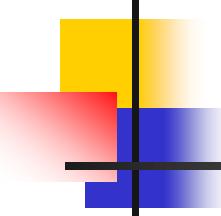


CHEMISTRY 2600

Topic #4: Electrophilic Addition Reactions of Alkenes and Alkynes

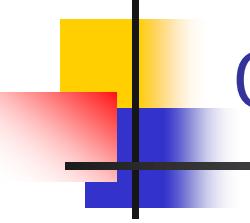
Fall 2018

Dr. Susan Findlay



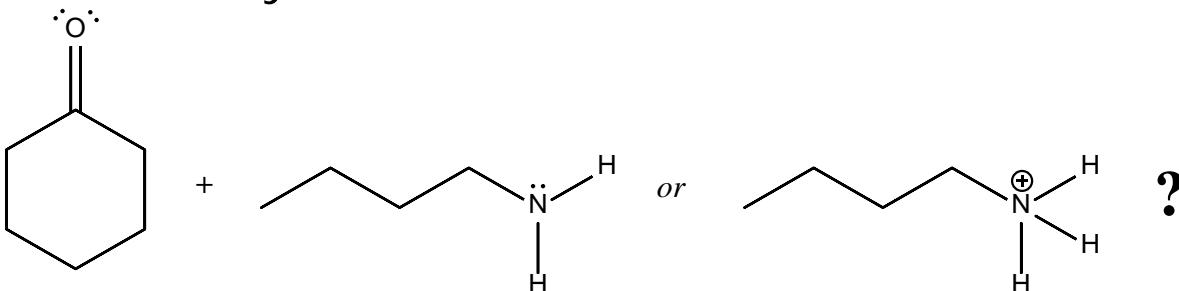
Organic Reactions (CHEM 2500 Review)

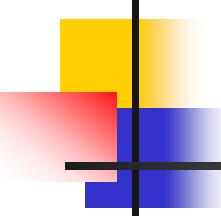
- Most reactions in organic chemistry fall into one (or more) of a few general categories:
 - Proton transfer reactions (Brønsted acid-base reactions)
 - Substitution reactions
 - Elimination reactions
 - Addition reactions
 - Rearrangements
 - Oxidation reactions (some are also additions or eliminations)
 - Reduction reactions (many are also additions)
- Which categories of reaction a molecule can undergo is determined by its composition. For example (list not exclusive),
 - Molecules with acidic hydrogens (or basic sites) can undergo proton transfer rxns
 - Molecules with π bonds can undergo addition rxns
 - Molecules with π bonds can be reduced
 - Alcohols and aldehydes can be oxidized
 - Molecules with good **leaving groups** can undergo substitutions or eliminations



Organic Reactions (CHEM 2500 Review)

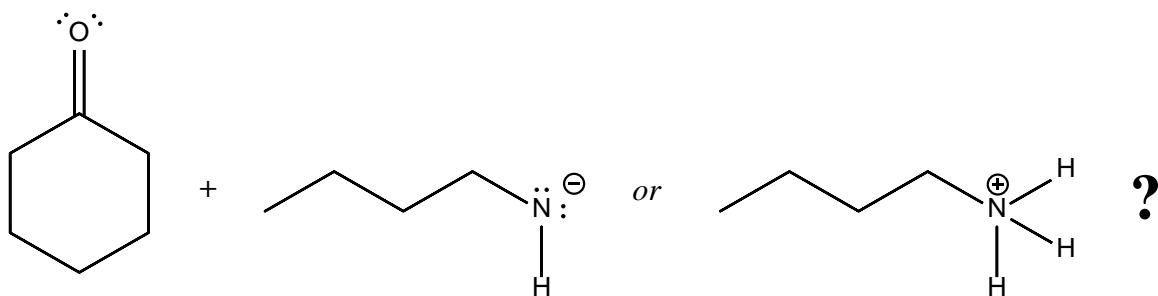
- When looking at a molecule to decide what types of reactions it is most likely to undergo, pay particular attention to any **nucleophilic** sites and **electrophilic** sites:
 - Nucleophilic site: electron rich atom(s) “looking for a nucleus”. Typically, an atom with a lone pair *or* a C-C π bond. A **nucleophile donates electrons** to an electrophile.
 - Electrophilic site: electron poor atom(s) “looking for electrons”. Typically, a carbon atom bonded to one or more electronegative atoms. An **electrophile accepts electrons** from a nucleophile.
- Which of the two nitrogen-containing molecules below can be a nucleophile? Find the most electrophilic site on cyclohexanone, and use “curly arrows” to show the attack of the nucleophile on cyclohexanone.





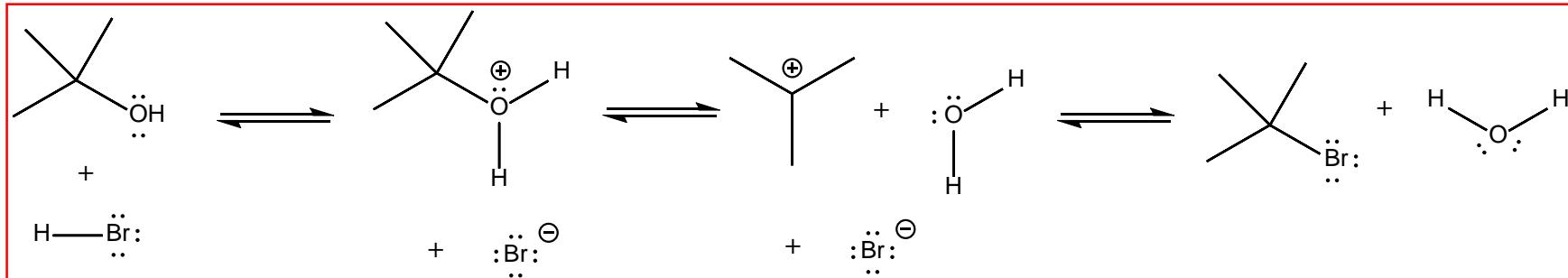
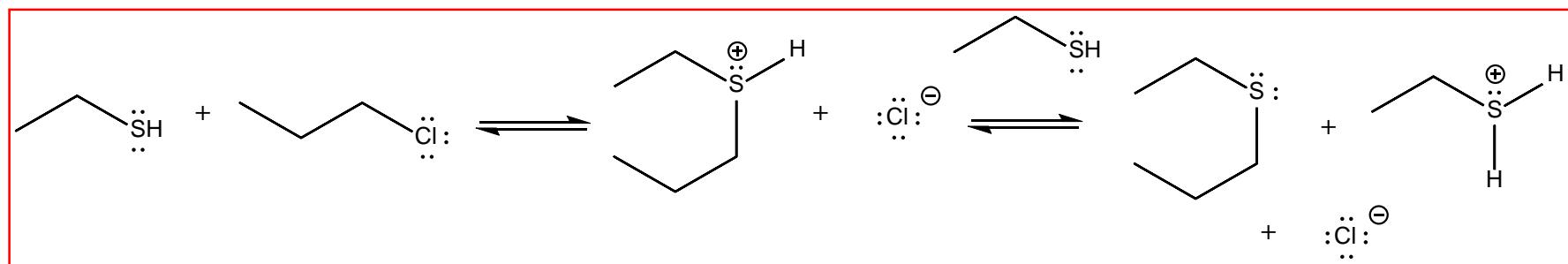
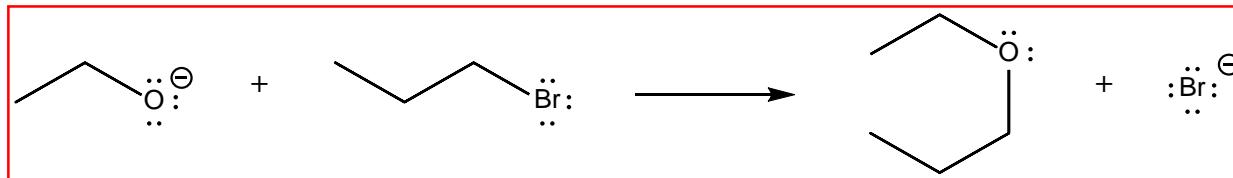
Organic Reactions (CHEM 2500 Review)

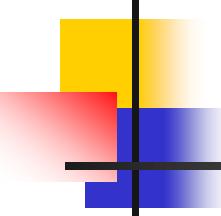
- It's also worth looking for acidic and basic sites:
 - Acidic site: hydrogen atom with a low pK_a value. To decide if a hydrogen is acidic, consider the stability of the compound formed when H^+ is removed (stable conjugate base = strong acid).
 - Basic site: electron rich atom(s) looking to acquire H^+ . Many (but not all!) nucleophiles are bases and vice versa.
- Which of the two nitrogen-containing molecules below can be a base? Find the most acidic site on cyclohexanone, and use "curly arrows" to show the attack of the base on cyclohexanone.



Substitution Reactions (CHEM 2500 Review)

- In a substitution rxn, a **nucleophile** attacks an **electrophile**, displacing a **leaving group**. Depending on the nature of the reactants, this may take one or more steps:



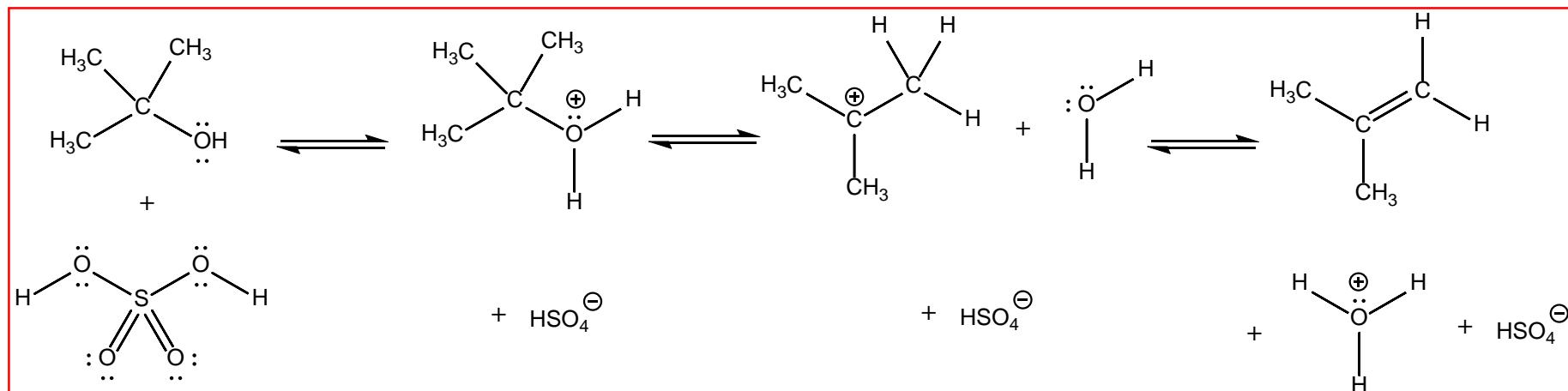
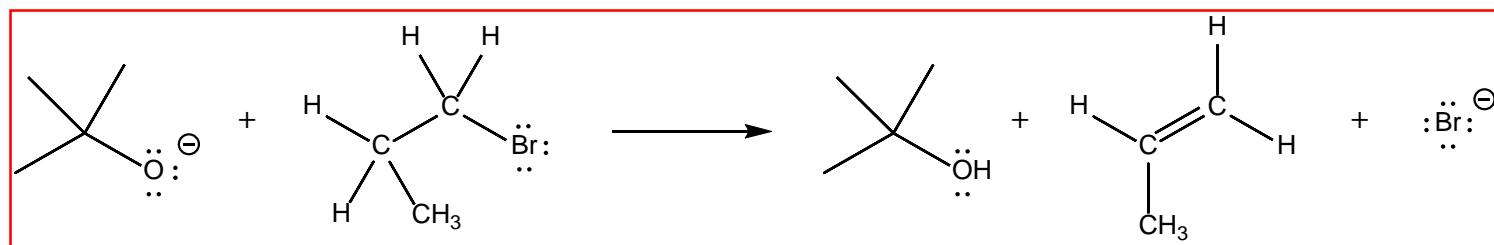


Substitution Reactions (CHEM 2500 Review)

- Upon closer examination of the substitution reactions on the previous page, they all had a few factors in common:
 - The geometry of the electrophilic carbon atom in an S_N1 *or* S_N2 reaction is **always** tetrahedral.
 - The “leaving group” always has a heteroatom bonded to the electrophilic carbon AND forms a stable molecule/ion upon departure. Note that $-OH$ had to be converted to $-OH_2^+$ first; water is much more stable than hydroxide. **Strong bases are bad leaving groups. Weak bases are good leaving groups.** *When we refer to a leaving group, we name the product made when it leaves.*
- The first reaction was drawn with a regular reaction arrow whereas the second reaction as a series of equilibria. Why?
- Which reactions on the previous page are S_N1 ? Which are S_N2 ?⁶

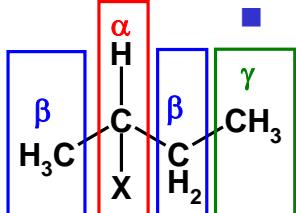
Elimination Reactions (CHEM 2500 Review)

- In an elimination rxn, a **base** attacks an **acidic hydrogen** that is **β - to a leaving group**, displacing that **leaving group**:
Depending on the nature of the reactants, this may take one or more steps:



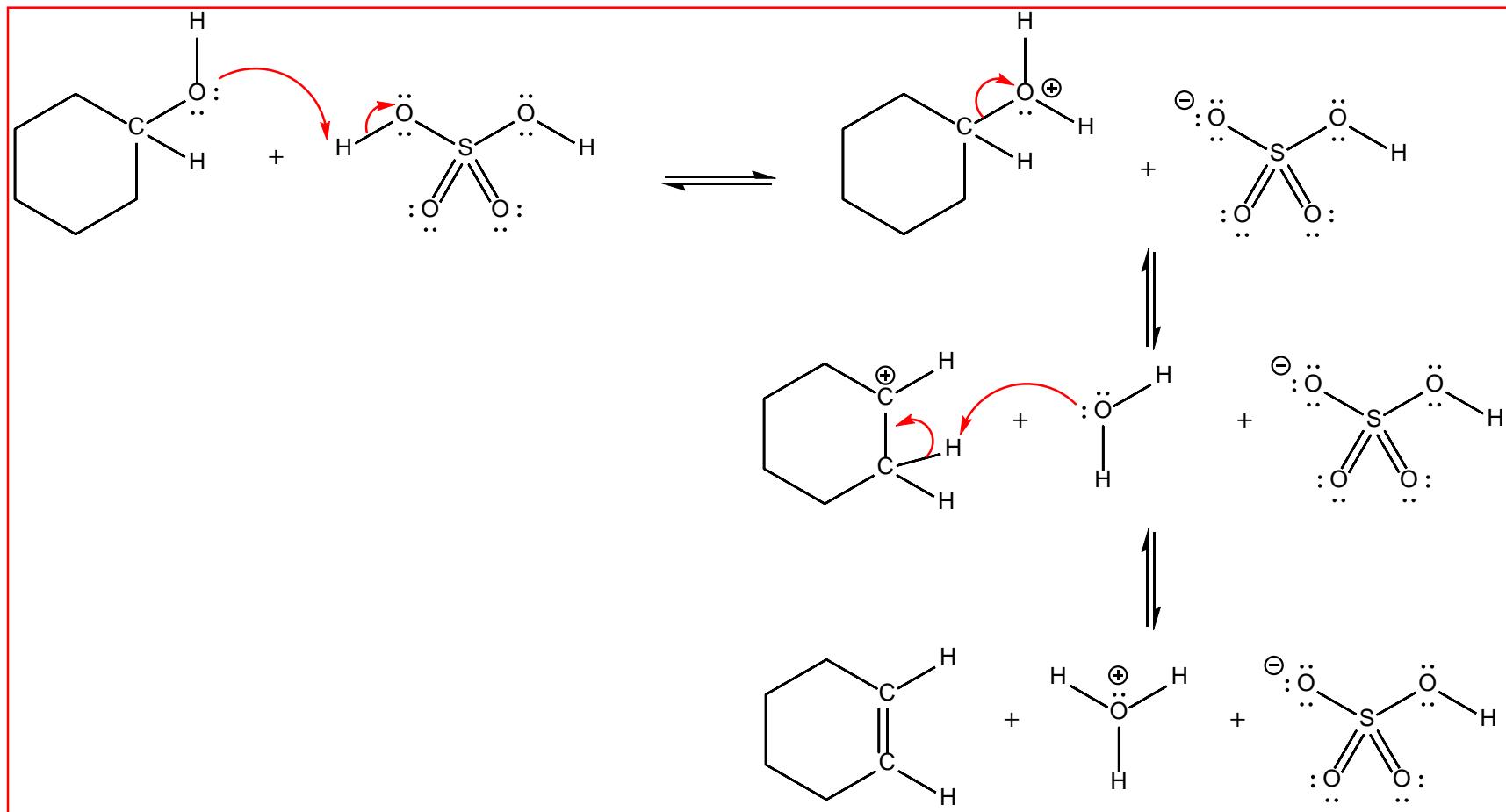
E1 vs. E2 vs. S_N1 vs. S_N2 (CHEM 2500 Review)

- As a general rule, the type of molecule that will readily undergo S_N1 reactions can also undergo E1 reactions. After all, they both have the same rate-determining step (leaving group loss)! To favour E1 over S_N1 for alcohols, choose an acid with a non-nucleophilic conjugate base. To favour S_N1 over E1, make sure a good nucleophile is available. (*You'll probably still see traces of E1 product.*)
- As a general rule, the type of molecule that will readily undergo S_N2 reactions can also undergo E2 reactions. To favour E2 over S_N2 , choose a bulky non-nucleophilic base. To favour S_N2 over E2, choose a weakly basic nucleophile (e.g. a halide).
- Before embarking on a " S_N vs. E" debate, confirm that the compound in question has one or more β -hydrogens! If not, elimination's not even an option...



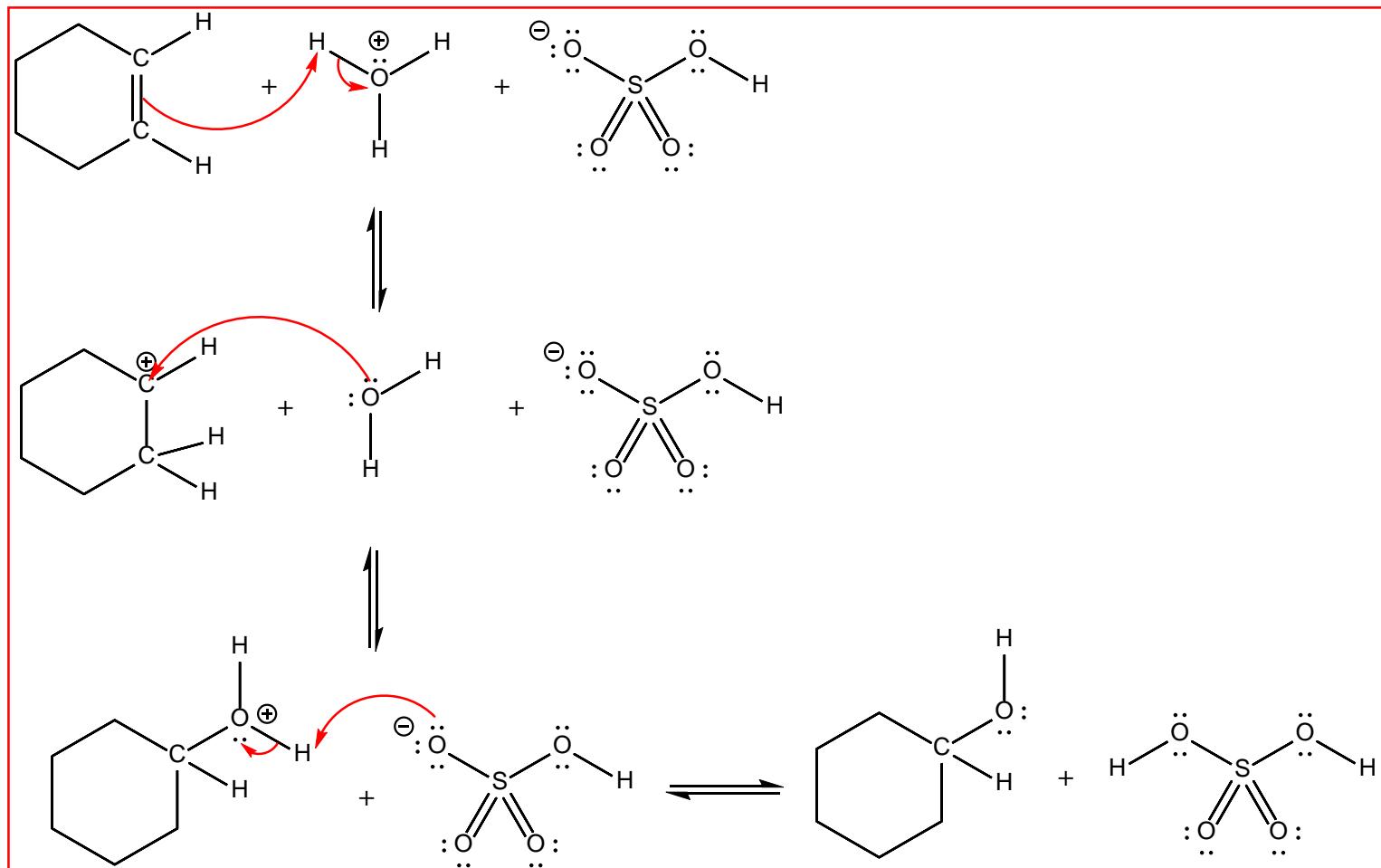
Electrophilic Addition Reactions of Alkenes (HX)

- When you looked at the mechanism for an E1 elimination reaction in CHEM 2500, you saw that every step was reversible:



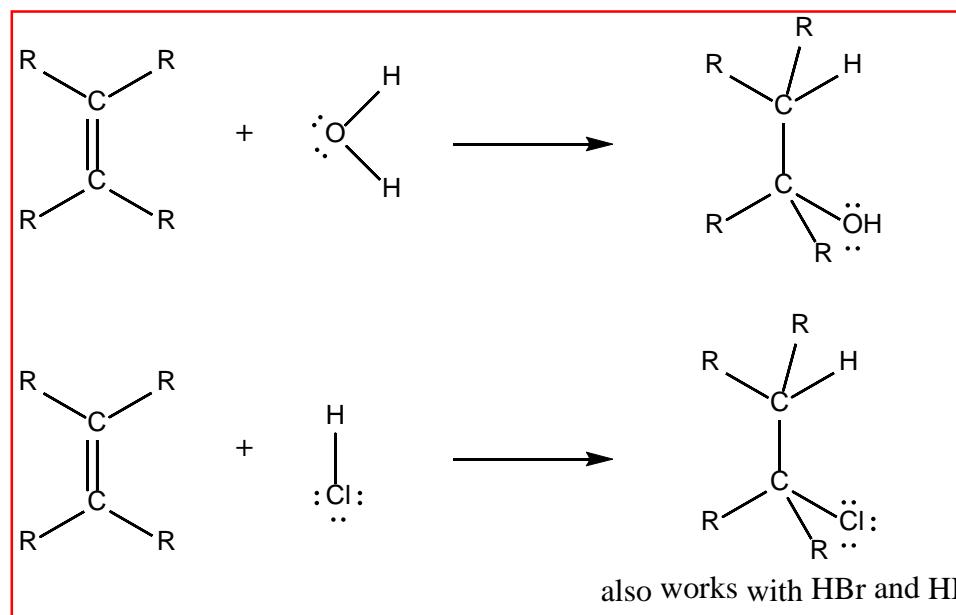
Electrophilic Addition Reactions of Alkenes (HX)

- As such, the reverse reaction (*below*) can also occur. How would you promote this reaction in which water is added to the alkene?

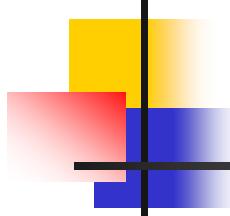


Electrophilic Addition Reactions of Alkenes (HX)

- The reaction on the previous page is an example of an **electrophilic addition reaction of an alkene**. In this type of reaction, a small molecule is “added” across a double bond:



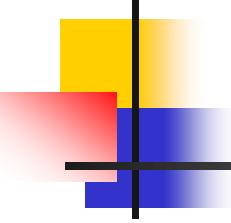
- In the first step of the mechanism, the small molecule being added serves as the electron recipient or “electrophile” (though, in some cases, it would be more accurate to say that the small molecule first acts as an acid). This is where the “electrophilic” in “electrophilic addition” comes from.



Electrophilic Addition Reactions of Alkenes (HX)

- Using the mechanism on slide #10 as a guideline, draw the mechanism for addition of HBr to *trans*-2-butene:
- Now, try drawing the mechanism for addition of HBr to 2-methyl-2-butene:

Here, you need to consider the regiochemistry of the product! 12



Electrophilic Addition Reactions of Alkenes (HX)

- When more than one constitutional isomer ("regioisomer") could theoretically be made in an electrophilic addition reaction, we look to the carbocation intermediate to tell us which will be the major product(s):

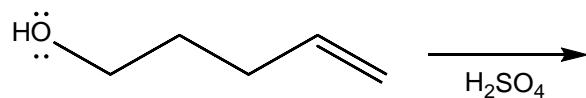
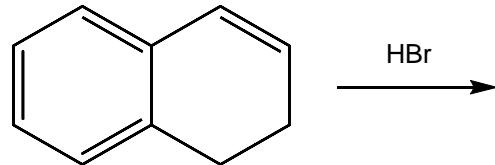
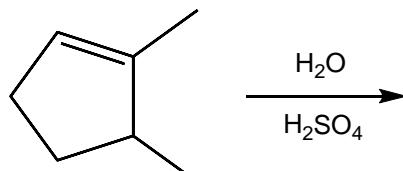
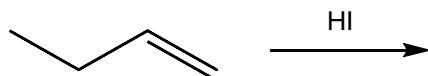
**THE MOST STABLE CARBOCATION INTERMEDIATE
WILL FORM MOST QUICKLY, LEADING TO THE MAJOR
ADDITION PRODUCT!**

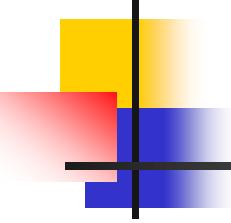
This is the rationale behind **Markovnikov's Rule** which was originally stated as:

This version works most of the time; however, if you plan to use Markovnikov's Rule, you must always watch out for resonance-stabilized carbocations!

Electrophilic Addition Reactions of Alkenes (HX)

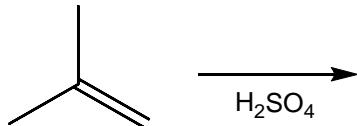
- Predict the major product(s) for each of the following electrophilic addition reactions:





Electrophilic Addition Reactions of Alkenes

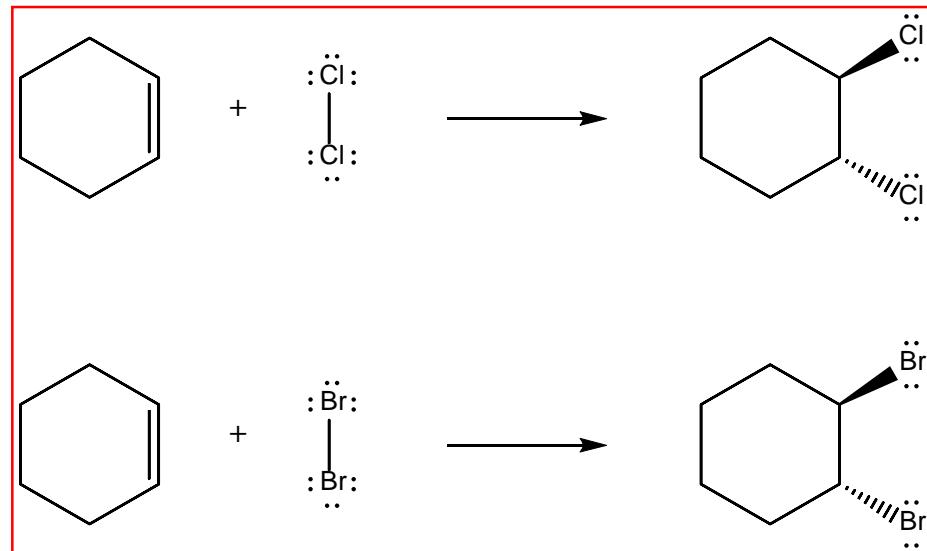
- What would happen if an alkene was treated with acid to make the carbocation, but there was no water or halide ion available?



- The example above was a dimerization; however, the reaction does not need to stop here. This is one way to make polymers.
- Biological systems use similar chemistry to make a wide variety of molecules including many hormones and steroids; however, they use enzymes instead of strong acid to generate the necessary carbocation-like intermediates.

Electrophilic Addition Reactions of Alkenes (X_2)

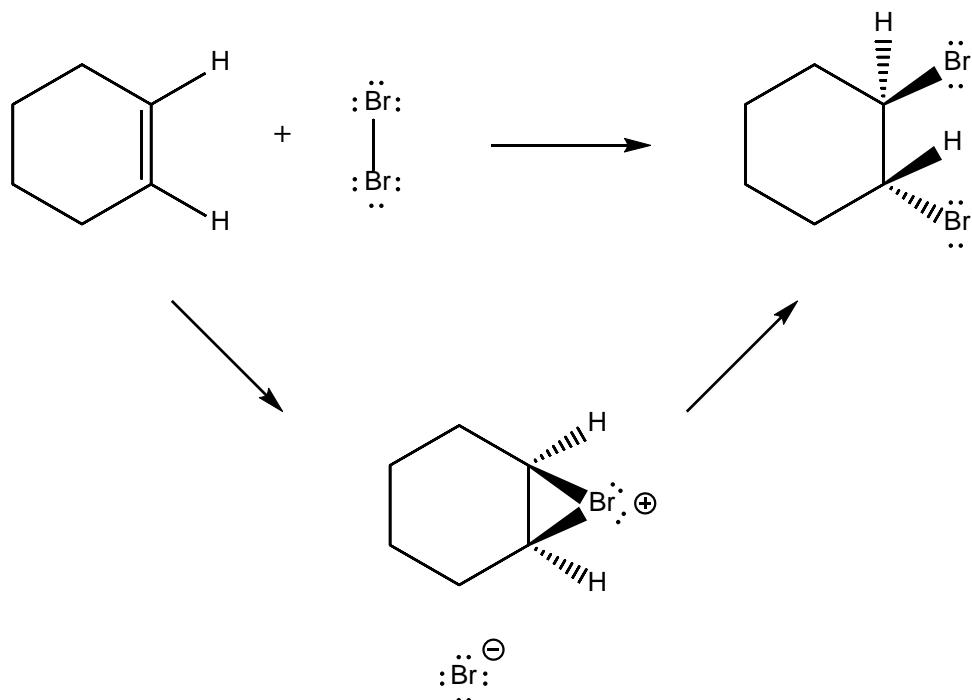
- Not all electrophilic addition reactions involve an acid (or water/acid combination). It's also possible to add halogens (usually Cl_2 or Br_2) across a double bond:



This is the basis for the most common test for presence of alkenes/alkynes – add Br_2 (a dark brown liquid) and see if its colour disappears.

Electrophilic Addition Reactions of Alkenes (X_2)

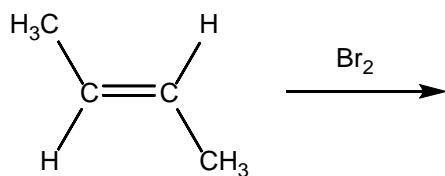
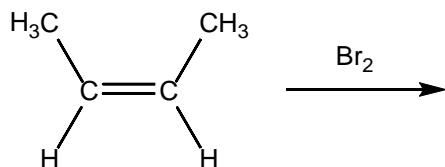
- Unlike addition of HX , addition of Cl_2 or Br_2 is **stereospecific**. The two halogen atoms **always add *anti*-** to each other. This is because of the reaction mechanism:



- The **bromonium ion** intermediate forces the bromide ion to attack in an S_N2 -like fashion from the opposite side of the Br^+ . 17

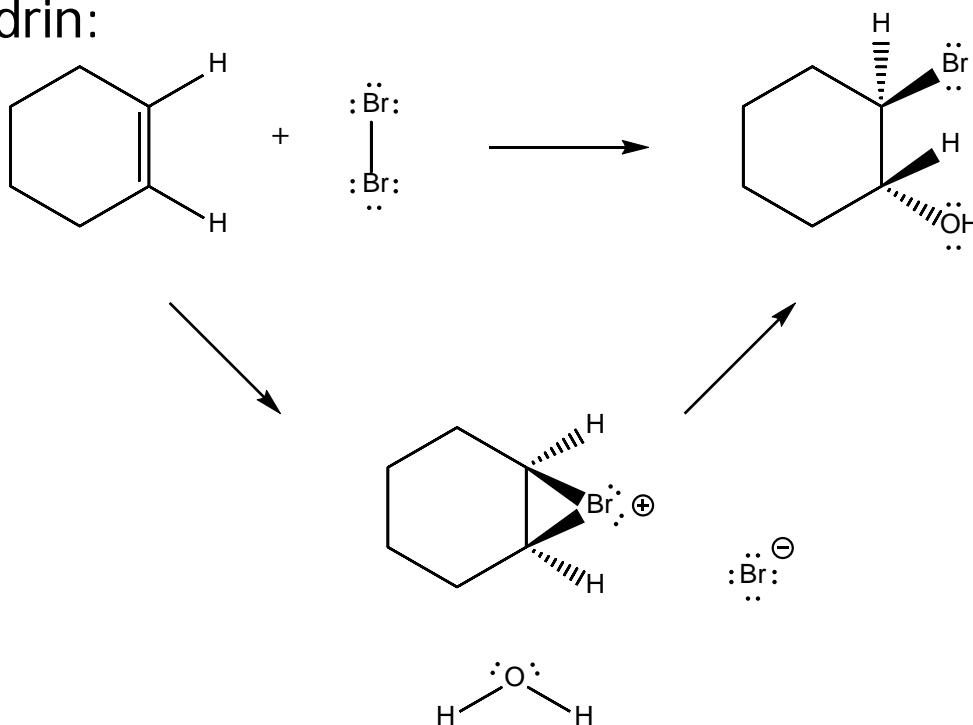
Electrophilic Addition Reactions of Alkenes (X_2)

- Even in acyclic systems, the stereospecificity of these additions often comes into play. Consider the bromination products from *cis*- and *trans*-2-butene:



Electrophilic Addition Reactions of Alkenes (X-OH)

- When an electrophilic addition is performed in a nucleophilic solvent (usually water), the solvent molecules will greatly outnumber the halide ions. Thus, in water, we get formation of a halohydrin:



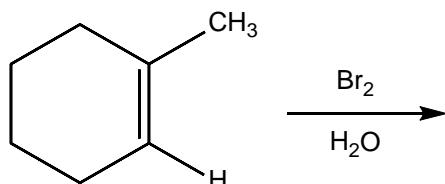
- Traces of the dibromocyclohexane will also form. Why?

Electrophilic Addition Reactions of Alkenes (X-OH)

- The bromonium ion is stabilized by resonance:

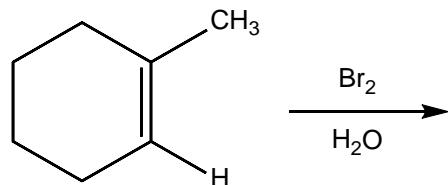
*Both C-Br bonds are strong enough that rotation is NOT possible!
The true picture is the weighted AVERAGE of these pictures.
We don't actually get "alternating" resonance structures!*

- If we generate a bromonium ion from an unsymmetrical alkene, which of the two carbocation resonance structures will be more stable? (*therefore weighted more heavily in the average picture*)



Electrophilic Addition Reactions of Alkenes (X-OH)

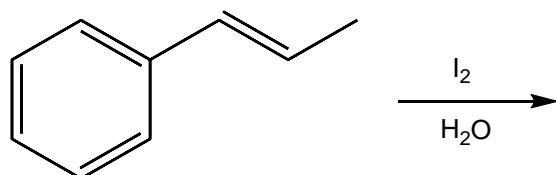
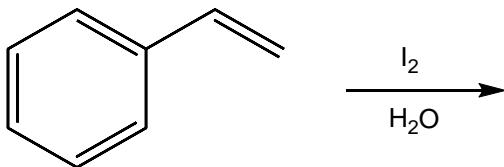
- So, the bromonium ion generated from an unsymmetric alkene will have the bromine atom pulled more tightly toward the carbon atom that makes a less stable carbocation. As such, the nucleophile will attack at the carbon atom that makes a more stable carbocation. **Markovnikov** strikes again!

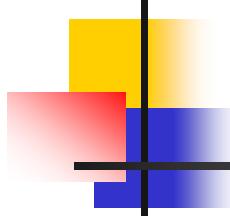


- Thus, formation of a halohydrin by reacting an alkene with a halogen in water is **stereospecific** and **regioselective**.

Electrophilic Addition Reactions of Alkenes (X-OH)

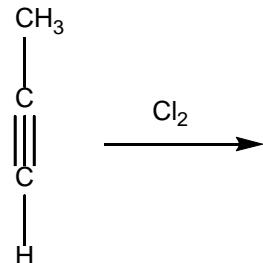
- In the presence of water, I_2 can also be used as the halogen. What are the major product(s) of each of the following reactions?





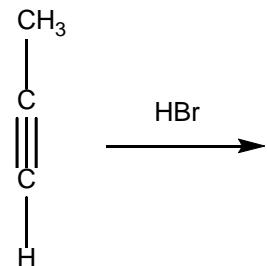
Electrophilic Addition Reactions of Alkynes

- Alkenes are not the only compounds containing π bonds. Electrophilic addition reactions can also be performed on alkynes (as well as C=O and C=N groups).
- When a halogen is added to an alkyne, two molecules of X_2 will be added per triple bond:



Electrophilic Addition Reactions of Alkynes

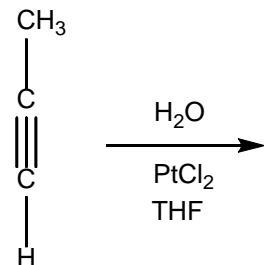
- When a hydrogen halide is added to an alkyne, two molecules of HX will be added per triple bond:



- Markovnikov's Rule applies to both additions.

Electrophilic Addition Reactions of Alkynes

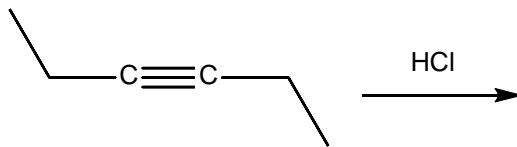
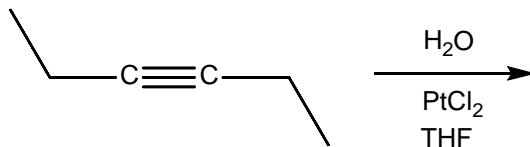
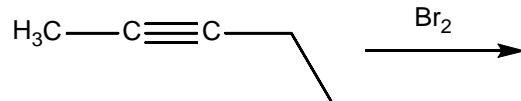
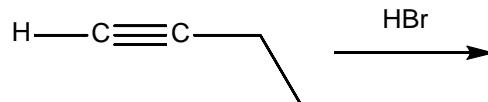
- When a water is added to an alkyne, a transition metal catalyst is necessary:



- Addition of one water molecule gives an enol. It **tautomerizes** to the corresponding ketone (a “keto-enol tautomerism”).

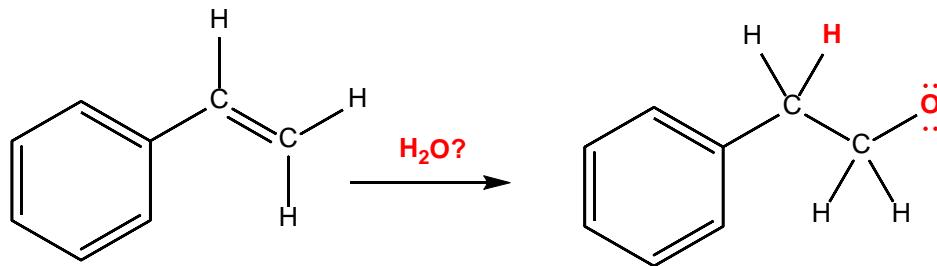
Electrophilic Addition Reactions of Alkynes

- Addition of unsymmetrical molecules (H_2O or HX) to an alkyne is only practical if the alkyne is either terminal or symmetrical. Why?
- What are the major products for each of the following reactions?



Hydroboration of Alkenes

- All electrophilic addition reactions follow Markovnikov's Rule, but sometimes, we really want to add the small molecule the other way around! How can we accomplish this? In other words, what can we do if we want to do the reaction below?

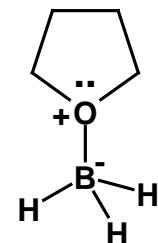
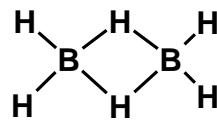


"anti-Markovnikov product"

- Problem: We can't add the water directly. We need to add something else that will put the hydrogen where we want it THEN convert the other group into an alcohol. That means we need to add a small molecule in which hydrogen is the MORE electronegative atom. The other part of the small molecule must be something we can convert into $-OH$ after the addition is done.

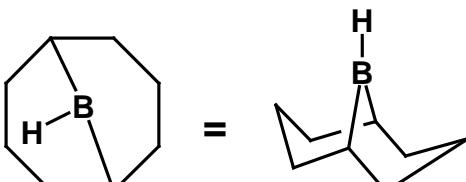
Hydroboration of Alkenes

- Solution: a borane ($\text{H-}\text{BR}_2$)
 - Hydrogen is more electronegative than boron.
 - The BR_2 part of a borane is bigger than H, so sterics will also help to put H on the more substituted carbon atom.
 - Boranes can be oxidized up to boronate esters (inserting an oxygen between the carbon and the boron) – which can be broken open, leaving behind an alcohol where BR_2 was.
- Two of the most common borane reagents are BH_3 (which MUST be in an ether solvent like THF) and 9-BBN:



Borane with no solvent is B_2H_6

Borane in THF

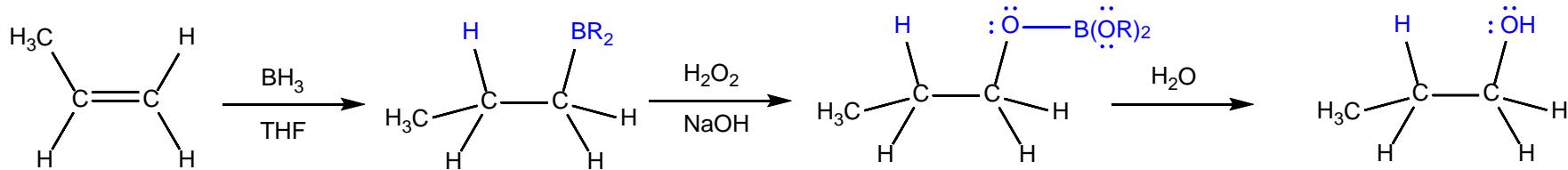


9-BBN
(9-borabicyclo[3.3.1]nonane)

If regioselectivity is a concern, choose _____.

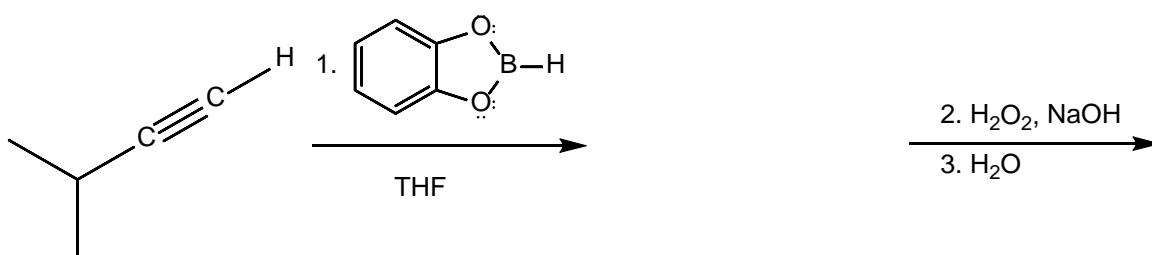
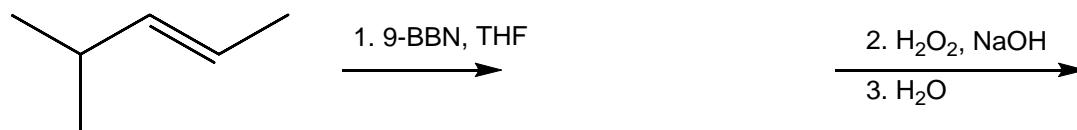
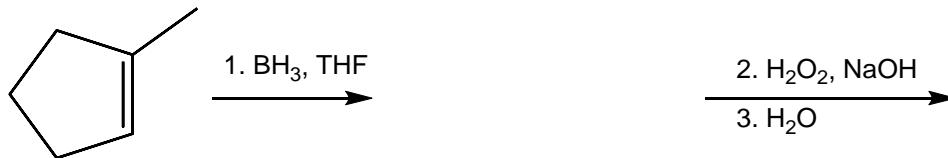
Hydroboration of Alkenes

- How does this give us the “anti-Markovnikov” alcohol (*even though we’re still following Markovnikov’s Rule at all times*)?



Hydroboration of Alkenes

- Note that, because both parts of the borane add simultaneously from the same molecule, this is always a *syn*-addition. That makes hydroborations **regioselective** and **stereospecific**.
- What are the major products for each of the following reactions?



Summary of Additions to Alkenes

