

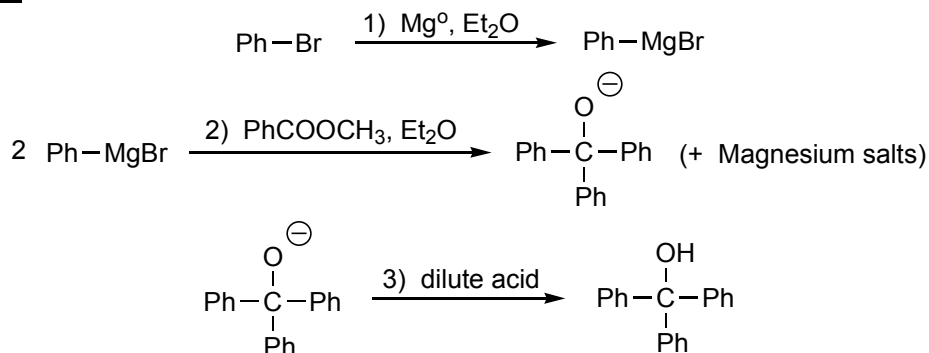
The Grignard Reaction: Triphenylmethanol from Bromobenzene and Methyl Benzoate

EVP/AEM Handout: Last modified 1/2019

Background

The Grignard reaction is a versatile method for the creation of new carbon-carbon bonds, which are otherwise quite difficult to make. The Grignard reagent (an alkyl or arylmagnesium halide) is a powerful nucleophile (reacting as a carbanion), and may be reacted with any substrate suitable for nucleophilic attack. One common practice is to react Grignard reagents with carbonyl compounds to yield alcohols. We will use this type of chemistry in this lab to generate a new alcohol from an ester.

Overall Reactions



Cautions and Warnings

AVOID EXCESSIVE HEATING. OPEN FLAMES PROHIBITED. Diethyl ether is a very volatile, highly flammable solvent. Care must be taken to avoid fires. Even hot plates have been known to ignite ether! Exercise extreme caution throughout this lab.

AVOID ALL WATER UNTIL THE WORKUP! Grignard reagents are very basic, and will react with water to give the conjugate acid (benzene, in this case). All glassware must be scrupulously dry.

Preparation of the Grignard Reagent (Phenylmagnesium Bromide)

Collect the glassware to prepare a macroscale addition apparatus: a 50 mL round-bottomed flask, a Claisen adapter, a water-cooled condenser, a separatory funnel (which will function as your addition funnel during the reaction), and a ground glass stopper. A diagram of how to put these items together will be presented in recitation. Each piece of glassware must be scrupulously dry, preferably by heating in an oven at 110° C overnight. (DO NOT heat the Teflon® stopcock – it will melt!). You should also have a dried 10 mL graduated cylinder to measure all of the amounts of liquids in the first two parts of the reaction sequence.

Add 0.5 g dry, crushed magnesium turnings and a stir bar to the round bottom flask. Assemble the apparatus (this may be done while still warm), taking care that all joints are well greased and well sealed; use the blue clips to hold the ground glass joints together. Add 5 mL of ANHYDROUS diethyl ether to the round-bottomed flask through the addition funnel, measured using the oven-dried graduated cylinder. Close the stopcock and replace the stopper on the funnel. Ensure a flow of cooling water through the condenser (check for leaks!).

With the stopcock closed, pour 2.4 mL bromobenzene (measure its mass) into the separatory funnel and add about 5 mL anhydrous diethyl ether. Swirl the mixture gently in the separatory funnel to obtain homogeneity.

Allow a small amount of this bromobenzene/ether solution (~0.5 mL) to run from the separatory funnel into the round-bottomed flask, stir, and observe. If bubbles are evolved, and/or the solution turns chalky, the reaction has started. The flask should become noticeably warmer due to

the exothermic nature of this reaction. If the reaction has not started in 10-15 minutes, you may warm the mixture using the hotplate. After 10 more minutes of warming, if the reaction has still not started, consult your instructor for alternate options.

With the reaction to form the Grignard reagent started, add 5 mL of additional anhydrous diethyl ether to the round-bottomed flask through the condenser and gently heat and stir the mixture on your stirring hotplate to obtain a smooth reflux. Add the remaining bromobenzene/ether solution from the addition funnel drop wise, such that smooth reflux is maintained. If the reaction becomes too vigorous, remove the heat source and cool the round-bottomed flask with an ice bath. After this addition is complete, continue to reflux for an additional 15 minutes. If necessary, add anhydrous diethyl ether to the reaction flask to maintain a minimum of about 15 mL of solution. As the reaction proceeds, the solution should take on a darker, chalky appearance. At the end of the reflux period, lower the hotplate and allow the solution to begin cooling.

Addition of the Methyl Benzoate

As the phenylmagnesium bromide solution is cooling, close the stopcock of the addition funnel, and add to it 1.2 mL methyl benzoate (measure its mass) and 5 more mL of anhydrous diethyl ether. Swirl the mixture in the separatory funnel to obtain homogeneity.

Once the phenylmagnesium bromide solution is near room temperature, cool it further with an ice bath. Remove the ice bath, and begin drop wise addition of the methyl benzoate/ether solution. Keep the ice bath nearby to cool the reaction if its rate becomes too vigorous. This is a very exothermic reaction, and it should reflux without external heating. If the condensate ring rises more than 1/3 of the way up the condenser, stop the addition and apply the ice bath until the solution is no longer refluxing, then cautiously resume the addition.

After the addition is complete, heat the reaction at reflux for 30 more minutes (time permitting). (If you do not have time to finish this reflux period, then cool the apparatus to room temperature, stopper the flask, and leave it until the next lab period.) Water is no longer a concern after the reaction of the Grignard reagent with the methyl benzoate is complete.

Workup

Pour the reaction mixture into an Erlenmeyer flask or a beaker containing 10 mL of cold 6 M sulfuric acid and an equivalent volume of crushed ice. Solvent-grade diethyl ether may be used to rinse the flask. Stir the resulting mixture until all solids have dissolved, adding additional 2-3 mL portions of ether and/or dilute aqueous acid if necessary. Verify that the aqueous layer is acidic; if not, add 6 M sulfuric acid in small portions until it is.

Transfer the entire mixture to your separatory funnel and shake gently while venting. Drain the aqueous layer, then extract the organic layer once with 5 mL of 3 M sulfuric acid, twice with 5 mL portions of saturated aqueous sodium bicarbonate solution, then finally once with 5 mL of saturated aqueous sodium chloride solution. CONSIDERABLE PRESSURE may build up during these washes; VENT frequently!

Pour the organic layer into an Erlenmeyer flask and dry it over anhydrous sodium sulfate for 10-15 minutes. Filter or decant the ethereal solution into a beaker, and let the ether gently evaporate. This crude triphenylmethanol product may be recrystallized from cyclohexane (about 10-20 mL / gram of product). Collect the purified crystals via vacuum filtration and set them aside to dry. Once dry, obtain the mass and compute the theoretical and percent yield. Characterize your triphenylmethanol product by measuring its melting point range, and its IR, proton and/or carbon NMR spectra, as indicated by your instructor.

CLEAN UP: Combine all aqueous extraction solutions, neutralize, and flush down the drain with lots of water. The cyclohexane mother liquor from the recrystallization should go in the liquid organic hazardous waste.