

CHEM 2229 EXP 2: The Grignard Reaction

Background:

The haloalkanes, also known as alkyl halides, R-X, are a group of chemical compounds comprised of an alkane "R" with one or more hydrogens replaced by a halogen "X" atom (fluorine, chlorine, bromine, or iodine). Halogens are more electronegative than carbons. This results in a carbon-halogen bond that is polarized. The carbon atom has a partial positive charge, while the halogen has a partial negative charge. In other words, the polarity of an alkyl halide, R-X, is such that R exhibits a carbocationic character. This allows R-X to undergo a multitude of nucleophilic substitution reactions. However, when R-X reacts with metallic magnesium, Mg, the product, RMgX, exhibits the *opposite* polarity (*i.e.*, R is now carbanionic in character). This phenomenon was discovered by Victor Grignard (Nobel Prize 1912) and RMgX is known as a Grignard reagent after its discoverer.

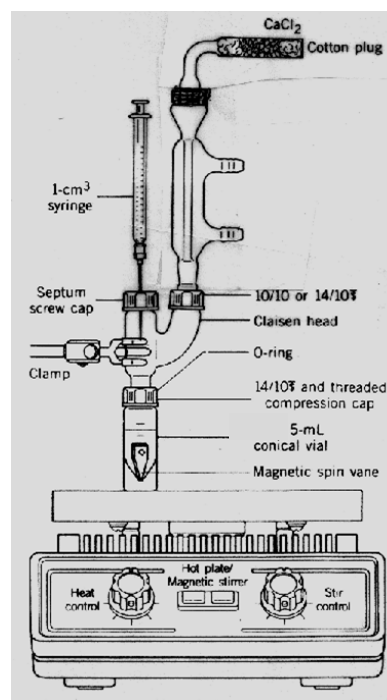
Because the R in RMgX has a carbanionic character, it can act as a nucleophile (and also as a strong base). The C in a carbonyl group, $>C=O$, bears a δ^+ because of the polarity and the polarizability of the carbon-oxygen bond. This makes such a C a likely site for the R of a Grignard reagent to attack: a C-C linkage is formed; the π bond of the carbonyl group is now changed to a σ bond linking the MgX moiety of the Grignard reagent. An aqueous work up leads to hydrolysis of the O...MgX bond. This type of strategy is exploited frequently in organic chemistry as a means of preparing alcohols.

It is absolutely essential that all reagents, solvents and glassware used in this preparation be exceptionally dry. (Why?)

IMPORTANT: All glassware and the stir bar should be very clean, placed in a labeled 600 ml beaker and dried at least overnight in an oven at 110 °C.

Required Glassware:

- 1 - 5 ml conical vial
- 2 - 3 ml conical vials
- 3 - caps and septa (not on vials) (replace damaged septa)
- 1 - Claisen head
- 1 - jacketed condenser
- 1 - drying tube (remove outer cotton plug only)
and desiccant (if pink, replace after oven drying)
- 1 - metal microspatula (clean) (not scoopula)
- 1 - teflon microstir vane
- 1 - 2 ml glass syringe (disassemble and clean)



I. Triphenylmethanol Preparation Summary:

First the Grignard reagent, phenyl magnesium bromide, will be prepared by reacting Mg with bromobenzene in anhydrous ether. To this reagent, an anhydrous ether solution of benzophenone is added. When the reaction is complete (~30 min), the product will be subjected to an acidic aqueous work-up whereby triphenylmethanol appears as a white precipitate. Isolation and recrystallization result in a relatively pure alcohol.

A. Preparation of the Grignard Reagent:

NOTE: The glassware is hot. Do not touch any glass surfaces with bare fingers. Wear gloves. Minute amounts of moisture are fatal to the experiment! The glassware should be assembled while still hot to minimize moisture gain and allowed to cool. Record all masses to the nearest 0.001 g.

1. Cap the 3 ml vials as soon as possible while the vials are still warm. Assemble the apparatus similar to that shown in Figure 3.18 on pg 31 of MTOL, adding a condenser between the Claisen head and the drying tube. Add desiccant (if needed) and cotton plug to the drying tube. Keep the vials capped and system closed unless otherwise noted.
2. Obtain 3 ml of anhydrous ether in a dry, labeled capped 3 ml conical vial. The closed vial is filled by injecting the ether via syringe needle through the septum. The cap should be loosened slightly during filling to allow pressure release.
3. Weigh ~40 mg of Grignard-quality Mg. Add the Mg into the 5 ml conical vial through the Claisen head and reclose the septum cap. Using the 2 ml glass syringe, add about 1 ml of anhydrous ether to the reaction mixture by withdrawing the ether from the 3 ml conical vial by puncturing the septum with the needle. (The cap on the 3ml vial will need to be loosened to permit withdrawal of ether.)
4. Weigh another labeled dry 3-ml conical vial, equipped with a septum cap. To this 3 ml vial, introduce ~0.17 ml of bromobenzene ($d=1.491$ g/ml) using a glass syringe. Reweigh the vial. Determine the mass of the bromobenzene and calculate the number of mmoles. Add 0.5 ml of anhydrous ether via syringe from the 3 ml ether vial to the bromobenzene vial and swirl to mix.
5. Fill the glass syringe with this solution. (The cap on the bromobenzene vial may need to be loosened slightly to withdraw material.) Be sure to close the valve on the syringe afterwards or the ether will squirt out of the syringe. Using the glass syringe, puncture the septum on the Claisen head and add about 0.2 ml of the bromobenzene/ether solution into the reaction vial containing the Mg turnings. Briefly remove the septum cap from the Claisen head and crush the Mg with a dry spatula to expose a fresh, reactive Mg surface. Quickly replace the septum cap.

Note: If the system is scrupulously clean and dry, bubbles should readily form on the surface of the metal. This signals the beginning of the reaction. The exothermic reaction is enough to start the ether boiling. The formation of a brownish-gray cloudy solution should accompany the gradual disintegration of the Mg metal. *If there is no evidence for a reaction going on, consult with the TA for choosing one or more possible remedies for starting the reaction.*

6. Once the reaction has started, introduce the rest of the bromobenzene solution in two portions via syringe. Rinse the bromobenzene vial with ~ 0.5 ml of anhydrous ether. Add this rinse to the reaction vial via syringe. (If some of the ether is lost during reflux, replace it with additional anhydrous ether.) Wait 45 minutes. During this time, Part B can be prepared. Once the 45 minutes have passed, most of the Mg turnings should have reacted.

B. Triphenylmethanol Synthesis:

While the Grignard reagent is being prepared, make the benzophenone solution.

1. Calculate the mass of 1.5 mmoles of benzophenone (MW = 182.220 mg/mmole) to the nearest mg. Record the calculation. Tare the capped dry 3 ml conical vial that was previously used for the bromobenzene. Add the 1.5 mmoles of benzophenone to the tared vial. Record the exact mass. Add 0.5 ml of anhydrous ether to this vial. Swirl to dissolve.
2. When the reflux period for part A is over, draw the benzophenone solution into the syringe and introduce it *slowly* into the Grignard reagent vial. (The reaction is exothermic and care should be taken that the reaction mixture does not boil.) When the addition is complete, cool the mixture to room temperature. As it cools the solution will turn pink/red and gradually solidify. If necessary, add ~ 0.2-0.3 ml of anhydrous ether, to replace any evaporated ether. Stir the mixture and let it stand for ~15 minutes. The color will fade back to white, indicating the reaction is complete. (If the color is still pink after 15 minutes, stir thoroughly with a microspatula until all pink coloring disappears.)

Acidic Aqueous work-up:

1. At this point the system no longer has to be protected from moisture. Leave the Claisen head on the vial to prevent product loss if foaming occurs. Using a glass Pasteur pipet, add dropwise 1.0 ml of 6M HCl to neutralize the reaction mixture and to induce the hydrolysis leading finally to the triphenylmethanol. (**Note:** HCl addition should be done cautiously because any unreacted Mg metal will generate H₂ gas as it reacts with the acid, which could cause liquid to foam out of the vial.)
2. Use a microspatula to stir the pasty product and ensure all of the magnesium has reacted. After all of the bubbling has stopped, remove the stir bar and transfer the contents of the vial to a storage vial (maybe, see below).

Clean-up & Storage: (Maybe, depending on the number of sections this semester)

1. Obtain a special storage vial from the TA. Label the storage vial with both first and last name, course number and section number. The following week's experiment will use the product in the upper ether layer. Any inorganic byproducts will be in the lower aqueous layer. Be sure to transfer both layers (i.e., all of the contents of the conical vial) to the storage vial. Place the labeled storage vial in the designated storage box.
2. Disassemble and rinse all glassware and glass syringe with acetone. Return the needle and valve to the instructor. Return the 600 ml beaker to the cart.

This is a good stopping point for the first week.

Week 2 – Recovery of the Product:

1. Obtain ~3 ml of ether (*ordinary, not anhydrous*) in a graduated cylinder. Place the 5 ml conical vial in the Al block to prevent tipping. Transfer contents of the storage vial to the 5 ml conical vial. Rinse the storage vial twice with ~0.5 ml portions of ether. Pour the rinsings into the 5 ml conical vial in order to transfer any remaining product from the storage vial and to replace any ether that may have evaporated from the previous week. Once all of the contents have been transferred, cap the 5 ml conical vial and mix by gentle shaking.* The contents should separate into a pale yellow top layer and a clear bottom layer.

***Note:** Be careful to shake gently, there may be some pressure buildup due to the ether. Excessive or vigorous shaking may lead to emulsion formation. Insufficient ether may also result in a turbid middle layer or some undissolved crystals of product. If this occurs, check with the TA.

2. With a pipet, remove the bottom H₂O layer adding it to a 3 ml conical vial. (Do ***not*** discard the H₂O layer yet.) Add another 0.5 ml of ether to the H₂O layer in the 3ml conical vial. With a pipet, remove the bottom H₂O layer adding it to a labeled waste beaker. Transfer the remaining contents from the 3ml conical vial into the 5 ml conical vial in order to combine the two ether portions. Verify that there are no longer two layers in the 5 ml conical vial.

***Note:** If iodine had to be added to help initiate the Grignard reagent, then the ether layer will be a dark reddish color. This may be removed by washing the ether layer with either sodium bisulfite (NaHSO₃) solution or sodium metabisulfite (Na₂S₂O₅) solution to reduce the iodine (I₂) to iodide ion (I⁻), which is colorless and water soluble.

3. Add 1 ml of an aqueous sodium bicarbonate (NaHCO₃) solution to the mixture in the 5 ml conical vial in order to wash the combined ether portions. Shake gently and allow the solution to separate into two layers. If there is any excess HCl from the previous Grignard workup, there may be fizzing. Using a pipet, remove the lower wash layer and add to H₂O waste beaker.
4. Add 1 ml of a saturated aqueous sodium chloride (NaCl) solution to the mixture in the 5 ml conical vial in order to wash the ether layer again. Shake gently and allow the solution to separate into two layers. Using a pipet, remove the lower wash layer and add to H₂O waste beaker. The H₂O layers in the waste beaker may now be discarded.
5. Transfer the ether mixture to a 50 ml beaker. Rinse the 5 ml conical vial with ~0.5 ml ether twice adding rinses to the 50 ml beaker. Add 3-4 spatulas of anhydrous Na₂SO₄ solid to dry the ether. Swirl the beaker to increase contact of sodium sulfate with the solution. The sodium sulfate will clump as it removes any remaining water in the solution. If only relatively large clumps form, add more sodium sulfate until it is “free-flowing.” Swirl occasionally for 5 minutes.
6. Weigh another 50 ml clean dry beaker. Record the mass to the nearest 0.001 g. Decant the ether solution into the 50 ml beaker. Rinse the sodium sulfate twice with 0.5 ml portions of ether. Add rinsings to the 50 ml beaker. (*The dried ether solution should be clear, not turbid. If cloudy, repeat the drying step.*)

7. Carefully evaporate the ether using a hair dryer or a hotplate on a low setting. Do ***not*** overheat and melt the sample. After the ether has evaporated, the distinct ether smell will no longer be present. The remaining residue or “crude product” will be a yellowish mixture of triphenylmethanol and biphenyl.
8. Weigh the beaker and contents. Record the mass to the nearest 0.001g. Subtract the mass of the beaker to determine the mass of the crude product.

Isolation of the Triphenylmethanol:

1. Add 2 ml of hexane to the crude product in the beaker. With the glass end of a stirring rod, triturate (*rub and grind*) the oily mixture for 2-3 minutes in order to extract the biphenyl.
2. Vacuum filter the crystals using the small (1 cm paper) Hirsch funnel. Rinse the crystals with 0.5 ml of cold hexane. Dry the crystals under vacuum. When crystals are dry, remove hose and shut off vacuum. Be careful when removing the Hirsch funnel not to spill any of the crystals. (Do ***not*** discard the filtrate yet.) Weigh the crystals to the nearest 0.001 g. Record this value as the mass of the triphenylmethanol.
3. To verify the identification of the product, add a few crystals of the triphenylmethanol to a disposable vial. Add a drop of concentrated sulfuric acid. If the triphenylmethyl carbocation is generated, a noticeable color change will occur. Observe and record the color of the conjugated carbocation.
4. Using a Fisher-Johns melting point apparatus, determine the melting point range of the product. Record the model and number of the MP apparatus. Record the melting point range.

***Note:** If time permits and the melting point of the triphenylmethanol is low or the crystals are darkly colored, a recrystallization may be done. To recrystallize the product, dissolve the crystals in a minimum volume of boiling isopropanol (start with 1 ml) using the microscale pipet technique. A Bunsen burner should be available in the hood for sealing the pipet tip. To decolorize, use activated carbon. Filter hot into a tared vial. Evaporate the solvent with a hair dryer under the hood. Reweigh and rerun the MP.

Recovery of the Biphenyl:

1. Weigh a small beaker. Record the mass of the beaker to the nearest 0.001 g. Transfer the filtrate from the trituration step to the preweighed beaker. Rinse the filter flask twice with 1 ml portions of hexane. Add rinsings to the beaker. (Note: It may be necessary to add more hexane to dissolve the crystals, as the vacuum filtration process tends to evaporate the hexane in the filter flask leaving biphenyl crystals in the bottom of the flask.)
2. Evaporate the hexane by gently heating the beaker with a hair dryer or on a hotplate. If the biphenyl deposits as an oil, it may be necessary to add a minimum amount of hot methanol to dissolve it; allowed to cool while covered; and then, cooled in ice to produce crystals. If crystals fail to form when cooled, add a few drops of water to precipitate the biphenyl.
3. Weigh the beaker and contents. Record the mass to the nearest 0.001g. Subtract the mass of the beaker to determine the mass of the biphenyl. Using a Fisher-Johns melting point apparatus, determine the melting point range of the biphenyl. Record the model and number of the MP apparatus. Record the melting point range of the biphenyl.

Post Lab Calculations: (*Label and show all calculations along with answers in lab report.*)

1. Determine the theoretical yield of the triphenylmethanol based on the moles of benzophenone.
2. Determine the overall percent yield of the crude product, the triphenylmethanol and the biphenyl.
3. Determine the percent yield of the triphenylmethanol and the biphenyl from the crude product.
4. Determine the percent error for the MP of both triphenylmethanol and biphenyl.

Post Lab Conclusion:

In your conclusion, discuss whether the experiment was successfully performed and / or any problems that arose during the experiment and your recommendation for how to avoid those problems if you were to redo the experiment.

Example Of How To Do The Equations

Part A on p2

“In another preweighed and dry 3-ml conical vial, equipped with a septum cap, introduce about 0.17 ml of bromobenzene (d=1.491 g/ml) using a glass syringe. Reweigh and calculate the number of mmoles.”

$$0.17 \text{ ml } (1.491 \text{ g / ml}) = 0.253 \text{ g}$$

When you added the bromobenzene, it probably wasn't exactly 0.253g. So you recorded the actual mass of the bromobenzene and converted it to mmole. For example, let's use 0.265 g.

$$0.265 \text{ g } (1 \text{ mole} / 157.01 \text{ g}) = 1.69 \times 10^{-3} \text{ mole } (1000 \text{ mmole} / 1 \text{ mole}) = 1.69 \text{ mmole}$$

If you used 0.253 g → 1.61 mmole

Part B on p 3:

“Triphenylmethanol synthesis. While the Grignard reagent is being prepared, make a solution by weighing 1.5 mmoles of benzophenone (MWt=182.22)...”

$$1.5 \text{ mmole } (182.22 \text{ mg} / \text{mmole}) = 273 \text{ mg (or } 0.273 \text{ g)}^*$$

*If you used a different number of mg, recalculate your number of mmole.

Notes:

1.) Since the reaction is 1:1, **verify that the benzophenone was your limiting reagent** (*i.e.*, there are fewer mmoles of benzophenone than your Grignard reagent). It should be if your masses were relatively close to the values in the directions.

2.) The reaction is also 1:1 for the reactants and the product triphenylmethanol. In which case, the number of mmoles of benzophenone should also be the number of mmoles of triphenyl methanol (*or the number of mmoles you'll use to calculate your theoretical yield*).

$$1.5 \text{ mmole of benzophenone } (1 \text{ Triphenylmethanol} / 1 \text{ benzophenone}) = 1.5 \text{ mmole TPM}$$

$$1.5 \text{ mmole TPM } (260.33 \text{ mg} / \text{mmole}) = 390.5 \text{ mg} \leftarrow \text{Theoretical Yield}$$

Grignard on p 5 paragraph 2:

“Carefully evaporate the ether using a hair dryer under your hood. Do not overheat the sample after the ether has evaporated. Weigh to get a yield of crude product, which at this point will be a yellowish, mixture of triphenylmethanol and biphenyl.”

For Example, your crude product weighs 0.141g. ← **Actual Yield of Crude**

$$\begin{aligned} \% \text{ Yield for crude product} &= (\text{Actual Yield} / \text{Theoretical Yield}) \times 100 \\ &= (0.141\text{g} / 0.391\text{g}) \times 100 \\ &= 36\% \end{aligned}$$

Page 5, Paragraph 3:

“Weigh, calculate the yield and run the MP of the crystals.”

For Example,

your crystals from the residue of the filtration weigh 0.112g. ← Actual Yield of Triphenyl methanol

$$\text{Overall \% Yield of TMP} = (0.112 \text{ g} / 0.391 \text{ g}) \times 100 = 28.6\%$$

$$\text{\% TMP Recovered from Crude} = (0.112 \text{ g} / 0.141 \text{ g}) \times 100 = 79.4\%$$

Presume that any of the Crude product that wasn't triphenylmethanol (TMP) is biphenyl (BP).

$$\text{Biphenyl expected mass} = 0.141 \text{ g} - 0.112 \text{ g} = 0.029 \text{ g}$$

After evaporating off the solvent of the filtrate, your crystals, for example, weigh 0.011g.

$$\text{Overall \% Yield of BP} = (0.011 \text{ g} / 0.391 \text{ g}) \times 100 = 2.8\%$$

$$\text{\% BP Recovered from Crude} = (0.011 \text{ g} / 0.141 \text{ g}) \times 100 = 7.8\%$$

$$\text{\% BP Recovered} = (0.011 \text{ g} / 0.029 \text{ g}) \times 100 = 37.9\%$$

For calculating the % Error for MP, use the midpoint of the range:

For example, Triphenylmethanol Literature: 160-163 °C Ref: Wikipedia
Experimental Range: 152-156 °C

$$\text{\% Error MP (TMP)} = [(\text{Theoretical} - \text{Observed}) / \text{Theoretical}] \times 100$$

$$= [(161.5 - 154) / 161.5] \times 100$$

$$= 4.64\%$$

Concepts To Consider Before Answering Prelab Questions on Canvas

(See Solomon's Organic Text for more information on Grignard reactions.)

1. Write the equations describing the reactions carried out in this week's experiment include the names of all of the reactants and products.
2. Explain why it is necessary to exclude and avoid all moisture in this experiment.
3. List 4 functional groups that must be avoided during the formation of a Grignard reagent.
4. For each of the functional groups listed in answer 3, write chemical equations that demonstrate why those particular functional groups should be avoided.
5. List 3 possible remedies to initiate a Grignard reaction that fails to start spontaneously.