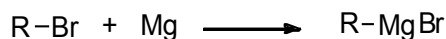


# GRIGNARD SYNTHESIS OF TRIPHENYLMETHANOL

CHM 222

## Background – forming Grignard reagents

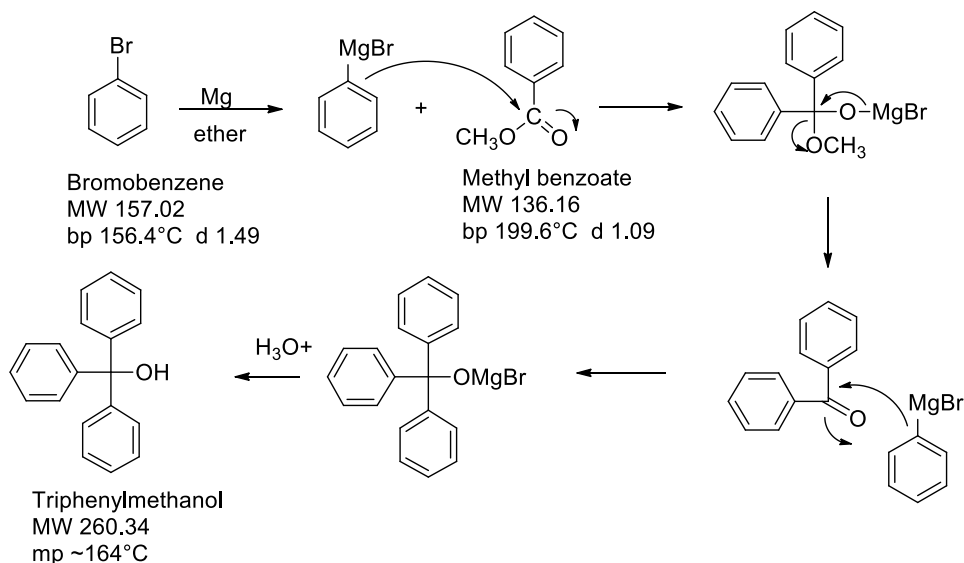
In 1912 Victor Grignard received the Nobel Prize in chemistry for his work on the reaction that bears his name, a carbon-carbon bond-forming reaction by which a variety of alcohols may be formed from appropriate alkyl halides and carbonyl compounds. The Grignard reagent is easily formed by reaction of an alkyl halide, in particular a bromide, with magnesium metal in anhydrous ether. Although the reaction can be written simply as below,



it appears that the structure of the material in solution is rather more complex. There is evidence that dialkylmagnesium is present,

## Background – synthesis of triphenylmethanol

In the experiment we will conduct, we shall carry out a common type of Grignard reaction, the formation of a tertiary alcohol from two moles of the Grignard reagent and one of an ester, as shown below. The initially formed product is unstable and eliminates a methoxy to form a ketone intermediate. The ketone intermediate is more reactive than the ester and immediately reacts with more Grignard reagent:



The primary impurity in the experiment is biphenyl, formed by the side reaction of phenylmagnesium bromide with unreacted bromobenzene. The most effective way to lessen this side reaction is to add the bromobenzene slowly to the reaction mixture so it will react with the magnesium and not be present in high concentration to react with previously formed Grignard reagent. The impurity is easily eliminated, since it is much more soluble in nonpolar hydrocarbon solvents (example: ligroin) than triphenylmethanol.

The experiment has been adapted from those in in Fieser and Williamson's **Organic Experiments**, 7<sup>th</sup> Ed.

Experiment (i.e.-the part that must be written into your notebook)

***\*All manipulations must be done in your fume hood.\****

a.) Formation of the phenylmagnesium bromide (aka phenyl Grignard) reagent

All apparatus and reagents must be **absolutely dry**. The Grignard reagent is prepared in a dry three-necked round-bottomed flask fitted with a long reflux condenser and a dropping funnel. A calcium chloride drying tube inserted into the thermometer fitment that will fit on the thermometer adapter and placed on the top of the condenser is also made ready. The flask, condenser, and magnesium (2 g = 0.082 mole of magnesium turnings) should be as dry as possible to begin with, and then the magnesium is placed in the flask, and the rest of the apparatus is assembled (except for the calcium chloride drying tube). The apparatus is heated gently but thoroughly with a cool luminous flame from the bottom to the top (note the appearance of water vapor condensing on the cool glass above the area you are heating--you need to drive that water up and out of the glassware). Do not overheat the magnesium. It will become deactivated through oxidation, or, if strongly overheated, can burn. Place the drying tube containing the calcium chloride onto your apparatus so that as the glassware cools, it pulls dry air through the calcium chloride. Cool to room temperature before proceeding! **Extinguish all flames** and wait until your instructor gives you anhydrous ether. Note that ether vapor is denser than air and can travel along bench tops and into sinks.

Make an ice bath ready in case control of the reaction becomes necessary, although this is usually not the case. Your instructor will pour into the flask, through the unused joint, 15 mL of *absolute* ether (absolutely dry, anhydrous). Being sure that your graduated cylinder is absolutely dry, add 9 mL (13.5 g = 0.086 mole) of bromobenzene. (More ether is to be added as soon as the reaction starts, but at the outset the concentration of bromobenzene is kept high to promote easy starting.) If there is no immediate sign of reaction, insert a *dry* stirring rod with a flattened end and crush a piece of magnesium firmly against the bottom of the flask under the surface of the liquid, giving a twisting motion to the rod. When this is done properly the liquid becomes slightly cloudy, and ebullition commences at the surface of the compressed metal. Be careful not to punch a hole in the bottom of the flask. Swirl the flask to provide fresh surfaces for contact, and, as soon as you are sure that the reaction has started, add 25 mL more absolute ether before spontaneous boiling becomes too vigorous. Note the volume of ether in the flask. Cool in ice if necessary to slow the reaction but do not overcool the mixture; the reaction can be stopped by too much cooling. Any difficulty in initiating the reaction can be dealt with by trying the following expedients in succession.

1. Warm the flask with your hands or a beaker of warm water. Then see if boiling continues when the flask (condenser attached) is removed from the warmth.
2. Try further mashing of the metal with a stirring rod.
3. Add a tiny crystal of iodine as a starter.
4. This can only be done with permission of the instructor: Start afresh, taking greater care with the dryness of apparatus and reagents.

Once the reaction begins, spontaneous boiling in the diluted mixture may be slow or become slow. If so, heat the flask with your heating mantle and reflux gently until the magnesium has disintegrated and the solution has acquired a cloudy or brownish appearance. The reaction is complete when only a few small remnants of metal (or metal contaminants) remain. Check to see that the volume of ether has not decreased. If it has, add more anhydrous ether. Since the solution of Grignard reagent deteriorates on standing, the next step should be started at once.

b.) Synthesis of triphenylmethoxy magnesium bromide

Your instructor will pour 15 mL of anhydrous ether into your separatory funnel, and then you will add 5 g (0.037 mole) of methyl benzoate to the separatory funnel, and swirl to mix. Cool the flask containing phenylmagnesium bromide solution briefly in an ice bath. Run in the methyl benzoate solution *slowly* with only such cooling as is required to control the mildly exothermic reaction, which affords an intermediate addition compound that separates

as a white solid. Swirl the flask continuously until the methyl benzoate is completely added. Complete the reaction by heating the mixture at reflux for one-half hour (hot water from the tap works well).

#### c.) Synthesis of triphenylmethanol & recrystallization

Pour the reaction mixture into a 250-mL Erlenmeyer flask containing 50 mL of 10% sulfuric acid and about 25 g of ice and use both ordinary ether and 10% sulfuric acid to rinse the flask. Swirl well to promote hydrolysis of the addition compound; basic magnesium salts are converted into water-soluble neutral salts and triphenylmethanol is distributed into the ether layer. An additional amount of ether (ordinary) may be required. Pour the mixture into a separatory funnel (rinse the flask with ether), shake, and draw off the aqueous layer. Shake the ether solution with 10% sulfuric acid to further remove magnesium salts, and wash with saturated sodium chloride solution to remove water that has dissolved in the ether. The amounts of liquid used in these washing operations are not critical. In general, an amount of wash liquid equal to one-third of the ether volume is adequate.

To effect final drying of the ether solution, pour the ether layer out of the neck of the separatory funnel into an Erlenmeyer flask, add about 5 g of granular anhydrous sodium sulfate. Swirl the flask from time to time, and after 5 min remove the drying agent by gravity filtration into a tared Erlenmeyer flask. Rinse the drying agent with a small amount of ether. Add 25 mL of 66-77°C ligroin and concentrate the ether-ligroin solutions (hot plate) in an Erlenmeyer flask in the hood. Evaporate slowly until crystals of triphenylcarbinol just begin to separate and then let crystallization proceed, first at room temperature and then at 0°C. The product should be colorless and should melt not lower than 160°C.

Turn in, as directed, the product in a vial labeled with your name, the name of the compound, its melting point, and the overall percent yield from methyl benzoate.

#### d.) Clean-up

Combine all aqueous layers, dilute with a large quantity of water, and flush the slightly acidic solution down the drain. The ether/ligroin mother liquor from the crystallization goes in the organic solvent container. Calcium chloride from the drying tube should be dissolved in water and flushed down the drain.