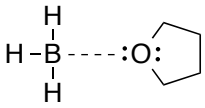
9. Hydroboration-Oxidation of Alkenes

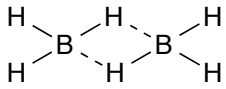
A. Introduction

1. Hydroboration-Oxidation of Alkenes

Alkenes can be oxidized to alcohols using a two-step method of hydroboration followed by oxidation. The first step of this process, the hydroboration, utilizes borane (BH_3), which is available commercially as a borane-tetrahydrofuran complex (BH3•THF). In this complex, THF acts as a Lewis base, stabilizing the electron deficient borane species. In the absence of THF, borane exists as diborane, B_2H_6, which is a toxic and colorless gas.

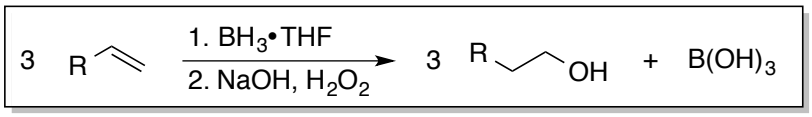


BH_3•THF



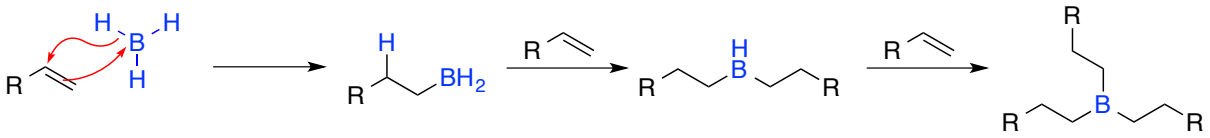
B_2H_6 (borane dimer)

In the hydroboration-oxidation process, three moles of alkene can be converted to three moles of alcohol using only one mole of BH_3. The reaction follows an anti-Markovnikov pathway where a hydrogen is added to the more substituted carbon while the hydroxyl group is added to the less substituted carbon. This regioselectivity is one of the major highlights of the hydroboration-oxidation reaction.

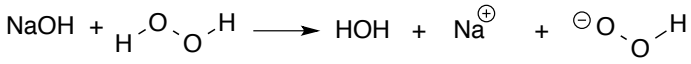


The hydroboration-oxidation mechanism is shown in figure 1. The first step of the sequence, hydroboration, involves addition of borane across the double bond. In this addition H and BH_2 are added to the alkene carbons. The hydrogen goes to the more substituted carbon while the BH_2 goes to the less substituted carbon. The BH_3 reagent is capable of reacting with three equivalents of alkene to form a trialkylborane species; this is possible because BH_3 has three hydrogens that can be added over the course of three hydroboration steps. Next, NaOH and H_2O_2 are added to oxidize the trialkylborane to three molecules of alcohol. The active oxidizing agent, HOO^-, is formed upon mixing sodium hydroxide and hydrogen peroxide. The nucleophilic HOO^- reacts with the electron deficient boron to form a negatively charged boron species. An alkyl shift from the boron to the oxygen with simultaneous loss of HO^- results in the formation of a borate ester R_3B-OR. Two more rounds of oxidation, results in the trialkyl borate ester $B(OR)_3$. Reaction of the trialkyl borate ester with NaOH and H_2O hydrolyzes the three B-O bonds, releasing three molecules of alcohol product. The byproduct is boric acid $B(OH)_3$, which can further react with NaOH to provide sodium borate Na_3BO_3.

1. Addition of B-H to three double bonds



2. Generation of the active oxidizing agent



3. Oxidation of the trialkylborane

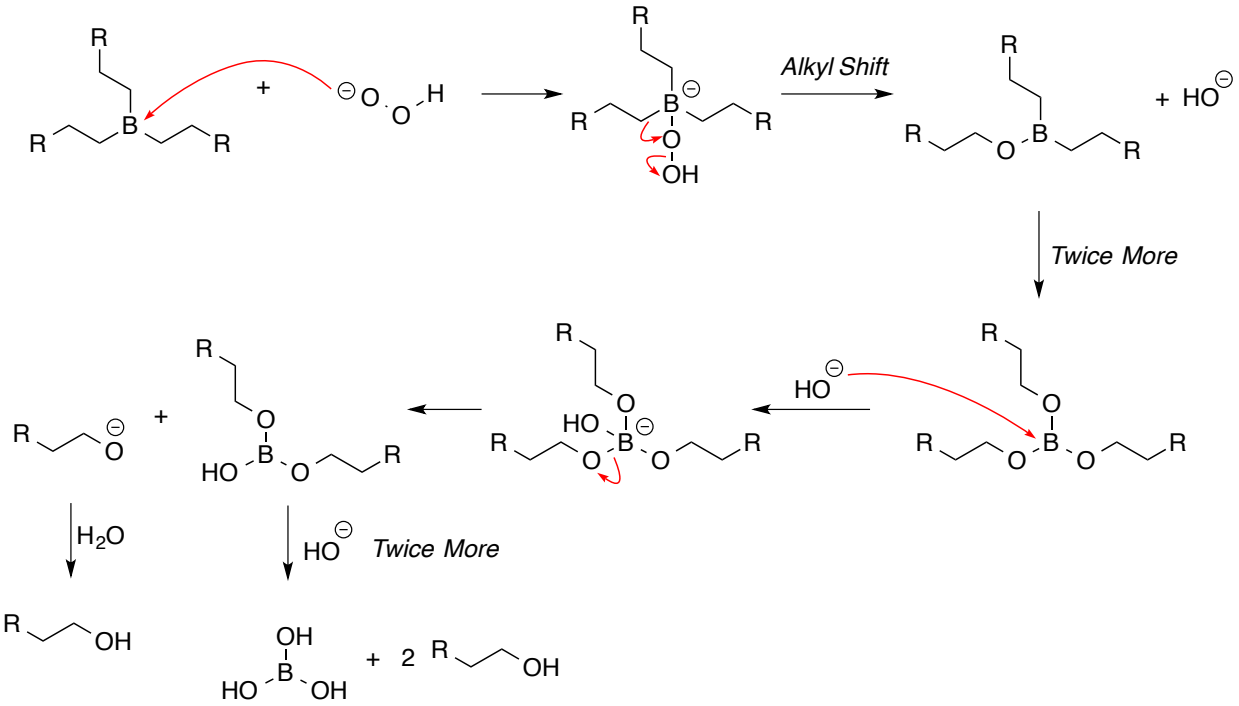
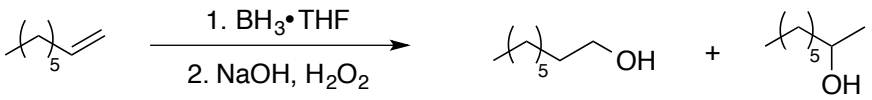


Figure 1. Mechanism of the Hydroboration-Oxidation Reaction

In the laboratory experiment, you will investigate the hydroboration-oxidation of 1-octene. The two possible products of the reaction are 1-octanol and 2-octanol. Because the reaction follows an anti-Markovnikov pathway, 1-octanol is expected to be the major product. Despite the regioselectivity, a small percentage of 2-octanol will be produced as a minor product.



Mol. Wt.	112 g/mol	130 g/mol	130 g/mol
Density (g/mL)	0.715	0.827	0.819
Boiling Point (°C)	122	195	180

Figure 2. The Hydroboration-Oxidation of 1-Octene

The products of the reaction will be examined by micro boiling point and IR spectroscopy. Additionally, it is possible to carry out GC analysis to determine the relative ratio of 1-octanol to 2-octanol that is produced.

2. Micro boiling Point

Throughout the course, you have obtained melting points on very small samples of solids using a mel-temp apparatus. Similarly, the boiling point of a liquid can be determined using a mel-temp. When the boiling point is determined via the mel-temp capillary tube method, the term micro boiling point is used.

A few microliters of liquid is loaded into a melting point capillary. There are two main ways to load the liquid. 1. Using a syringe equipped with a needle and 2. Heating the bottom half of a capillary tube on the hot plate, which drives some air out of the tube. The tube is removed from heat and the open end is then quickly placed into the liquid sample. The liquid will be sucked into the capillary tube. To get the liquid to the bottom of the tube, it can be centrifuged on low for a minute or two.

Obtain a microcapillary tube that has one open end and one sealed end and place the open end into the melting point tube and immerse the microcapillary down into the liquid. This provides a site for bubble formation during the boiling process.

Place the melting point tube into the mel-temp apparatus and heat the sample until boiling begins. You should observe fine bubbles coming out of the microcapillary tube. At this point, turn off the heat and continue to observe the sample. The temperature at which boiling ceases is recorded as the micro boiling point. You may re-heat your sample to confirm the micro boiling point if you wish.

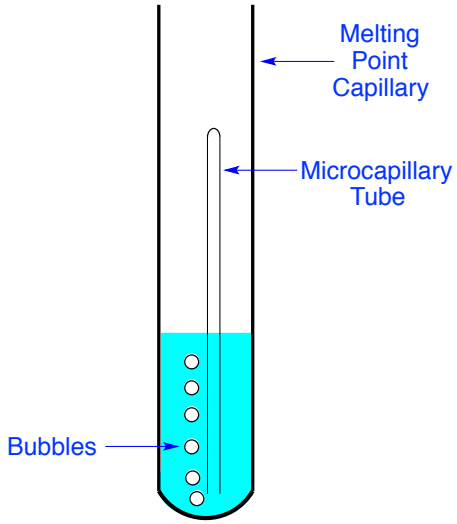
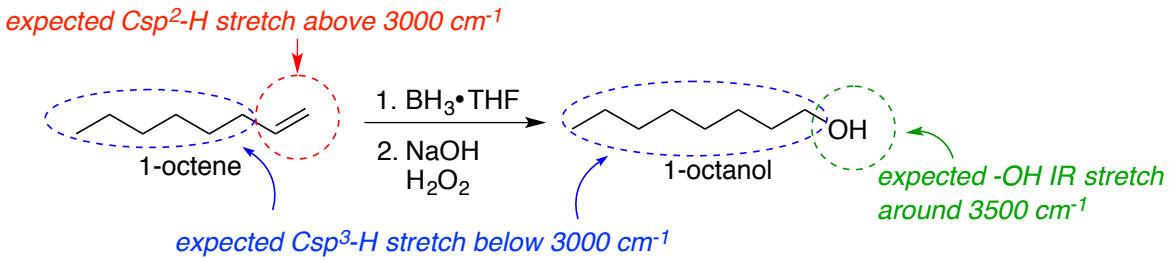


Figure 3. Micro Boiling Point Capillary

3. Infrared (IR) Spectroscopy

In this experiment, an alkene will be converted to an alcohol via a hydroboration-oxidation sequence. In going from the starting material (1-octene) to product (1-octanol), you would expect the disappearance of Csp^2-H peaks which come just above 3000 cm^{-1} and the disappearance of the C=C stretch at 1650 cm^{-1}. In the product, the appearance of an –OH stretch is observed at *ca* 3500 cm^{-1}.



You should obtain an IR spectrum of both 1-octene and the product that you isolate from the hydroboration-oxidation reaction. You will analyze both spectra to confirm that the reaction went to completion.

B. Experimental Procedure

Add 150 mg (0.210 mL) of 1-octene to a dry 5-mL conical vial with a spin vane. Attach a screw cap and septum and place this vial in the aluminum block on the stir-plate. Next, using a dry syringe fitted with a needle, withdraw approximately 0.8 mL of the 1.0 M BH_3•THF reagent.[1] Inject the BH_3•THF into your vial slowly over approximately 1 min. Slower addition results in better regioselectivity. Once the reagent has been added, let the solution stir for an additional 5 min. At this point, the hydroboration step should be complete.

To destroy excess BH_3, add 15 drops of acetone via pipet and allow the solution to stir for 2 min. Next, to carry out the oxidation step, add 4 drops of water followed by 0.3 mL of 3 M NaOH and 0.3 mL of 30% H_2O_2. ***Use caution when working with the concentrated hydrogen peroxide!*** Each of these reagents should be added over approximately 30 sec. Once both are added, allow the reaction mixture to stir for 1 min. Next, place the vial in a 50 mL beaker that is half-filled with water and heat the water bath to approximately 60 °C. Heat the reaction for 5 min at this temperature.

Workup. Add 1 mL of saturated aqueous NaCl solution (brine). A two-phase mixture should result. If insoluble material appears at the bottom of the vial, continue heating until a clear two-phase solution results. Next, cool the mixture to room temperature and add 1 mL of diethyl ether. Stir the solution rapidly to affect extraction of the organic product into the ether layer. Stop stirring and allow the layers to separate. Carefully remove the lower aqueous layer via pipet and transfer it to a supported test-tube. *This layer can eventually be discarded, but it should be retained until you know that your extraction and product isolation was successful.* Add 0.5 mL of brine to wash the ether layer. Stir the mixture, allow the layers to separate, then pipet out the lower aqueous layer and transfer it to the test tube containing the initial aqueous later. Repeat this washing procedure with one additional 0.5 mL portion of brine.

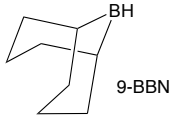
Prepare a sodium sulfate drying column (a small pipet plugged with a wad of cotton followed by the addition of 0.5 cm of sand and 3 cm of anhydrous Na_2SO_4). Transfer your organic layer to the drying column and collect the dried solution in a pre-weighed conical vial. Rinse the vial with approximately 0.5 mL of ether and pass this rinse solution through the drying column as well.

[1] BH_3 reacts violently with water. Use caution and be sure your glassware and syringe are completely dry. The BH_3 solution degrades over time resulting in a lower concentration. It may be necessary to use additional reagent if the BH_3 solution is not fresh.

Evaporate the ether using a stream of nitrogen and **very gentle** heating. Continue the evaporation process until a constant weight of material is obtained. Determine the yield, micro boiling point, and record an IR spectrum of the product.

C. Pre-Lab Questions

1. 9-borobicyclononane (9-BBN) is a hydroboration reagent that provides excellent regioselectivity. If 9-BBN were used to hydroborate one mole of 1-octene, how many moles of 9-BBN would be required? Explain.

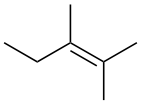


9-BBN

2. Propose a mechanism for the reaction of BH_3 with water. The products of the first reaction are H_2 gas and BH_2OH. What are the products after reaction with two additional water molecules?

3. Draw the Lewis-Acid base adduct with formal charges for the reaction of BH_3 with diethyl ether.

4. If the alkene below were subjected to hydroboration-oxidation, predict all of the possible products including stereoisomers.



D. Post-Lab Questions

1. Carbocation rearrangement is not observed in the hydroboration reaction. Explain.

2. What was the micro boiling point of your product? How does this value compare with the literature values of 1-octanol (195 °C) and 2-octanol (178.5 °C)? Based on this data, what can you conclude about the identity and purity of your product?

3. What characteristic absorption did you observe in the IR spectrum of 1-octene and your product?

4. Did the hydroboration-oxidation reaction go to completion? Is there any evidence of 1-octene remaining after the reaction?