

Grignard Reaction: Synthesis of Benzoic Acid

Background

Grignard Reaction

A Grignard reaction is based around the formation of a Grignard reagent. An organohalide reacts with magnesium metal in the presence of ether to make the reagent, such as the example shown in Figure 1. The resulting Grignard reagent is a strong nucleophile and base. As a base, the Grignard reagent reacts with the acidic protons in water, which is a common competing reaction for the desired Grignard reaction.

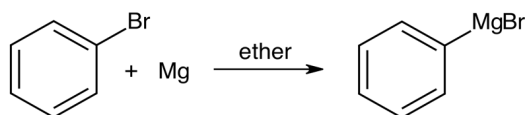


Figure 1 Example preparation of Grignard reagent from bromobenzene and magnesium

Once the Grignard reagent is formed, it acts as a nucleophile that can attack electrophiles, such as carbon dioxide, as shown in Figure 2. The carbon attached to the magnesium is nucleophilic with a partial negative charge. The nucleophilic carbon attacks the partially positive part of the electrophile, like the carbon in a carbonyl or carbon dioxide. The resulting compound can be considered ionic, with an anionic organic molecule and the cationic magnesium portion of the Grignard reagent. A final step in many Grignard reactions is the addition of acid to protonate the anionic oxygen.

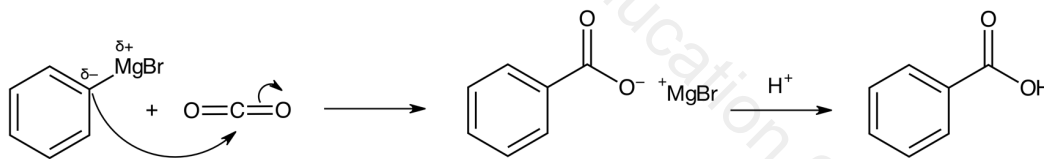


Figure 2 Reaction of a Grignard reagent with carbon dioxide and subsequent protonation

In this experiment, a phenylmagnesium bromide Grignard reagent will be reacted with CO_2 to form a benzoate salt, which is then hydrolyzed to form benzoic acid.

Ultrasound Modification in Grignard Reagent Preparation

Since the 1920's, many applications of ultrasound to accelerate reactions have been identified. Reactions involving metals have had the biggest impact from sonication. In general, ultrasonic waves passing through a liquid cause the formation of bubbles that collapse along with powerful high-energy shock waves. The shock waves are believed to clean the metal by removing the oxide coating from the magnesium metal during preparation of a Grignard reagent. The fresh metallic surface is then present for the reaction between magnesium and the organohalide. The use of ultrasound during preparation of a Grignard reagent will allow the reaction to be performed with ether solvent that has not been thoroughly dried and with glassware that does not need to be oven-dried and cooled under N_2 atmosphere immediately before use.

Objectives

- Prepare a Grignard reagent from bromobenzene
- React the Grignard reagent with carbon dioxide to produce benzoic acid

Materials

- | | |
|----------------------------|-------------------------------|
| • Bromobenzene | • Graduated cylinder |
| • Diethyl ether | • Vials |
| • Magnesium filings | • Test tubes |
| • Iodine crystals | • Watch glass |
| • Dry ice | • Cotton ball |
| • 6M HCl | • Ultrasonic water bath |
| • Methyl tert-butyl ether | • Ice bath |
| • 5% aqueous NaOH | • Vacuum filtration apparatus |
| • 125-mL separatory funnel | • Melting point apparatus |
| • 150-mL beaker | • IR instrument |

Diethyl ether is extremely volatile and flammable. There must be no flames or sparking sources present in the laboratory during this experiment.

Avoid breathing bromobenzene or ether fumes.

Bromobenzene is a skin irritant. Wear gloves, goggles, and a lab coat to avoid skin and eye contact with all chemicals.

Procedure

Grignard Reaction Week 1

Formation of the Grignard Reagent

Note: Use the same balance for all mass measurements in the experiment (± 0.001 g).

1. Measure about 10 mL of diethyl ether in a small graduated cylinder and pour it into a large vial.
2. Bromobenzene will be supplied in another vial. Weigh the vial + cap and contents.
3. Add the bromobenzene to the large vial containing the ether. Gently swirl the large vial to mix the contents.
4. Weigh the empty vial + cap to obtain the mass of bromobenzene used in the reaction.
5. Add 0.5 g of magnesium filings to a large test tube.
6. Add the bromobenzene/ether solution to the test tube containing the magnesium. Loosely place a cotton ball in the open end of the tube. Do not stuff the cotton down the test tube. The purpose of the cotton ball is to minimize exposure to atmospheric water and oxygen and to help absorb any ether that might evaporate during the reaction.

7. To initiate the reaction, place the test tube in an ultrasonic water bath. When the solution begins to turn cloudy gray, white, or brownish the reaction has begun. The ether should begin to boil spontaneously due to the exothermicity of the reaction.
8. If the reaction becomes too vigorous, remove it from the bath for a short period.
9. If the reaction fails to start, add a crystal of I_2 , which can initiate a sluggish reaction.
10. You should continuously monitor the reaction in your test tube, observing any changes taking place, and record the observations in the notebook.

Reaction of the Grignard Reagent with CO_2

1. When the Grignard reaction begins to slow down, place ~10 g of crushed dry ice in a 150-mL beaker labeled with your name. Do not take time to weigh the dry ice. Use approximately the amount in the beaker indicated by your instructor. The CO_2 is in large excess and will not affect your calculation of percent yield of benzoic acid product. Cover the beaker with a watch glass.
2. When most of the magnesium has reacted and the ether boiling subsides, quickly pour the contents of the tube into the beaker containing dry ice.
3. Add a few milliliters of ether to the test tube and swirl to rinse. Add the rinse liquid to the beaker.
4. Cover the beaker with the watch glass and allow it to stand until the next lab period. During the interim, the excess dry ice will have sublimed.

Grignard Reaction Week 2

Hydrolysis

1. Hydrolyze the Grignard addition product by slowly adding ~ 30 mL of 6M HCl to the beaker with the sublimed dry ice and reaction mixture. Stir the mixture with a glass stirring rod. If there is excess magnesium present, it will react with the HCl to evolve hydrogen gas – *add HCl slowly!*
2. Add ~30mL of methyl-*tert*-butyl ether (MTBE) to the beaker. Stir the mixture. There should now be two distinct liquid layers.
3. If there is solid other than magnesium present, add a little MTBE with a transfer pipette. If the solid is still not dissolved, add a little more HCl. Stir. Avoid adding excess HCl.
4. Pour the contents of the beaker into a 125-mL separatory funnel (use a glass funnel in the neck of the separatory funnel), leaving behind any residual magnesium in the beaker.
5. Rinse the beaker with a few milliliters of MTBE and add it to the separatory funnel.

Isolation of Benzoic Acid

Refer to Figure 3 for the isolation procedure and to follow the location of the compounds through the washes and extractions.

Wash with water

1. Stopper the separatory funnel. Carefully invert the separatory funnel and vent through the stopcock. Close the stopcock and gently shake the separatory funnel. Vent again. Repeat.
2. Separate the layers by draining the aqueous layer into a labeled waste beaker. Do not discard the beaker contents until after you have isolated your product.
3. Add 5 mL of distilled water to the organic phase remaining in the separatory funnel. Perform another wash by venting and shaking the separatory funnel. The drained aqueous layer can be added to the aqueous waste beaker.
4. Repeat a wash with another 5 mL of distilled water.

Extraction with base

5. Add 5 mL of 5% aqueous NaOH to the organic phase in the separatory funnel. Shake the mixture gently, with venting.
6. Drain the aqueous layer into a clean, dry 150-mL labeled beaker. Do not combine this aqueous layer with the aqueous waste from the wash steps.
7. Repeat the extraction with two more portions of 5 mL of 5% aqueous NaOH, draining the aqueous layers into the same beaker as the first extraction.
8. Place the organic layer into separate waste container to be disposed of at the end of the experiment as instructed. Do not discard the liquid until after you have isolated your product.
9. Gently heat the combined aqueous extracts (~15 mL) containing the benzoate salt on a hot plate, set to 4-5, for about 10 minutes to remove any residual MTBE, which is slightly soluble in water. Small bubbles will boil off. Do not boil the water.
10. Let the solution cool to room temperature.
11. Add 10 mL 6M HCl and stir. A precipitate will form in the beaker. Cool the mixture in a water/ice bath.
12. Assemble a vacuum filtration apparatus and vacuum filter the product using a Buchner funnel.
13. Wash the crystals on the filter paper with 2 portions of 5 mL cold distilled water.

Recrystallization of Benzoic Acid

14. Carefully transfer the solid to a 50-mL Erlenmeyer flask. Add ~15mL distilled water.
15. Heat the solution to just below the boiling point, swirling the mixture occasionally, until all the solid is dissolved.

16. Allow solution to cool slowly to room temperature. If the cooled solution does not have sufficient water to suspend the purified crystals as a slurry, add 10 mL distilled water, redissolve the crystals by heating the mixture, and cool again slowly to room temperature.
17. Weigh a piece of vacuum filter paper and then vacuum filter the product crystals. Wash the crystals with 5 mL cold distilled water.
18. Remove the filter paper and crystals from the Buchner funnel. Place both in a clean, dry, labeled, pre-weighed weighing tray until the next lab period.
19. Weigh the dry benzoic acid + filter paper + weighing tray. Place the benzoic acid in a clean, labeled vial.
20. Take a melting point of the recrystallized product.
21. Take an IR of the recrystallized product.

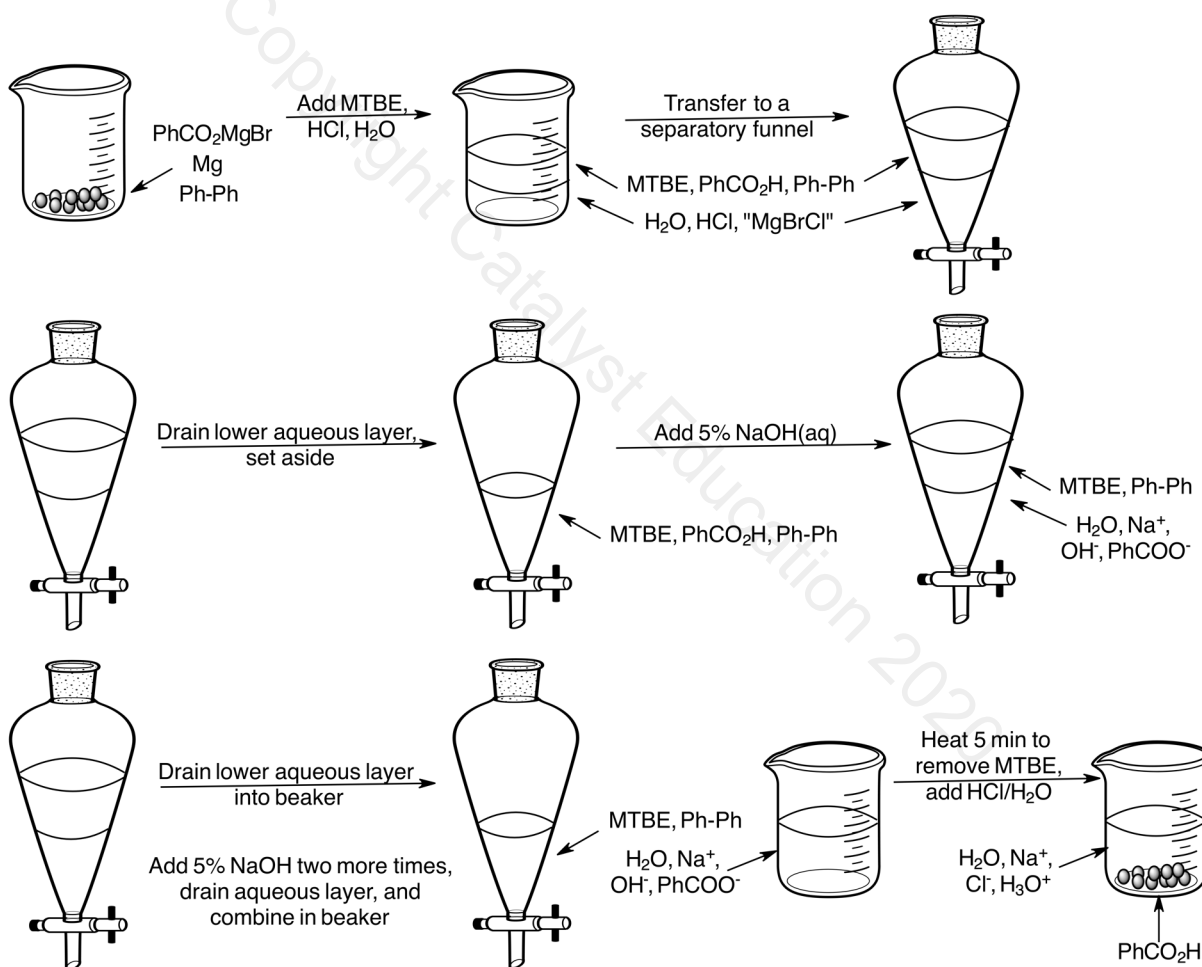


Figure 3 Product isolation procedure

Pre-Lab Questions

Prepare for lab by completing and understanding the answers to these questions. Refer to the Background or another resource, such as your textbook, if necessary.

1. Explain why the Grignard reagent is more reactive than the starting organohalide.

2. Propose a mechanism for the undesired reaction of a Grignard reagent with water.

3. Describe the benefits of ultrasound to a Grignard reaction.

Grignard Reaction Report Sheet

Name _____

Lab section _____

Date _____

Instructor _____

Grignard Reaction

Reaction Characterization

Type of reaction (not Grignard) _____

Write the overall balanced equation and mechanism for the transformation of bromobenzene into benzoic acid through a Grignard reaction.

Calculation of Theoretical Yield

Mass of vial + cap + bromobenzene _____
(grams)

Mass of vial + cap (grams) _____

Mass of bromobenzene used (grams) _____

Moles of bromobenzene used _____

Space for calculations:

Mass of magnesium used (grams) _____

Moles of magnesium used _____

Space for calculations:

Limiting reagent _____

Benzoic acid theoretical yield (grams) _____

Space for calculations:

Benzoic acid obtained (grams) _____

Benzoic acid percent yield _____

Space for calculations:

Benzoic acid melting point (lit) _____

Benzoic acid melting point (exp) _____

Post-Lab Questions

1. Draw a separation scheme for the isolation of benzoic acid from the reaction mixture.

2. Label both the literature and experimental IR spectra for the benzoic acid product, identifying the bond in the structure corresponding to at least three peaks on each spectrum.

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