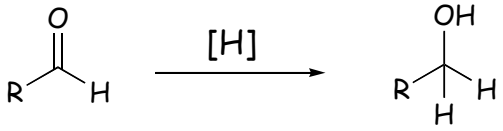
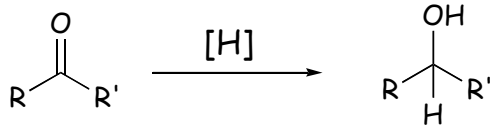
Expt 3: Reduction of Vanillin with Sodium Borohydride to form Vanillyl Alcohol

INTRODUCTION

One of the most commonly used methods for preparing 1° and 2° alcohols is the reduction of aldehydes [equation (1)] or ketones [equation (2)]. Although many different reagents can be used to achieve tis transformation, sodium borohydride ($NaBH_4$) or lithium aluminum hydride ($LiAlH_4$), are employed most recently. Sodium borohydride was originally developed by H.C. Brown (who developed the hydroboration-oxidation reaction of alkenes) in the 1940's, in the context of uranium enrichment for the production of nuclear weapons. As a result, the synthetic applications of this reagent in organic chemistry were only declassified and published in 1953 after the conclusion of World War II.

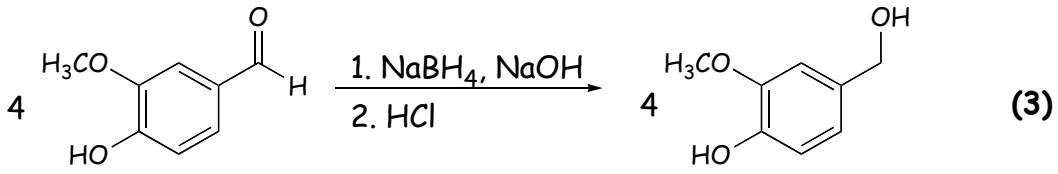


(1)



(2)

As a reducing agent, $NaBH_4$ has several distinct advantages over $LiAlH_4$. First, $NaBH_4$ is much safer to use in a laboratory setting since $LiAlH_4$ can react explosively with water. In contrast, freshly prepared solutions of sodium borohydride in water or methanol are stable at room temperature for several hours. Moreover, $NaBH_4$ exhibits excellent chemoselectivity, and will generally only react with aldehydes and ketones. Lithium aluminum hydride is a much stronger reducing agent and will reduce virtually all carbonyl-containing organic compounds (esters, carboxylic acids, amides, ketones, etc.).



(3)

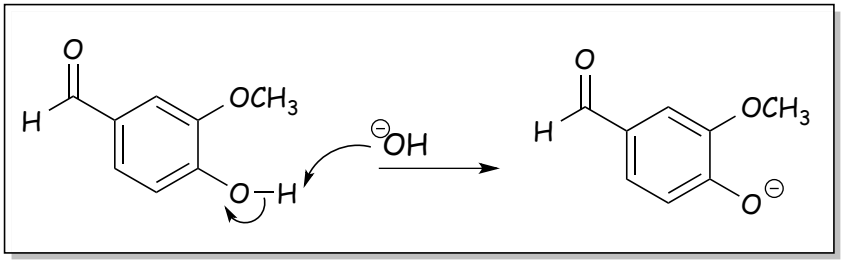
Vanillin, **1** Vanillyl alcohol, **2**

This preparation involves the reduction of the aldehyde group in vanillin (**1**, a flavoring compound found in vanilla) [See Note 1] to produce vanillyl alcohol (**2**) using sodium

borohydride as the reducing agent [equation (3)]. The overall, balanced equation for this reaction is given in equation (3); it is balanced with respect to the key reactants, vanillin, **1**, and sodium borohydride, and the product, vanillyl alcohol, **2**.

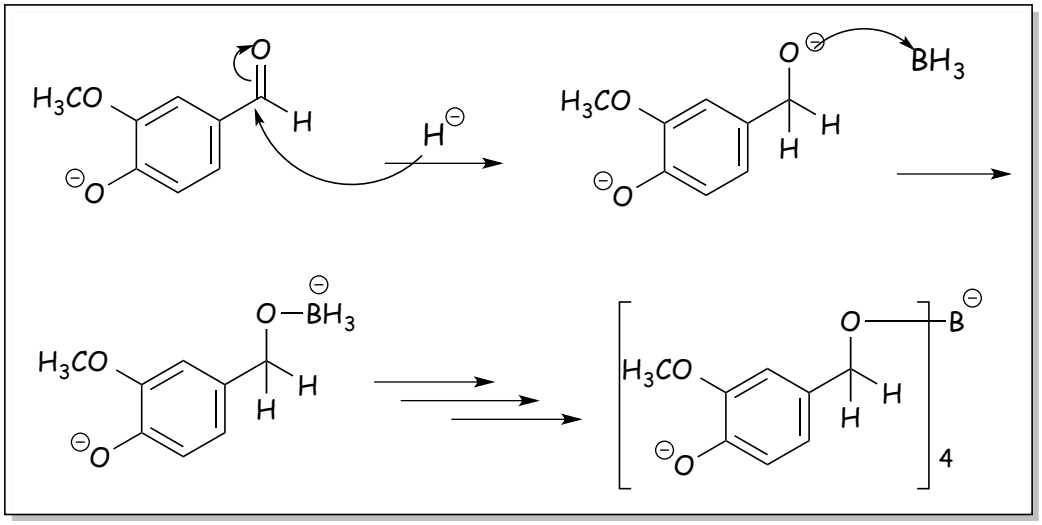
EXPERIMENTAL OVERVIEW

In this experiment, you will use sodium borohydride to reduce the aldehyde functional group in Vanillin. Since the reaction will be conducted in aqueous solution, vanillin must first be deprotonated with the strong base sodium hydroxide in order for it to dissolve. Phenols (pK_a = 10) are considerably more acidic than ordinary alcohols (pK_a = 16-18) because the conjugate base (called a phenolate) is resonance stabilized. Since sodium hydroxide is the conjugate base of water (pK_a = 15.7), the deprotonation of vanillin will be essentially quantitative, giving a homogenous solution.

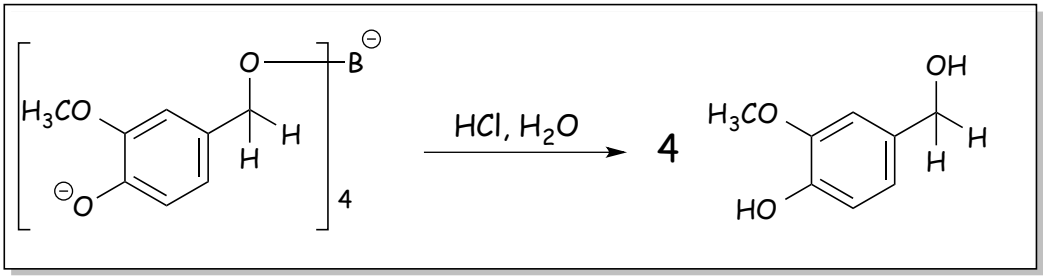


In theory, one equivalent of $NaBH_4$ could reduce four equivalents of vanillin since all four of the hydrides could react. Nevertheless, it is very common to use a stoichiometric (or near-stoichiometric) amount of $NaBH_4$ since the rate of hydride transfer decreases significantly as more alkoxy groups are added to boron.

The mechanism for the reduction involves the transfer of hydride ions from $NaBH_4$ to the carbon of the carbon-oxygen double bond (the carbonyl of the aldehyde group) in vanillin. The polarity of the carbonyl group, due to the greater electronegativity of the oxygen atom results in a partial positive charge on the carbon. As such, the carbon acts as the electrophile for the nucleophilic hydride to attack. The new oxygen anion that forms then reacts with the Lewis Acid in solution, BH_3, and forms an oxygen-boron bond, regenerating the negatively charged boron atom. This allows the borane to be recycled and continue to donate hydride equivalents, until potentially all four hydride nucleophiles have reacted [See Note 3].



The oxygen-boron bonds are hydrolyzed by making the reaction mixture distinctly acidic (pH 1) with 3M aqueous HCl solution.



This addition of HCl (Step 7 in the Experimental Procedure) causes four reactions to occur:

a. it hydrolyzes the O-B bond in the intermediate and protonates the oxygen atom that was originally the oxygen atom in the carbonyl group
b. it destroys any excess $NaBH_4$ that may be present in the reaction mixture
c. it neutralizes excess NaOH and
d. it protonates the phenolic oxygen.

ISOLATION AND PURIFICATION OF PRODUCT

After Vanillin and $NaBH_4$ have been mixed together in the presence of aqueous NaOH, the reaction mixture is stirred at room temperature for about 20 minutes to ensure complete reduction of the carbonyl group. During the reaction process, small bubbles of hydrogen gas should be observed rising through the reaction mixture. Hydrogen gas is formed because $NaBH_4$ reacts slowly with water; the unbalanced equation for this reaction is $H:^{\ominus}$ (from $NaBH_4$) + H_2O → H_2 (gas) + $^{\ominus}OH$.

After transfer to a small beaker, the reaction mixture is acidified with excess HCl, which causes the four reactions described previously to occur. Mention is made in Step 7 of the **Experimental Procedure** that vigorous bubbles of hydrogen gas will be observed when HCl is added, as a result of destroying excess $NaBH_4$. The unbalanced equation for the reaction that occurs is $H:^{\ominus}$ (from $NaBH_4$) + $H^{\oplus}$ (from HCl) → H_2 (gas). Because this is an acid-base reaction, heat is liberated and the reaction mixture becomes slightly warm.

All boron atoms from $NaBH_4$ are converted to boric acid, H_3BO_3, which is water-soluble. This and all other inorganic ions, such as $Na^{\oplus}$, $H^{\oplus}$, $Cl^{\ominus}$, are removed from the product by washing the solid product with water after it is collected by vacuum filtration. Washing with water also removes unreacted vanillin (if any) which is more soluble in water than the product.

Since Vanillyl alcohol is not soluble in water, it will begin to precipitate from solution during the slow acidification. The process of crystallization is completed by cooling in an ice-water bath. The solid that crystallizes (vanillyl alcohol) is collected by vacuum filtration, washed with water and allowed to air dry. In the next lab period, you will measure the mass of the vanillyl alcohol and calculate the percent yield. The purity of the product will be determined by melting point analysis and you will collect the infrared (IR) spectrum of this compound.

NOTES FOR THIS EXPERIMENT:

Note 1: The IUPAC name for vanillin is 4-hydroxy-3-methoxybenzaldehyde and of vanillyl alcohol is 4-hydroxy-3-methoxybenzyl alcohol.
Note 2: In contrast, lithium aluminum hydride reacts explosively with water to yield hydrogen gas and basic salts of Li(I) and Al(III). Its use requires anhydrous conditions in a solvent such as ether, followed by very careful hydrolysis.
Note 3: The use of brackets for the intermediate structure in the mechanism indicates that four molecules such as that drawn in the brackets are attached to boron.

REAGENT/PRODUCT TABLE:

Reagents	**MW (g/mol)**	**MP (°C)**	**BP (°C)**	**Density**	**Concentration**
vanillin	152	81-83	170/15mm	1.056	
sodium borohydride	37.83	400	dec.		80 mg/mL
Product	**MW (g/mol)**	**MP (°C)**			
vanillyl alcohol	154.17	113-115			

FOR YOUR SAFETY:

1.Wear gloves when weighing out or transferring vanillin or vanillyl alcohol.

2. Sodium borohydride, sodium hydroxide and hydrochloric acid are corrosive; if any of these solutions come in contact with your skin, rinse immediately with cold running water.

3. Hydrogen gas is highly flammable.

EXPERIMENTAL PROCEDURE:

1. Place 380 mg (0.380 g) of vanillin in a clean 5 mL conical reaction vial containing a spin vane.

2. Using the color-coded syringe provided in the hood, add 2 mL of 1 *M* NaOH to the vanillin in the conical vial.

3. Place the vial in the aluminum block in the center of the stirring hot plate. Commence slow stirring (setting of 5), and continue to stir during Steps 4 and 5.

4. Using the color-coded 1.0-mL syringe provided in the hood, transfer 1.0-mL of a solution containing 1 *M* NaOH and $NaBH_4$ (80 mg/mL) to a clean, small sample vial. With a Pasteur pipette, transfer the contents of the small vial to the stirring conical vial containing the vanillin and aqueous NaOH.

5. Stir the reaction mixture for about 20 minutes after adding the $NaBH_4$/NaOH. The color of the solution should slowly change from bright yellow to pale yellow or almost colorless. Small bubbles of hydrogen gas should be observed rising through the solution.

6. Pour the reaction mixture into a clean 30-mL beaker. Rinse the conical vial with two 1-mL portions of water and add them to the beaker. Use a Pasteur pipette from your drawer for the measurement of the water – each pipette, when filled, holds approximately 2 mL of liquid.

7. **This step requires patience and the slow *drop-wise* addition of HCl with stirring!!!** Obtain about 3 mL of 3 *M* HCl in a clean, small sample vial. Using a pipette, add **one drop** of 3 *M* HCl solution to the contents of the beaker, and **stir** with a clean stirring rod. When the bubbling and foaming stop, add a **second** drop of HCl; stir the mixture vigorously until the bubbling and foaming stop. Note that crystals of vanillyl alcohol usually start to form in the foam after the first few drops of HCl are added (foaming is a good thing!). Continue the **drop-wise** addition

of the 3 *M* HCl solution (with stirring after each additional drop) until no more foaming or bubbles are observed **and** until the solution is pH = 1. You can check the acidity of the aqueous solution by using the glass stirring rod – stir the solution and then touch the glass rod to the pH paper. **Do not stick the pH paper in the solution**, as this will dissolve the dye of the paper and cause the solution – and thus your product – to be colored! If the pH is not 1, add more HCl solution drop-wise and with stirring until it is. Less than 3 mL of 3 *M* HCl should be required to obtain pH 1. Note that it may not be necessary to add the entire 3 mL of aqueous HCl.

8. Add 1 mL portion of water to the acidic reaction mixture in the beaker and stir to mix completely.

9. If very little solid forms, scratch the side of the beaker with a clean stirring rod to induce crystallization. With stirring, cool the beaker in a larger beaker containing an ice-water bath to complete the crystallization process.

10. Collect the product by filtering the contents of the beaker through a Hirsch funnel (Technique A.2 in Appendix A). Rinse the beaker with 2 mL of **ice** water from the ice-water bath, and pour over the solid in the funnel. Repeat this rinsing process with two additional 2-mL portions of **ice** water.

11. Carefully place the Hirsch funnel containing the vanillyl alcohol product into a beaker, and leave it in your locker so the solid can dry until the next lab period. The solid maybe left on the Hirsch funnel to dry (place funnel inside a beaker and carefully place inside locker drawer) until the next lab period.

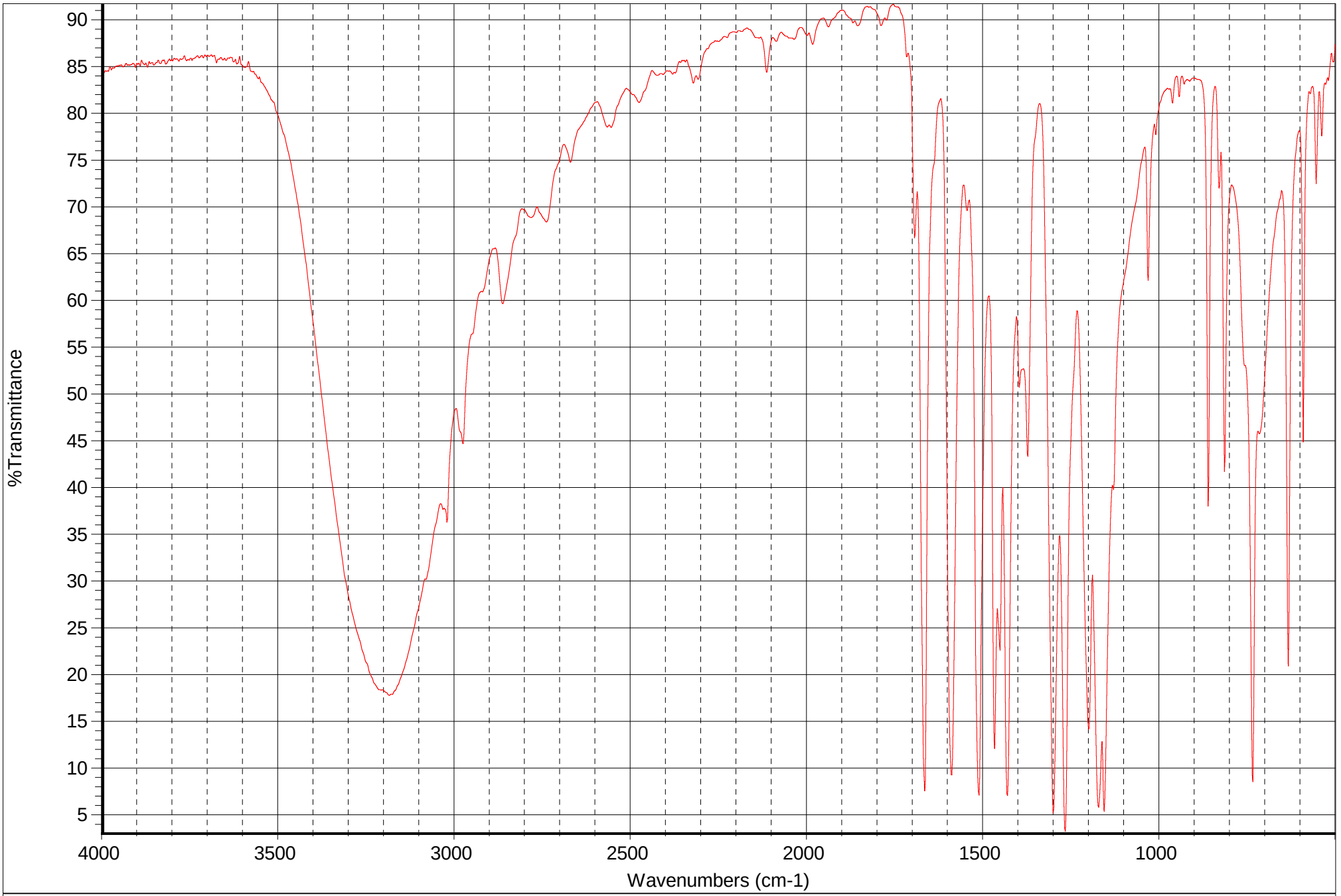
12. In the next lab period, determine the mass and melting point of your product. Weigh an clean and dry empty SMALL sample vial with cap. Transfer your product carefully and reweigh the vial and cap. Obtain a MP of your product as well as an IR of your product. Submit your product in a properly labeled SMALL sample vial

WASTE DISPOSAL

1. Put the filtrate from the filter flask (Step 10) in the "aqueous acid waste" container provided in the waste hood.
2. Carefully wash all the apparatus used in this experiment in the sink.

CALCULATIONS

1. Calculate the number of moles of vanillin that were used.
2. Calculate the number of moles of $NaBH_4$ that were used and then determine the number of moles of hydride that were in the reaction.
3. Determine which component is the limiting reagent – vanillin or hydride
4. Calculate the theoretical yield for vanillyl alcohol.
5. Calculate the percent yield of vanillyl alcohol.



Date: Wed Dec 02 21:17:52 2009 (GMT-05:00) Vanillin (cast film, NaCl)

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