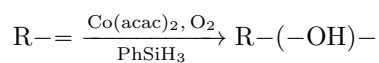


Week 7

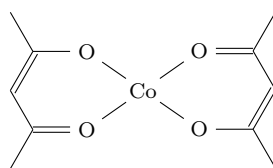
Reactions of Alkynes

7.1 Methods of Hydration

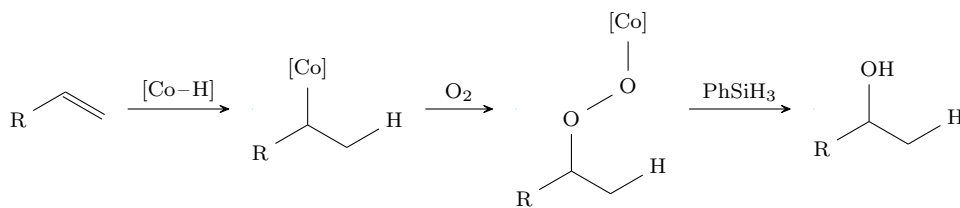
- 11/9:
- Mukaiyama Hydration.
 - A “greener” method.
 - General form.



- Mechanism:



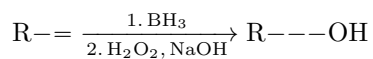
(a) Cobalt catalyst.



(b) Mechanism.

Figure 7.1: Mukaiyama hydration mechanism.

- Note that $\text{Co}(\text{acac})_2$ is a catalyst.
- Hydroboration/oxidation of alkene.
 - Nobel Prize (1979).
 - Discovered by a UChicago undergrad, H. C. Brown.
- General form.



- Regioselective (anti-Markovnikov).

- Stereospecific (H and OH add cis).
- Covers BH_3 with its empty p orbital that makes it a good Lewis acid and dimerizes to B_2H_6 with its “3C-2e” bond in the gas phase.

• Mechanism:

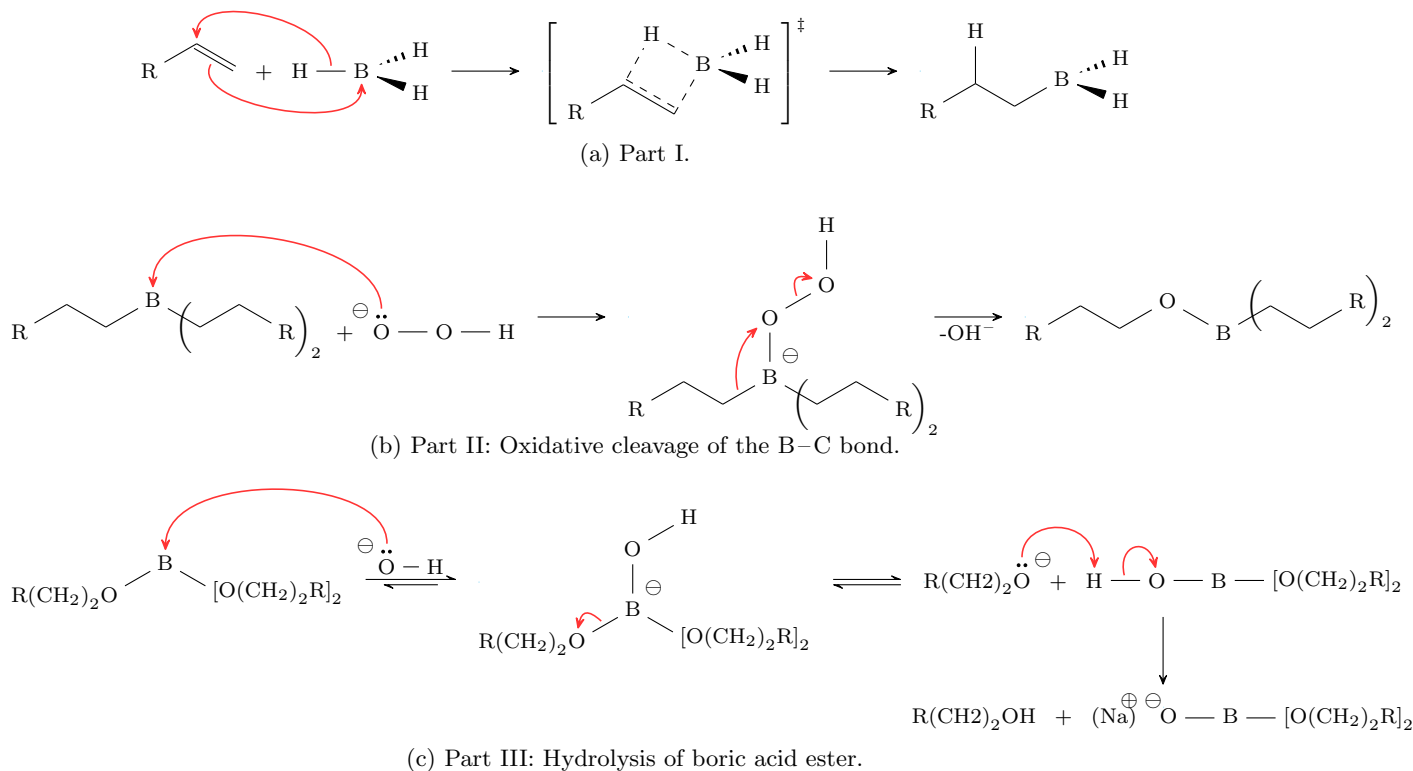


Figure 7.2: Hydroboration mechanism.

- The step in Part I is a concerted step (this is key for cis addition).
 - BH_3 adds the way it does in part I (with the H put on the more substituted carbon) due to sterics (bulky group attaches to the less bulky side) and electronics (the π -bonding electrons of the alkene connecting to the boron first will create a partial positive charge, and it is more stable to have that partial positive on the more substituted position).
 - The alkene does not attack an H on BH_3 because said H's are not acidic (it is the boron that is electron deficient).
 - Each part repeats an additional two times with the product of the n^{th} run the reactant of the $(n + 1)^{\text{th}}$ run to create the reactant of the next part.
 - In part II, mixing H_2O_2 with OH^- yields a deprotonated peroxide (HO_2^-).
 - The final product of part II is the boric acid ester.
 - Part III has a borate salt as a final byproduct.
 - The mechanism implies that the hydrogen added comes from BH_3 , and the oxygen added (as part of the hydroxide) comes from H_2O_2 .
- If we add to an alkene borane, and then a strong acid and heat, we end up hydrogenating it.
 - Summary of alcohol synthesis:
 - If you want Markovnikov addition, use...

- Acid-catalyzed hydration.
 - Oxymercuration/reduction.
 - Mukaiyama hydration.
- If you want anti-Markovnikov addition, use...
 - Hydroboration.
- Ozonolysis of alkenes.
 - An **oxidation** reaction (adding oxygen or removing hydrogen).
 - Treat an alkene with ozone and dimethyl sulfide to cleave the C=C bond and add oxygen onto each carbon, forming carbonyls (and associated groups).
 - Note that if we consider the resonance structures of ozone, we will find that charge separation is unavoidable, i.e., that the molecule must have a plus and a minus charge somewhere. This makes it very reactive.
- Mechanism.

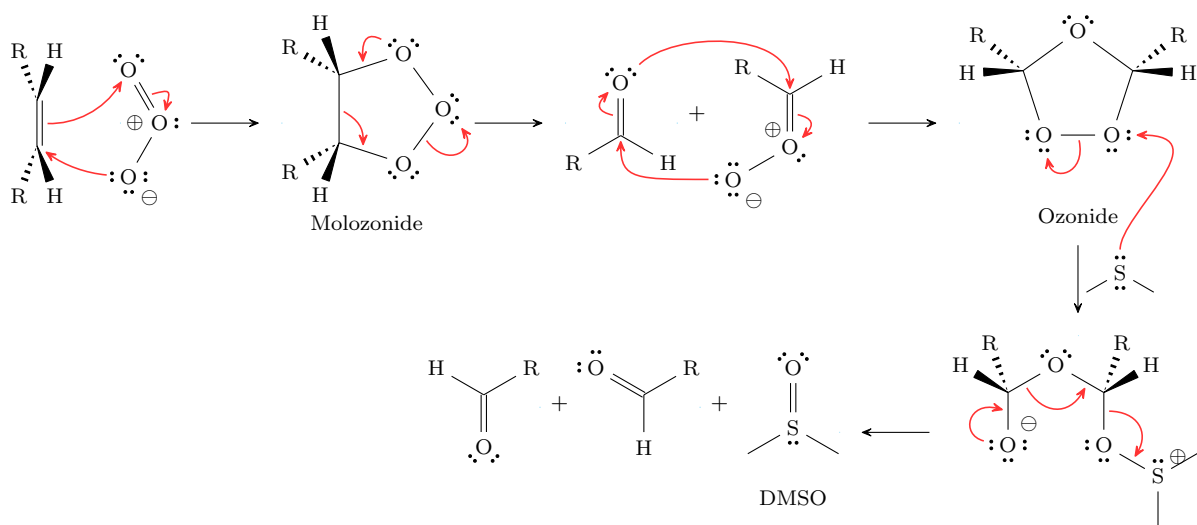


Figure 7.3: Ozonolysis of alkenes.

- The first step of the reaction is a concerted 3 + 2 addition.
 - The ozonide intermediate is more stable than the molozonide owing to its symmetry.
 - Motivation for the last intermediate to split is eliminating charge separation.
- Dihydroxylation of alkene (creation of a 1,2-diol).
- General form.

$$R- \xrightarrow[2. \text{NaHSO}_3]{1. \text{OsO}_4} R-(\text{OH})-\text{OH}$$
 - Stereospecific (*cis*).
 - Compare to bromination, which gives the *trans*-product (the difference is for mechanistic reasons).
 - The product is a 1,2-diol, or a vicinal diol.

- Mechanism.

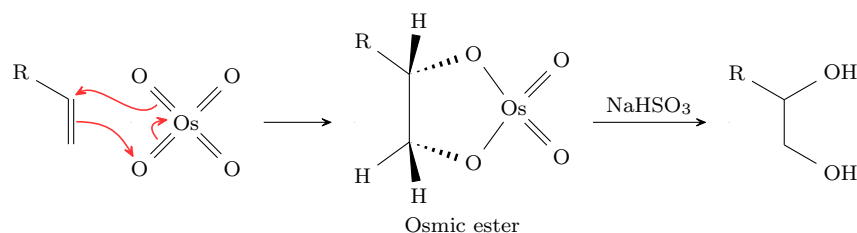
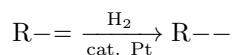


Figure 7.4: Dihydroxylation.

- The first step is concerted, once again.
- Osmium gets reduced in the first step (oxidation number goes from +8 to +6).
- In the second step, sodium bisulfite cleaves the two osmium oxygen bonds in a very complex process.
- Problems: OsO_4 is very expensive and very toxic.
- Solutions:
- UpJohn process (1976).
 - The same as dihydroxylation but with only 1% OsO_4 and NMO (N-methylmorpholine oxide) and H_2O added second instead of NaHSO_3 .
- Sharpless asymmetric dihydroxylation.
 - Nobel prize (2001).
 - Gives high ee for each product.
 - Conditions are catalytic potassium osmium salt ($\text{K}_2\text{OsO}_2(\text{OH})_4$), potassium carbonate (K_2CO_3), and potassium iron cyanate ($\text{K}_3\text{Fe}(\text{CN})_6$).
- Alkene dihydrogenation.

11/13:

- General form:



- A reduction reaction.
- The catalyst can be Pd, Ru, Rh, Ir, etc.
- This reaction happens on the solid surface of a metal catalyst.
- Most of the time, this is *cis*-addition (as we can determine with deuterium labeling).

7.2 Alkynes

- Review of bonding.
 - Consider acetylene, or ethyne ($\text{H}-\text{C}\equiv\text{C}-\text{H}$).
 - Bond angle 180° .
 - Linear.
 - *sp* hybridization.
 - Orbital diagram (similar to homework 1.7b).
 - Driving force: Break weaker π bonds.

- IUPAC nomenclature.
 - If there is a stereocenter, we need (R/S). If there is *cis/trans*, we need that, too.
 - Same rules as for alkenes except with “-yne.”
 - No E/Z for alkynes.
 - Alkenes have higher priority than alkynes, e.g., we have but-1-ene-3-yne, not but-1-yne-3-ene.
 - Alkenes have higher priority than alkynes, have higher priority than halogens, e.g., we have 3-bromo-3-methyl-1-butyne.
- Acidity of terminal alkynes.
 - Recall that sp hydrogens are more acidic than sp^2 hydrogens, are more acidic than sp^3 hydrogens (more s character means that the charge on the conjugate base is held closer to the positive nucleus and thus stabilized better).
 - Indeed, $R-C\equiv C-H$ is a reasonable Brønsted acid (it can react with a strong base).
 - For example, acetylene and sodium amide react to establish an acid-base equilibrium to the right.
 - Take home message: Strong bases can remove hydrogen from terminal alkynes to give $R-C\equiv C^-$.
 - Two more strong bases (that can fully remove a hydrogen from a terminal alkyne): NaH (sodium hydride) and LDA (lithium diisopropylamide).
 - NaOH cannot remove a hydrogen from a terminal alkyne.
- Reactions of alkynes.
 - Tip: Learn alkyne reactions simply by making an analogy to an alkene reaction.
- Hydrohalogenation.

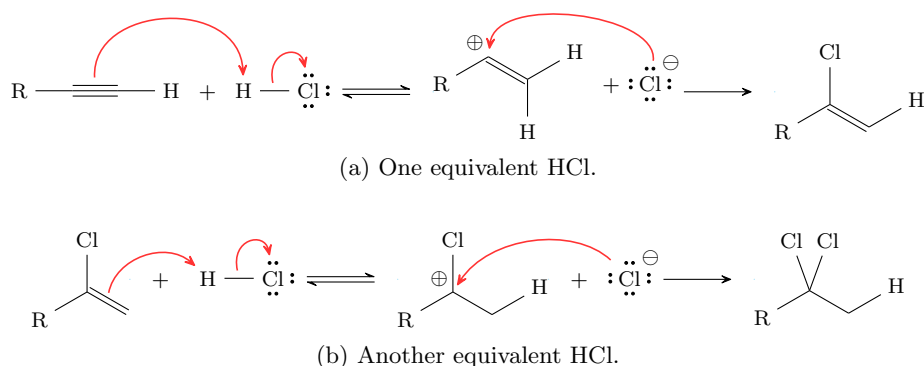


Figure 7.5: Hydrohalogenation mechanism (alkynes).

- Two equivalents of HCl yields a **geminal dichloride**.
- Still Markovnikov addition.
- If we wanted to form a vicinal (or 1,2-) dichloride, we would use chlorination of an alkene, but if we want to form the geminal chloride, we must start with an alkyne.
- Halogenation.
 - Similarly, one equivalent yields a *trans* alkene.
 - Two equivalents yield a tetrahalo alkyne.

- Acid-catalyzed hydration.

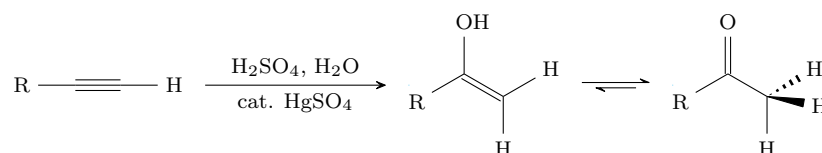
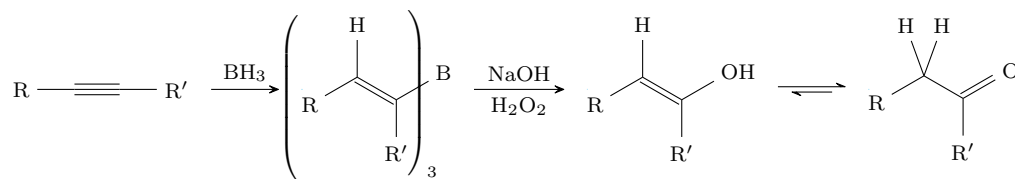
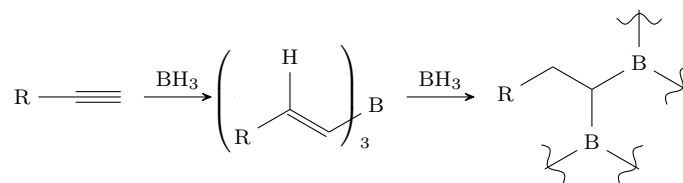


Figure 7.6: Hydration mechanism (alkynes).

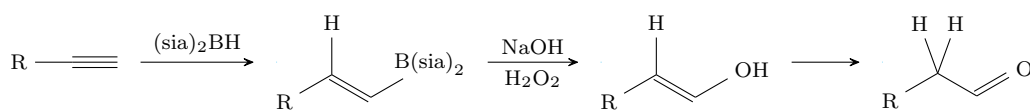
- For an alkyne, we need a more forcing condition. In particular, we will add catalytic HgSO_4 .
 - After running once, we will form an enol.
 - Enols are unstable and undergo enol-keto tautomerizations, forming a ketone.
 - If we are asked to draw the products of this reaction, draw *only* the ketone.
 - The tautomerization favors the ketone for thermodynamic reasons: The ketone is more stable (by about 15 kcal mol^{-1}), and the O–H and C–H bonds have similar BDEs.
 - This is Markovnikov.
 - A good method for ketone synthesis: Alkyne to ketone.
 - We do not need to know the mechanism because the introduction of the mercury catalyst goes beyond this class; it will be covered third quarter, though.
 - Know, however, that alkyne hydration requires a more forcing condition because alkynes' hybridization leads to tighter holding of electrons relative to alkenes. Thus, we say that alkenes are more electron rich.
 - There are some alternative greener methods, but we will not cover them.
- Hydroboration.



(a) Alkyne hydroboration.



(b) Over hydroboration.



(c) Solving over hydroboration.

Figure 7.7: Hydroboration mechanism (alkynes).

- Three equivalent of the reactant go through at once to form three equivalents of the product.
- The product results from typical hydroboration *cis*-addition followed by the keto-enol tautomerization.

- The R' group in the normal hydroboration prevents boron from adding to the alkene again via steric hindrance.
- We can solve over hydroboration by using (sia)₂B–H instead of BH₃, which only works one molecule at a time and is too bulky for over hydroboration.
 - The sia ligand is sec-isoamyl (5 carbons, prong at the end, bonds through the second carbon along the tail).
 - The full name of (sia)₂BH is di-sec-iso-amylborane.
- Three ways to make ketones:
 1. Ozonolysis of alkenes.
 2. Acid-catalyzed hydration of alkynes.
 3. Hydroboration of alkynes.
- Reduction (hydrogenation).
 - The reaction is hard to stop at the alkene if we use catalytic platinum and hydrogen.
 - To stop at the alkene stage, we can use a Lindlar catalyst (has some Pd, CaCO₃, and PbO).
 - A **poisoned catalyst** that does not have the same reactivity as platinum. It can bind with the alkyne, but not the alkene.
 - Alternatively, we can use Ni₂Br.
 - We can get the *trans* product with a special condition called dissolving metal reduction.

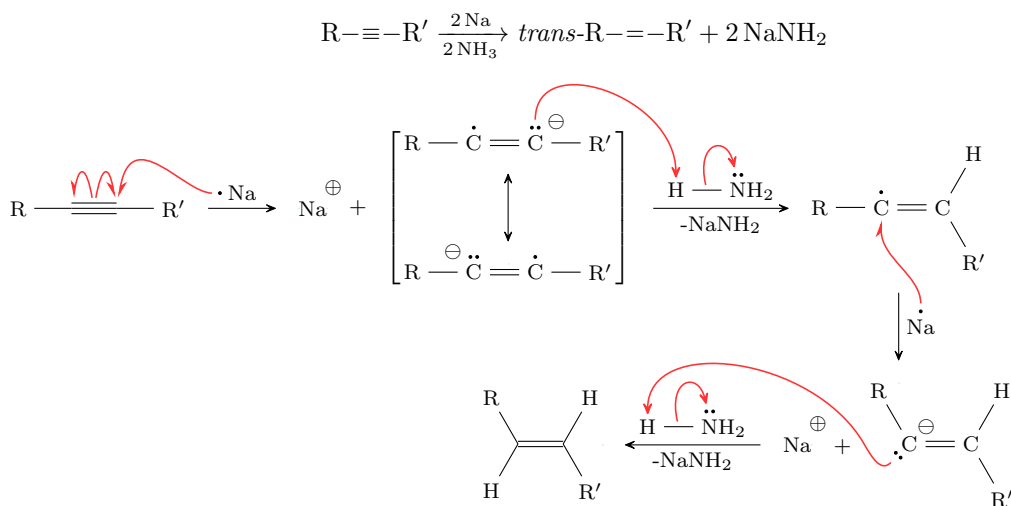


Figure 7.8: Monohydrogenation of an alkyne.

- Dissolve two equivalents of sodium in NH₃.
- Stereospecific (*trans*).
- Sodium is very electropositive, a single-electron donor. On the other hand, the alkyne is electron poor.
- We favor the *trans* intermediate for steric reasons.