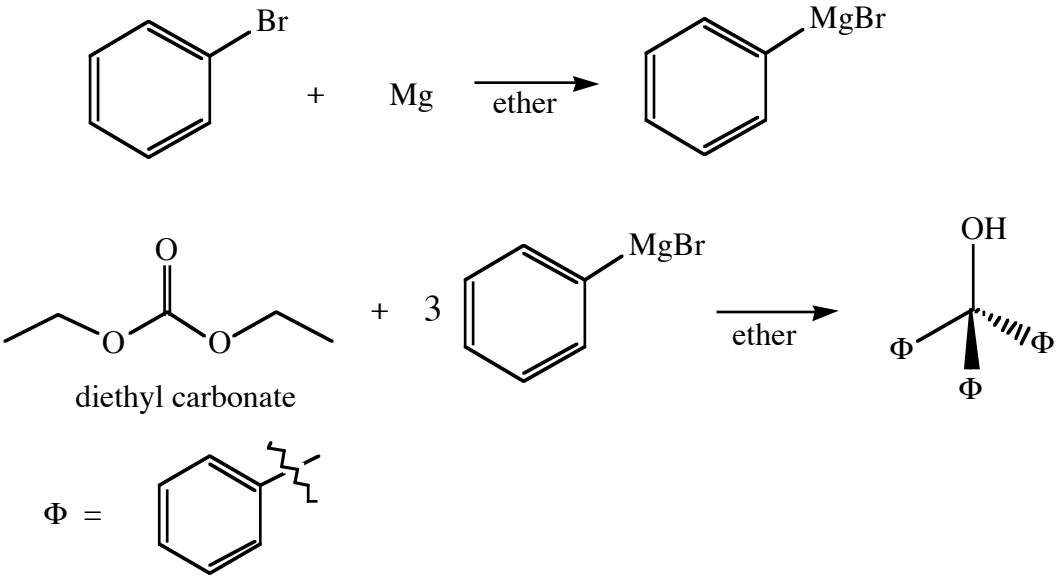
The Grignard Reaction revisited
or
There is more than one way to skin a cat

Reactions:



Experimental Procedure:

Note: Water is the enemy! All equipment and reagents must be dry! The glassware that you will be using - the 5 mL long-necked round-bottomed flask, two vials, the air condenser from the Williamson kit, the magnetic stir-bar, and a stirring rod - should be placed in the drying oven the lab period before the one in which you will be beginning this experiment.

Remove the glassware from the oven and place the vials and the magnetic stir-bar into the dessicator located next to the oven. Secure the air condenser on the round-bottomed flask using the rod connector, place a septum on the air condenser, and place a needle in the septum for pressure relief (you must have this pressure relief needle in the septum at all times during the reaction!).

While this apparatus is cooling, obtain a piece of the magnesium ribbon, sand it to remove the oxide coating, cut it into small pieces, and place 150 mg (approximately 6 mmoles) into the cooled round-bottomed flask. Place an equimolar amount of bromobenzene (approximately 6 mmoles, 0.942 g, 0.63 ml) into an oven-dried vial, add 1.0 mL of anhydrous diethyl ether to this vial, and cap the vial.

Remove the air condenser from the flask and quickly add approximately 0.25 mL of the bromobenzene/ether solution to the magnesium. Crush a piece of the magnesium with your dry stirring rod, add the dry stir-bar, and replace the air condenser. When the reaction starts, you should see a reddish-brown color and bubbles on the surface of the magnesium, and the solution will become cloudy.

Once the reaction has started, begin stirring the mixture with a magnetic stirrer, and add 1.0 mL of anhydrous diethyl ether with a clean syringe through the septum. Then use your own syringe to slowly add the rest of the bromobenzene/ether solution through the septum. Add this solution at

such a rate so as to maintain a gentle reflux. After the addition is complete, rinse your vial with 0.25 mL of ether, and add this rinse all at once to the reaction mixture. Then continue stirring and reluxing the mixture for an additonal 20 minutes until most of the magnesium has reacted. You may need to warm the reaction with a warm water bath to maintain the reflux.

While this reaction is refluxing, place the appropriate amount of diethyl carbonate (about 2 mmoles, 0.236 g, 0.24 mL) in the same vial you used for the bromobenzene. Base this amount on the limiting reagent from the formation of the Grignard reagent, keeping in mind the balanced equation for the addition to the diethyl carbonate. Add 1.0 mL of *tert*-butyl methyl ether and mix this solution thoroughly.

After the formation of the Grignard reagent is complete, cool the reaction down to room temperature, and slowly add the diethyl carbonate/ether solution through the septum to the reaction mixture. Add the solution at such a rate so as to maintain a gentle reflux. If this reaction becomes too vigorous, you may have to cool the reaction with an ice-water bath, so have one ready if needed. After this addition is complete, reflux the reaction for 15 minutes, using a warm water bath to heat the reaction flask. You may store the reaction in your locker overnight at this point. Remove the air condenser, and place a septum on your flask. You should parafilm the septum as well.

Hydrolysis of the Alkoxide:

Place 5 mL of 10% H_2SO_4 in the centrifuge tube and cool it in an ice-water bath. Slowly add the Grignard solution (use a pipet) to the centrifuge tube while vigorously stirring with your spatula. If you have alot of magnesium metal remaining in your reaction mixture, this bubbling may be very vigorous - so be careful here! Rinse your reaction flask with 1-2 mL of ether and add this to the centrifuge tube as well. Once the bubbling has stopped and your addition is complete, cap the centrifuge tube and gently shake the contents. If there is any solid remaining or your ether layer is cloudy, add enough ether to dissolve any solid. Spot a small amount of the ether layer on a TLC plate.

Pipette the aqueous layer into a separate centrifuge tube, add 0.5 mL of ether, cap the tube, and shake. Add this small ether layer to the larger ether layer remaining from the initial hydrolysis described above. Wash these combined ether layers with 1 mL of water, followed by 1 mL of saturated sodium bicarbonate solution, followed by 1 mL of saturated NaCl solution. Remember to remove the aqueous layer after each washing. After you have removed the saturated NaCl solution, add anhydrous calcium chloride to the centrifuge tube until the drying agent no longer clumps together. This drying should take 5-10 minutes. Decant the ether solution from the drying agent into a clean,dry, and tared 25 mL Erlenmeyer flask. Rinse the calcium chloride with 1 ml of ether and add this to the Erlenmeyer flask as well. Spot a small amount of ether layer on the same TLC plate used before (make a separate spot).

Isolation and Recrystallization of the Product:

Remove the ether by heating gently (use a boiling stick). Be careful not to overheat your solution! Obtain a weight of your crude product and determine the yield of crude product. Can you smell the biphenyl? Dissolve the crystals in the smallest amount of warm diethyl ether possible (1-2 mL will be more than enough), and add 1.5 mL of ligroin. Add a boiling stick to the solution, and boil off some of the ether until the solution is slightly cloudy. Add one drop of warm ether (just enough to make the solution clear again), and allow the solution to cool slowly to room temperature. Then cool the solution in an ice bath, spot a small amount of the solvent that is above the recrystallized product (to see what we lose in the solvent), collect the crystals by vacuum filtration, wash the

product with a few drops of cold 1:4 ether-ligroin mixture, and determine the melting point, weight, and yield of the pure product.

Analysis of the product:

Dissolve a small amount of your final product in ether and spot this solution on your TLC plate. Your TLC plate should now have 4 separate spots, from 4 separate phases of your reaction and purification procedures. Develop the TLC plate with a hexane/ethyl acetate (10/1) mixture.

Take an IR of your product and analyze the IR and NMR spectra of your product, assigning the major peaks.

Questions:

1. What do you notice when looking at your developed TLC plates? What spot(s) are no longer in the final product? What impurities do these missing spots represent?

2. Show the mechanism for the reaction of 3 equivalents of the Grignard reagent with the diethyl carbonate.

3. What would be the final result if only 2 equivalents of the Grignard reagent had been used? If only one equivalent of the Grignard reagent had been used?

4. Compare the reactivities of all of the carbonyl compounds in your mechanism from question 2. Explain this difference in reactivity.