

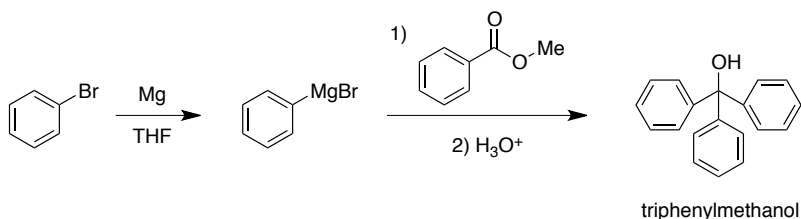
Addition of a Grignard Reagent to an Ester: Formation of a Tertiary Alcohol

Introduction:

Grignard reagents are important and versatile reagents in organic chemistry. In this experiment, you will prepare a Grignard reagent and react it with an ester to prepare a tertiary alcohol. Specifically, in this reaction you will prepare phenyl magnesium bromide from bromobenzene and magnesium metal and then react it with methyl benzoate to prepare triphenylmethanol (Figure 1). In this reaction, two equivalents of phenylmagnesium bromide add to methyl benzoate.

Note: Grignard reagents are sensitive to water. ALL glassware must be completely clean and dry. Reagents have been stored over molecular sieves to keep them dry in storage, but you should also keep containers closed as much as possible. Finally, water in the air can also react with the Grignard reagents over time. To successfully prepare triphenylmethanol in this experiment, you will need to be well organized and not take too much time between steps.

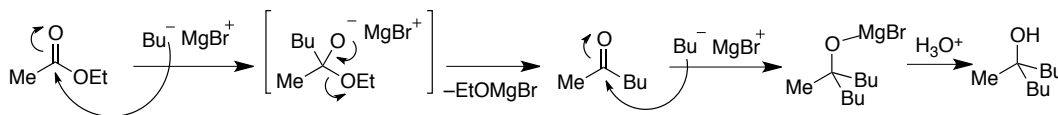
Figure 1.



Mechanism:

The formation of Grignard reagents from aryl halides is a complex mechanism, which takes place on the surface of the magnesium metal. You do not need to concern yourself with the details of this step of the mechanism.

Figure 2.



The mechanism of the reaction of a Grignard reagent with an ester is shown in Figure 2 (using methyl propionate and butylmagnesium bromide). Grignard reagents are potent nucleophiles and react with electrophilic esters. The initial attack gives rise to a tetrahedral intermediate, which collapses to give a ketone and bromomagnesium ethoxide. The resulting ketone rapidly reacts with a second equivalent of Grignard reagent, giving rise to the tertiary alkoxide. Work-up with acidic water protonates the alkoxide, giving rise to the observed tertiary alcohol.

Equipment:

- ring stand, small
- 10- and 100-ml graduated cylinders
- clamps
- 100-mL round bottom flasks (may be in oven-hot)
- hoses
- pan or beaker for ice
- 125-mL separatory funnel
- flask heater for 100 mL rb flask
- cork ring
- 250-mL round bottom flask
- 250-mL Erlenmeyer flask
- reflux condenser (may be in oven-hot)
- 20 mL vials with caps
- pipets and bulbs
- melting point capillaries

Reagents:

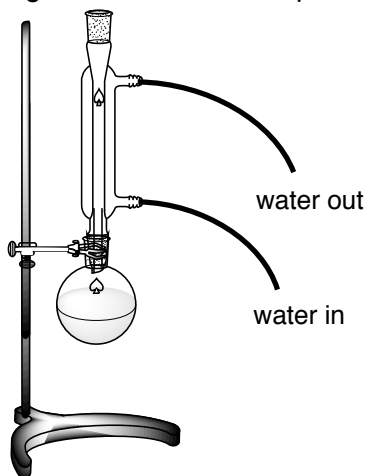
- bromobenzene^a
- magnesium turnings
- methyl benzoate^a
- iodine (crystalline)
- anhydrous THF^{a,b}
- ethyl acetate
- 10% sulfuric acid
- wash acetone
- 1 M HCl (for TA's to decompose Mg)
- saturated NaCl solution

^a Stored over activated 4Å Mol. Sieves. ^b Fresh bottle for each lab.

Procedure:

Prepare a solution of methyl benzoate in THF by adding 2.5 g of methyl benzoate and 8 mL of anhydrous THF to a clean, dry 20-mL vial. CAP THE VIAL WITH A PLASTIC CAP and set it aside until you have prepared the Grignard reagent. (Note: Capping the solution is important so that the THF does not evaporate and so that the solution does not pick up excess water from the air during the time you are working on the Grignard reagent.)

Figure 3. Reactor Setup.



Next you will prepare the Grignard reagent. Make sure that your round-bottom flask, reflux condenser and graduated cylinder are absolutely dry. Clamp a clean, dry 100-mL round bottom flask securely to a ring stand, and allow enough room to slide an ice bath under the flask (Figure 3). Make sure you clamp the flask (not the condenser) and do not use a ring to support the flask. Although you may not need it, have a pan or beaker of ice water ready in case you need to control the exothermic reaction with cooling.

Place 1.34 g of dry, shiny magnesium turnings in the round-bottom flask. Do not use magnesium that is dark and oxidized and do not touch it with your fingers. Add one or two crystals of iodine to the flask. (Note: The iodine is added to the reaction to activate the surface of the magnesium. Do not add too much.)

Next attach a reflux condenser onto the neck of the flask and start the flow of water through it. Add 8 mL anhydrous THF to the flask via the condenser and wait for the color of the iodine

(purple) to disappear. Next add 5 mL bromobenzene to the flask by pouring carefully down the condenser. Warm the flask by placing the palms of your hands around the outside of the flask. Be patient, but if a visible reaction has not started within 10 minutes, see your TA. In exceptional cases, the reaction can become too vigorous (boiling to the top of the reflux condenser). If this happens, temporarily cool the flask with the ice bath until the reaction is under control. Do not cool it for too long, however, as too much cooling can quell the reaction.

When the reaction has clearly begun, noted by cloudiness and bubbling around the magnesium, swirl the flask to provide fresh surfaces for the reactants and then add 12 mL more anhydrous THF down the condenser. Let the reaction proceed until most of the magnesium is consumed and the solution turns the cloudy, brownish color that is characteristic of a Grignard reagent.

Once the Grignard reagent is formed, cool the round-bottom flask in an ice-water bath and wait about 1 min. Using a pipet, slowly add the solution of methyl benzoate that you prepared previously to the reaction in a drop-wise fashion. The addition should take about two minutes. It is important that you do this slowly as adding the solution quickly can cause heat from the reaction to build up and lower the yield of your product.

Once the methyl benzoate solution is added, wait two more minutes and then remove the ice bath and allow the reaction to warm to room temperature. Swirl the flask until it is at room temperature and the reaction has subsided. (Note: An intermediate product may separate at this point as a white solid. This is okay.) Place the reaction on the flask heater and gently reflux your reaction mixture for 25 minutes. Then shut off the flask heater, remove the reaction from the heat and cool the reaction to room temperature.

Once the outside of the flask is cool to the touch, transfer your reaction mixture into a 250-mL Erlenmeyer flask containing 20 mL of 10% sulfuric acid and about 10 g of ice. Rinse the reaction flask with approximately 20 mL ethyl acetate and add this rinse to the Erlenmeyer. Swirl well. The acid hydrolyzes the addition product, neutralizing the basic magnesium salts so they become water soluble, and the triphenylcarbinol disperses in the organic ether portion. Transfer the liquid contents to a 125-mL separatory funnel, rinse the flask with approximately 15 mL of ethyl acetate, and then also transfer this rinse to the separatory funnel. (Note: Give the round-bottom flask containing remaining magnesium and solid residue to your TA at this point for treatment with HCl and disposal.) Shake the funnel using proper, safe techniques (ask TA if not sure) and remove the aqueous layer. Shake the organic phase with additional 15 mL 10% sulfuric acid solution to further remove magnesium salts. Again draw off the aqueous layer. Add 15 mL of saturated sodium chloride solution to the separatory funnel to dry the ethyl acetate layer. Draw off the aqueous layer. Pour the remaining ethyl acetate layer out the neck of the funnel into a 125 mL Erlenmeyer flask, add a few grams of anhydrous sodium sulfate, swirl occasionally for 5 minutes or so, and decant the solution into a clean, **tared** (pre-weighed) 250-mL round-bottom flask. Concentrate using the rotary evaporator to dryness and weigh the flask containing the solid product.

Determine the yield and collect a melting point. Don't forget to clean and dry your glassware, and place the clean 100-mL round-bottom flasks and reflux condensers in the oven so that they are dry for the next lab.

Prelab Questions:

1. What is the limiting reagent in this reaction?
2. How many equivalents of Grignard reagent are used in this reaction compared to the limiting reagent?
3. If water is not excluded from the reaction, what by-product(s) are expected to form?
4. What is the fate of the methoxy group from the methyl benzoate in this reaction?

Postlab Questions:

1. Determine the percent yield.
2. How does your melting point compare to the reported value?
3. If there were time to recrystallize the product, predict how its melting point might change.
4. In this reaction, we isolated a tertiary alcohol and not the intermediate ketone. This is due to the reactivity of the ketone compared to the starting ester. Explain why it is not possible to isolate the ketone from these reaction conditions, even if we had used less Grignard reagent.
5. Describe ways in which the yield of this reaction might be improved.