

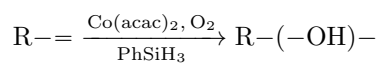
## Week 7

# Reactions of Alkynes

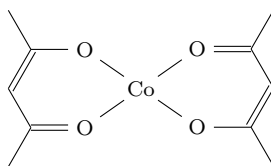
### 7.1 Methods of Hydration

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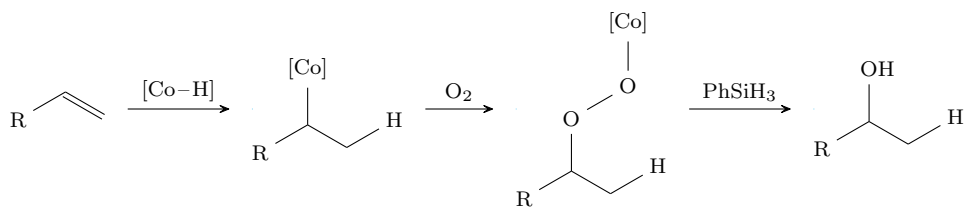
- Mukaiyama Hydration.
  - A “greener” method.
- General form.



- Mechanism:



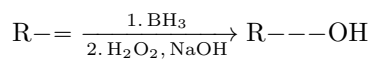
(a) Cobalt catalyst.



(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  $\text{BH}_3$  with its empty  $p$  orbital that makes it a good Lewis acid and dimerizes to  $\text{B}_2\text{H}_6$  with its “3C-2e” bond in the gas phase.

• Mechanism:

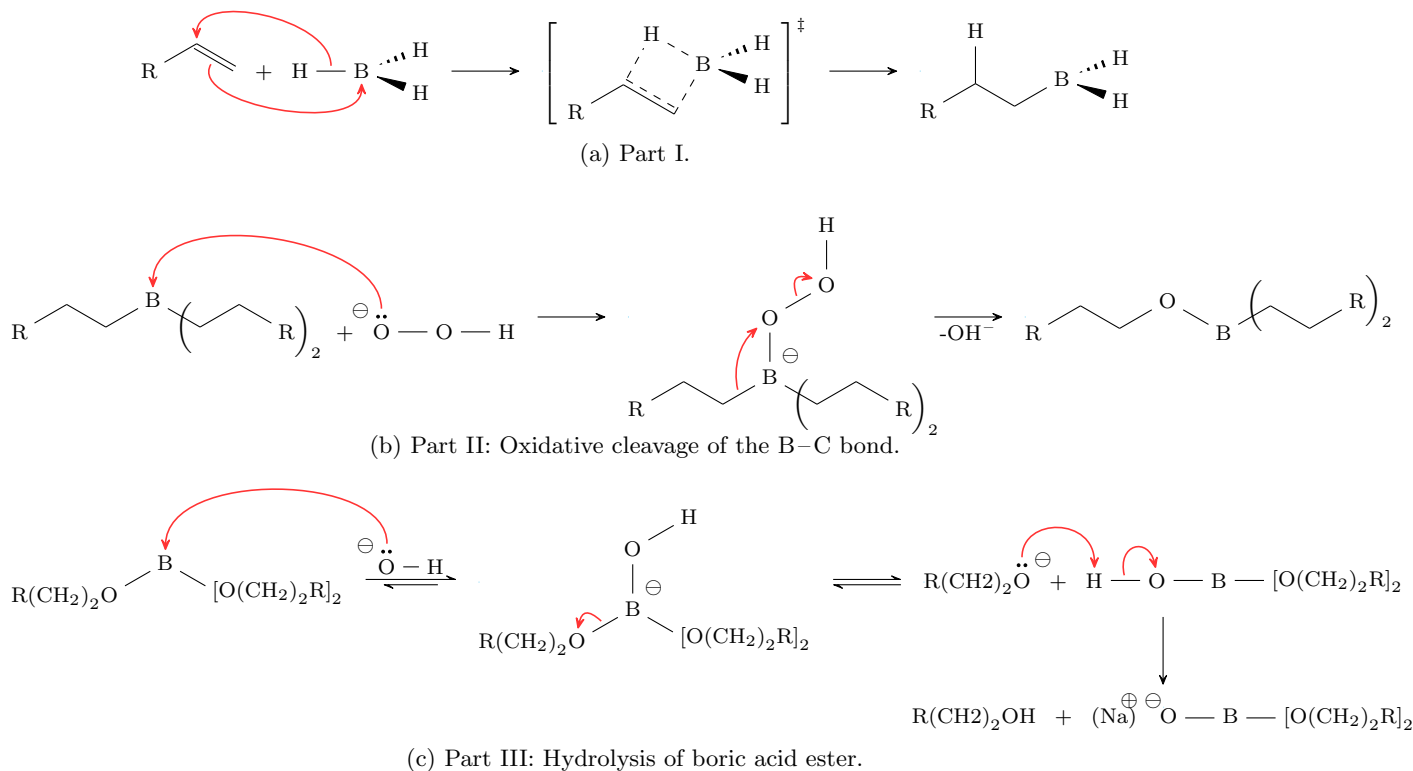


Figure 7.2: Hydroboration mechanism.

- The step in Part I is a concerted step (this is key for cis addition).
  - $\text{BH}_3$  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  $\pi$ -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  $\text{BH}_3$  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  $n^{\text{th}}$  run the reactant of the  $(n + 1)^{\text{th}}$  run to create the reactant of the next part.
  - In part II, mixing  $\text{H}_2\text{O}_2$  with  $\text{OH}^-$  yields a deprotonated peroxide ( $\text{O}_2\text{H}^-$ ).
  - 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  $\text{BH}_3$ , and the oxygen added (as part of the hydroxide) comes from  $\text{H}_2\text{O}_2$ .
- 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.

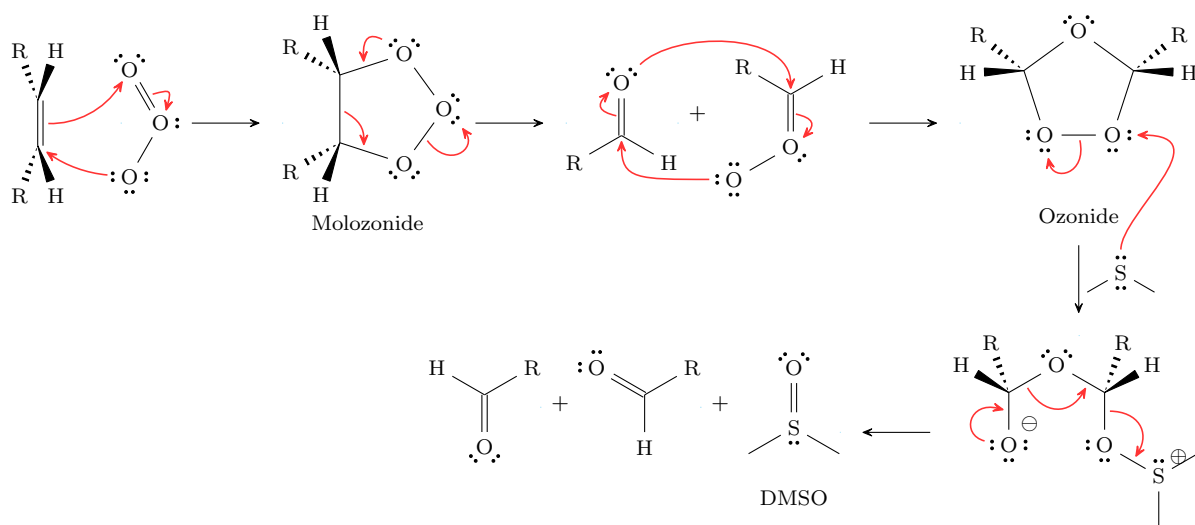


Figure 7.3: Ozonolysis of alkenes.

- 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.

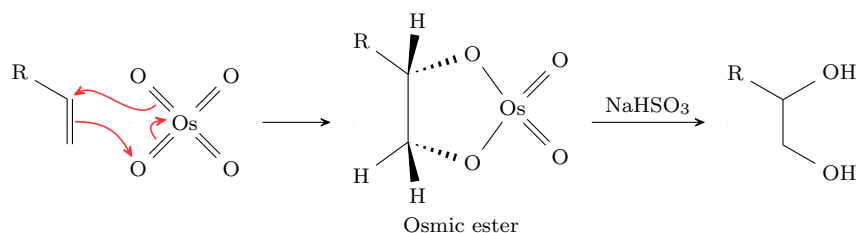
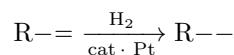


Figure 7.4: Dihydroxylation.

- 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:  $\text{OsO}_4$  is very expensive and very toxic.
- Solutions:
- UpJohn process (1976).
  - The same as dihydroxylation but with only 1%  $\text{OsO}_4$  and NMO (N-methylmorpholine oxide) and  $\text{H}_2\text{O}$  added second instead of  $\text{NaHSO}_3$ .
- 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 ( $\text{K}_2\text{CO}_3$ ), 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  $180^\circ$ .
    - Linear
    - $sp$  hybridization.
    - Orbital diagram (similar to homework 1.7b).
  - Driving force: Break weaker  $\pi$  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 Z/E for alkyne.
  - 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.

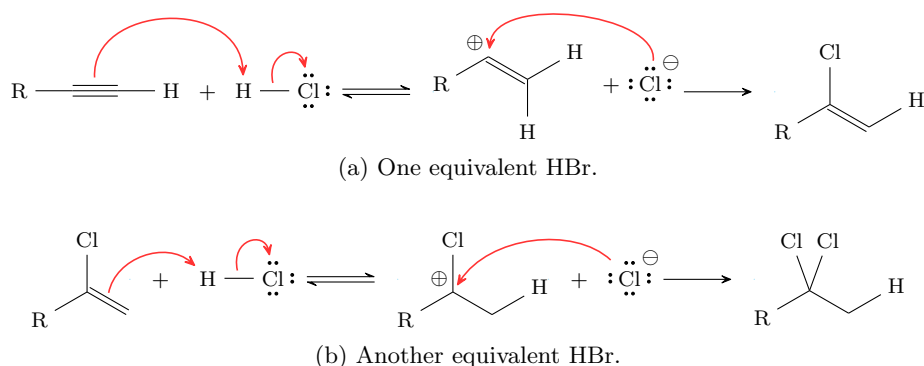


Figure 7.5: Hydrohalogenation mechanism (alkynes).

- Two equivalents of HBr yields a **geminal dichloride**.
- Still Markovnikov addition.
- If we wanted to form a vicinal (or 1,2-) dichloride, we would use chlorination, 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.

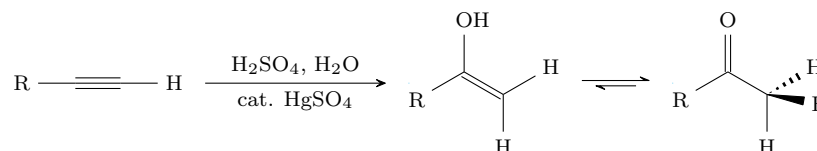
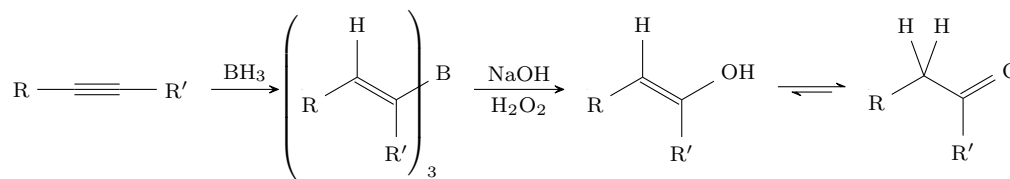


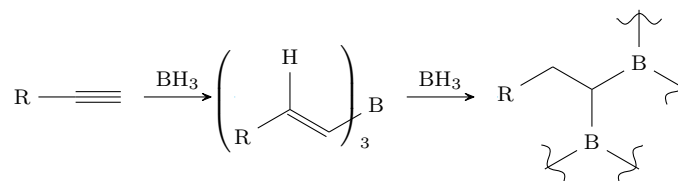
Figure 7.6: Hydration mechanism (alkynes).

- For an alkyne, we need a more forcing condition. In particular, we will add catalytic  $\text{HgSO}_4$ .
- 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  $15 \text{ kcal mol}^{-1}$ ), 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.
- 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.

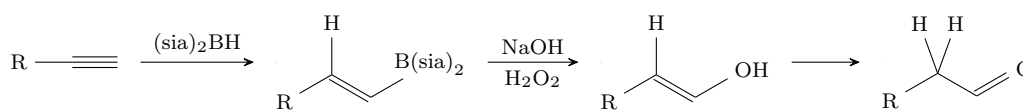
- Hydroboration.



(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)<sub>2</sub>B–H instead of BH<sub>3</sub>, 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)<sub>2</sub>BH 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, CaCO<sub>3</sub>, 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 Ni<sub>2</sub>Br.
  - We can get the trans product with a special condition called dissolving metal reduction.

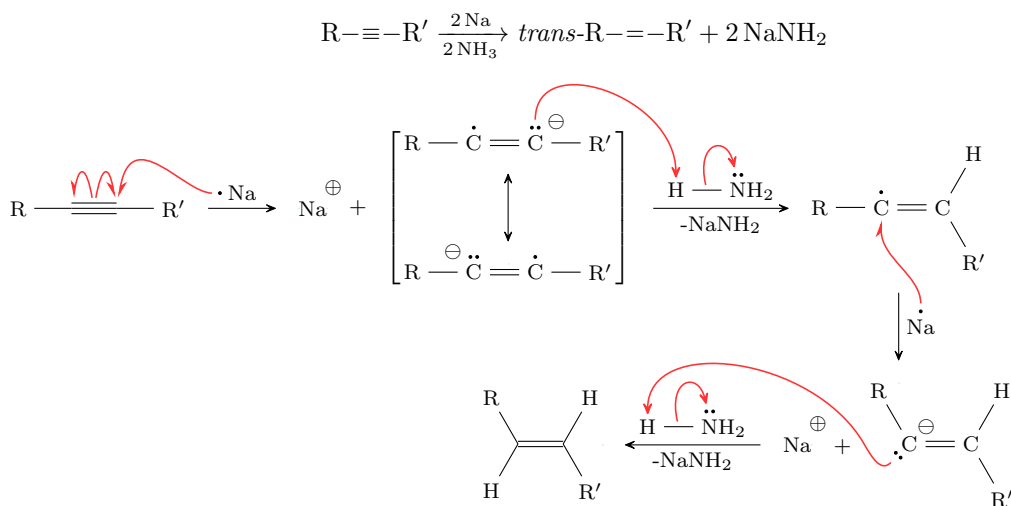


Figure 7.8: Monohydrogenation of an alkyne.

- Dissolve two equivalents of sodium in NH<sub>3</sub>.
- 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.