ORGANIC SYNTHESIS: BENZOIC ACID VIA A GRIGNARD REACTION

EXPERIMENTAL PROCEDURE  Work in pairs but hand in separate, individual reports.

- Diethyl ether is highly flammable. MAKE SURE there are NO FLAMES nearby when using it.
- Dry ice is a cryogen. Avoid skin contact as it will cause cold burns.
- This reaction should be performed in a fumehood.

Preparation of Benzoic acid from Bromobenzene via a Grignard Reaction

1) Preparation of Phenylmagnesium Bromide

In order for this experiment to work, your glassware must be clean and dry. If needed wash the glassware and then ask your TA to show you how to dry it.

In a fumehood, set-up a dry 100 mL round-bottomed flask in a heating block on a hotplate stirrer - make sure the heating is turned off and that the hotplate can be quickly removed if needed by carefully clamping the neck of the flask (then it could be lifted up if needed). Add a stirrer bar.

Weigh out 1.74 g (0.072 g atom) of magnesium. Crush the magnesium in a mortar and pestle to "activate it" (this process provides the clean metallic surfaces necessary to initiate the reaction). Transfer the activated magnesium to the reaction flask and add a single crystal of iodine. Assemble the reflux with addition apparatus. Equip the 100mL round bottomed flask with a dry reflux condenser and a dry dropping funnel using a Claisen head (see diagram on the left).

(If required (unlikely in the dry air of Calgary), the CaCl₂ drying-tube can be fitted onto the top of the condenser. Do not pack the CaCl₂ too tightly or you will close off the system and not allow air to escape when the system is heated (a drying tube is required on humid days (or in humid climates) to ensure that water vapour does not interfere with the reaction)).

Make sure to start the cooling water in the condenser and that all the glass joints are well sealed.
Introduce 7.0 mL of bromobenzene (10.4g; 0.066 mole) in 10 mL of anhydrous ether into the dropping funnel. The funnel should be kept stoppered when the contents are not being added to the reaction flask but the stopper must be removed to allow addition of the bromobenzene solution to be made.

With gentle stirring, carefully add 5.0 mL of the bromobenzene / ether solution to the flask making sure it mixes and warm the flask gently with your hands. The appearance of cloudiness, with spontaneous bubbling and heat generated by the reaction will indicate the start of the reaction and the formation of the phenylmagnesium bromide. If the reaction proceeds too vigorously it should be moderated by momentarily cooling the flask using an ice-bath. However, once the reaction has started make sure you keep it going. DO NOT TURN ON THE HEAT UNTIL ALL THE ETHER SOLUTION HAS BEEN ADDED.

If you encounter difficulty in initiating the reaction, talk to your TA. They may suggest one of the following measures:

a) Warm the reaction flask using the heating block and then see if boiling continues when the flask (condenser attached) is removed from the heat.

b) Add another iodine crystal (or a few drops of methyl iodide (this forms a Grignard reagent very readily and will expose fresh magnesium)).

c) Start again! Take greater care with respect to the dryness of the apparatus and the seals at the ground glass joints.

Once the reaction is initiated, add a further 20 mL of anhydrous ether to the remaining bromobenzene solution in the dropping funnel. Add this solution to the reaction vessel gradually over 5-10 mins, at a rate sufficient to maintain boiling of the reaction mixture and making sure it mixes. Once the addition is almost complete, starting heating to continue the gentle reflux of solution for 30 minutes until the magnesium has nearly all disintegrated and the solution has acquired a cloudy or brownish appearance.

2) **Preparation of Benzoic Acid**

**CAUTION:** Exercise caution in handling dry ice.

Contact with the skin can cause severe frostbite or cold burns.

Always use cotton gloves or tongs.

Moisture from the atmosphere will condense on dry ice to form a coating of water ice over its surface so it is important to try to keep it protected from the moisture in the air to avoid side reactions caused by this condensed water. Therefore, collect your 10g of dry ice just before you need to use it. If it looks frosted, wipe the surface of the dry ice pellets with a clean, dry paper towel to remove any surface
frost and place it in a beaker covered with a watch glass until you are ready to use it.

When the phenylmagnesium bromide has been prepared and the mixture has stopped refluxing, remove the condenser from the flask and pour the liquid contents of the flask slowly but steadily over approximately 10g of dry ice contained in a 200 mL beaker - try to leave as much of the unreacted magnesium metal behind in the round bottomed flask. Rinse the flask with a small amount of anhydrous ether if needed and add that to the reaction mixture (again without transferring the unreacted magnesium). Cover the reaction mixture with a watch glass and allow it to stand until the excess dry ice has completely sublimed. The Grignard addition compound will appear as a viscous glassy mass. If the mass is too viscous to stir, add an additional 5-10 mL of ether (or more) as needed.

Before starting the work-up, draw a flow chart that summarises what is happening at each stage of the work-up process and that allows you to track the location of the product and shows how it is purified at each step. Show this to your TA before you start the work-up process.

The following steps are the work-up. Hydrolyse the Grignard addition product by carefully adding the mixture of about 25g of crushed ice (ordinary water ice), stir the mixture. If there is any magnesium in the bottom of the beaker then pour (i.e. "decant") the liquid into another beaker leaving the magnesium behind. Now carefully add concentrated hydrochloric acid DROPWISE while stirring. Check the pH with blue litmus paper (or pH paper) after you have added 8mL of conc. HCl, if it is not acidic then continue to add more conc. HCl until the solution is acidic. At this point any remaining solid material should have dissolved completely, if not, then you may have to add some extra hydrochloric acid (and maybe diethyl ether) to get any remaining solid material to dissolve completely. Stir the mixture until two clear layers appear (add more diethyl ether and acid if needed). Transfer the mixture to a separatory funnel. Remove the lower aqueous layer and discard it. Wash the upper ether layer by adding a mixture of 12.5mL of water and 2.5 mL of a saturated solution of sodium thiosulfate solution, stoppering the funnel and shaking as before. Allow the layers to separate and remove the water layer. If the ether layer still appears dark yellow or brown because iodine is still present repeat the thiosulfate wash process. Extract the ether layer three times with successive 12.5 mL portions of 10% sodium hydroxide solution to remove the benzoic acid. Combine the basic extracts. Once you are sure you have the right layer, discard the ether layer, which contains the by-product biphenyl, into the organic waste container in the fume hood.

Transfer the combined basic extracts into a clean round bottom flask - do not overfill the flask, it should not be more than about half full. Use a rotary evaporator remove the dissolved ether (ether is soluble in water to the extent of 7%) - your TA’s will demonstrate the correct use of this invaluable (but expensive) equipment. Unless the ether is removed before the benzoic acid is precipitated, the product may appear as a waxy solid instead of crystals. IF YOU HAVE ANY PROBLEMS WITH THE ROTARY EVAPORATOR AT ANYTIME ASK YOUR TA. Carefully remove the flask from the rotary evaporator and precipitate the benzoic acid by carefully adding ~8 mL of concentrated hydrochloric acid (test with litmus
paper that the solution is acidic). Collect the precipitated benzoic acid on a Büchner funnel by vacuum filtration. Wash the collected crystals with several portions of cold water and allow the crystals to dry thoroughly at room temperature or in a cool oven. When the crystals are dry, weigh the product and calculate the percentage yield.

Determine the melting point of the product and compare to the literature value. Hand in a small amount of your product in a clearly labelled container with your laboratory report.

**CLEAN UP**
- Aqueous solutions should be poured into the container for aqueous waste.
- Organic waste should be poured into the container for organic waste in the fume-hood.
- Used pipettes should be rinsed with acetone then put into the special container provided.

**REPORT**
The report for this experiment is a formal report. More details on writing formal reports can be found in the introduction to this manual. Remember that more it not necessarily better. It is important to be accurate and concise rather than verbose and vague (4-5 pages maximum). Proper English should be used and it should be written in your own words. A guide to the sections you should include is shown below.

1. Title and Date
2. Introduction: Describe the purpose of the experiment, include equations of the reactions.
3. Procedure
4. Results – g yield, % yield, melting points etc.
5. Analysis of product spectra
6. Discussion - (e.g. yield, purity, success, sources of error etc.)
7. Conclusions - summarise your results and discussion
8. References
9. Questions:
   (a) What are the mechanisms for the reactions involved starting from the reaction of the Grignard reagent, PhMgBr, with carbon dioxide through the work-up to give the desired product, benzoic acid?
   (b) Why do the Grignard reagents have to be kept away from water and oxygen? Show the by-products formed if the Grignard reagent reacts with water or oxygen.
   (c) Show (using a flow chart) how the product is separated from the unwanted by-products of the reaction during the “work-up”.