INTRODUCTION

A common method for preparing alcohols is the reduction of aldehydes to form primary alcohols [equation (1)] or of ketones to produce secondary alcohols [equation (2)]. Some commonly used reducing agents are lithium aluminum hydride (LiAlH₄), sodium borohydride (NaBH₄) or catalytic hydrogenation.

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. 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.

Either LiAlH₄ and NaBH₄ could be used for this reduction, but sodium borohydride is the reagent of choice for this reaction because it is safer and easier to use. The advantage to sodium borohydride is its stability in aqueous solutions [See Note 2] for short periods of time (several hours), and the reduction will be carried out in aqueous solution containing NaOH and NaBH₄ and provides a homogeneous reaction mixture. Aromatic alcohols, commonly referred to as phenols, dissolve readily in dilute NaOH to form water-soluble ionic sodium salts: ArOH + NaOH → ArONa + H₂O.
The acidity of the phenol proton is greater than that of an aliphatic alcohol (pKa = 10 versus pKa = 16). Alcohols do not react with NaOH to form sodium alkoxide salts.

For every one equivalent of NaBH₄ there are four equivalents of hydride (H⁻) to react. The mechanism for the reduction involves the transfer of hydride ions from NaBH₄ 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, BH₃, 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 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 aqueous HCl solution. The addition of HCl (Step 7 in the Experimental Procedure) causes these 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 NaBH₄ that may be present in the reaction mixture
c. it neutralizes excess NaOH and
d. it protonates the phenolic oxygen
Equation (4), shown below, shows the detailed mechanistic sequence of events described above that lead to the final product, vanillyl alcohol.

**ISOLATION AND PURIFICATION OF PRODUCT**

After Vanillin and NaBH₄ have been mixed together in the presence of aqueous NaOH, the reaction mixture is allowed to remain 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 NaBH₄ reacts slowly with water; the unbalanced equation for this reaction is 

\[ \text{H}^- \text{(from NaBH}_4\text{)} + \text{H}_2\text{O} \rightarrow \text{H}_2 \text{ (gas)} + \text{OH}^- \]

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 NaBH₄. The unbalanced equation for the reaction that occurs is \( \text{H}^+_\text{from NaBH}_4 + \text{H}^+_\text{from HCl} \rightarrow \text{H}_2 \) (gas). Because this is an acid-base reaction, heat is liberated and the reaction mixture becomes slightly warm.

All of the boron from NaBH₄ is converted to boric acid, H₃BO₃, which is water-soluble. This and all other inorganic ions, such as Na⁺, H⁺, Cl⁻, are removed from the product by washing the solid 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.

Vanillyl alcohol forms as a solid during 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.

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:

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

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 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, and continue to stir during Steps 4 and 5.

4. Using the 1.0-mL syringe provided in the hood, transfer 1.0-mL of a solution containing 1 M NaOH and NaBH₄ (80 mg per 1 mL of solution) 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 NaBH₄/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. After stirring for about 20 minutes, 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 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. (This is the gas given off when the NaBH₄ is destroyed). Continue the drop-wise addition of the 3 M HCl solution (with stirring after the addition of each drop) until no more foaming or bubbles are observed and until the solution is pH = 1. Use pH paper to check the acidity by using a pipette tip to place a drop of the solution on a piece of 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. Crystals of vanillyl alcohol usually start to form in the foam after the first few drops of acid are added. Foaming is a good thing!

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. Filter the contents of the beaker through a Hirsch funnel ( Technique A.2). 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. 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. Do not recrystallize the alcohol unless told to do so by your instructor. If required, the dry vanillyl alcohol may be recrystallized from hot ethyl acetate to yield fine white crystals. Use as little solvent as possible.
12. Determine the weight and melting point of your product. Hand in the product in a properly labeled vial.

WASTE DISPOSAL

1. Carefully wash all the apparatus used in this experiment in the sink.
2. Put the filtrate from the filter flask (Step 10) in the “aqueous acid waste” container.
4-Hydroxy-3-methoxybenzyl alcohol (vanillyl alcohol) (KBr pellet)