

Organic Chemistry II

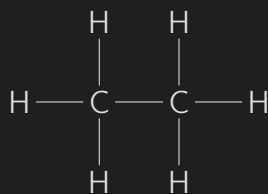
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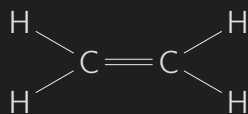
14: Alkenes

Alkenes Basics/Review

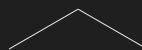
- Alkanes vs alkenes:



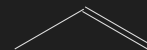
Saturated
alkanes ethane



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

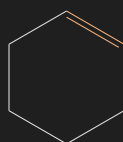
- Basic types of alkenes:



Terminal Alkene

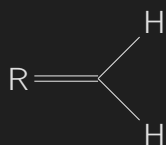


Internal Alkene



Cycloalkene

- Types of terminal alkenes:



Methylene



Vinyl

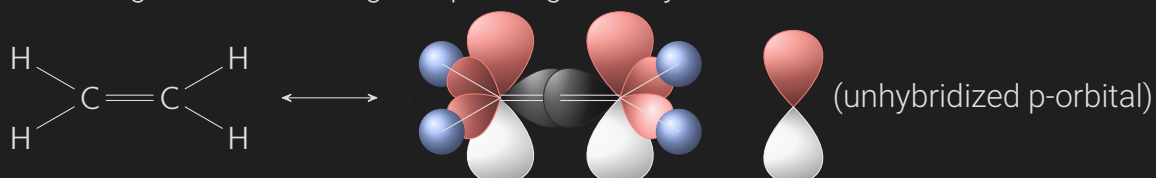


Allyl

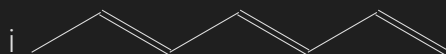
- "R" always tells you it's a carbon containing functional group, or hydrogen.
- "A" can be used to represent any functional group.

Relevant Review

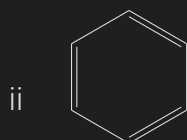
- **Electronegativity:** negative charges on atoms with lower hybridization result in greater stability due to proximity (overlap) to positive nucleus. More s character results in greater stability.
 - I.e., sp (50% s) > sp^2 (33% s) > sp^3 (25% s)
 - E.g., ethene has two carbons that are both sp^2 due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

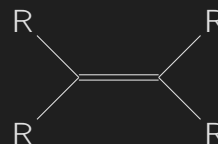


i $\frac{1}{2}(2(7) + 2 + (0) - (3 + (5(1)) + 2) - 0) = 3$



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

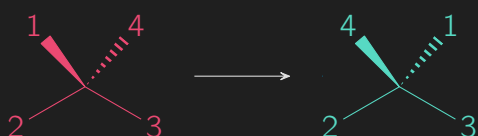
- **Achiral (nonsuperimposable)**: when an object's mirrored version is identical to the actual object.
- **Chiral**: objects that are not superimposable.
 - The most common source of molecular chirality is the presence of a **carbon bearing four different groups**.
- All three-dimensional objects can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

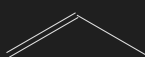
Nomenclature of Alkenes

Basic Alkene Nomenclature Rules

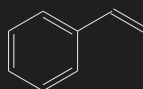
- Alkenes are named using the same four steps in the previously used nomenclature, though the suffix of "ane" is replaced with "ene."
- When choosing the parent chain, choose the parent chain that **includes** the double bond.
- When numbering the parent chain, the double bond should receive the **lowest**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



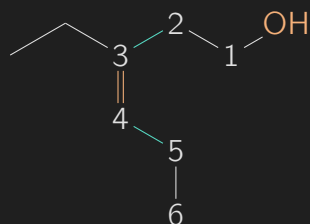
Styrene

- 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:

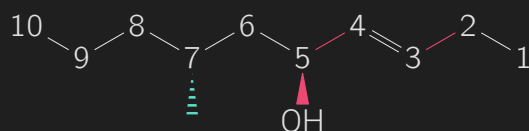


(3Z)-3-propyl-hex-3-en-1-ol

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:



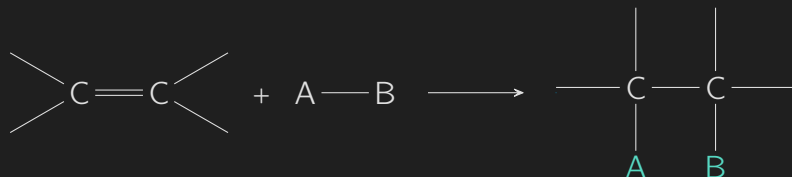
(3E,5S,7R)-4-methyl-3-en-5-ol

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

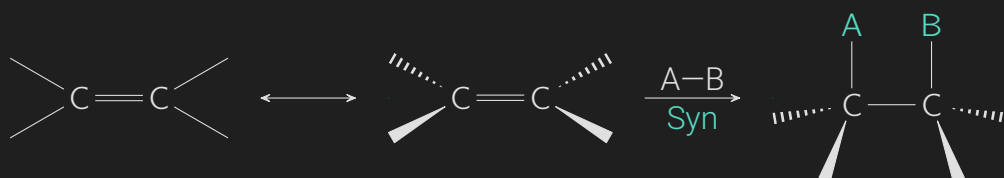
Addition Reactions of Alkenes

Syn Addition

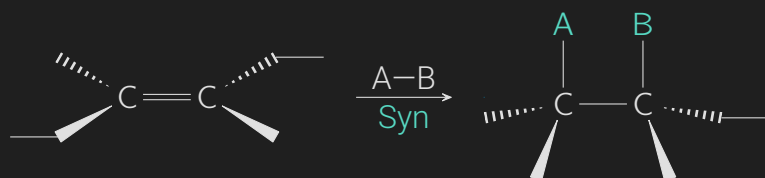
- Syn addition means that both components (A & B) came in from the same side.



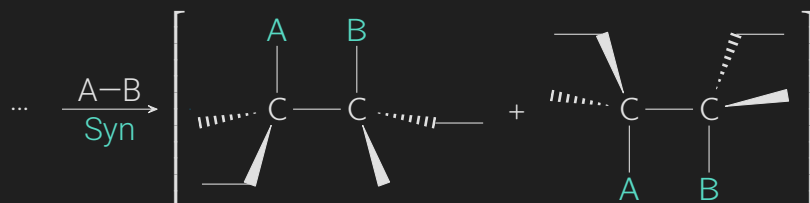
- When there is mixture of products, then the stereochemistry is important—A & B could come from different directions.
- Switching to a 3D perspective, with groups pointing towards and away from the viewer, rather than a flat view:



- 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.

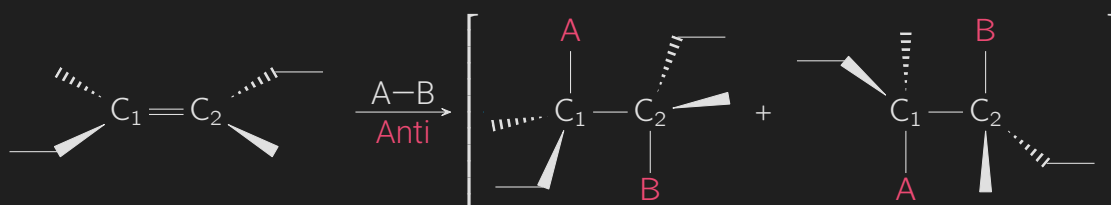


- The product in this case has **chiral centers**, so enantiomers must be considered.



Anti Addition

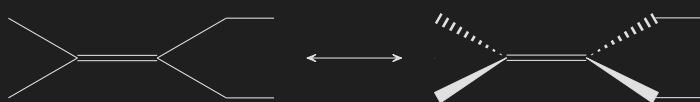
- Anti addition means that the added components come in from different sides.



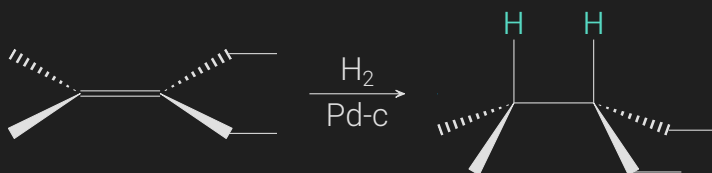
Hydrogenation

- **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:

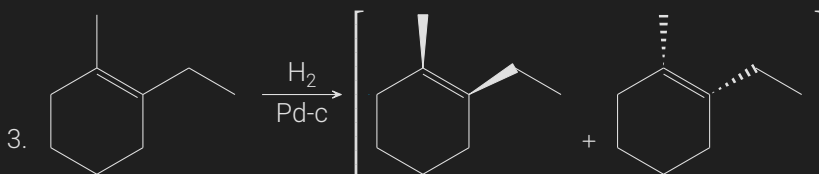
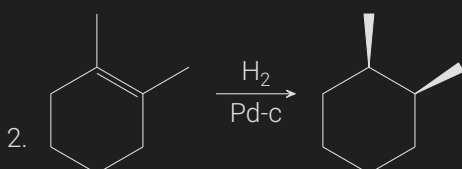
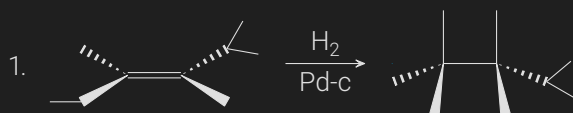


- Then apply H_2 with catalyst to trigger syn addition:



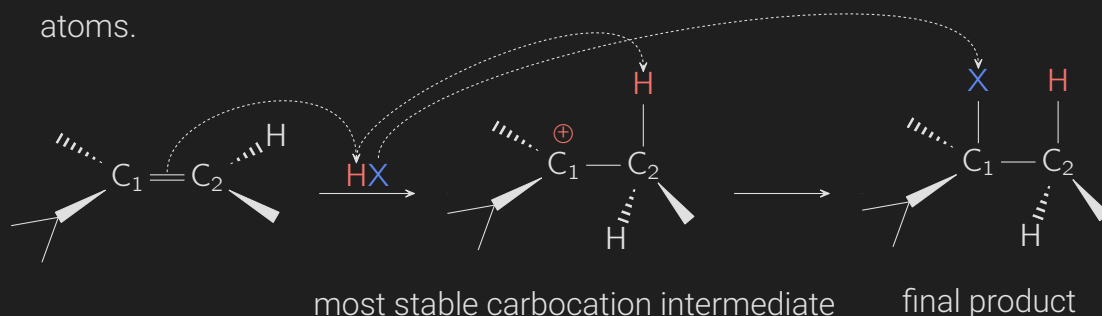
- Product is achiral; no enantiomers. Bottom would attack just flips the orientation; not a different product.

Hydrogenation Practice Problems

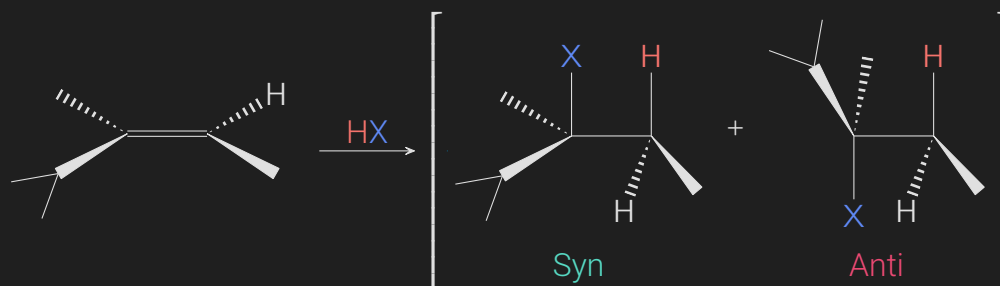


Hydrohalogenation

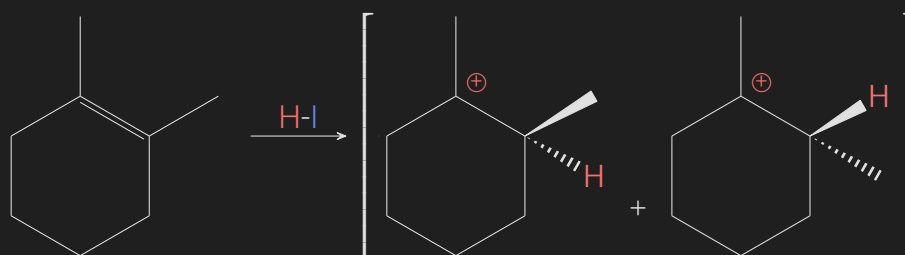
- **Hydrohalogenation:** the electrophilic addition ($\pi \rightarrow 2\sigma$ bonds) of hydrohalic acids (HX, e.g., HCl or HBr) to alkenes to yield the corresponding haloalkanes.
- **Markovnikov's Rule:** an addition of a protic acid (HX) or other polar reagent to an asymmetric alkene results in the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



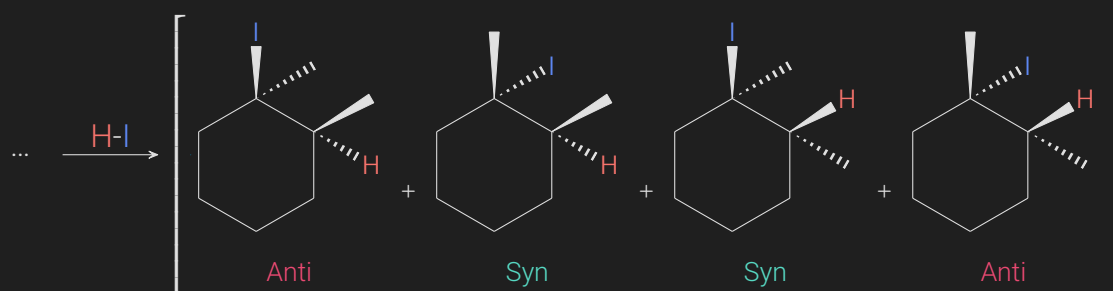
- However, we have a chiral carbon, so we have to take enantiomers into account:



- 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:

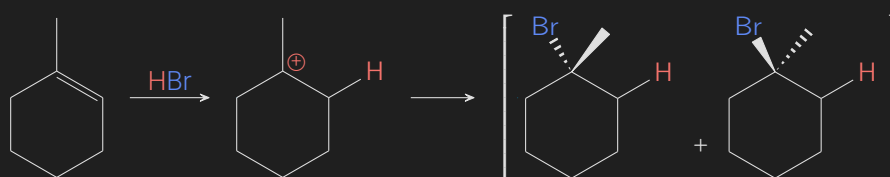


- Again, this first step shows the most stable carbocation intermediate, which helps determine where the H^+ will attach to. In this case either location works, so four products are formed, each with syn and anti enantiomers.



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

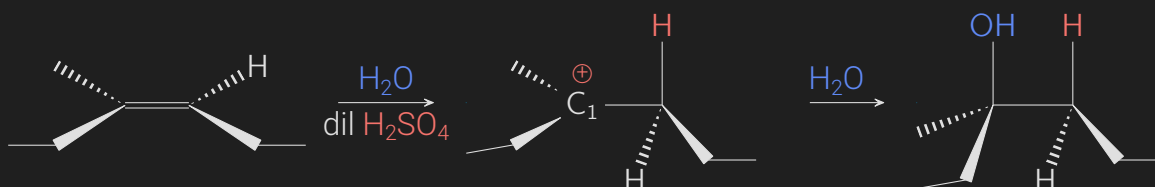
Hydrohalogenation Practice Examples



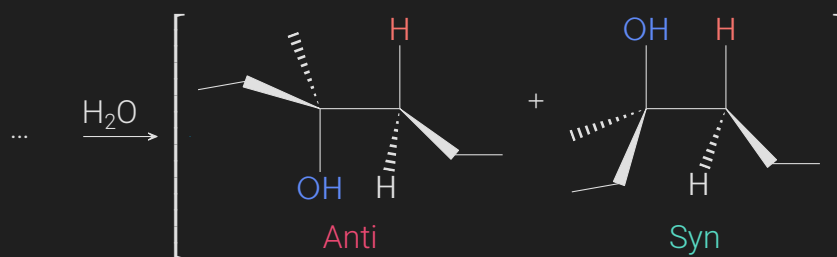
Addition of Water or Alcohol

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.

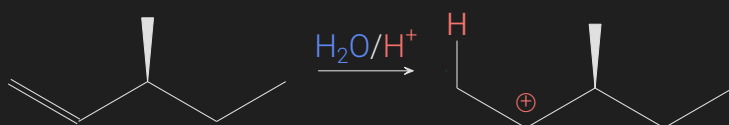
- Note: the hydronium ion (H_3O^+) forms via the reaction of H_2SO_4 with H_2O , and is the source of the proton that reacts with the starting alkene.
- $\text{H}-\text{OH}$ and $\text{RO}-\text{H}$ helps to visualize where the proton is coming from. What ever works with water also works with alcohol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



- Note: 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:

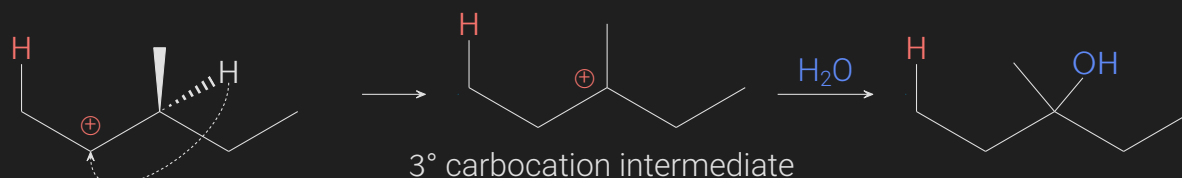


- Example 2:

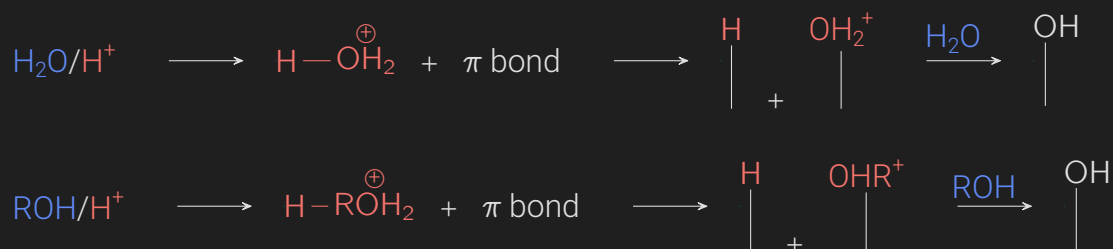


- **Rearrangement** \rightarrow is always a possibility to be considered when cation are generated. In this case, a 2° carbocation was generated, but we can do better:

- 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.



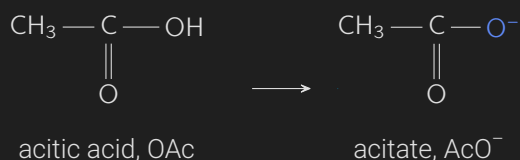
- **Problems of going through carbocation intermediate:**

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

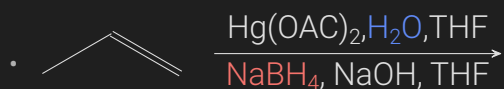
- C^+ can cause rearrangements leading to **multiple products**.

Oxymercuration-Demercuration

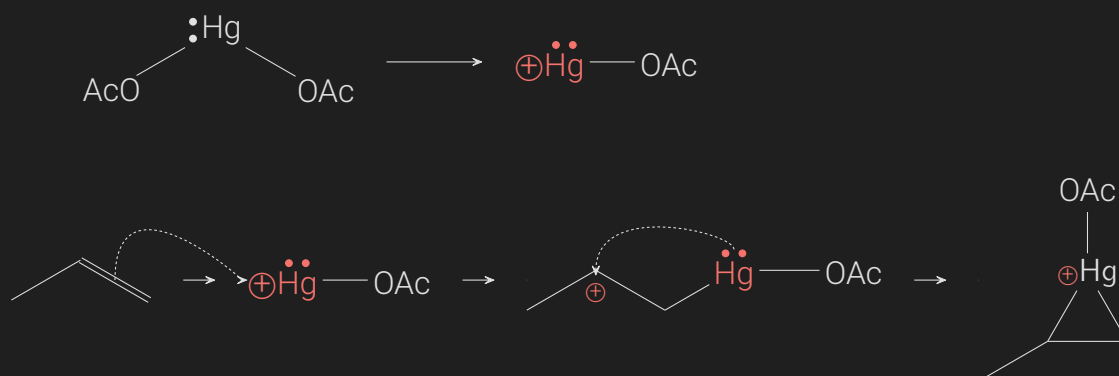
- **Oxymercuration-Demercuration** is another electrophilic addition organic reaction that transforms an alkene into a neutral alcohol.
- Reacts with mercuric acetate ($AcO-Hg-OAc$) in aqueous solution to yield the addition of an acetoxymcury ($HgOAc$) group and a hydroxy (OH) group across the double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



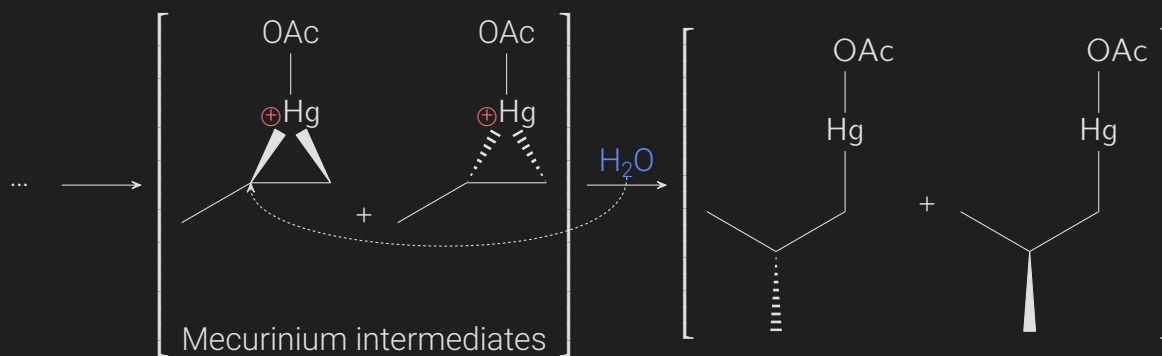
- Carbocations are not formed in this process and thus rearrangements are not observed.
- The reaction follows **Markovnikov's rule**.
- The reaction is stereospecific—it is always an **anti addition**.
- Example using propylene:



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

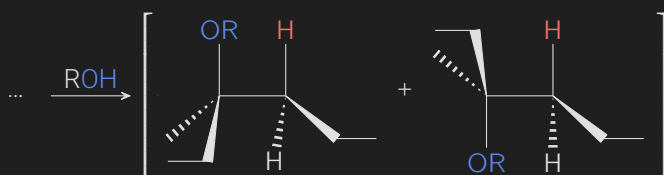
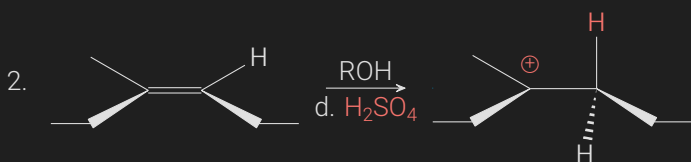
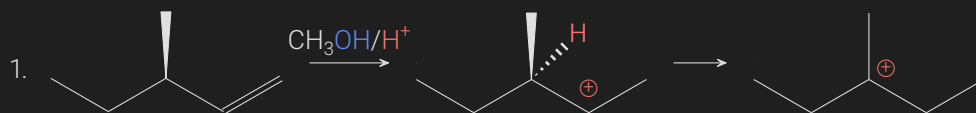


- Note: the above is a concerted (one step) process, but drawn out for illustration.
- Also, we are not done, we have a chiral center that forms, plus it is just an intermediate step, a nucleophilic attack will occur on the strained (highly reactive) epoxide:

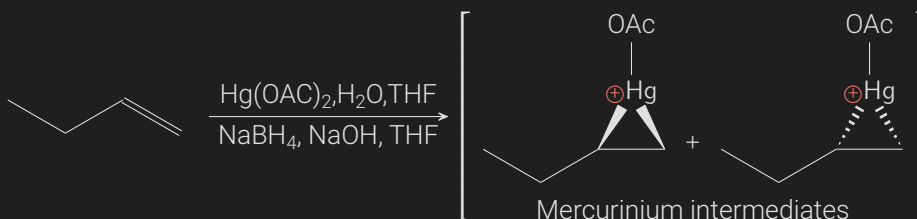


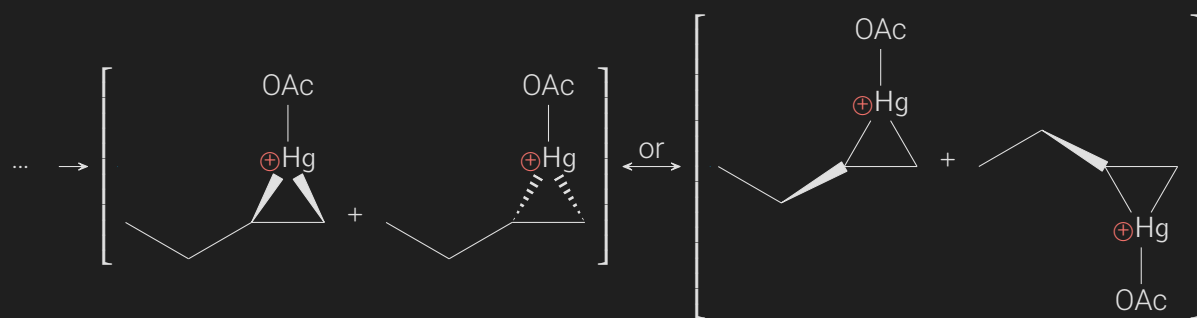
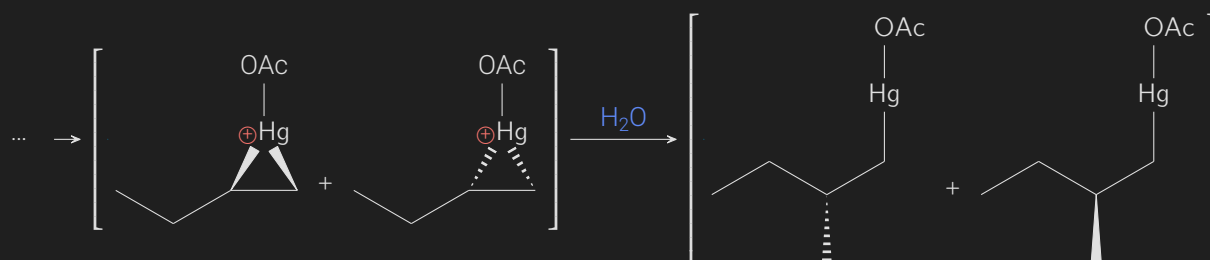
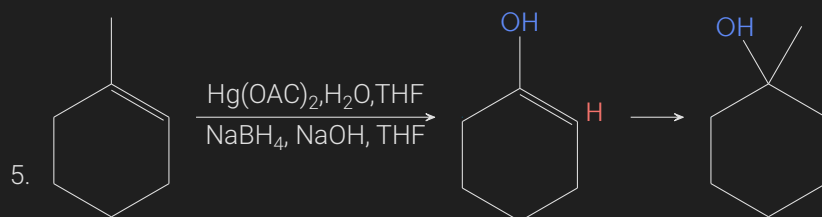
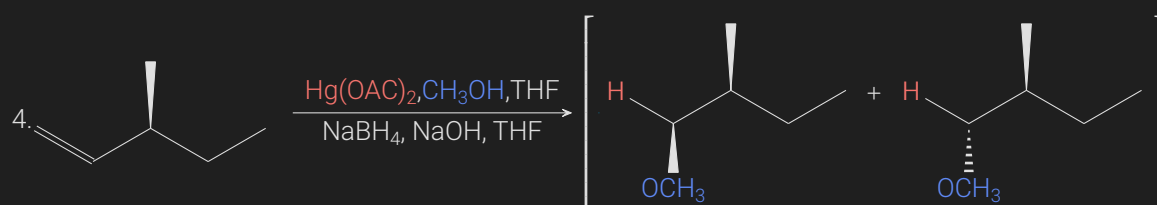
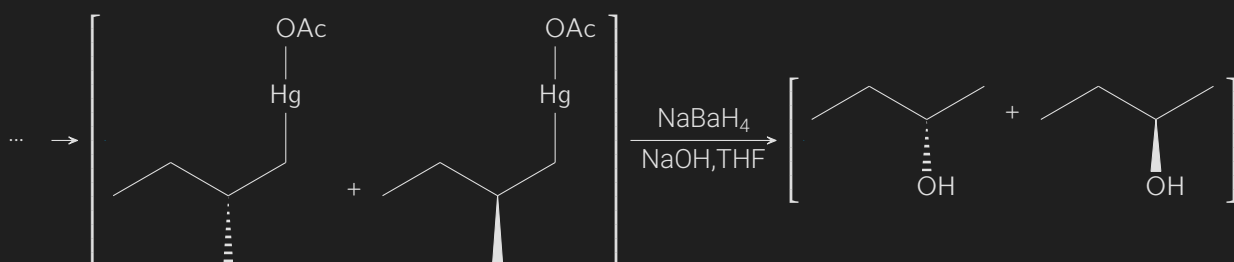
- Notice the nucleophile attack the carbon with the greater flow of electrons (more substituted), since there was a positive charge on mercury. Epoxides with no charge are attacked on the side with less steric hindrance.
- Also, the nucleophilic attack occurs on the opposite side of the plane since there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

Related Practice Problems

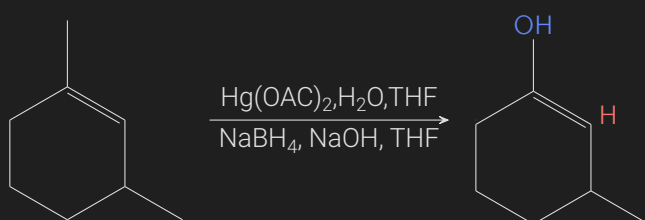


3. + Alternate ways of drawing rings (was done in lecture):

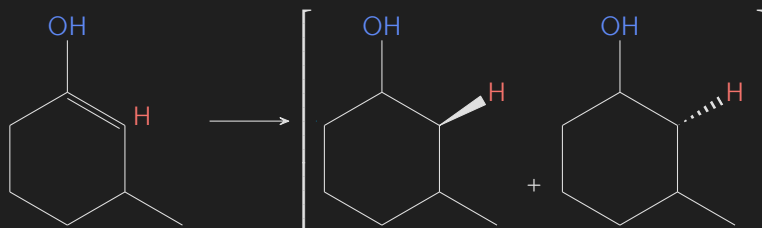


**Oxymercuration:****Demercuration:**

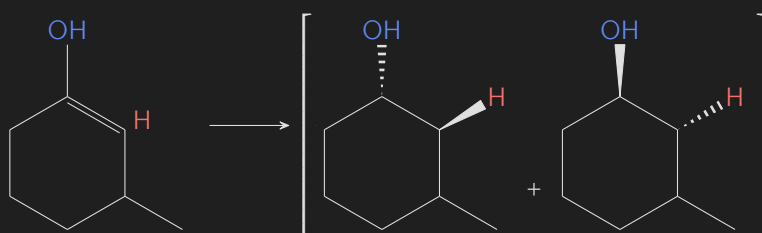
6. (was done in lecture)



- 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:

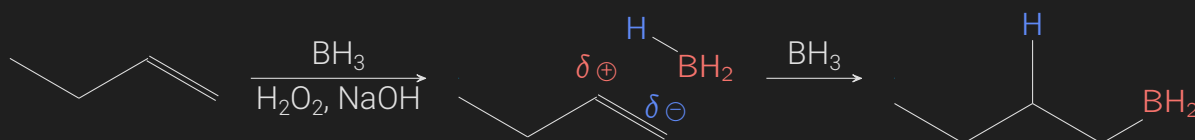


Hydroboration-Oxidation

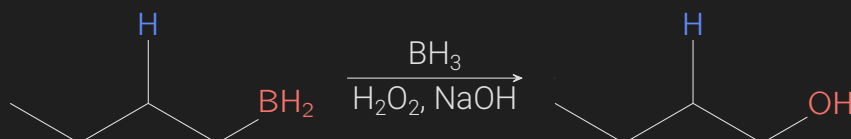
- Hydroboration-Oxidation:** a two-step hydration reaction that converts an alkene into an alcohol.
 - Results in the **syn addition** of a hydrogen and a hydroxyl group where the double bond had been.
 - An **anti-Markovnikov reaction**—the hydroxyl group attaches to the less-substituted carbon.
 - 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.



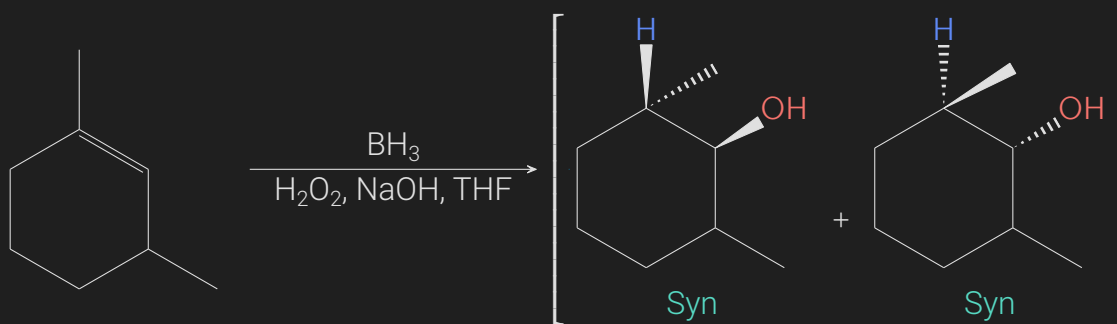
- There are no chiral centers, but there is still one more step—the oxidation:



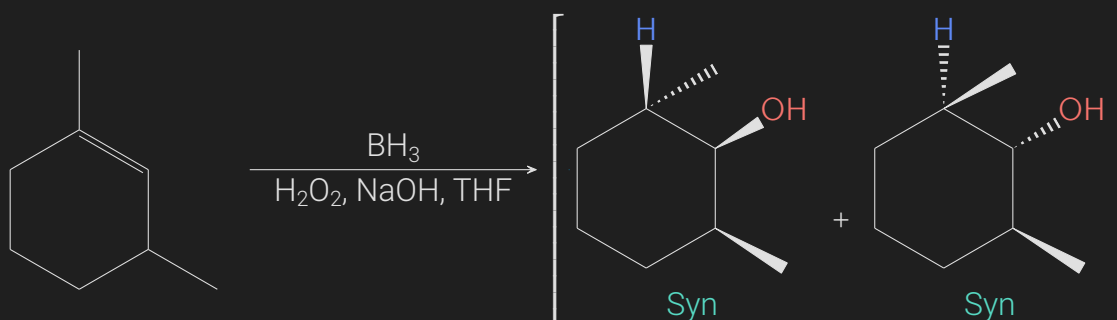
- If we had used $\text{Hg}(\text{OAc})_2$, then the above reaction would be different; partial charges change the possible final products: $\text{H}^{\delta-}-\text{BH}_2^{\delta+}$ vs. $\text{H}^{\delta+}-\text{OH}_2^{\delta-}$:



- Revisiting a practice example, using different reagents:

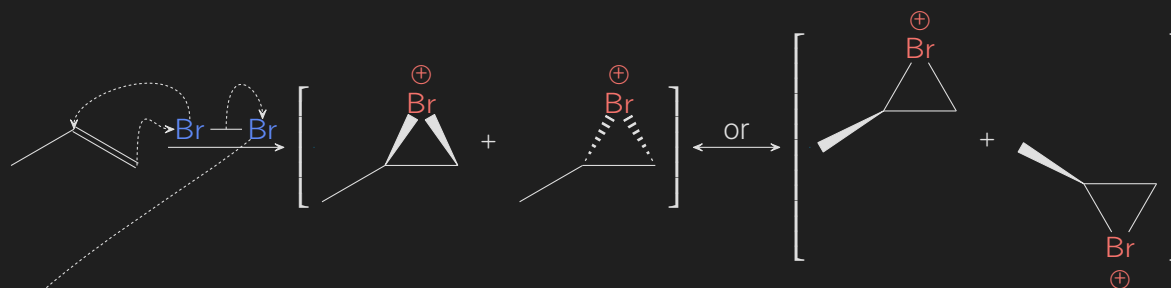


- If the untouched methyl happened to be above or below the plane initially, then you would keep that the same, e.g:

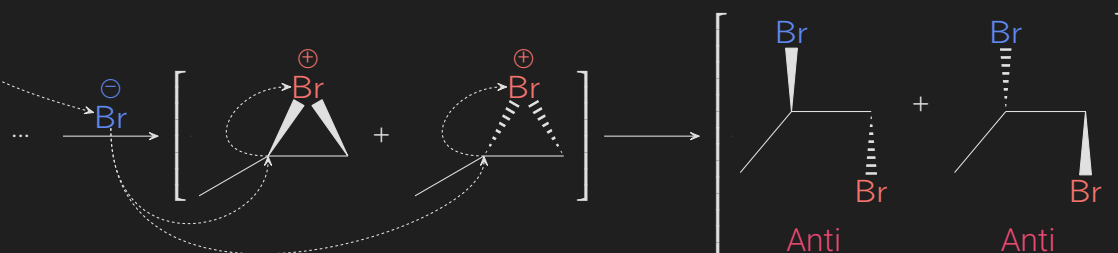


Halogenation

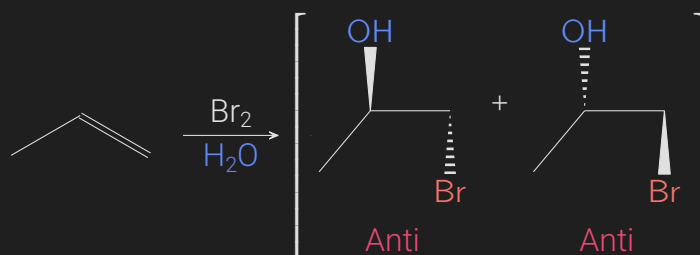
- Halogenation:** a reaction that involves the addition of one or more halogens to a compound or material.
 - The addition of halogens to alkenes proceeds via intermediate halonium ions.
 - Halonium ion:** any onium ion containing a halogen atom carrying a positive charge. This cation has the general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



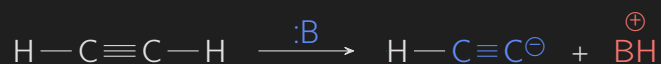
15: Alkynes

Alkynes Basics/Review

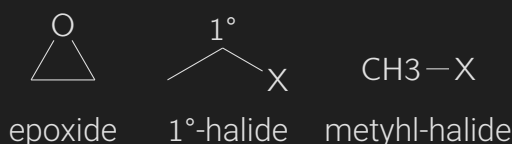
- **Alkynes**: an unsaturated hydrocarbon containing at least one carbon—carbon triple bond.
 - Contains two unhybridized p-orbitals (sp) on each carbon.
- $$\begin{array}{ccccccc} \delta+ & \delta- & \delta- & \delta+ \\ \text{H} & -\text{C} & \equiv & \text{C}-\text{H} \end{array}$$
- Large amount 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 C₂H₂ (ethyne)

Acetylides

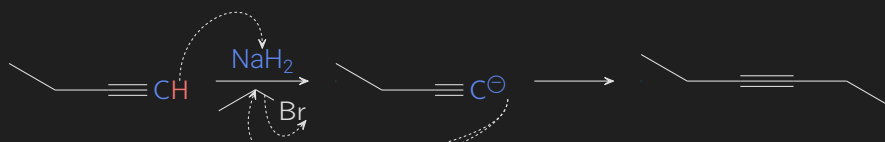
- **Acetylide**: an alkyne with a negatively charged carbon on one end, e.g.,



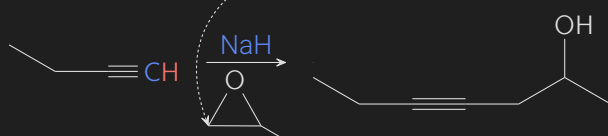
- :B is a name of generic base, typical bases used:
 - NaNH₂ → sodamide, or NaH → sodium hydride.
- Acetylide acts as a nucleophile when it reacts with an epoxide, 1°-halide, or a methyl-halide.



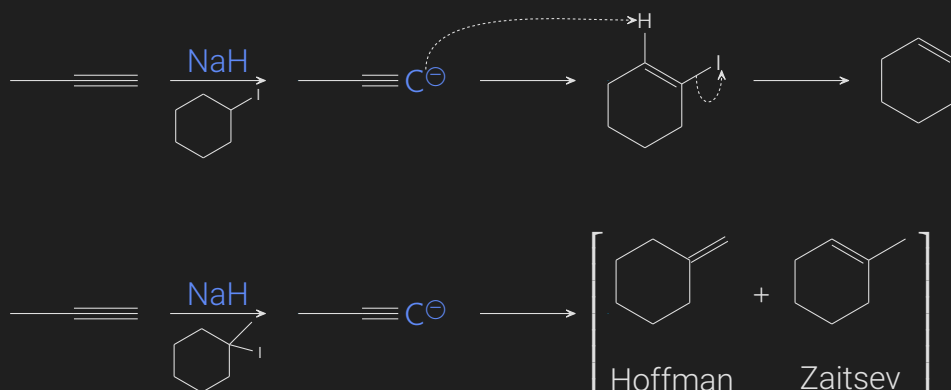
- Is a S_N2 reaction.
- Can be used for chain extension, e.g.,



- Example two:



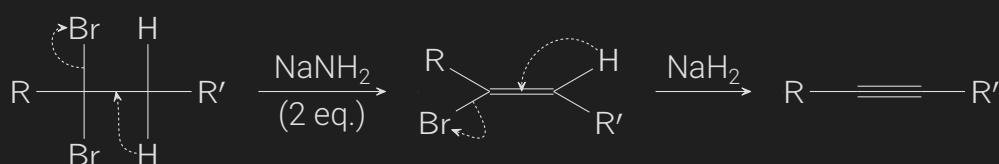
- Acetylide acts as a **base** when it reacts with 2°-halide or a 3°-halide due to steric crowding.
 - Is an E2 reaction.



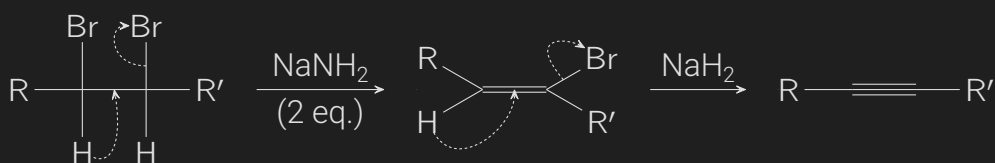
- The Zaitsev product is more likely to be the major product due to the thermodynamics (more energetically stable) than the Hofmann product; a bulkier base would likely increase the Hofmann product.

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.

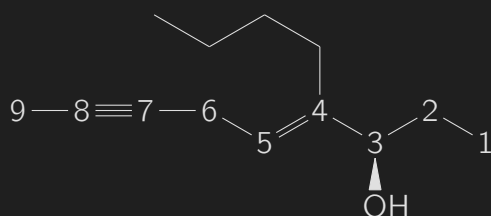
Alkyne Nomenclature

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:

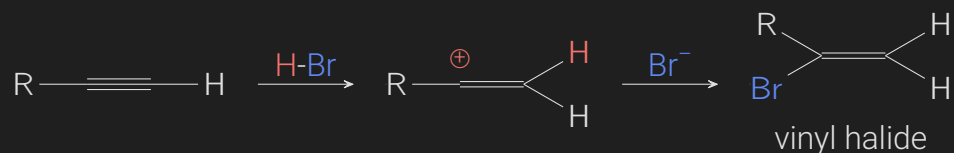


(3R,4E)-butylnon-4-en-7-yn-3-ol

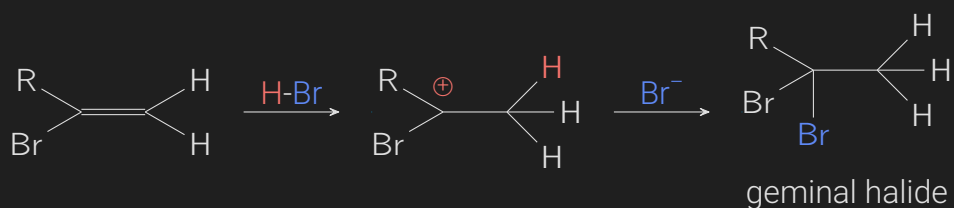
Addition Reactions of Alkynes

Hydrohalogenation of Alkynes

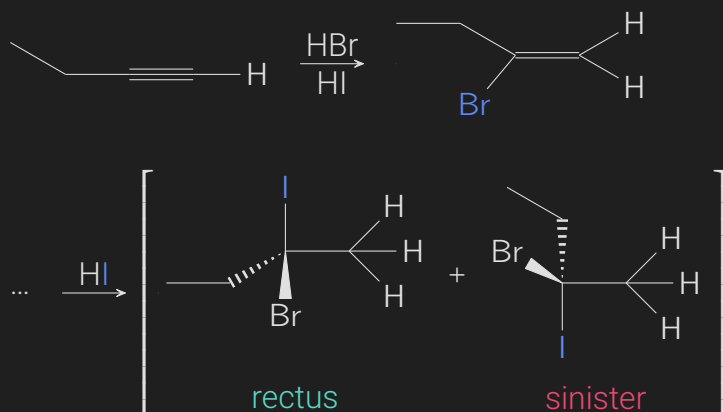
- Introductory example:



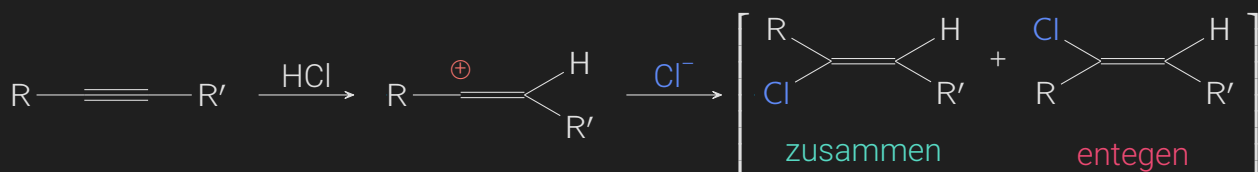
- Is **Regioselective** ↗
- Follows **Markovnikov's Rule** ↗
- This reaction can be done again (2 equiv):



- 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):

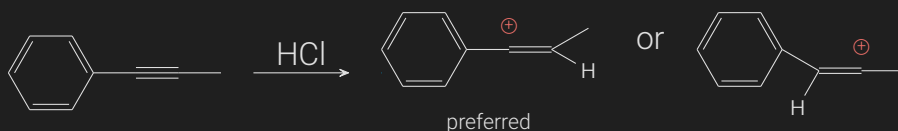


- Example with an internal alkyne; either side can be chosen if the R groups are not specified:

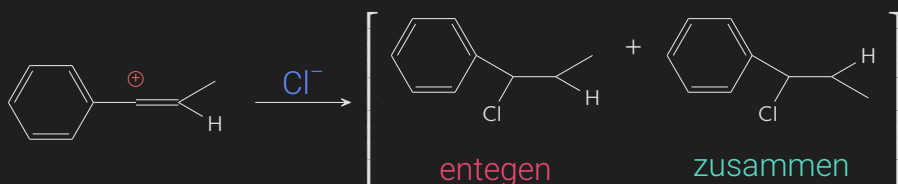


- Cl is higher priority than any carbon containing group (R), and any R' is higher than H, so both top and bottom attacks are possible.

- Related practice problem:

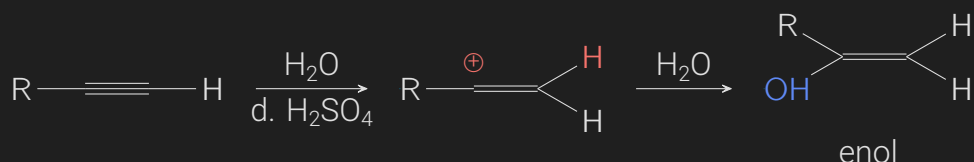


- The former carbocation intermediate is preferred due to resonance of the benzene ring, which does a better job stabilizing the carbocation.
- Continuing the reaction:

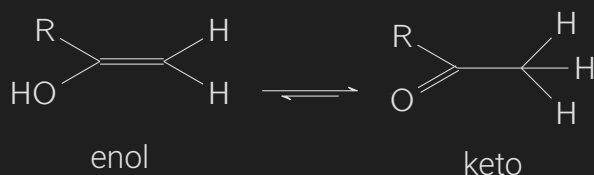


Hydration of Alkynes

- Introductory example:



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



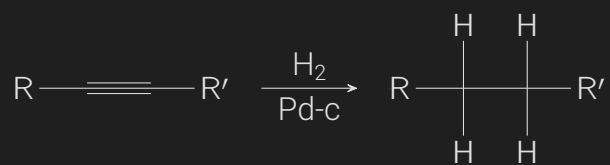
- **Tautomers:** a class of structural isomers (constitutional isomers) that readily interconvert, commonly due to the relocation of a proton (protonation-deprotonation) across a π bond.
 - The chemical reaction is called tautomerization; the concept is referred to tautomerism, which is sometimes desmotropism.
- 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 ↗:

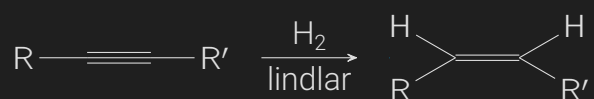
- o **Aldehyde:** generally created by removing a hydrogen from an alcohol; in our case it is generated by the **anti-Markovnikov** reaction that results in a terminal enol, which then undergoes tautomerization and produces the aldehyde as the major product.

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:

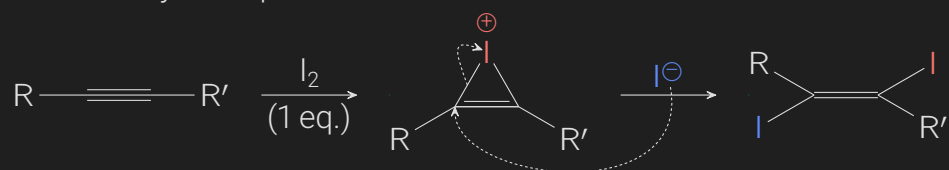


- Alkyne → **trans**-alkene; using generation of free radicals (•, single electron) that pair up with another electron generated by the dissociation of $\text{Na} \rightarrow \text{Na}^+ + \text{e}^-$ to create a free pair of electrons that then receive a hydrogen from NH_3 :

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

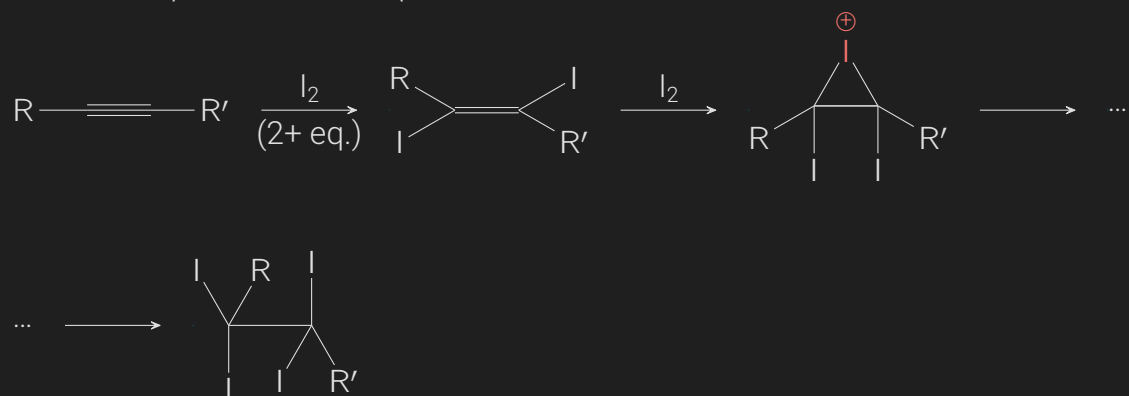
Halogenation of Alkynes

- 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:

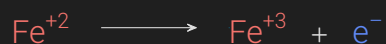


- Note: if you had controlled the second addition and added a different halide, then stereochemistry would have been important to consider since the products would have had chiral carbons.

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.



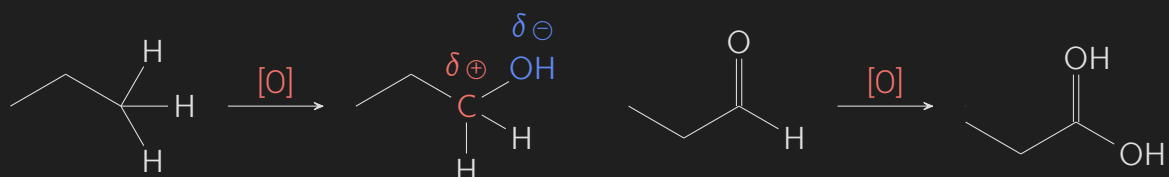
- **Reduction:** is the **gain of electrons** or a **decrease in the oxidation state** of an atom, an ion, or of certain atoms in a molecule (a reduction in oxidation state).



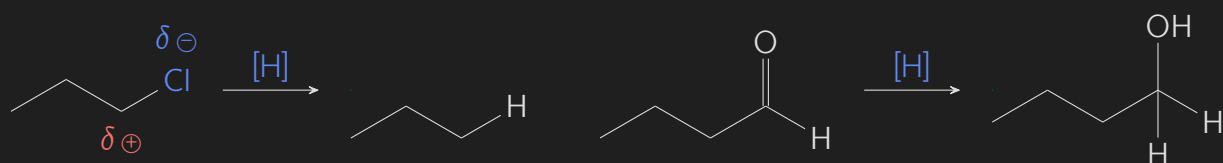
- **Redox (reduction-oxidation):** a type of chemical reaction in which the oxidation states of atoms are changed.
 - Characterized by the actual or formal transfer of electrons between chemical species.
 - Most often one species (**the reducing agent**) undergoing **oxidation** while another species (**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:



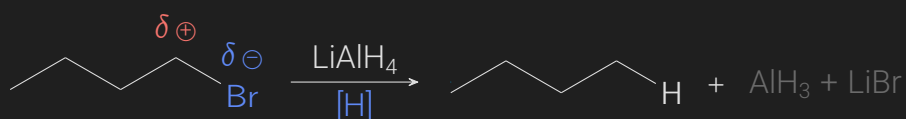
Reduction Reactions

Reduction Agents

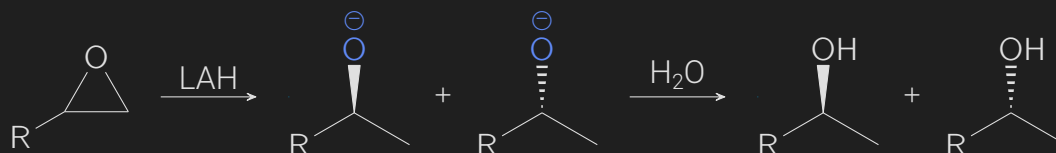
- **Hydride:** H^- , a negatively charged hydrogen ion (anion); commonly used as a **strong base** that react with **weak acids**, releasing H_2 .
- NaBH_4 : sodium borohydride.
- LiAlH_4 (LAH): lithium aluminum hydride.
- Both NaBH_4 and LiAlH_4 are **hydride donors**; they give up a hydride to become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



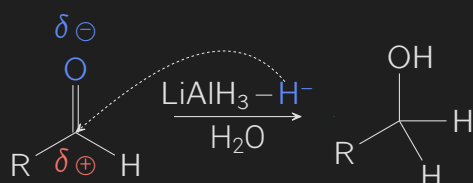
- Example with an epoxide:



- 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).

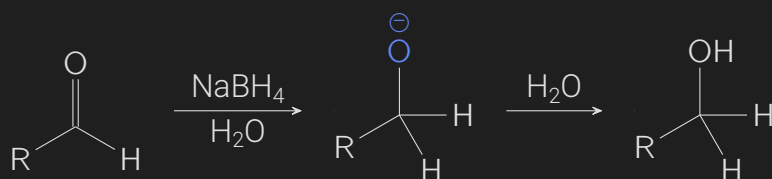
Reduction of Aldehydes

- Example of reduction to 1° alcohol:



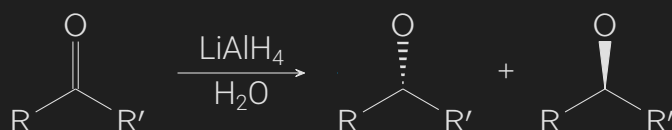
- Note: the reaction is done in two steps, but the addition of water was omitted here.

- 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

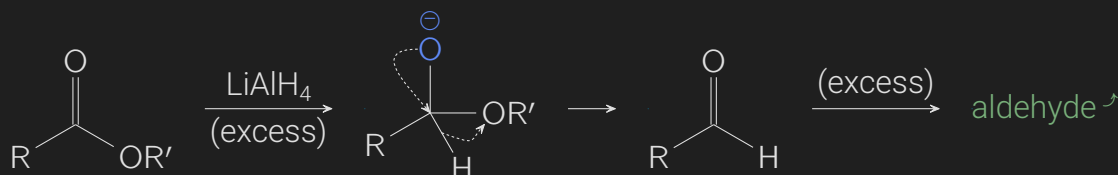
- Examples of generating racemic mixtures of 2° alcohols:



- 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

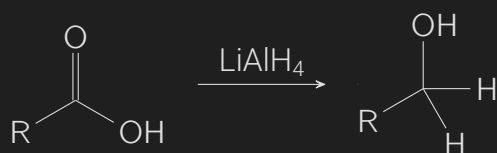
- First the ester is reduced to an aldehyde, then in presence of excess it will be further reduced from an aldehyde to a 1° alcohol.



- 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

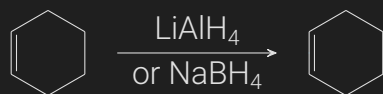
- Very similar to Esters, which ends up producing a 1° alcohol:



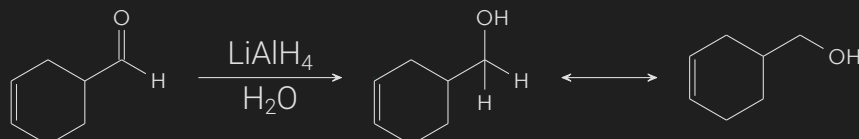
- Again, the presence of resonance will only allow the use of LiAlH_4 ; the first step will not occur if NaBH_4 is used as it is too weak to be a reagent.

Reduction Practice Problems

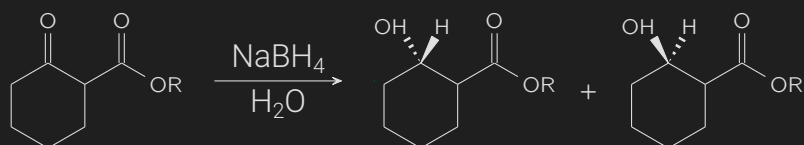
1. No reaction, needs carbonyl (C=O) functional group to proceed:



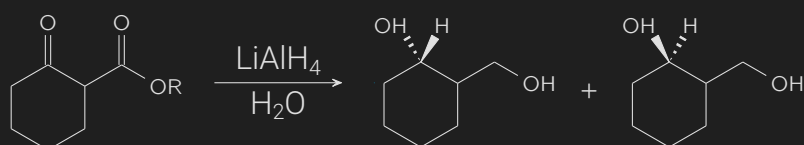
2. Example that contains a carbonyl group:



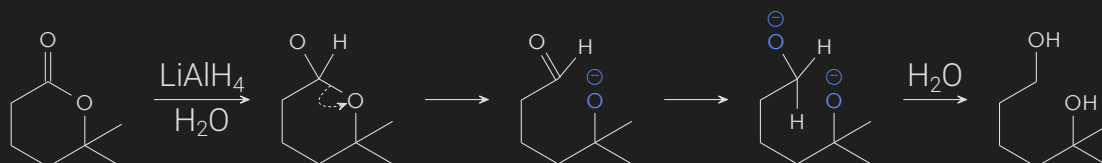
3. Example with a ketone and an acyclic ester:



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



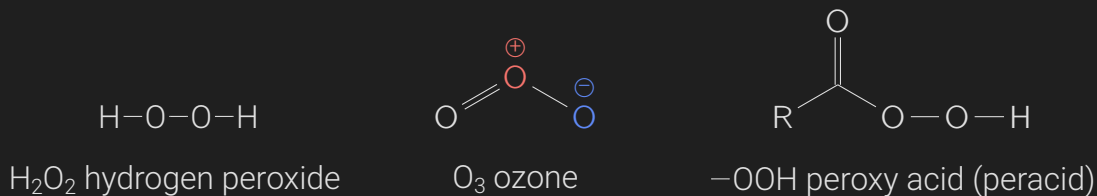
4. Example with a cyclic ester (assuming excess):



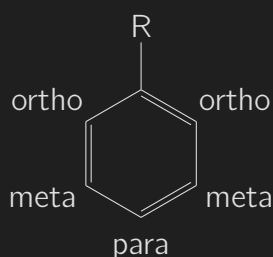
Oxidation Reactions

Oxidizing Agents

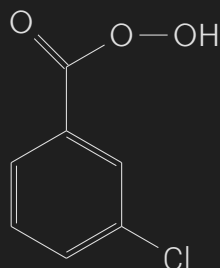
- **Peroxide reagents:** reagents that contain O—O linkage of some kind:



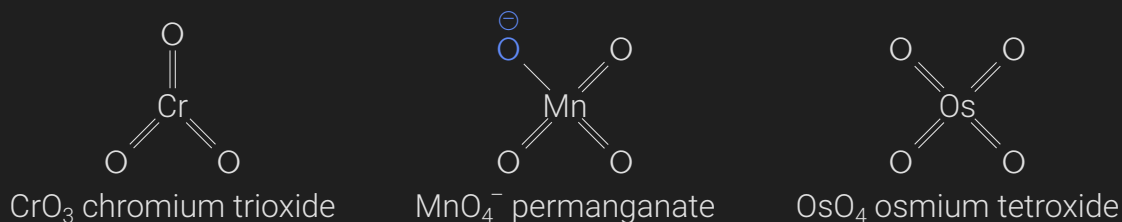
- **Arene substitution patterns:** IUPAC nomenclature for naming substituents other than hydrogen in relation to each other on an aromatic hydrocarbon:



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

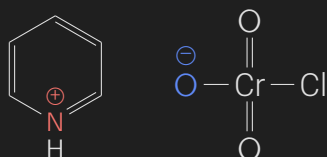


Metal Based Oxidizing Agents



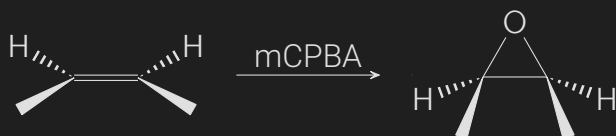
- KMnO_4 is **inexpensive**, but a very **strong oxidizing** agent and is **not soluble** in organic solvents.
 - MnO_4^- comes as KMnO_4 ; the anion must be created in order to be used as a reagent.
 - Keeping KMnO_4 cold can help reduce activation energy, leading a reduction of the more oxidized byproduct.

- 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.
- 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:
 - 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.

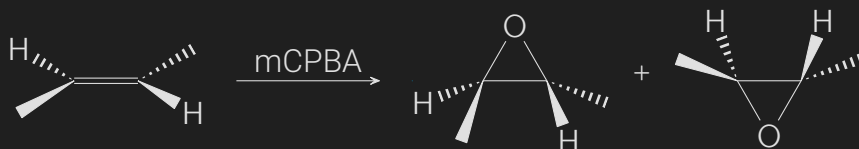


Epoxidation

- 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.

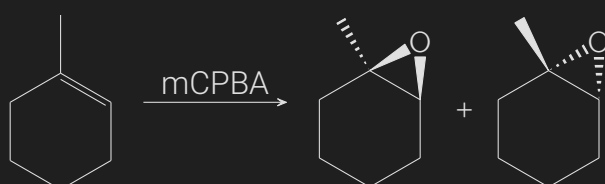
- These examples show that epoxidation reactions are **concerted** reactions, since there is no mixture of products between cis and trans products; it's dependent on the starting compound.

Epoxidation Practice Problems

1.

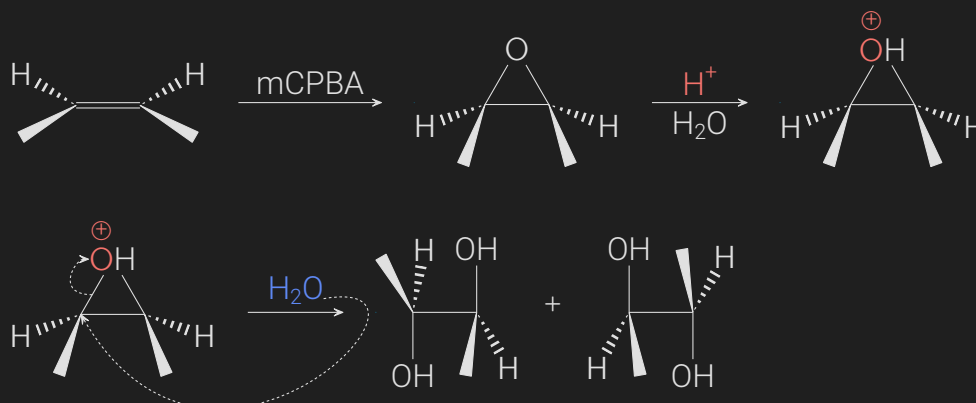


2.



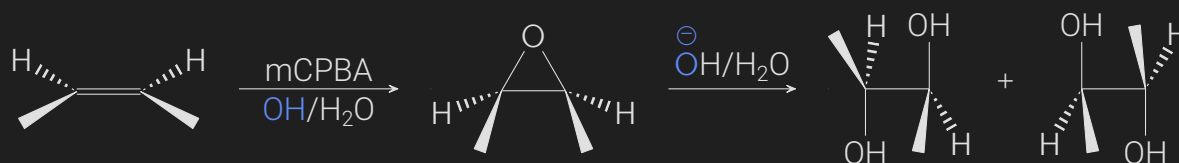
Trans Dihydroxylation

- 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:

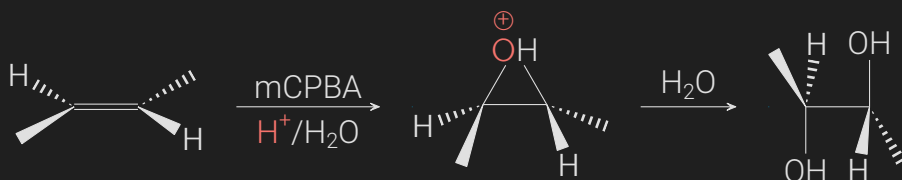


- Note: the result is the same as acid catalyzed conditions when both sides of the alkene are equally substituted.

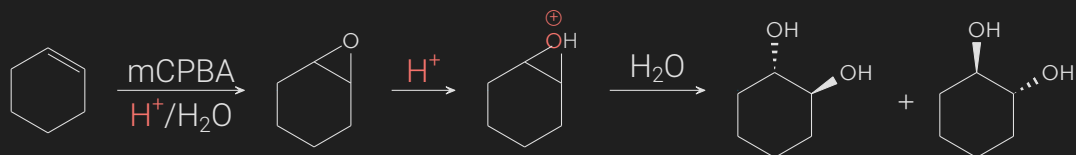
- However, under **acidic conditions** then the **more substituted** side will get attacked, while under **basic conditions** then the **less substituted** side will get attacked.

Trans Hydroxylation Practice Problems

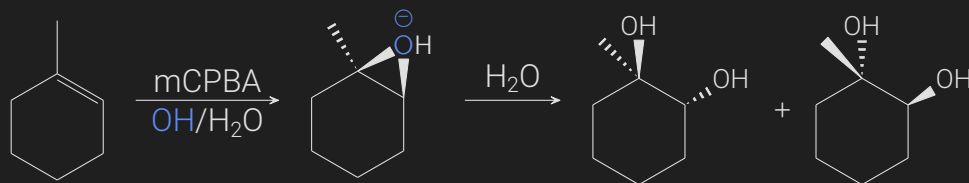
- *Trans*-alkene reactant (**acid catalyzed** in this case, but a **base catalyzed** would produce same product):



- Cyclohexene reactant:

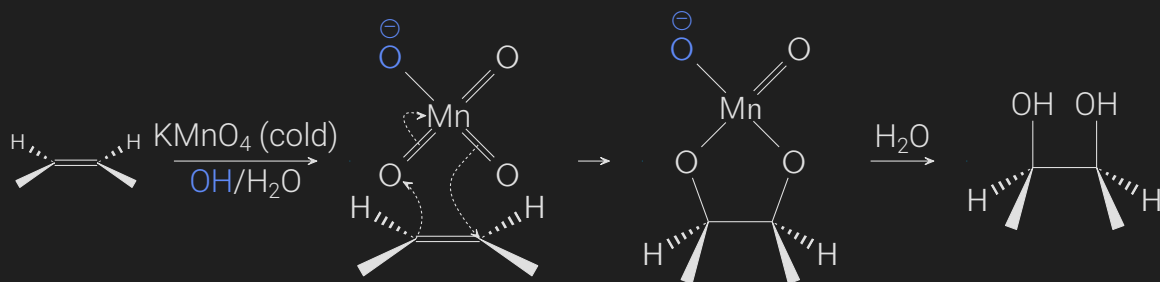


- 1-methylcyclohexene reactant:

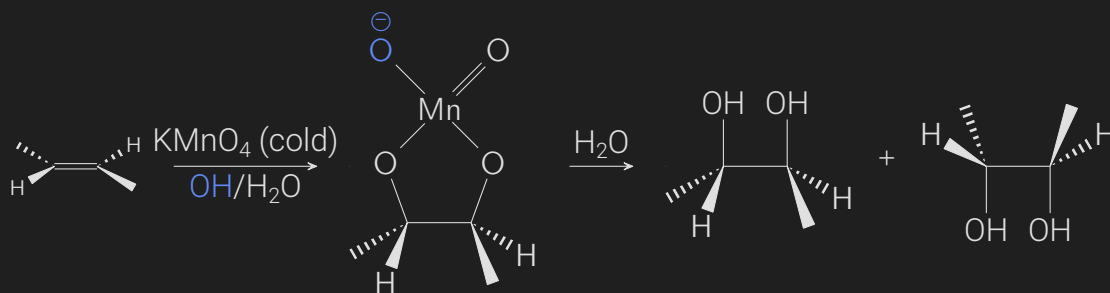


Syn Dihydroxylation

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



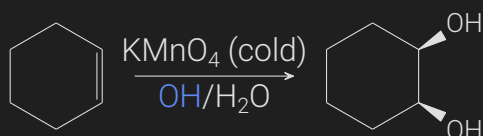
- The addition of MnO_4^- is a **concerted** reaction, which is then replaced by hydroxyl groups due to addition of water to create a syn product.
- The product is a meso compound, so it is achiral, making it have no enantiomers.
- Same reaction, but on a *trans*-alkene:



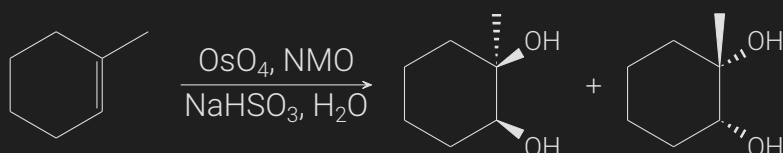
- The product is no longer chiral, giving us different products depending on which side MnO_4^- attached to.

Syn Dihydroxylation Practice Problems

- Cyclohexene with cold potassium permanganate:

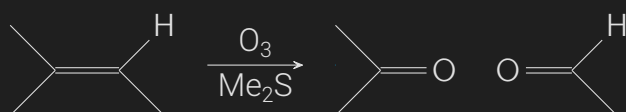


- 1-methylcyclohexene with osmium tetroxide:

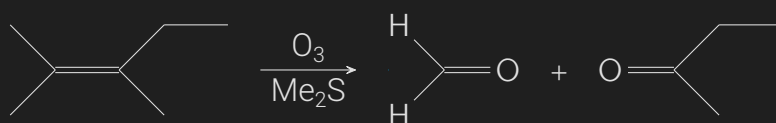


Ozonolysis

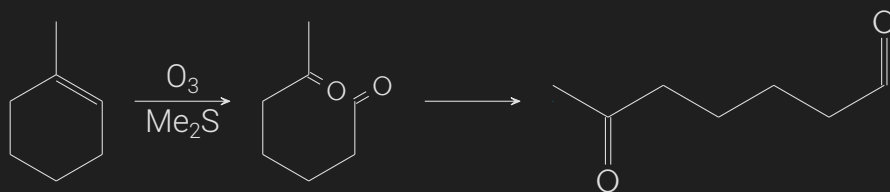
- Ozonolysis:** when the unsaturated bonds of alkenes, alkynes, or azo compounds (azo compounds not important for this class) are **cleaved** with ozone.
- Basic example demonstrating bond cleavage:



- Me_2S : 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:



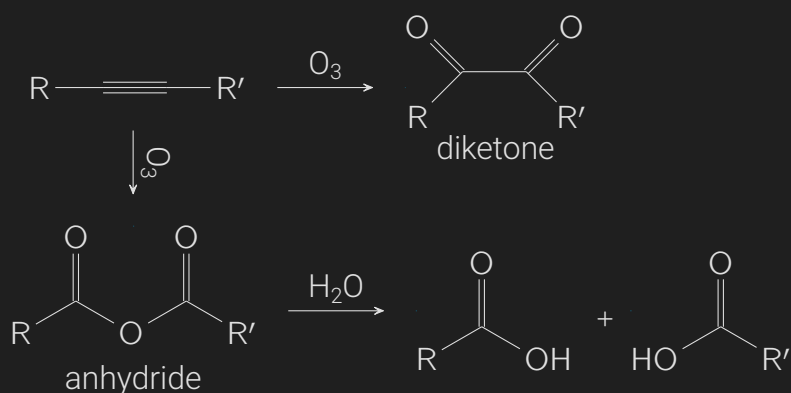
- Example with 1-methylcyclohexene:



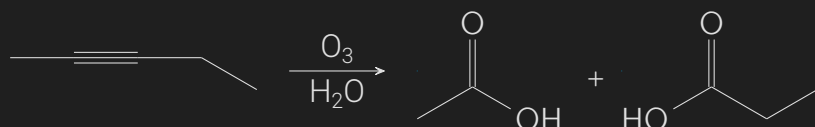
- Ozonolysis of alkynes generally gives an acid anhydride or diketone product, unlike the complete fragmentation in alkenes.

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

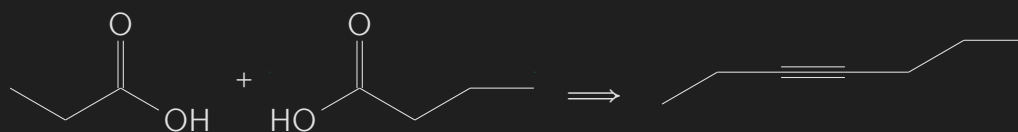
- Example of ozonolysis on alkynes:



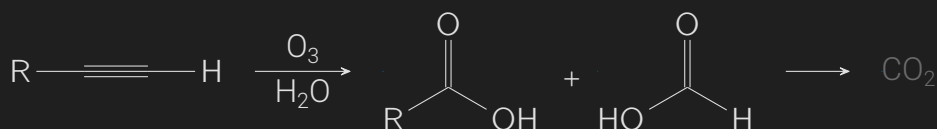
- Example of alkyne with different substituents:



- 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 CO₂.

17: Mass Spectrometry and Infrared Spectroscopy

Infrared Spectrometry

- **IR spectroscopy:** measurement of the interaction of infrared radiation with matter by absorption, emission, or reflection.
 - Used to study and identify chemical substances or functional groups.
 - Uses an infrared spectrometer to produce an infrared spectrum.
- The infrared spectrum is plotted on a graph with absorbance (or transmittance) vs. frequency.
- **Wavelength** λ : the distance over which a wave shape repeats.
- **Frequency** ν , f : number of occurrences per unit of time (period; T), i.e., $\nu = \frac{1}{T}$
- λ and ν are inversely proportional:

$$c = \lambda\nu \qquad \frac{c}{\lambda} = \nu \qquad \lambda \propto \frac{1}{\nu} \qquad c \left(\frac{1}{\lambda} \right) = \nu \qquad c\tilde{\nu} = \nu$$

- **Wavenumber** $\tilde{\nu} = \text{cm}^{-1}$: wave number is the spatial frequency of a wave, rather than number of waves per distance, making $\tilde{\nu} \propto \nu$
 - Energy: $E = h\nu$; h = Planck's constant.
 - Thus, $E \propto \nu \propto \tilde{\nu}$
 - Charts usually use frequency represented in wavenumbers.
- Bonds can be thought of as springs that are constantly moving. IR graphs exploits the fact that molecules absorb frequencies that are characteristic of their structure.
 - Peaks in the IR spectrum arise when a bond absorb energy that matches its vibrational energy, provides it has a dipole moment.
 - The **stronger the bond**, the faster its vibrations and the **greater the $\tilde{\nu}$** .
 - The **smaller the atoms** in a bond, the faster its vibrations and the **greater the $\tilde{\nu}$** .
- Calculating $\tilde{\nu}$:

$$\tilde{\nu} = \frac{1}{2\pi c} \sqrt{\frac{k}{\mu}}$$

Where k is the spring constant for the bond, c is the speed of light, and μ is the relative mass.

- A spectrograph is often interpreted as having two regions:
 - **Functional group region:** $\geq 1500 \tilde{\nu}$.
 - Most work done in this class will be in functional group region.
 - Shapes of the troughs help determine compounds in functional group region:

- -OH has a large wide “tongue shape”.
- -COOH has a wide and staggered “beard shape”.
- R-NH_2 has a double “fang shape”.
- $\text{R}_2\text{-NH}$ has a single “fang shape”.
- **Fingerprint region:** $< 1500 \tilde{\nu}$.
 - Generally there are many troughs which form intricate patterns, which can be used to determine certain compounds.
- **Conjugation:** alternating σ and π bonds. Allows for electron delocalization which in general lowers overall energy of the molecule and increases stability.
 - This leads to **lower $\tilde{\nu}$** due to the electron delocalization.
- Strong inductive effects towards electronegative atoms can retain double bond character if it is near one. This double bond “sealing” increases $\tilde{\nu}$ relative to resonance found in anhydrides due to increased double bond character.
 - Inversely, inductive effects towards double bonded oxygen decrease $\tilde{\nu}$ due to decreased double bond character.
- Carboxylic acid has even more increased resonance if it is close to another one, which decreases overall double bond character and thus decreases $\tilde{\nu}$.
 - Likewise, with NH_2 rather than OH , then there is even more of a tendency to enter resonance.

Mass Spectrometry

- **Mass Spectrometry (MS):** an analytical technique that is used to measure the mass-to-charge ratio of ions; typically presented as a mass spectrum.
 - **Mass-to-charge ratio $\frac{m}{Q}$:** a physical quantity that is used in electrodynamics of charged particles; two particles with the same mass-to-charge ratio move in the same path in a vacuum when subjected to same magnetic field.
 - **Mass spectrum:** an intensity of $\frac{m}{z}$ (a dimensionless unit of $\frac{m}{Q}$) representing chemical analysis; used to represent the distribution of ions by mass in a sample.
- Basic technique involves taking a sample, vaporizing it to gas form, then bombarding the ions with high energy electrons, then analyzing the unstable radical cations in order to determine relative abundance of ions by mass.
 - **Molecular ion peak M^+ :** corresponds to that of the molecule with all of its atoms intact, rather than a fragment, which themselves cause other minor peaks.
 - **Base peak:** The tallest peak, often is the same as the molecular ion peak, but not always.

- **M + 1 peak:** peaks that are due to molecular ions containing heavier isotopes of their atoms.
 - E.g., relative intensity of M+1 peak divided by 1.1 gives you the number of carbon atoms if the M peak has an intensity of 100%.
- **M + 2 peak:** used to determine if there are halogens in the molecule.
 - Relative natural abundance of chlorine: 3:1
 - Relative natural abundance of bromine: 1:1
 - Thus, roughly equal M + 2 peaks signal for Br, while uneven peaks signal for Cl.
- The atoms or molecules can then be identified by correlating known masses of the molecule or atoms to the identified masses through characteristic fragmentation patterns.
- Molecules containing only C, H and/or O atoms will have an even molecular weight.
- **Nitrogen rule:** molecules with an odd number of nitrogen atoms will have an odd molecular weight.
- In general, one can do the following to find the molecular formula:
 1. Assign M, M + 1, and M + 2 peaks.
 2. Multiple peaks by what ever factor makes M's peak 100%.
 3. Use M to determine if nitrogen is present, most of the time there will just be 1 if there is.
 4. Estimate number of carbons by dividing M + 1 relative abundance by 1.1.
 5. Determine if Cl or Br is present by comparison of M + 2 peaks. (use lower number isotope for calculation)
 6. Determine if oxygen is needed after accounting for halides and nitrogen.
 7. Add remaining hydrogens needed to reach M's amu.

18: Nuclear Magnetic Resonance Spectroscopy

NMR Basics

- **NMR spectroscopy:** a technique to observe local magnetic fields around atomic nuclei using excitation of nuclei with radio waves.
 - Radio waves triggers nuclear magnetic resonance, which changes resonance frequency, giving access to detail of the electronic structure of a molecule and its individual functional groups.
- NMR usually involves three sequential steps:
 - Alignment (polarization) of magnetic nuclear spins in an applied, constant magnetic field B_0 .
 - Perturbations of the nuclear spins by weak oscillating magnetic fields, usually referred to as a radio-frequency (RF) pulse.
 - Detection and analysis of electromagnetic waves emitted by the nuclei of the sample as a result of the perturbation.
- Organic chemist are usually limited to proton (1_1H) and carbon-13 ($^{13}_6C$), but can be used on more.

Proton NMR Spectroscopy

- **Proton NMR:** specific application of NMR spectroscopy with respect to hydrogen-1 nuclei within the molecule of a substance in order to determine structure.
 - There are four main characteristics analyzed in order to determine the structure, signal quantity, location (shift), area (integration), and shape (spin-spin).

Signal Quantity

- The number of signals identifies the number of different types of protons in the sample.
- **Chemically equivalent proton:** protons that share the same chemical environment.
 - CH_3 , CH_2 , and CH will always be non-equivalent to each other.
 - Protons are chemically equivalent if they are equivalent via symmetry considerations.
- Differences in chemical environment will show up as the same peak.
 - E.g., ethane has 6 hydrogens that all have the same chemical environment, while butane has two different chemically equivalent groups $2 \times (CH_3, CH_2)$

Signal Location

- **Chemical shift** δ : the resonant frequency of a nucleus relative to a standard in a magnetic field, i.e., **where** the signal shows up on the **x-axis** of the NMR spectrum.
 - $\delta = \frac{\nu_{sample} - \nu_{ref}}{\nu_{ref}}$
 - ν_{sample} : absolute resonance frequency of the sample.
 - ν_{ref} : absolute resonance frequency of a standard reference compound in the same applied magnetic field B_0 .
 - δ expressed in parts per million.
- Chemical shift can have deviations; exact value depends on molecular structure of solvent, temperature, magnetic field, and neighboring functional groups.
 - Tells us about the chemical or electrical environment in regard to proton NMR.
- NMR plots have an x-axis of 14–0 ppm.
 - Closer to 0 is the “upfield.”
 - Closer to 14 is the “downfield.”
 - Comparisons are relative.
- **Shielding**: an opposed magnetic field (B_i) to an applied field (B_0) induced by circulating electrons from adjacent bonds and atoms.
 - $B = B_0 - B_i$
 - **Shielded**: when nucleus of interest is surrounded by high electron density, making it more **upfield**.
 - **Deshielded**: the inverse of shielded; when electron density is pulled away from the nucleus, making it more **downfield**.
- Increased electronegativity of nearby atoms decreases shielding (increasing deshielding), thus making the chemical shift more downfield.
- Inductive effect decreases with distance, decreasing degree of chemical shift.
- Electron donating groups: OH, OCH₃, R, NR₂.
- Electron withdrawing groups: carbonyl groups (must be attached to ring), nitro groups.

Signal Integration

- NMR plots give the number of hydrogens responsible for a given peak by using an integration curve (area under the curve).

Signal Shape

- The splitting pattern of signal peaks reveal how many hydrogens neighbors exist for a particular group of equivalent hydrogens.
- In general, splitting will result in $N + 1$ peaks, where N is the number of hydrogens on the adjacent atom(s).
- **Singlet**: no hydrogens on adjacent atom.
- **Doublet**: one hydrogen on adjacent atom, resulting in two peaks of equal size.
- **Triplet**: two hydrogens on adjacent atom, with three peaks with an area ratio of 1:2:1.
- **Quartet**: three hydrogens on adjacent atoms, with four peaks with an area ratio of 1:3:3:1
- A peak is split by n identical protons into components whose sizes are the ratio of the n th row of Pascal's triangle.

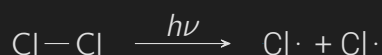
19: Free Radical Reactions

Free Radical Basics/Review

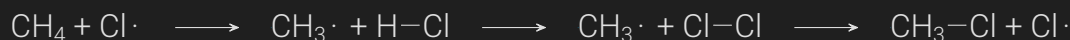
- **Free radical:** a highly reactive intermediate atom, molecule, or ion that has an unpaired valence electron formed upon homolytic cleavage, or homolysis.
 - Homolytic cleavage occurs when breaking a covalent bond, leaving each fragment with **one electron**.
 - Breaking bonds require energy, so **heat (Δ)** or **light ($h\nu$)** is needed for homolysis to take place.
 - Radical forming reactions proceed in **nonpolar solvents**, since radicals do not have a charge.
 - No rearrangements are possible with radicals.
- **Bond-dissociation energy (BDE):** one measure of strength of a chemical bond.
 - BDE is based on energy required for homolytic bond cleavage:
 - Higher BDE = less stable radical formed.
 - Lower BDE = more stable radical.
- Carbon radical geometry is not perfectly trigonal planar, instead it is a hybrid between trigonal pyramidal and trigonal planar.
- Compounds bearing C–H bonds react with radicals in the following order, reflecting C–H BDE:
 - Least stable \leftarrow $\text{CH}_3^\bullet < 1^\circ\text{C} < 2^\circ\text{C} < 3^\circ\text{C} < \text{benzyl} < \text{allyl} \rightarrow$ most stable
- **Captodative effect:** the stabilization of radicals by synergistic effect of electron-withdrawing group (EWG; “captor” group) and an electron-donating group (EDG; “dative” group)
 - Free radical can be **stabilized by resonance** in a manner directly analogous to that of carbanions and carbocations.

Radical Halogenation of Alkanes

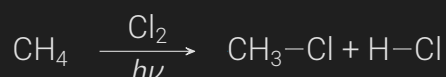
- **Free-radical halogenation:** a type of halogenation typical of alkanes and alkyl-substituted aromatics under application of UV light that proceeds by a free-radical chain mechanism.
- General mechanism (using chlorination of methane as example):
 - **Initiation:** homolysis of halogen by light or heat forming free radicals:



- **Chain propagation:** a hydrogen is pulled off the carbon leaving a methyl radical, then the methyl radical pulls a $\text{Cl}\cdot$ from Cl_2 :



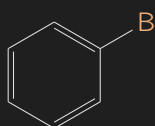
- If there is sufficient chlorine, then other products could be formed, for example a continuation to CH_2Cl_2 .
- **Chain termination:** recombination of two free radicals, needed to stop the reaction. Could result in two methyl radicals forming an impurity in final mixture. Ideally, however, the following net reaction occurs:



- Radical halogenation allows for the addition of a halogen on an alkene or other substituent, thus allowing for further reactions to take place on such normally unreactive substituents (e.g., haloalkanes) which are often needed in other reactions.
- **Statistical product distribution:** when all hydrogens in a substituent are equivalent and have equal chance of being replaced.
 - Hydrogens that form CH_2 or CH will be preferred on propane and above for alkanes.
- The reactivity of different halogens varies considerably.
 - $\text{F} > \text{Cl} > \text{Br} > \text{I}$.
 - Fluorine is difficult to control (too exothermic), with chlorine moderate to fast, bromine slow (with high UV levels) and iodine practically nonexistent (since it's endothermic).
 - Use of bromine will increase BDE preference and form a major product due to lower thermodynamic activation energy available.
 - Use of chlorine will typically create all possible products since activation energy is higher.

Allylic Bromination

- Benzylic position: the position next a benzene ring:



- **N-Bromosuccinimide (NBS):** a chemical reagent with a weak $\text{N}-\text{Br}$ bond that is highly conducive to homolytic cleavage.
 - Leads to bromine radical formation in presence of peroxides or light.

- Avoids competitive alkene addition by limiting presence of Br present in the reaction medium.
- Allylic and benzylic radicals intermediates formed are more stable than other carbon radicals; major products are allylic and benzylic bromides.
- Use of NBS in allylic or benzylic bromination is also called Wohl-Ziegler reaction.

Anti-Markovnikov Addition of HBr to Alkenes

- Recall that normal **hydrohalogenation** follows Markovnikov's Rule due to carbocation intermediate forming on the more substituted side and the **hydrogen coming in first** on the less substituted side.
- Free radical conditions result in anti-Markovnikov reactions in contrast, since the less substituted carbon is **brominated first**, then the more substituted side forms the free radical.
- This only works well with Bromine, since chain propagations using HCl or HI is more endothermic.