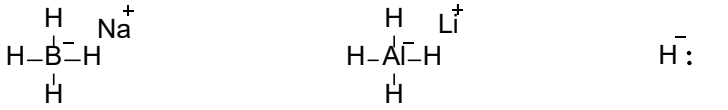
Sodium Borohydride Reduction of Benzoin

Introduction:

The most common and useful reducing agents for reducing aldehydes, ketones, and other functional groups are metal hydride reagents. The two most common metal hydride reagents are sodium borohydride ($NaBH_4$) and lithium aluminum hydride (LAH, $LiAlH_4$). These reducing agents contain a metal hydrogen bond that serve as a source of the hydride ion (a good nucleophile). Sodium borohydride is a weaker reducing agent than lithium aluminum hydride because the B-H bond is less polar than the Al-H bond. $NaBH_4$ is more selective than LAH because the former will only reduce aldehydes and ketones, whereas LAH will reduce almost anything. We will not be using LAH as it is flammable upon exposure to air, and scrupulously dry solvents are needed (as it reacts extremely violently with water).



Sodium Borohydride	Lithium Aluminum hydride	Hydride Ion
$NaBH_4$	$LiBH_4$	

When an aldehyde or ketone is reacted with $NaBH_4$ or $LiAlH_4$, followed by an acidic-water workup, an alcohol is the product. The carbonyl bond is reduced by the formal addition of H_2 across the C=O π-bond (Figure 1). Note the hydrogen atom from the reducing agent (red) is attached to the carbon, and the acidic hydrogen (blue) is the alcohol proton. Note also from figure 1 that $NaBH_4$ is generally used with water or alcoholic solvents, whereas LAH must use aprotic, ether solvents.

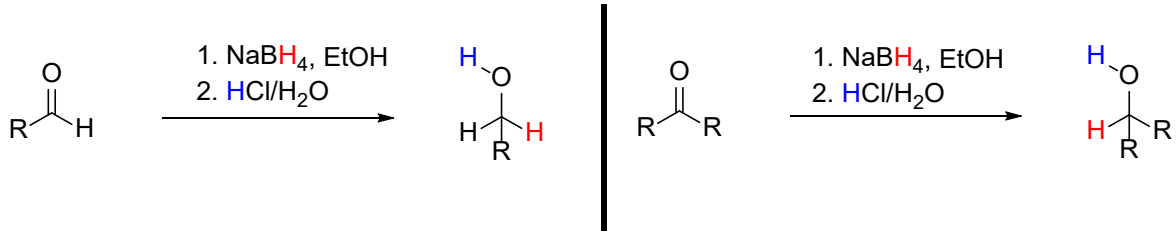


Figure 1. Reduction of an aldehyde (left) and a ketone (right) via sodium borohydride.

Figure 2 shows the rate of nucleophilic (hydride in this experiment) attack on a C=O, which is dependent on the identity of Y and Z. Thus, the more electron deficient the carbon (acid chloride, or aldehyde) the faster the attack, and the more electron rich (ketone to carboxylate), the slower the attack. In this way, more reactive carbonyl compounds can be selectively reduced in the presence of less reactive carbonyl groups.

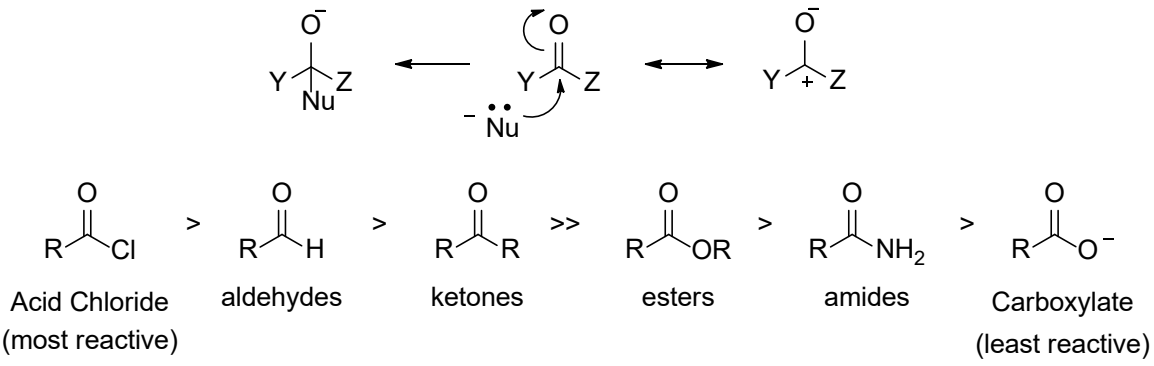
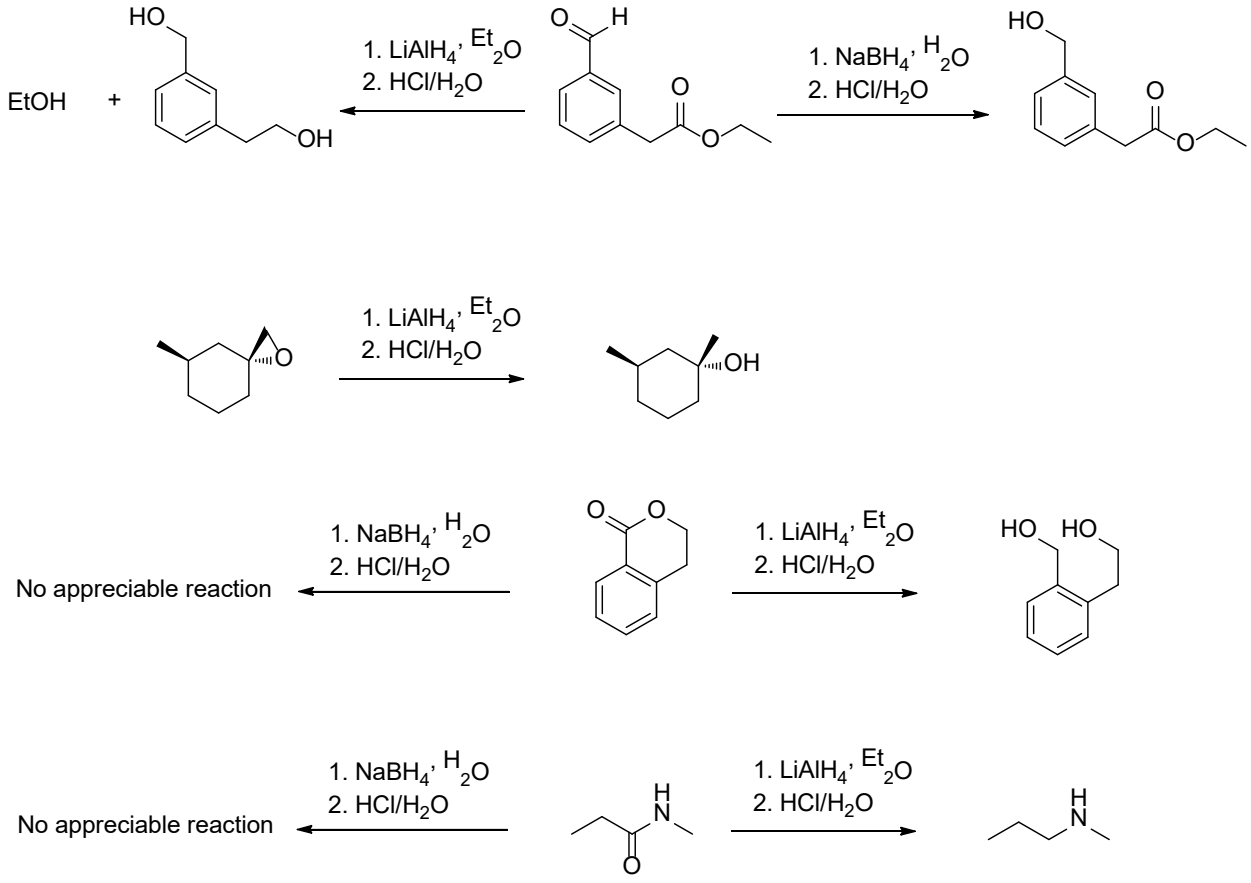


Figure 2. Relative reactivity of carbonyl groups.

Some examples of the uses of these reducing reagents are outlined below:



The Prelab:

Your table of reagents should always include molar equivalents of any non-solvent or catalytic species. Make it look like the table below. A hyphen indicates that data is not needed for that substance. This table is not entirely complete. Don't forget hazards, MPs, or any other relevant data.

Substance	mmol	MW ($g*mol^{-1}$)	Density ($g*ml^{-1}$)	Mol eq	amount
benzoin			-		
95% ethanol	-	-		-	
sodium borohydride			-		

In addition to the standard prelab write-up, provide answers to the following questions:

1. Provide a mechanism for the reduction of benzoin with sodium borohydride. Be sure to include all steps and protonations.

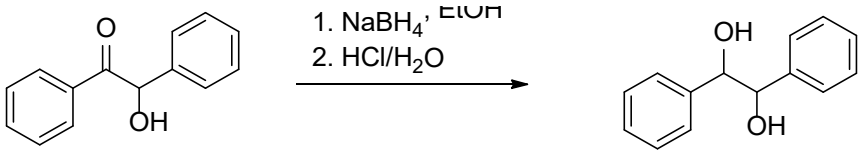
2. State why we employ $NaBH_4$ for the reduction in this reaction as opposed to using $LiAlH_4$.

3. What are two specific examples of solvents that could be used in the presence of the very powerful reducing agent $LiAlH_4$?

Prelab: You may either print out your prelab and bring it with you to lab, or bring your computer. Your TA will grade it on the spot before you begin the experiment. For the in lab observations, you may use scratch paper and record later in your ELN, or bring your computer and record directly in your ELN.

Postlab Report: Make sure to use the Formal postlab report template on the course website!

The Reaction:



Benzoin 1,2-diphenylethane-1,2-diol

Part I: Procedure for the Reduction of Benzoin

1. Add benzoin (0.5 g) and ethanol (4 mL) to a 25-mL Erlenmeyer flask and swirl gently at room temperature for several minutes. Note that the benzoin may not completely dissolve. This is okay. Move on to step 2.

2. Add sodium borohydride (0.1 g) using a microspatula in several small portions over 5 minutes.

3. Gently swirl the mixture at room temperature for 20 additional minutes.

4. Cool the mixture in an ice-water bath, then add water (5 mL) and **6M HCl** (0.3 mL). After 15 minutes, add an additional portion of water (2.5 mL). This last step is called *quenching*.

5. Collect the product via vacuum filtration on a Hirsch funnel, and wash the solid with small portions of ice-cold water.

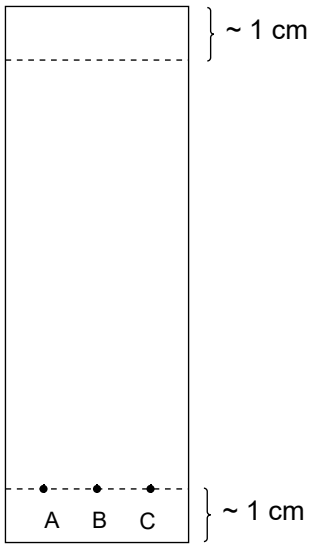
6. Allow the product to dry on the filter for 15 minutes, then determine the crude yield and mp. **Reserve a small portion (1-2 mg) of the crude material for TLC analysis.**

7. Recrystallize the crude solid from acetone. Use a 25 mL Erlenmeyer flask in which to recrystallize the sample. You must determine the amount of solvent to use. Let the crystals dry until you are able to obtain a melting point. Go on to the TLC analysis portion of the experiment.

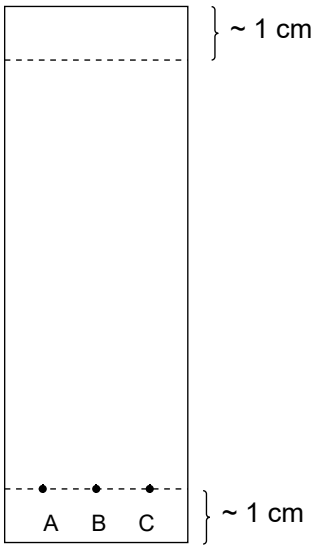
8. Determine the MP and yield (% and mass) of purified 1,2-diphenylethane-1,2-diol. Obtain an IR of the product with assistance from your TA.

Part II: TLC

1. Dissolve a small amount of benzoin (the starting material), your recrystallized product, and your reserved crude product (1-2 mg) in ethyl acetate in each of three vials.
2. Spot 2 TLC plates, as shown below, with starting material (sm), reserved crude product (c), recrystallized product (p), and a spot that contains both (a co-spot). Be careful to leave sufficient space between the lanes. Also, be careful to keep the spot's diameter small as you apply it to the baseline.
3. Run the TLC plates in 9:1 CH_2Cl_2:ethanol (this solution will be prepared for you).
    a. Add your eluant to a TLC developing chamber.
    b. Using tweezers, carefully place the TLC plate in the developing chamber and slowly screw on the cap.
    c. Allow the solvent to run from the baseline to about 1 cm from the top (marked line) of the TLC plate.
    d. Remove the TLC plate, mark the solvent front and allow it to dry in your fume hood.
    e. Once the plate is dry, visualize the spots under UV light and circle them with a pencil.
4. With your phone, take a picture of all relevant TLC plates and then insert the photos into your ELN and your post-lab formal report.



A: SM
B: Your rec. product
C: SM and rec. Product



A: Starting Material
B: Crude product
C: Starting Material and Crude Product

Formal Report Requirements:

1. Compose a formal report that includes a title, a purpose, a balanced reaction equation, a procedure, and a results and discussion. Use the example in the first synthetic experiment as your guide. Remember to also use the formal report template and look at the rubric, downloadable on the course website.

3. Address the following questions in your discussion section:

How do you know you have the desired reaction product? Address your TLC plate. Are there 2 spots other than starting material?

How could you improve the yield and/or purity?

When addressing methods to improve yield and purity:

–Examine possible modifications to the reaction equation (alternate reagents or conditions).

–Examine possible modifications to the stoichiometry of the reaction.

–Justify change in catalyst, solvent, reagents, temperature, time, and molar ratio using your chemical and mechanistic understanding of the reaction.

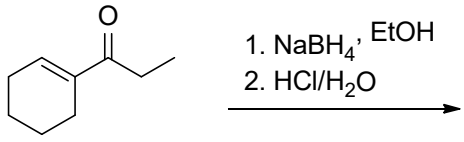
–Be sure to be clear and logical about what this change would accomplish. Make sure your modification is something that you could actually attempt in lab.

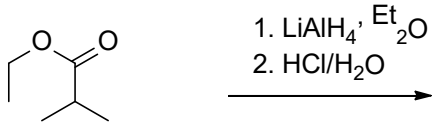
Post lab Question:

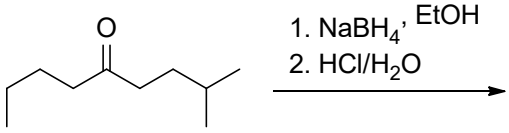
Let's say you have 3 UV active spots in the crude material and co-spot TLC plate. One has the same R_f value as the starting material and the other 2 are very different. What could these 2 non-starting material spots be? Use structures and words. Hint: think about the nucleophilic addition of the hydride.

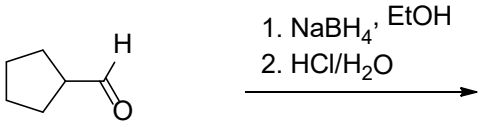
Practice Problems:

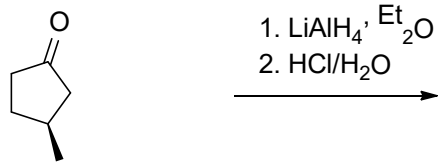
Predict the major organic product for the following reactions:

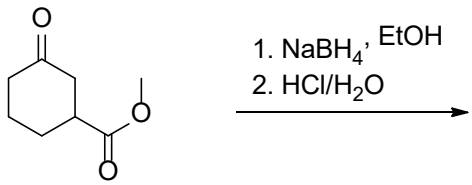


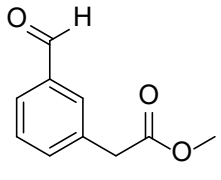




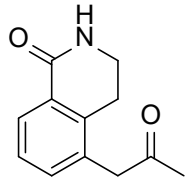








1. $LiAlH_4$, Et_2O
2. HCl/H_2O



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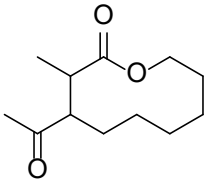

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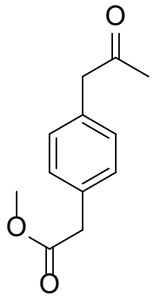
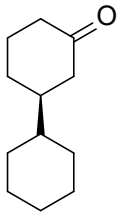


1. $NaBH_4$, EtOH
2. HCl/H_2O



1. $NaBH_4$, EtOH
2. HCl/H_2O

Study Guide

1. Be able to write the mechanism of the reaction.

2. Understand the purpose of adding HCl at the end of the reaction.

3. Be able to predict the product of a reaction of $NaBH_4$ with a given aldehyde or ketone.

4. Know why $NaBH_4$ was used in this reaction instead of $LiAlH_4$.

5. Be able to predict the products of a reaction with $LiAlH_4$ with a given carbonyl compound, and know the selectivity difference between $NaBH_4$ and $LiAlH_4$