LABORATORY 9

The Grignard Reaction: A Microscale Preparation of Benzoic Acid

Introduction

Your laboratory skills have grown considerably since the first of the semester, and you are ready for the challenge of a famous reaction--one marked by unusual materials and striking chemical and physical changes. Try, especially, to understand exactly which chemical structure and equation corresponds to each stage of this dramatic synthesis.

Your work in this laboratory is a departure from your previous experience. You will work on a micro scale. Microscale apparatus is used throughout the second semester organic laboratories (CHEM 2130).

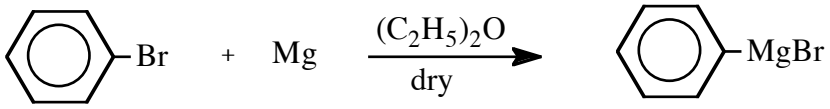
Working on a microscale greatly reduces both the quantities of material and the reaction time. The regular scale reaction requires nearly two full periods. The microscale work can be done in one period. Further, the reduced scale minimizes the hazard of working with ether, a very flammable solvent with a low flash point. You must eliminate flames and sparks when working with ether.

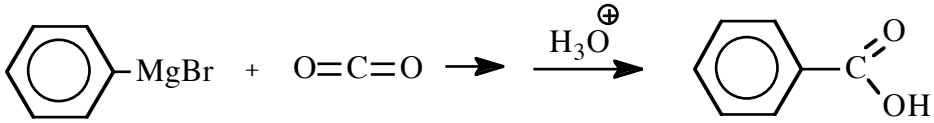
To run a successful Grignard reaction, it is essential that moisture (including water vapor from the air) be excluded from the reaction apparatus. Septa (rubber caps) on the reagent bottles and on the reaction tubes effectively exclude moisture, so that a calcium sulfate drying tube is unnecessary.

A syringe, with a needle, is used to remove reagents from septum protected storage bottles and to add the reagent to a reaction tube. Thus, use of a syringe and septum eliminates the need for an addition funnel and a costly three-necked round-bottomed flask. There is less set-up time, less clean-up time and less breakage of expensive glassware.

The Reactions

Running two separate reactions carries out this preparation. The second reaction has two separate steps. The first reaction is the preparation of phenyl-magnesium bromide, the Grignard reagent. The second reaction is the preparation of benzoic acid from the Grignard reagent and solid carbon dioxide. The two reactions are:





Phenylmagnesium bromide, the Grignard reagent, reacts with moisture to form benzene. So, no moisture can be present. The product formed by reaction with phenylmagnesium bromide and solid carbon dioxide ("Dry Ice") is a magnesium salt of benzoic acid. As

such, this magnesium salt is ionic and insoluble in the ether solvent. The reaction mixture will look like "gunk" at this point. The addition of aqueous hydrochloric acid adds the proton to the benzoate anion, giving the final product—benzoic acid. The benzoic acid can be purified by micro-recrystallization to remove the major side product, biphenyl, a neutral hydrocarbon. Benzoic acid is soluble in hot water and slightly soluble in cold water. Benzoic acid is soluble in sodium hydroxide solution and biphenyl is not.

Apparatus

The following apparatus is located at the front of the room for short loan for today's preparation:

1 – 30-mL or 50-mL beaker or flask
2 – glass Pasteur pipettes
1 – Pasteur pipette bulb
1 – 1-mL syringe with **blunt** needle
1 – specially dried microscale reaction tube with vented septum cap.
(This tube has been dried in an oven and stored in a desiccator.)

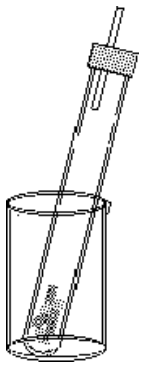
Chemicals

- Anhydrous diethyl ether ("Ether") in septum-capped bottles.
- 1-mL bromobenzene in anhydrous diethyl ether solution
  - Concentration = 340 mg bromobenzene/1-mL ether solution.
- 52 mg fresh, bright magnesium turnings.
- "Dry Ice," solid carbon dioxide, CO_2
- 3 M Hydrochloric Acid

Procedure

A. Preparation of Phenylmagnesium Bromide

In all that follows fire safety is essential since the diethyl ether solvent is extremely flammable. There can be no open flames or sparks.



Obtain one of the specially dried microscale reaction tubes with a vented septum cap, and support it in an Erlenmeyer flask or a small beaker. This tube was dried in an oven at 110° to remove moisture and then cooled in a desiccator. A 2 cm piece of plastic tubing was inserted through the septum to serve as a pressure release vent. To the reaction tube, add 52 mg (2.14 mmol) of magnesium metal turnings. Use a clean glass stirring rod to crush the magnesium turnings in the tube. Replace the septum on the tube. The magnesium is rarely completely reacted. While you should carefully record the exact mass of the metal, you should base your yield calculations on the bromobenzene as limiting reagent.

Using a dry syringe, inject 0.5 mL of dry, anhydrous ether directly through the septum into the reaction tube containing the magnesium. Recall that ether is flammable. Next, fill the syringe with exactly 1 mL of the bromobenzene-ether solution. 1 mL of this solution contains exactly 340 mg (2.1 mmol) of bromobenzene. Insert the syringe

needle through the septum and inject about 6-8 drops of the bromobenzene-ether solution into the reaction tube. If reaction does not begin in two minutes, you may need to remove the septum and grind the magnesium chips with the tip of a dry, glass rod. If this second strategy does not succeed, add a small iodine crystal and continue grinding the magnesium with the stirring rod. A stirring rod that has successfully started one student's reaction will contain some active Grignard reagent and will act as a "Magic Wand" to initiate other students' reactions.

You will know when the bromobenzene and the magnesium have begun to react. The clear, colorless solution will become slightly turbid with a greenish-yellow tint. Small bubbles will begin to spontaneously form on the magnesium surface. Once the reaction begins, heat is given off and the ether boils spontaneously. Gradually, a few drops at a time, add the rest of the bromobenzene-ether solution to the boiling reaction mixture so that boiling and refluxing is maintained at a controlled, steady rate. If boiling gets out of control, cool the reaction tube in cold water. Heat the tube in warm water when the boiling slows down. Too much boiling will reduce the volume of the ether and make transfer difficult. Before proceeding with the next step, add sufficient ether so that you have 1-1.5 ml of ether in the reaction tube.

B. Reaction of the Grignard Reagent with the Carbonyl Compound.

Obtain a small amount of Dry Ice weighing around 500 mg in a small (30-50 mL), clean, dry beaker. The minimum weight required is 2.00 mmol or 22.0 mg. Dry Ice sublimes rapidly. Excess is used to insure complete reaction since the bromobenzene is the limiting reagent. Moisture from the atmosphere will form "water" ice on the surface of the "Dry" Ice. This water will destroy the Grignard reagent. Work rapidly once you place the Dry Ice in your beaker. Remove the septum from the reaction tube and pour the ether solution of the phenylmagnesium bromide directly onto the Dry Ice. A vigorous reaction results producing a mud-like, viscous mess. Stir this mixture with a glass rod until all the Dry Ice has sublimed. Warm the beaker or flask in your palm or in a beaker of warm water until all the ether has evaporated and a glassy solid remains.

C. Neutralization of the Reaction Mixture and Isolation of the Product

The next reaction is the protonation of the glassy solid which is a magnesium bromide salt of benzoic acid. A proton from the hydronium ion in the acid solution is added to the benzoate anion to make benzoic acid. Add 10 mL of dilute (1-3 M) hydrochloric acid to the glassy solid in the beaker or flask. Stir thoroughly until the mixture is no longer gummy and any magnesium metal has dissolved. Crude benzoic acid will precipitate from the solution.

Pure product will be obtained if the benzoic acid is crystallized from the hydrochloric acid solution. Place a wooden applicator stick into the beaker and heat the mixture on the hot plate, under the hood, until boiling. The Benzoic acid should completely dissolve with some stirring. Excess unreacted bromobenzene, or biphenyl impurity may be present in the beaker. Rapidly transferred the hot liquid to a clean container (beaker, flask or clean scintillation vial). As the liquid cools, large needles of benzoic acid will crystallize from the solution. Chill the mixture on ice to reduce the solubility of the benzoic acid in water.

Set up the Hirsch funnel and the 25-mL filter flask for suction filtration. Put a small circle of pre-weighed filter paper into the Hirsch funnel. Wet the paper and suck it onto the Hirsch funnel so that it sticks into place. Stir the mixture of benzoic acid and water and pour it quickly into the Hirsch funnel and remove all the water with suction. Rinse the container with about 5-mL of ice water and pour this into the Hirsch funnel and suction the water through the benzoic acid to wash out soluble reaction products. Continue to suck air through the benzoic acid for at least one minute. Dry the product on a filter paper for a few hours or overnight.

Weigh the product, determine the melting point range and calculate the percent yield based on bromobenzene.

Results, Discussion and Conclusion

Write your results, discussion of your results and your conclusion. Complete any post-lab questions.

Abstract

This part should be filled in after the completion of the experiment and analysis of all data. When submitting the report, the abstract should appear at the beginning of the report.

Report

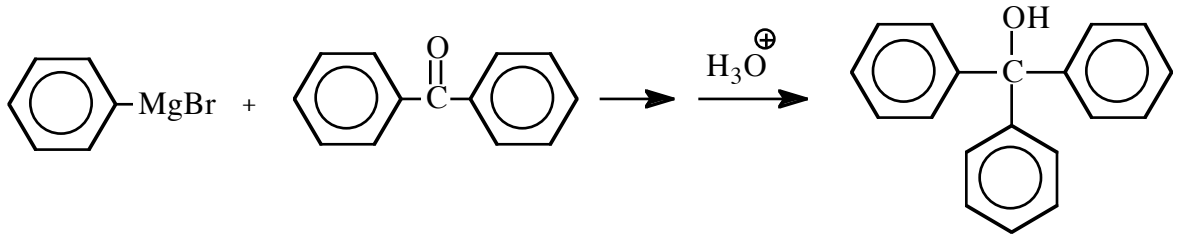
Adhere to the format required by your instructor and submit the report on time.

Summary

1. Grignard reagents are organo magnesium halides (RMgX).
2. Grignard reagents react with carbonyl (C=O) compounds.
3. Grignard reagents are prepared and worked with under dry conditions.
4. The typical solvent used in a Grignard reaction is anh. diethyl ether.
5. The nucleophile in a Grignard reagent is the carbon center (R^-).
6. Grignard reagent can also act as a base in presence of acidic groups.

Questions

Your instructor may have substituted the experiment in Appendix F as an alternate preparation using a Grignard synthesis. This experiment illustrates the classic synthesis of a tertiary alcohol by reaction of a Grignard reagent with a ketone. The Grignard reagent is the same phenylmagnesium bromide prepared experiment 9. This organomagnesium bromide is alternately reacted with benzophenone to give, after neutralization, triphenylmethanol.



The problems below use the chemistry and stoichiometry of both of these reactions. Your instructor may assign some or all of these questions as pre- or post-Laboratory assignments. These particular problems are particularly good pre-lab questions.

By this third synthesis experiment you should be familiar with the procedure for calculating theoretical and percent yields.

1. Write balanced equations for the preparation of phenylmagnesium bromide and its reaction with benzophenone followed by neutralization in acid.

2. Calculate the theoretical yield of a microscale reaction of these materials in which 300 mg of bromobenzene, 50 mg of magnesium, and 350 mg of benzophenone were used.

3. If 350 mg of triphenylmethanol product were collected, what is the percent yield?

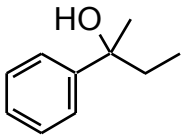
Reaction of a Grignard reagent with water is an important competing reaction in Grignard syntheses and a major cause of lower yields of products.

4. Write an equation for the reaction of phenylmagnesium bromide with water. Name the product of this reaction.

5. Calculate the mass of frost (water ice) on a piece of dry ice that would completely react with 2 mmol of phenylmagnesium bromide.

6. If there are 25 mg of water in a typical drop of water, how many drops of water would react completely with 2 mmol of phenylmagnesium bromide?

7. If phenylmagnesium bromide is added to a different ketone, you will obtain a different alcohol product. What ketone would you need to use to obtain the following from reaction with the phenylmagnesium bromide:



8. Grignard reagents can react with a number of different electrophiles to give a wide variety of products. Suggest mechanisms for each of the following: