Purpose

To generate a Grignard reagent from bromobenzene and magnesium and to use that Grignard reagent in the synthesis of triphenylmethanol.

Learning Objectives

To describe the properties of a Grignard reagent and explain the mechanism of a Grignard reaction.

To explain the importance of the anhydrous reaction conditions.

To describe the role of the trituration.

Theory and Background

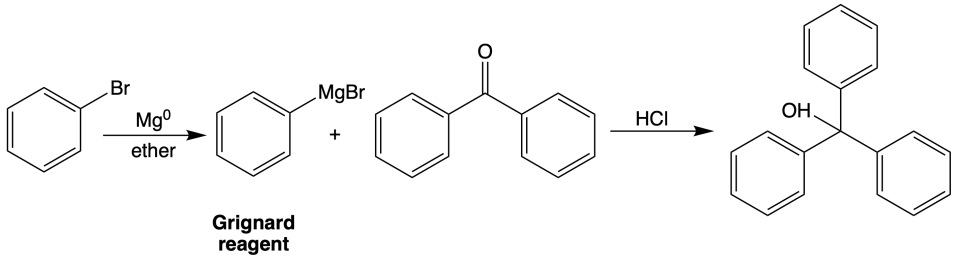

Figure 15B.1: Grignard reaction adding a phenyl group to benzophenone.

The Grignard reaction (Figure 15B.1) is an important carbon–carbon bond-forming reaction that was discovered by Victor Grignard. (Grignard later won the 1921 Nobel Prize in Chemistry for this discovery.) Grignard's breakthrough came with two discoveries—that an ether solvent was vital and that the reaction must be carried out under stringent anhydrous conditions. The Grignard reaction begins by reacting elemental magnesium with various alkyl, aryl or vinyl halides. It has since been discovered that the magnesium inserts itself into the carbon–halogen bond, forming what is known as a **Grignard reagent**. The ether solvent is necessary for stabilization of the Grignard reagent because the magnesium is electron deficient (it is only surrounded by 4 electrons). The ether solvent is able to use its lone pair electrons to coordinate to the magnesium and donate electron density to it. The anhydrous conditions are required because the Grignard reaction is a very good nucleophile AND a very strong base.

The nucleophilic carbon species (RMgX) readily reacts with carbonyl compounds to form new carbon–carbon bonds. However, because the Grignard reagent is such a strong base, we must take special precautions to ensure that the reaction is run under anhydrous (or water-free) conditions. This also means that Grignard reactions

cannot be performed on molecules that have acidic hydrogens (such as alcohols or carboxylic acids).

Mechanism

The reaction begins with the insertion of magnesium into the carbon–bromine bond to generate the Grignard reagent. This then acts as a nucleophile and attacks the carbonyl carbon of benzophenone. An acidic workup then forms the alcohol as the final product.

Techniques

Drying Agents

Drying agents such as $CaCl_2$ readily hydrate. It is important to remove it from your drying tube as soon as possible after you are done with it to prevent it from clumping up. Other agents such as Na_2SO_4 and $MgSO_4$ are obtained from bottles marked as anhydrous. **DO NOT LEAVE THE TOP OFF THESE DRYING AGENT CONTAINERS!**

Trituration

The final purification step in this experiment is **trituration** in petroleum ether. Trituration is the process of grinding an impure solid in a solvent in which the desired compound is insoluble and the impurities are soluble. This places the impurities in the liquid, which we can remove by filtration.

Reading

For more information on the reactivity of Grignard reagents, see Bruice textbook.

Reagents

Table 15B.1: Table of Reagents

Reagent	For-mula	Equiv	MW	Den-sity (g/mL)	Vol-ume (mL)	Mass (g)	mmol	m.p. (°C)	b.p. (°C)
Bromobenzene								31	155-156
Magnesium				—				—	—
Diethyl ether (anhydrous)		Solvent		0.713				—	34.5
Benzophenone				—				48.5	—
3 N HCl			36.46	—				—	—
Triphenyl-methanol				—					—

Procedure

Safety Precautions

Syringes: Never replace the needle cap and dispose of the syringe in the sharps container. **Do not** recap the syringe before disposal.

A few steps in this experiment call for slow addition of reagents. It is very important you follow these instructions and pay attention to your reaction to avoid the reaction becoming too exothermic.

The setup for this experiment is complex; make sure that you follow each step closely. You should sketch the glassware setup (Figure 15B.2) in your lab manual.

Your TA will provide you with two syringes and two needles. At the end of the experiment, these should be disposed of in the sharps container. This is extremely important; any student that does not follow this instruction will receive a zero for the entire experiment.

Prepare the Glassware

1. Bring a 25 mL round bottom flask with stir bar, Claisen adapter, water condenser, drying tube, and 5.0 mL conical vial into the fume hood. Once the glassware is ready, notify your TA and they will dry your glassware.

2. Once the glassware is cool enough to touch, assemble the glassware as indicated in Figure 15B.2. To do this, place the 25 mL round bottom flask in a heating mantle on the hot plate. Attach the Claisen adapter to the round bottom flask and attach a water condenser to the Claisen adapter. Prepare the drying tube with calcium chloride and attach this to the water condenser. Cap both the open end of the Claisen adapter and the 5.0 mL conical vial. Attach the rubber tubing to the water condenser.

3. To prepare a drying tube-like apparatus for the conical vial, remove the plunger from one of the syringes, affix the needle (but do not remove the needle cover) and pack the syringe with a small amount of cotton, and fill with $CaCl_2$ and then cap with another small amount of cotton. *Carefully* remove the needle cover and insert into the capped conical vial. Note: you will never pass any liquid through this syringe. It is to equalize pressure as you add/remove liquids from this conical vial later in the experiment. You may reuse this syringe-drying tube throughout the entire experiment.

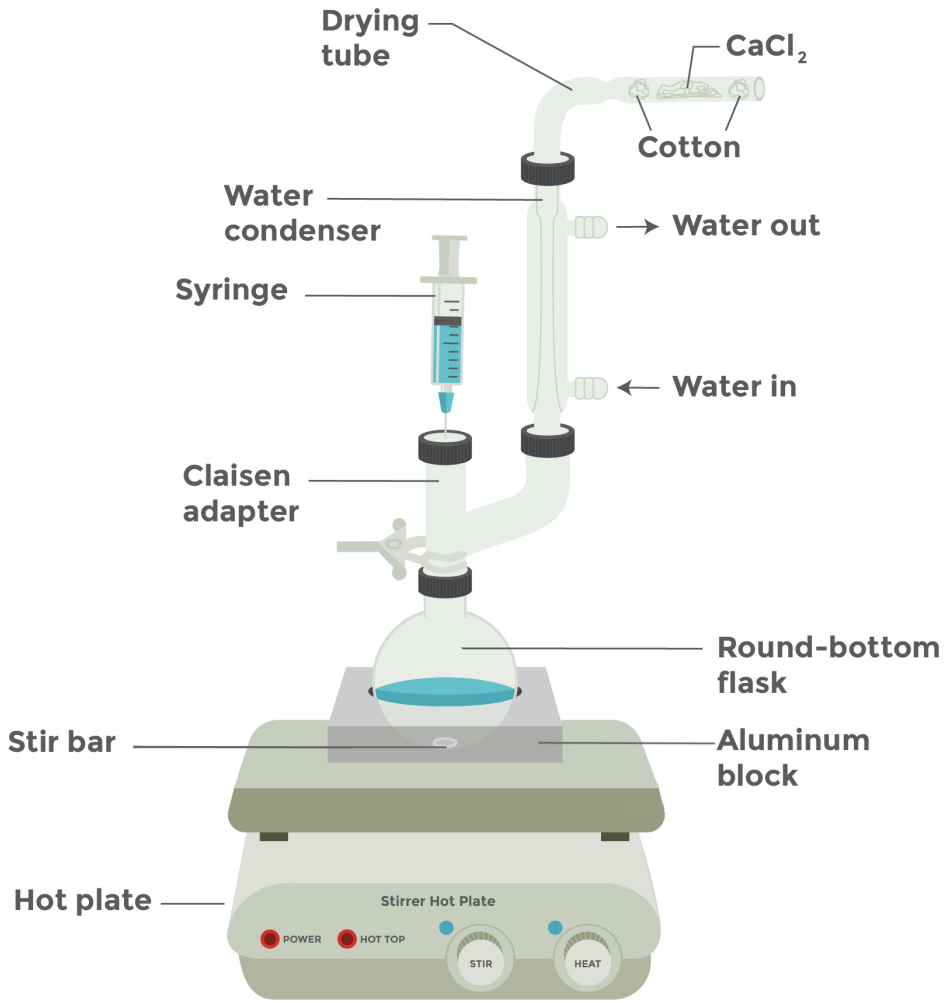

Figure 15B.2: Glassware setup for the Grignard Reaction.

Prepare the Grignard Reagent

4. Weigh 96 mg of magnesium turnings and grind them with a mortar and pestle. This will help remove any magnesium oxides from the surface of the magnesium. Then add the turnings into the 25 mL round bottom flask by briefly lifting up the Claisen adapter. At the same time, add a single crystal of iodine and a tiny drop of 1,2-dibromomethane to the round bottom flask.

5. Measure out 2.0 mL of anhydrous diethyl ether from the amber colored 30 mL bottles and add this to the capped 5.0 mL conical vial. Add the ether through the septum, do not remove the cap. Make sure the ether you are using is labeled anhydrous and it is not labeled pet ether (aka petroleum ether).

6. Add 0.42 mL of bromobenzene to the conical vial. Make sure the tip of the syringe-drying tube apparatus remains above the liquid level at all times.

7. Using the other syringe and needle, draw up 1.0 mL of the solution in the conical vial and add it slowly over 5 minutes into the 25 mL round bottom flask through the septum of the Claisen adapter. You should see cloudiness and bubbling on the surface of the magnesium within 5–10 minutes. If you don't see this, you can speed up the reaction by lifting up the round bottom flask off the heating block and holding it in the palm of your hand for a few minutes. If you still don't see cloudiness or bubbling, consult with your TA.

8. Once you see the reaction initiate, turn on the stirrer and add any remaining bromobenzene solution into the round bottom flask very slowly (over 5–10 minutes), rinsing the conical vial with 1.0 mL of anhydrous ether and adding this rinse to the round bottom flask.

9. Turn on the hot plate on the very low setting and reflux the reaction until most of the magnesium is consumed and the solution is cloudy (about 15–30 minutes). While the solution is refluxing, proceed to the next step.

Make the New Carbon–Carbon Bond

10. In a separate clean, dried, and capped 5.0 mL conical vial dissolve 730 mg of crushed benzophenone into 2.0 mL of anhydrous ether. Add this solution dropwise into the 25 mL round bottom flask. You will notice the reaction refluxing; control your rate of addition to make sure the reaction rate stays under control. The solution should turn pink and a red precipitate will form, indicating the presence of a benzophenone radical. As the reaction proceeds, this will be consumed.

11. Let the reaction sit for a few minutes and once it has cooled to room temperature add any additional ether as necessary to maintain the original volume.

Purify the Product

12. Remove the Claisen adapter and other glassware from your round bottom flask. Remove the stir bar with the magnet wand (ask your TA where it is). Prepare an ice bath for use in case the next step becomes too exothermic.

13. Carefully add 3M HCl(aq) dropwise to the round bottom flask containing the reaction mixture. Use your spatula to break up any large precipitates that form. If the bubbling becomes very intense place the round bottom flask in the ice bath to cool it.

14. Continue adding 3M HCl(aq) until you have achieved a pH between 2 and 3. This should take approximately 2–3 mL of 3M HCl(aq). During this process the mixture should separate into two layers. Once the correct pH is reached, add more ether to dissolve any remaining precipitate.

15. Prepare 2 centrifuge tubes. Transfer the entire mixture to one of the centrifuge tubes. Out of this centrifuge tube transfer the aqueous layer into the empty centrifuge tube. Extract this aqueous layer with ether (1.0 mL x 2) and add these ether extracts into the original centrifuge tube.

16. Wash this combined ether solution with a sodium bisulfate solution (1.0 mL x 2) and then brine (1.0 mL x 1). Transfer the ether solution into a clean Erlenmeyer beaker and dry it with anhydrous sodium sulfate.

17. Filter the ether solution into a 25-mL beaker, using a cotton plugged pipette as the filter. Add a boiling stick to the beaker and evaporate the solvent over low heat.

18. To further purify the reaction add about 2.0 mL of petroleum ether (NOT diethyl ether) and stir it around with a spatula, mixing it well. This process is known as trituration. Collect the crystals through vacuum filtration and rinse them with a small amount of petroleum ether while they are still on the filter.

19. Weigh the crystals after they are dry and calculate the percent yield.

20. Obtain an IR spectrum and measure the melting point range of your product. If necessary, you may do this on your next lab day.

Discussion

In addition to the regular guidelines for the lab report, include the following in your write up.

1. Compare your experimental data to the actual data for triphenylmethanol. What data from the melting point measurement and the IR, ^{1}H-, and ^{13}C-NMR spectra suggest that the reaction worked to produce triphenylmethanol?
2. Why is it necessary for the reaction to be anhydrous? How did you ensure it was anhydrous?
3. What was the impurity removed during the trituration?

Volume of bromobenzene used (mL) _____

Mass of benzophenone used (g) _____

Mass of product (g) _____

Percent yield _____