Experiment 31 Grignard Addition to a Carbonyl – Alcohol Synthesis

Objectives

- Prepare an alcohol through the addition of a Grignard reagent to a carbonyl compound
- Use micro-scale techniques to carry out a reaction in a dry environment
- Introduce a second reactant to a dry system using a syringe with a needle and a rubber septum
- Use a separatory funnel to separate immiscible liquid phases
- Calculate a theoretical and percent yield of product
- Verify the structure of the product through comparison of M.P. and an IR spectra

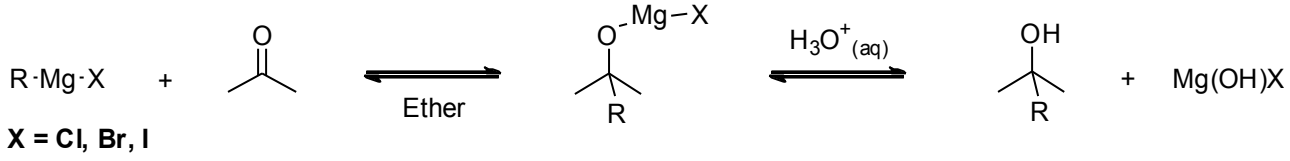
Pre-Lab Reading

Read the sections on extraction (pp. 116-118 of your Padias text) and controlled atmosphere reactions and adding reagents during a reaction (pp. 32-36 of your Padias text). Read the material on Grignard addition to aldehydes and ketones in your lecture text (Sections 17.5 and 19.7 in the 7th edition of McMurry).

Prior to beginning this reaction, all glassware to be used needs to be thoroughly dried by rinsing with anhydrous acetone and leaving the glassware open in your drawer for at least 24 hrs. The glassware to be dried includes the 25 mL r.b. flask, the Claisen head adapter, a 4 mL conical reaction vial and the drying tube in your kit. A small magnetic stir bar (**not** a spin vane) should be similarly prepared. A pre-dried glass stoppered 20 mL Erlenmeyer flask containing anhydrous ether will be provided to you the day of the experiment.

Introduction

One of the most general and versatile synthetic routes to the preparation of an alcohol is to add a Grignard reagent to an aldehyde or ketone, followed by an acidic-aqueous work-up of the addition product. The reaction requires the preparation and the maintenance of a dry environment for the addition phase, as Grignard reagents react readily with even trace amounts of water. This reaction can be used to prepare primary, secondary and tertiary alcohols, depending on the aldehyde or ketone that is used.



X = Cl, Br, I

In this experiment you will be using a commercial preparation of phenyl magnesium bromide in ether and benzophenone. After completing the nucleophilic addition reaction and the aqueous acidic work up of the final product, triphenylmethanol, you will determine the mass and percent yield of the product. You will also document the structure of the product by its M.P. and its IR spectrum. The IR spectrum of the starting reagent, benzophenone, is shown in Figure 31.1 below.

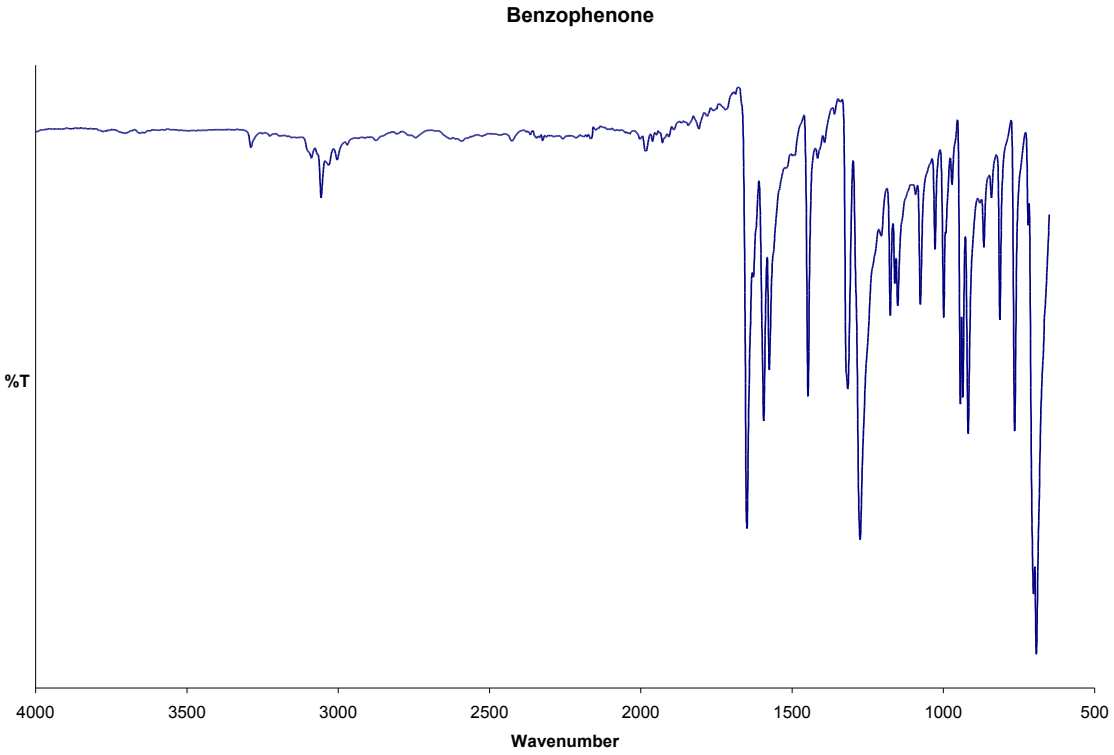
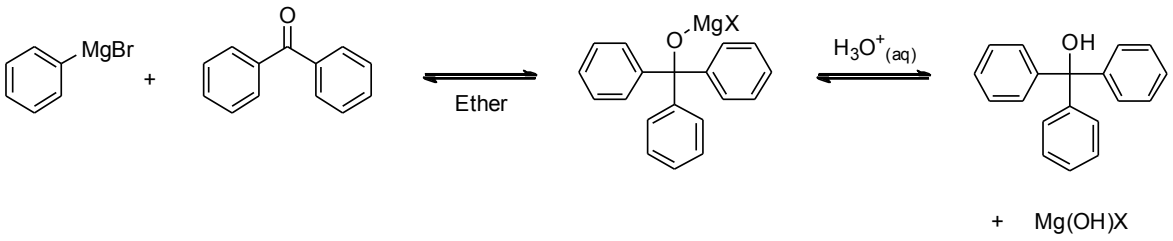


Figure 31.1. Infrared spectrum of benzophenone (neat)

Reactions



Pre-Lab Questions

1. Why is it important that the glassware be specially dried prior to performing the reaction? (Hint: what happens to a Grignard reagent in the presence of water?)

2. The experiment calls for 2.5 mL of a 3.0 M phenyl magnesium bromide solution in ether. Calculate the moles of phenyl magnesium bromide you will be using.

3. The experiment calls for 1.1 g of benzophenone. Calculate the moles of benzophenone to be used. Compare this with the number of moles of Grignard reagent calculated in question 2 and determine the limiting reagent.

Waste Disposal

Your instructor will safely dispose of any unused Grignard reagent. Any extra ether or ether/benzophenone solution should be discarded in the non-halogenated liquid waste container. Any waste from the water/acid workup may be flushed down the drain

Apparatus

The apparatus is shown in Figure 31.2 below.

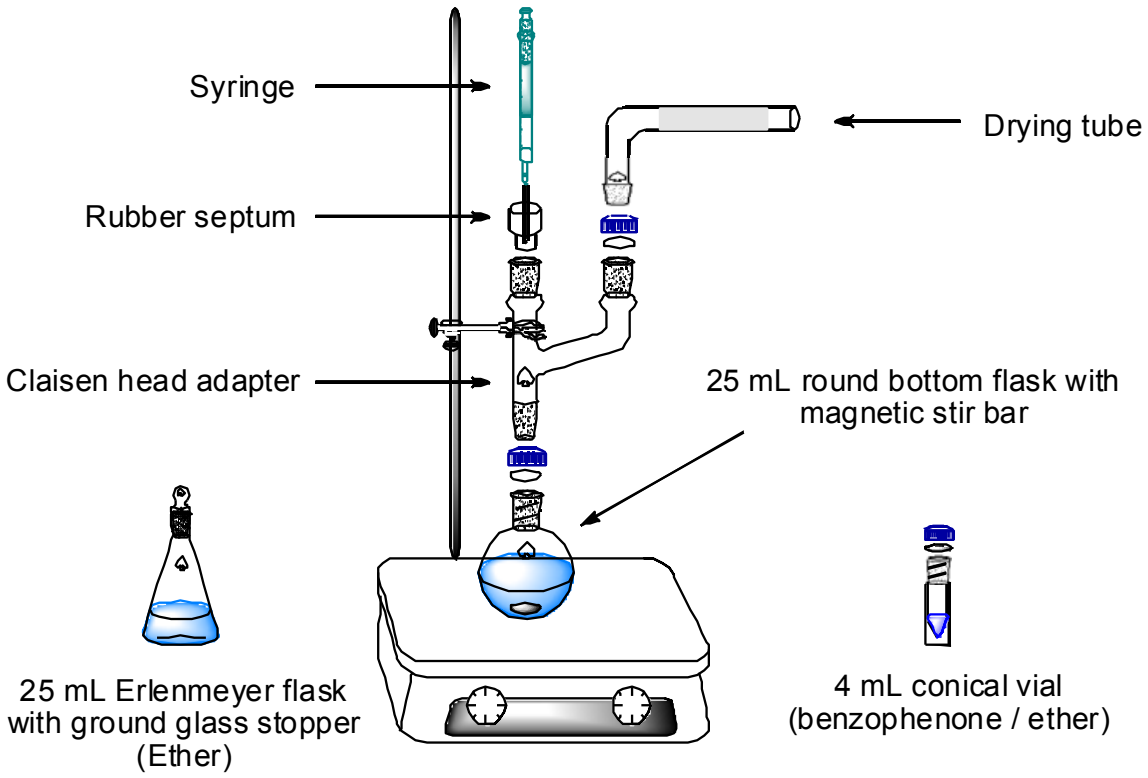


Figure 31.2. Apparatus assembly for the Grignard reaction.

Experimental Procedure

Preparation of Reactants

1. Prepare your drying tube by placing a small amount of cotton along the longer side, adding enough $CaCl_2$ pellets to form 1-1.5 inches of $CaCl_2$, and enough cotton in the end to keep the pellets in place. Your instructor will demonstrate the preparation of the drying tube. It is important that the cotton plugs be sufficient to hold the drying agent in place, but not so large that they restrict air flow.
2. Assemble your apparatus using the pre-dried glassware and magnetic stir bar.
3. Prepare your benzophenone solution by weighing 1.1 g of benzophenone, placing it in the pre-dried 4 mL conical vial, adding approximately 2 mL of dry ether and capping it with a rubber septum or Teflon plug and blue cap
4. Take your assembled apparatus to your instructor who will use an Eppendorf pipette to discharge 2.5 mL of 3.0 M phenyl magnesium bromide directly into your 25 mL rb flask. Immediately re-attach the remainder of your apparatus. The phenyl magnesium bromide solution may be slightly brownish and / or contain some white crystalline Grignard reagent.
5. Secure your apparatus to a ring stand and begin stirring.

Formation of Addition Product

6. Using a syringe with a needle and pushing the needle through the rubber / Teflon septum, draw up some of the benzophenone solution from the 4 mL conical vial and add it to the stirring Grignard solution. The addition needs to be steady, but not all at once. Add the remainder of the benzophenone solution in the same manner. Rinse the vial with 1 mL of dry ether and add this rinse to the reaction mixture. Note: the addition of benzophenone solution should be fairly steady but gradual enough that the reaction mixture in the round bottom flask does **not** begin to boil. Once the addition is complete, the reaction mixture will become red and then will change into a pink-white solid over several minutes.
7. After the pink-white solid has formed and stirring is no longer possible, remove the round bottom flask from the apparatus, stir the mixture with a spatula and then cap it.
8. Let the reaction mixture stand for about 15 minutes before hydrolysis of the initial addition product.

Hydrolysis of Product

9. Add 6 mL of 6M HCl to the reaction mixture, dropwise at first until the mixture is neutralized, and then more quickly. Use your spatula and shaking to break up lumps and dissolve the solid. You may need to add additional 6M HCl and/or ether to completely dissolve the solid.

Separation and Drying of Product (Your instructor will demonstrate the proper use of a separatory funnel)

10. Transfer the reaction mixture to a small separatory funnel, rinsing the round bottom flask with a small amount of ether and adding the rinse solution to the separatory funnel. If more solid appears and/or three layers appear in the separatory funnel, add small additional amounts of ether and/or 6M HCl. Adding some water may also help – your goal is to have two distinct layers in the separatory funnel. *Caution: remember to frequently "vent" the liquid contents of the separatory funnel to avoid a build up of pressure.*
11. Withdraw the lower aqueous layer (containing Mg salts) into a beaker. *Caution: remember to remove the glass stopper from the separatory funnel before trying to withdraw the lower layer through the stopcock.* Pour the top ether layer (with dissolved triphenylmethanol product) into a second dry beaker.
12. Return the aqueous layer to the separatory funnel and add 5 mL of ether to extract any remaining product. The lower, aqueous layer from this second extraction may be discharged down the sink. Combine the top ether layer in the beaker with the earlier ether layer.
13. Dry the combined ether extracts with anhydrous Na_2SO_4. When the solution becomes clear (after about 5 minutes) decant it into a pre-weighed beaker. You can rinse the drying agent with additional dry ether and decant this ether into the same pre-weighed beaker.
14. Evaporate the ether by setting the beaker in a fume hood. The white product residue that remains after evaporation of the ether is the triphenylmethanol.
15. After the evaporation of the ether, weigh your initial product and determine the mass and the M.P. If time permits, obtain an IR spectrum of your product. Your instructor may direct you to recrystallize your product from 2-propanol and to record the mass, M.P. (Lit. Value = 162°C), and IR spectrum on the purified product.

Questions

1. Show how the sequence of reactions used in this experiment may also be used to prepare the following alcohols.

   (a) Benzyl alcohol

   (b) Isobutyl alcohol

   (c) 3-Pentanol

   (d) 3-phenylpentan-3-ol

2. Benzene is sometimes produced in this reaction. Write the equation showing how the benzene is formed?

3. Identify the major IR absorptions you are looking for in your product. Compare with the given IR spectrum of benzophenone. Did a reaction occur?