In this experiment, you will be reducing carbonyl groups on the compound benzil with sodium borohydride. In general chemistry, you learned about redox reactions in terms of the transfer of electrons; however, in organic chemistry, oxidation reactions are generally defined as a net loss of hydrogen atoms or a net gain of oxygen atoms. Conversely, organic reductions are usually defined as a net gain of hydrogen atoms or a net loss of oxygen atoms. (Scheme 1)

![Scheme 1 - Reduction and Oxidation Reactions](image)

This lab will focus on the reduction of ketones to alcohols. Reductions occur when hydrogen is incorporated into a functional group, either through high pressure hydrogenation (with hydrogen gas and a metal catalyst) or through a metal-hydride transfer reaction. The most common reducing agents for carbonyl chemistry are lithium aluminum hydride (LiAlH₄) and sodium borohydride (NaBH₄). Both are excellent reducing agents, however LiAlH₄ is stronger with the ability to reduce ketones, aldehydes, esters, and carboxylic acids, over NaBH₄’s ability to only reduce ketones and aldehydes. Unfortunately, LiAlH₄ is so strong that it reacts violently with water or any other protic solvent, making NaBH₄ the preferred reducing agent. It is stable to most protic solvents and not nearly as reactive in water.

Mechanistically, NaBH₄ works through a hydride transfer, in which a hydride is transferred from an electropositive boron to an electropositive α-carbon in a carbonyl. (Scheme 2) The hydride can attack from either the front or back side of a ketone (a back side attack is shown in Scheme 2), creating a new chiral center. As the hydride attacks the carbonyl’s carbon, the π-electrons in the carbonyl move onto the oxygen. This in turn causes a lone pair from the oxygen to bond to the electropositive boron. As a final step, this intermediate is hydrated by a protic solvent, creating the newly formed chiral alcohol and an oxyborohydride byproduct. This oxyborohydride then has the ability to reduce more carbonyls with its remaining hydrides.

![Scheme 2 - Reduction of a ketone using sodium borohydride](image)
Reducing Benzil

Benzil has two chemically equivalent carbonyls, thus it can produce an array of stereoisomeric products, as seen in Scheme 3.

The first carbonyl on benzil can be attacked by the hydride either on the front (path a) or the back (path b) resulting in (+)- and (-)-benzoin enantiomers. The reduction could stop here, but there is another carbonyl that can be reduced, and, depending on whether this carbonyl is attacked on the front or the back, several different stereoisomers products can be produced. Both pathways d and e will yield meso-hydrobenzoin, a stereoisomer with an internal mirror plane. However, paths c and f will yield two different diasteromers (+) and (-) hydrobenzoin.

The first reduction on benzil should give a racemic mixture of (+/-)-benzoin since the molecule is symmetric and attacks on one face aren’t favored over the other. However, when a second stereocenter is being set, the reaction can be diastereoselective. Meaning that benzil can either predominately produce the meso-hydrobenzoin product, or a mixture of both enantiomers of hydrobenzoin.

Your goal will be to discover which product(s) the reduction of benzil actually makes: (+/-)-benzoin, (+/-)-hydrobenzoin, or meso-benzoin. Through using Chart 1, you should be able to narrow your reduction product(s) down to one of the three options using melting points, TLC, and IR.
Reducing Benzil


**Data Table:** Have a copy of this table in your notebook prior to the beginning of lab. Fill in the amount, mmol, and mole ratio of each substrate when you actually complete that portion of the experiment. Sections with a “–” do not need to be filled in or included in your report.

<table>
<thead>
<tr>
<th></th>
<th>Benzil</th>
<th>95% Ethanol</th>
<th>Sodium Borohydride</th>
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<tr>
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<td>Mole Ratio</td>
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Reducing Benzil

Procedure:

Start by weighing out 1 g of benzil into a 125 mL Erlenmeyer flask. You should record the exact mass you weighed out. Next add 10 mL of 95% ethanol to the benzil. The benzil will not dissolve so don’t be alarmed. Make an ice-water slurry in a large beaker and set your 125 mL Erlenmeyer in the ice bath to cool to 0 ºC.

Next, while the flask is still in the ice bath, weigh out 0.2 g of sodium borohydride and add it to the ice-cold benzil and ethanol mixture in small portions (8-10) over the next couple minutes. Keep mixing the solution by gently swirling the flask between additions.

You can now remove the flask from the ice-bath, and let the reaction warm to room temperature. Keep swirling the flask as it warms. Make sure to record any changes that occur as the reaction is going.

As your solution is warming, heat 50 mL of DI water in a beaker on your hot plate. It should reach about 80 ºC then add 10 mL of the hot water to your reaction mixture. Add a boiling chip and heat the reaction mixture to boiling on the hot plate. If the solution is not clear, do a hot vacuum filtration and collect the clear filtrate.

The boiling chip can be removed from the mixture and then 15-20 mL of hot DI water (70-80 ºC) should be added to the mixture. Swirl to mix, and then set the Erlenmeyer down and let the mixture cool to room temperature. Once it reaches room temperature, cool it in an ice-bath for 5 minutes. If you see no precipitate, try scraping the bottom of the Erlenmeyer with a glass rod or spatula. While you are waiting on your solution to cool in the ice bath you can add 10 mL of DI water to a test tube and cool it in an ice-bath.

Weigh a filter paper and vacuum filter your ice-cold solution to collect all of the crystals that have precipitated from your mixture. Rinse the Erlenmeyer with the chilled water from your test tube. Let the crystals dry in your drawer until the next lab period.

At the next lab period, weigh your dried crystals and identify the product using the flow chart provided in the handout above. You can use the “General Techniques”, “Recrystallization”, and “Chromatography” handouts if you need help taking an IR, MP, or TLC.
Prelab Questions:

1.) Why is it important to add the sodium borohydride to your solution at 0 °C and in small portions?

2.) Which would you expect to have a higher Rf on a TLC, (+/-)-benzoin or meso-hydrobenzoin? Explain.

3.) The following reaction can potentially make 8 different stereoisomeric products. Please provide each of the eight structures and label each chiral center as (R) or (S).