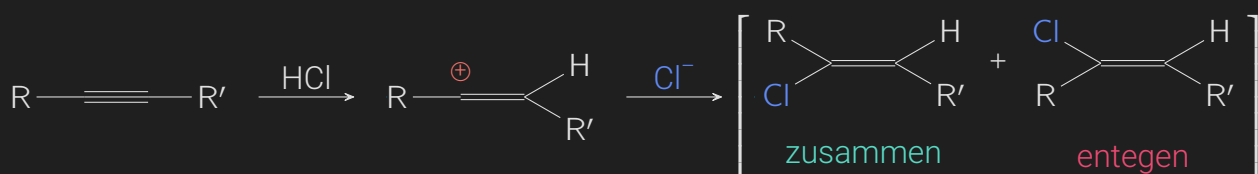
- Is **Regioselective** ↗
- Follows **Markovnikov's Rule** ↗
- This reaction can be done again (2 equiv):



- 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):

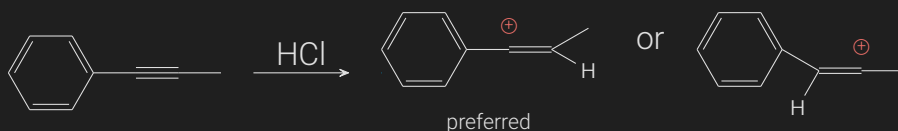


- Example with an internal alkyne; either side can be chosen if the R groups are not specified:

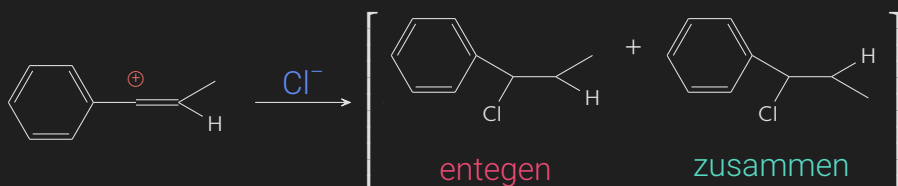


- Cl is higher priority than any carbon containing group (R), and any R' is higher than H, so both top and bottom attacks are possible.

- Related practice problem:

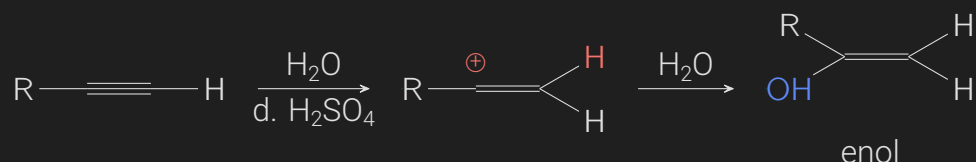


- The former carbocation intermediate is preferred due to resonance of the benzene ring, which does a better job stabilizing the carbocation.
- Continuing the reaction:

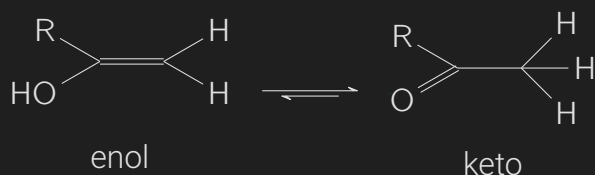


Hydration of Alkynes

- Introductory example:



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



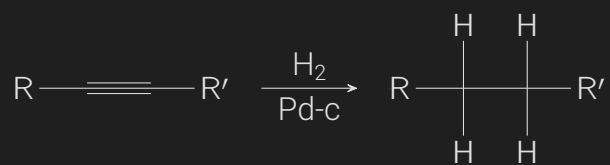
- **Tautomers:** a class of structural isomers (constitutional isomers) that readily interconvert, commonly due to the relocation of a proton (protonation-deprotonation) across a π bond.
 - The chemical reaction is called tautomerization; the concept is referred to tautomerism, which is sometimes desmotropism.
- Keto-enol tautomerism major product is the keto form, which does not allow for a second addition reaction.
- HgSO_4 is frequently used instead of d. H_2SO_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 ↗:

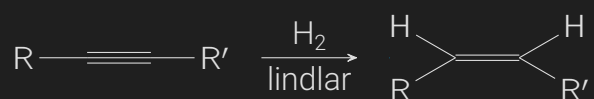
- o **Aldehyde:** generally created by removing a hydrogen from an alcohol; in our case it is generated by the **anti-Markovnikov** reaction that results in a terminal enol, which then undergoes tautomerization and produces the aldehyde as the major product.

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:

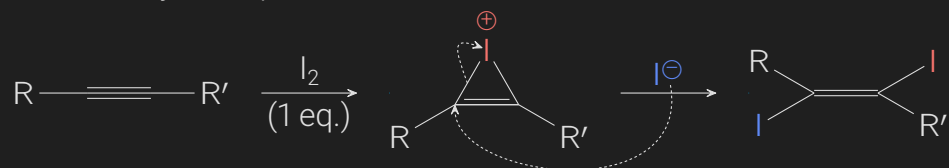


- Alkyne → **trans**-alkene; using generation of free radicals (•, single electron) that pair up with another electron generated by the dissociation of $\text{Na} \rightarrow \text{Na}^+ + \text{e}^-$ to create a free pair of electrons that then receive a hydrogen from NH_3 :

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

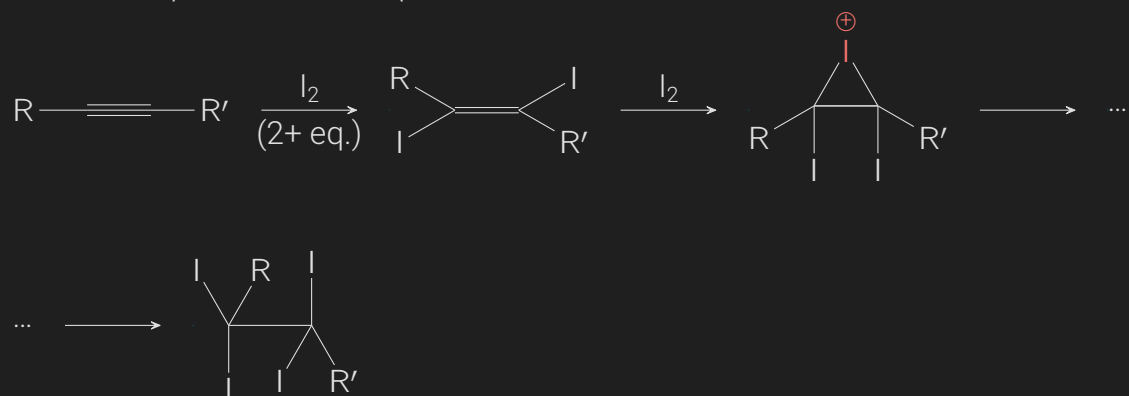
Halogenation of Alkynes

- 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:

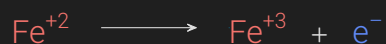


- Note: if you had controlled the second addition and added a different halide, then stereochemistry would have been important to consider since the products would have had chiral carbons.

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.



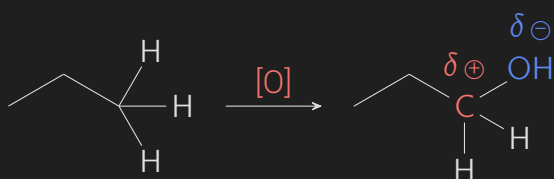
- ▷ **Reduction:** is the **gain of electrons** or a **decrease in the oxidation state** of an atom, an ion, or of certain atoms in a molecule (a reduction in oxidation state).



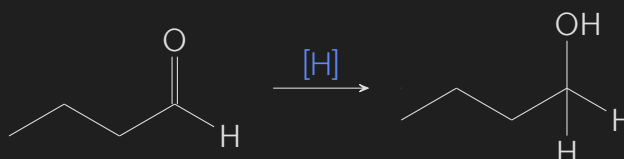
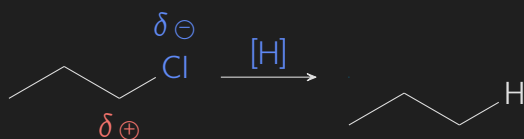
- ▷ **Redox (reduction-oxidation):** a type of chemical reaction in which the oxidation states of atoms are changed.
- Characterized by the actual or formal transfer of electrons between chemical species.
 - Most often one species (**the reducing agent**) undergoing **oxidation** while another species (**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– δ^{\ominus} bond; pulls **electron density away** from the carbon.
 - **Reduction [H]:** going from a C– δ^{\ominus} → C–H bond; pulls **electron density towards** the carbon.

Redox Practice Examples

- Examples of oxidation reactions:



- Examples of reduction reactions:



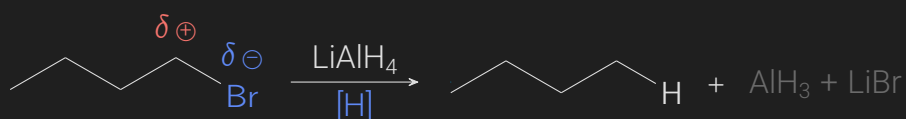
Reduction Reactions

Reduction Agents

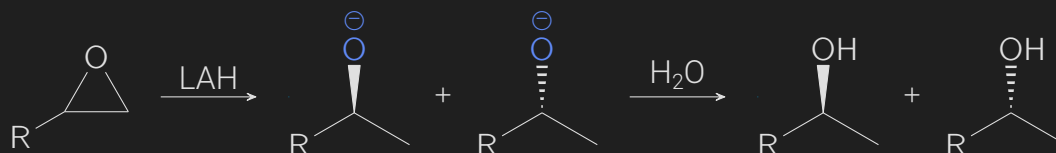
- **Hydride:** H^- , a negatively charged hydrogen ion (anion); commonly used as a **strong base** that react with **weak acids**, releasing H_2 .
- NaBH_4 : sodium borohydride.
- LiAlH_4 (LAH): lithium aluminum hydride.
- Both NaBH_4 and LiAlH_4 are **hydride donors**; they give up a hydride to become 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:
 - LiAlH_4 is a **stronger** reducing agent.
 - NaBH_4 is a **weaker** reducing agent.

Reduction with LiAlH_4

- Example with an alkyl halide:



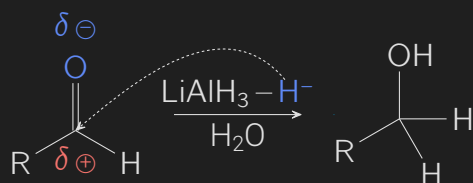
- Example with an epoxide:



- 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 H_2O for the negatively charged oxygen in this case).

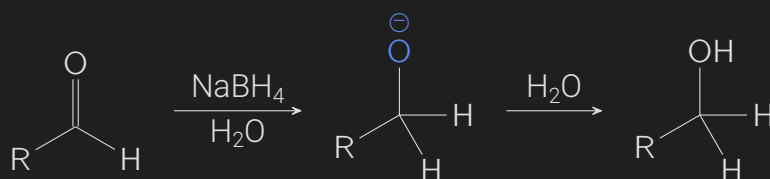
Reduction of Aldehydes

- Example of reduction to 1° alcohol:



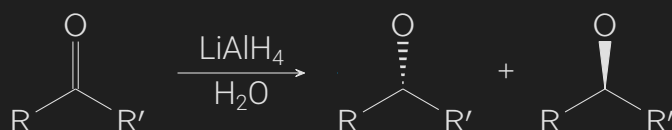
- Note: the reaction is done in two steps, but the addition of water was omitted here.

- 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 NaBH_4 and showing the intermediate step:



Reduction of Ketones

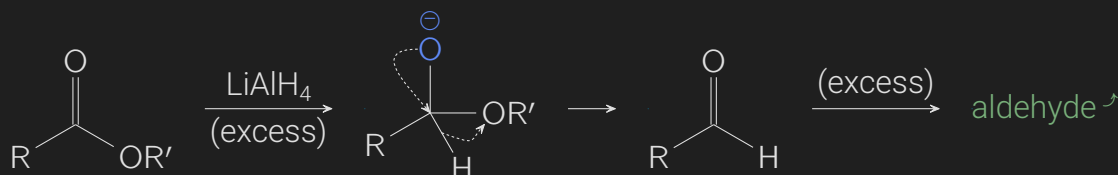
- Examples of generating racemic mixtures of 2° alcohols:



- Note: the above can be done with 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

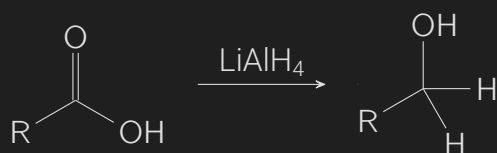
- First the ester is reduced to an aldehyde, then in presence of excess it will be further reduced from an aldehyde to a 1° alcohol.



- Resonance (shared electron density due to delocalization of electrons between either oxygen) is stronger than inductive effect, so **only reduction using LiAlH_4** works.

Reduction of Carboxylic Acids

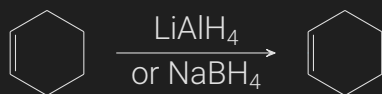
- Very similar to Esters, which ends up producing a 1° alcohol:



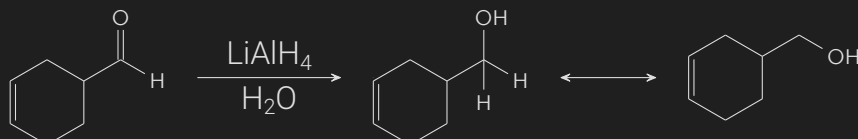
- Again, the presence of resonance will only allow the use of LiAlH_4 ; the first step will not occur if NaBH_4 is used as it is too weak to be a reagent.

Reduction Practice Problems

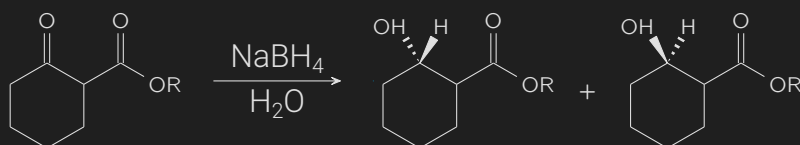
1. No reaction, needs carbonyl (C=O) functional group to proceed:



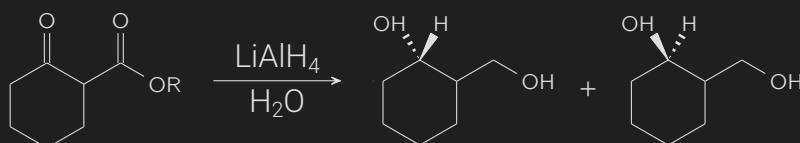
2. Example that contains a carbonyl group:



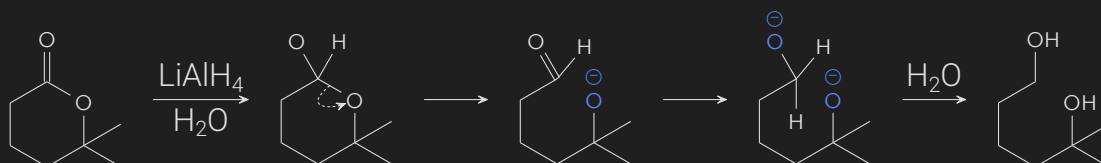
3. Example with a ketone and an acyclic ester:



- 3b. Same example as above but with LiAlH₄ (assuming excess):



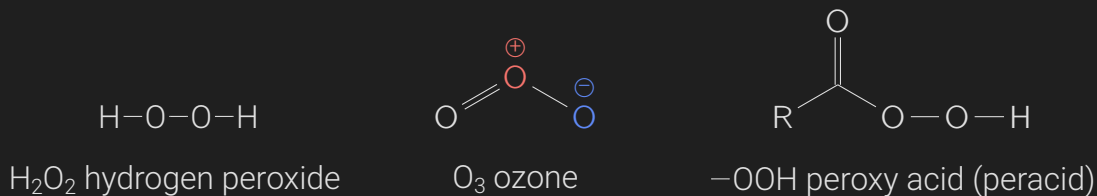
4. Example with a cyclic ester (assuming excess):



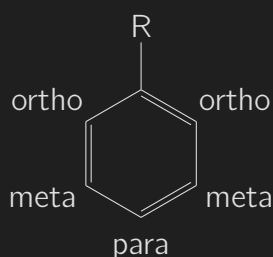
Oxidation Reactions

Oxidizing Agents

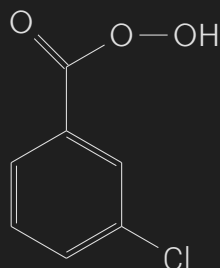
- **Peroxide reagents:** reagents that contain O—O linkage of some kind:



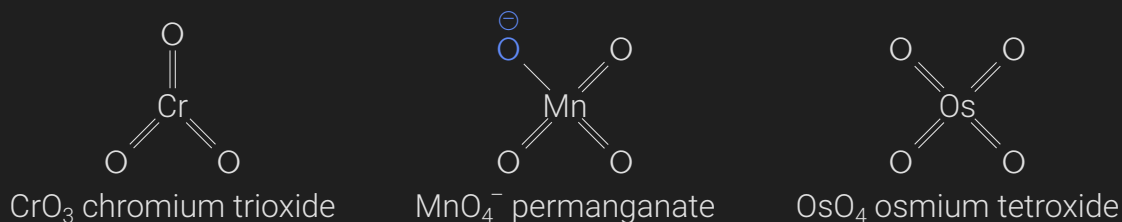
- **Arene substitution patterns:** IUPAC nomenclature for naming substituents other than hydrogen in relation to each other on an aromatic hydrocarbon:



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

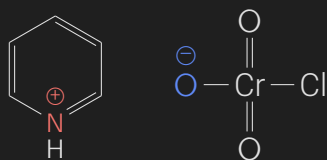


Metal Based Oxidizing Agents



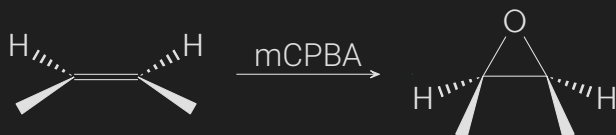
- KMnO_4 is **inexpensive**, but a very **strong oxidizing** agent and is **not soluble** in organic solvents.
 - Keeping KMnO_4 cold can help reduce activation energy, leading a reduction of the more oxidized byproduct.
 - MnO_4^- comes as KMnO_4 . The anion must be created in order to be used as a reagent.

- OsO_4 is **very expensive**, but a **mild oxidizing** agent that is **soluble** in organic solvents.
 - N-methylmorpholine N-oxide (NMO): used with OsO_4 to reduce cost; it oxidizes the byproduct (Os^{+6}) back to OsO_4 in solution, allowing for reuse.
- **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.

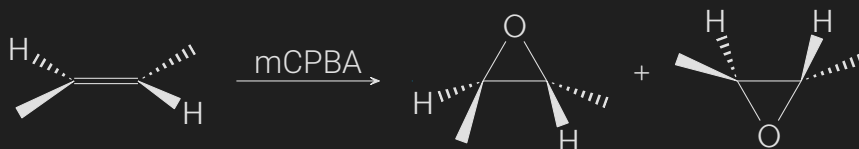


Epoxidation

- 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:



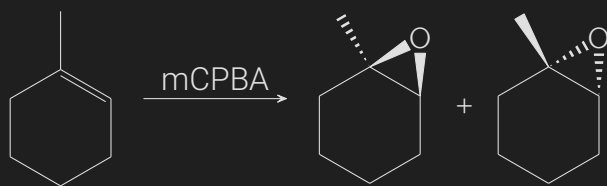
- The *trans*-epoxide ring is no longer a meso compound, so you must show both products; one when the ring forms on the top and one where the ring forms on the bottom.
- These examples show that epoxidation reactions are **concerted** reactions, since there is no mixture of products between *cis* and *trans* products; it's dependent on the starting compound.

Epoxidation Practice Problems

1.

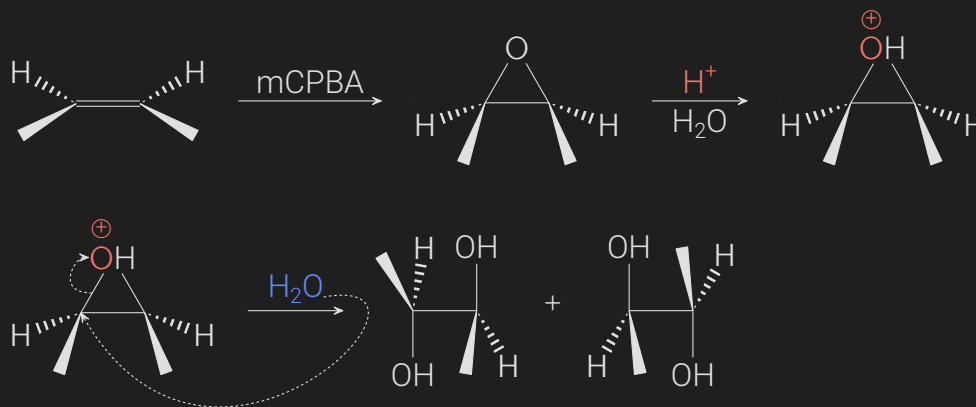


2.



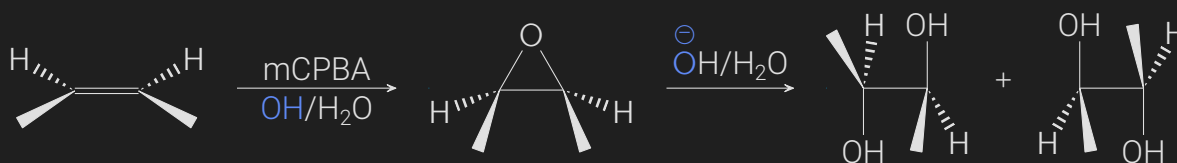
Trans Dihydroxylation

◦ 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.

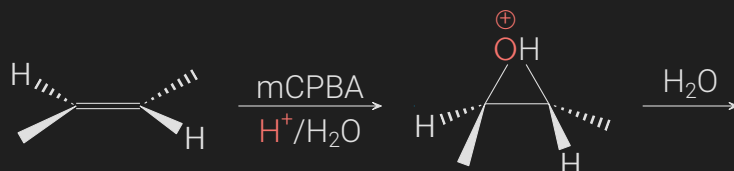
◦ Base catalyzed:



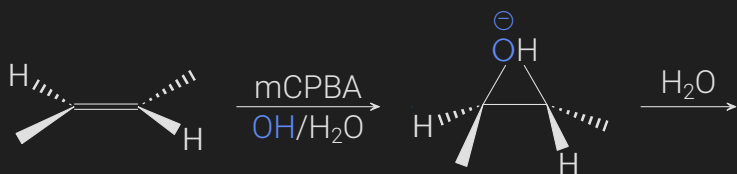
- Note: the result is the same as acid catalyzed conditions when both sides of the alkene are equally substituted.
- However, under **acidic conditions** then the **more substituted** side will get attacked, while under **basic conditions** then the **less substituted** side will get attacked.

Trans Hydroxylation Practice Problems

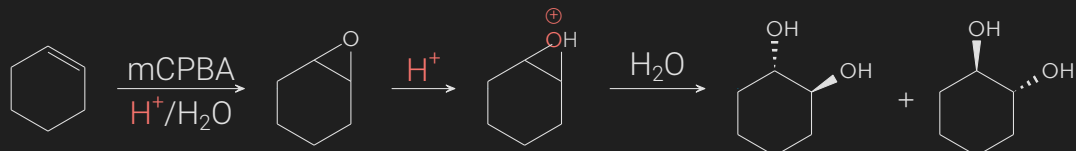
◦ *Trans*-alkene reactant (**acid catalyzed**):



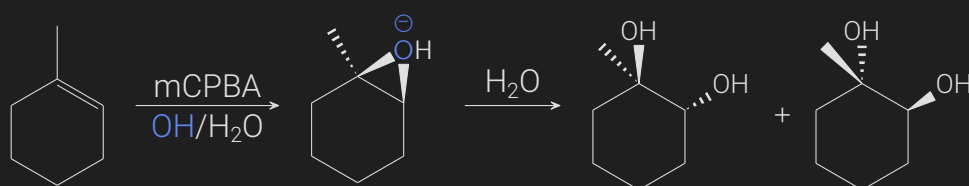
- *Trans*-alkene reactant (base catalyzed):



- Cyclohexene reactant:

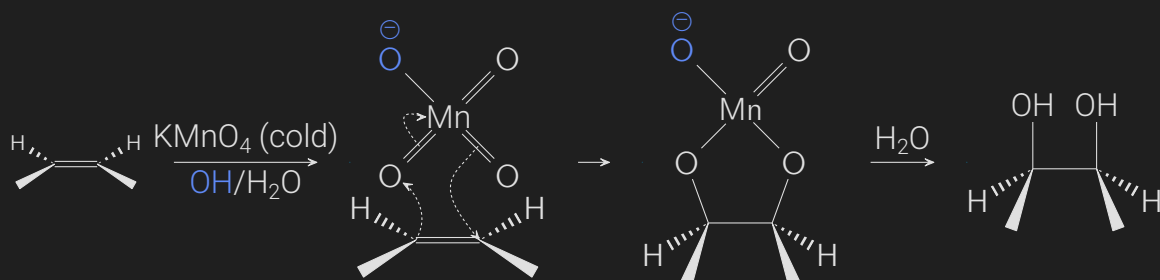


- 1-methylcyclohexene reactant:



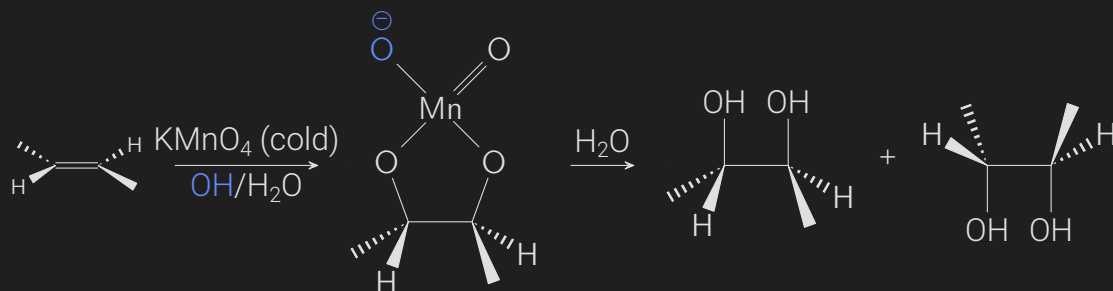
Syn Dihydroxylation

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



- The addition of 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 MnO_4^- attached to.