One common method for the preparation of organic acids is by a Grignard reaction. The French chemist Victor Grignard won the 1912 Nobel Prize in Chemistry for his discovery of the organomagnesium reagents that now bear his name. Grignard's discovery was that organic halides react with magnesium in dry ether to form organo-magnesium compounds, which are very effective and versatile *carbon-centred nucleophiles*. Grignard reagents react with many classes of organic compounds. With carbonyl compounds, they add across the C=O double bond to create a new carbon–carbon link.

In this experiment, a substituted bromobenzene will be converted to a substituted benzoic acid *via* a Grignard reaction (see procedure below). The bromobenzene compound is first reacted with magnesium to form a Grignard reagent, a phenylmagnesium bromide. The phenyl carbanion present in phenylmagnesium bromide then adds to one of the carbonyl groups in carbon dioxide. Hydrolysis of the reaction complex yields benzoic acid.

By-products are also formed in the Grignard reaction: some of the bromobenzene is converted to a biphenyl, and some of the phenylmagnesium bromide is intercepted by water and converted to a benzene derivative. In designing the work-up of the reaction, the desired product (a carboxylic acid) must be separated from inorganic salts and the neutral by-products.

In the second week of this experiment, the pK_a of benzoic acid compound will be determined using titration, and a pH meter. pK_a is defined by equation (1)

$$pK_a = -\log_{10} K_a \qquad (1)$$

Where the acid dissociation constant, K_a, is the equilibrium constant associated with the equilibrium,

$$HA \rightleftharpoons H^+ + A^-$$

and given by equation (2).

$$K_a = \frac{[H^+][A^-]}{[HA]} \qquad (2)$$

The acid dissociation constants of weak acids vary widely. In aqueous solutions, acids with pK_a less than 0 are essentially completely ionised, and can be considered strong acids. Carboxylic acids generally fall within the range pK_a = 2 to 7.

pK_a can be determined from the pH at the half-equivalence point of a titration, which is where there are equal numbers of moles of weak acid and its conjugate base present. The **equivalence point** is the theoretical point where equal moles of acid and base are present (in contrast to the **endpoint**, which is the experimental approximation to the equivalence point, measured by methods such as colourimetric indicator). For the titration of a weak acid with a strong base, the pH of the equivalence point will be above 7.

1. LEARNING OUTCOMES

After undertaking this experiment, you will have the following laboratory skills:

- Working with water-sensitive reagents
- Use of dry ice
- Use of a separating funnel
- Filtration techniques
- Manipulation of volumetric glassware
- Weighing by difference
- Use of a pH meter

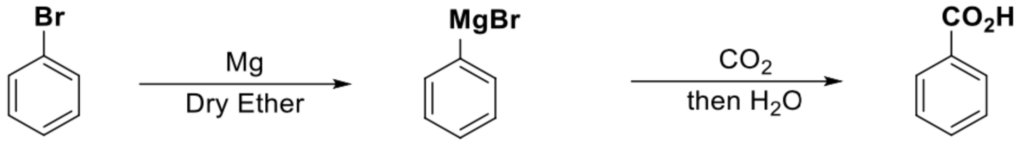
After undertaking this experiment and writing the lab report, you will understand:

- Organomagnesium compounds
- Use of Excel for plotting and fitting data
- Determination of pK_a from titration data

Experiment 2 – Preparation and analysis of an organic acid

This experiment will take place over two weeks and will involve the preparation of an organic acid (week 1), and the determination of its pK_a by a pH titration (week 2). You should form pairs in week 1. You and your partner will work individually on the same bromobenzene starting material in week 1 and analyse one of your compounds in week 2 together. As a pair you will present your findings in an oral presentation.

One common method for the preparation of organic acids is by a Grignard reaction. The French chemist Victor Grignard won the 1912 Nobel Prize in Chemistry for his discovery of the organomagnesium reagents that now bear his name. Grignard's discovery was that organic halides react with magnesium in dry ether to form organo-magnesium compounds, which are very effective and versatile *carbon-centred nucleophiles*. Grignard reagents react with many classes of organic compounds. With carbonyl compounds, they add across the C=O double bond to create a new carbon–carbon link.



Bromobenzene
MW 157.0, bp 155°C

Phenylmagnesium bromide
(a Grignard reagent)

Benzoic Acid

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1. LEARNING OUTCOMES

After undertaking this experiment, you will have the following laboratory skills:

- Working with water-sensitive reagents
- Using a multi-necked round-bottomed flask with condenser and dropping funnel
- Use of dry ice
- Use of a separating funnel
- Filtration techniques
- Manipulation of volumetric glassware
- Weighing by difference
- Use of a pH meter

After undertaking this experiment and writing the lab report, you will understand:

- Organomagnesium compounds
- Use of Excel for plotting and fitting data
- Determination of pK_a from titration data

2. CHEMICALS USED AND SAFETY DATA

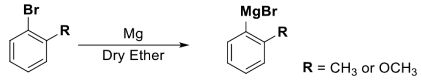
1-Bromo-2-methylbenzene	**Irritant**
Bromobenzene	**Causes skin and serious eye irritation, flammable**
Magnesium	**Highly flammable**
Diethyl ether	**Highly flammable, irritant**
Iodine	**Irritant**
Carbon dioxide(s)	**Avoid skin contact; can cause cold burns**
Hydrochloric acid	**Corrosive, toxic**
2-Methylbenzoic acid	**Irritant**
Benzoic acid	**Causes skin and serious eye irritation**
Sodium hydroxide	**Corrosive on contact with skin, eyes and respiratory tract**
Ethanol	**Highly flammable**

3. PROCEDURE

Week 1 – Preparation of substituted benzoic acid

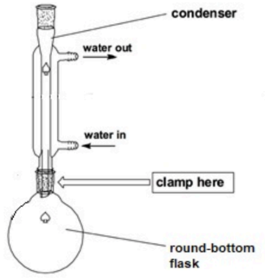
This experiment will take the full 4 hours, so you need to be prepared ahead of class. Demonstrators will show groups of students how to set up the experiment at the start of the session, and will assign you a substituted bromobenzene starting material.

Formation of the Grignard reagent



The following glassware has been pre-dried and provided for you: 50 mL round-bottomed flask, B19-joint water condenser, two 100 mL beaker and a 25 mL measuring cylinder.

Check that the glassware is completely dry before use, or this reaction will not work.

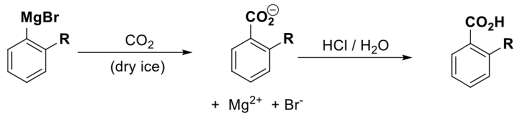


Using a 100 mL beaker, collect your assigned substituted bromobenzene (3.0 g / 2.0 mL) from the dispenser in the front fumehood. Using the *dry* measuring cylinder, collect *anhydrous* ether (~10 mL) from the PureSolv (with the help of a demonstrator) and add it to your substituted bromobenzene in the beaker. Place a watch glass on your beaker to avoid moisture from getting in.

Weigh magnesium granules (0.3 g) into the 50 mL round bottomed flask using the plastic powder funnels and rubber/cork rings next to the balances. Attach the condenser as indicated in the diagram to the right. More information about using clamps can be found in Appendix 6.

Add the prepared mixture into the round bottom flask, then add one small crystal of iodine into the flask. Put the condenser onto the round-bottom flask and *turn the condenser water on*. Heat the mixture to reflux with a hair-dryer for 20 minutes. The orange colour from iodine shall disappear after 7min of refluxing and the mixture shall get cloudy and pale yellow. A small amount of magnesium metal should remain. *Use your Grignard reagent* ***immediately*** *in the next step.*

Conversion of the Grignard Reagent into Substituted Benzoic Acid



Collect dry ice (solid carbon dioxide pellet, ~ 3 g, issued by a demonstrator – wait until you are ready to use it before you obtain it to avoid condensation of water) in a dry 100 mL beaker. *You should use gloves for this step.* Decant the substituted phenylmagnesium bromide solution onto the dry ice with swirling. Decant it slowly so that any remaining solid magnesium is left behind. Rinse the flask with 5 mL of 3 M HCl solution to convert any remaining elemental Mg to its chloride salt, then dispose of it in the magnesium waste container. After the dry ice has disappeared, continue swirling and add ice-cold water (20 mL) to decompose the reaction complex.

The remaining operations are necessary to isolate the substituted benzoic acid from the other components. Acidify the two-phase system with 10M hydrochloric acid (5 mL). *Add the acid in portions and with gentle swirling to avoid frothing over as the dissolved carbon dioxide is liberated.* Transfer your two-phase solution into a 100 mL separating funnel, rinsing the beaker with ether (2 × 10 mL).

Shake thoroughly in a 100 mL separating funnel (venting frequently) and allow the layers to separate. Run off the bottom acid layer (which contains water-soluble impurities plus some of your substituted benzoic acid) into a 100 mL beaker; pour the top ether layer into a clean 100 mL beaker (most of your product is in here, along with some organic impurities).

Pour the bottom acid layer back into the separating funnel and extract with two further portions of ether (2 × 10 mL each) as above, collecting the organic layer in the same flask. Pour the organic extract back into the separating funnel, then extract the combined ether layers with 10% sodium carbonate (15 mL), collecting the bottom (alkaline) layer. *Make sure you vent the separating funnel frequently!* Add a second 15 mL of 10% sodium carbonate solution to the organic layer in the separating funnel and repeat.

Combine the two basic extracts in a 100 mL beaker placed on ice and acidify slowly with 10M hydrochloric acid while swirling the beaker carefully. Add the acid slowly in order to minimise frothing as CO_2 is produced. *Be careful: many students add too much, too quickly, and dissolve their product.* Continue until the solution is acidic (to test this, dip your Teflon rod into your solution and dab it onto universal indicator paper provided); about 9 mL should be enough.

Collect the precipitated substituted benzoic acid product by filtration using a filter flask and Hirsch funnel, and wash with a little bit of ice-cold water. *Do not forget to clamp your filter flask while it is under vacuum.* Leave your product on the Hirsh funnel for 10 min under vacuum to dry your product. While waiting for the drying, put a label with your name on it onto a glass vial and record the weight of that vial (without a cap). Collect your product into that vial and then leave your product to dry in a desiccator in the service room. More information about filtration techniques can be found in the Appendix 6.

Waste Disposal:

- Dispose of any solid magnesium by washing with 3 M HCl into the "magnesium waste container".
- Combine your aqueous waste from your separating funnel and your filtration into a large ice basin. Add 10% sodium carbonate solution slowly until the solution turns red litmus paper to blue (pH 8-10). Pour this alkaline solution down the sink.
- Dispose of acetone and ether into the "non-halogenated organic waste container (Non-Cl)".
- Dispose of used gloves into the cardboard "Broken glass" bins.

Submit your product to the Service Room, in a weighed vial labelled with your SID and day of attendance, to be placed in a desiccator cabinet before you leave the lab. Your sample will not be fully dried by the end of the session, but will be by the time you are ready to start part b.

Week 2 – Determination of the pK_a of substituted benzoic acids

Collect your dried substituted benzoic acid from the Service Room and weigh it to determine your yield for inclusion in your presentation. Quote your yield both in grams, and as a percentage (based on the amount of bromobenzene you started with).

Titration of substituted benzoic acids

You will complete this part of the experiment in pairs. For more information about the volumetric techniques you will be performing today, refer to Appendix 7.

Your demonstrator will show you how to calibrate a pH meter using the available buffer solutions. You should calibrate your pH meter before beginning the experiment.

Weigh ***approximately*** 0.25 g of your substituted benzoic acid (prepared in part 1 of this experiment) into a clean and **dry 250 mL beaker**. Place a clean, dry magnetic stir-bar in your beaker, and first carefully dissolve your acid in 40 mL ethanol. You can carefully use the magnetic stirrer to aid dissolution. Once dissolved, carefully add 60 mL of distilled water, taking care not to create any splashes or have undissolved material on the walls of the beaker. Carefully secure the electrode with a boss head and clamp attached to the burette retort stand, ensuring it is sufficiently immersed in the solution for measurement and not coinciding with the burette or stirrer bar.

Record the initial pH reading and initial volume. Titrate your acid solution with approximately 1 mL increments of the 0.1M NaOH solution. After each addition of base, record accurate volumes and corresponding pH readings on the results sheet. Make sure that the tip of the burette is above the solution at all times, and that you continue your titration well past the equivalence point (to pH ~12).

At this point, perform the calculations for this titration, plotting your results on Excel (see below). Determine the equivalence point for this titration.

Repeat the titration, using smaller increments (approximately 0.1 mL) of base in the region of the half-equivalence point. Continue the titration and again use smaller increments in the region of the equivalence point. This will ensure that you can accurately calculate the pK_a from the pH at the half-equivalence point.

You will be given a different substituted benzoic acid to study – at the end of the session, you will share your results with the rest of your group. Repeat the entire protocol using 0.25 g of this substituted benzoic acid.

Waste Disposal:

- Dispose of the titrant and titrand solution and (washing) acetone into the "Non-halogenated organic waste (Non-Cl)".

Calculations

Use Excel to plot pH (y-axis) against volume of NaOH added (x-axis). To improve the accuracy of your equivalence point, you will also plot the first and second derivatives of this raw data, as shown by your demonstrator, and using the example Excel table provided. From your second titration (for which you collected more values in the important regions), calculate the value of the pK_a as the pH at the half-equivalence point.

Example Excel Table:

V reading (mL)	Titration V (mL)	pH	ΔV	ΔpH	ΔpH/ΔV	V(ave)	$\Delta(\Delta pH)/\Delta V^2)$
	0						

Once you have calculated the pK_a of your substituted benzoic acid, write it on the board. You should record all the results obtained from the other groups, to include in your report. You will be able to access your group's pK_a via the Scilearn site (see Canvas).

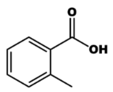
The number of moles of NaOH added to reach the equivalence point should match the number of moles of benzoic acid you weighed out. On this basis make an assessment (as a percentage) of the purity of your benzoic acid product and include this alongside your product description and yield calculation in your report.

4. DATA ENTRY & SAMPLE HAND-IN

Before you leave the lab, enter the pK_a values that you obtained for both your synthesised and assigned benzoic acid derivatives onto one of the laptop computers in the lab. Please be careful with your analysis the first time, because repeating and re-entering results will incur a penalty.

You should also submit your remaining synthesised aromatic acid to the service room in a sample vial with a label stating your SID and chemical name or structure, and yield (mass) obtained.

123456789



Experiment 3a
2-Methyl benzoic acid 2.1 g

5. ORAL PRESENTATION

This experiment is assessed by a six-minute oral presentation (see Canvas for a template). You will present <u>with your partner</u>. Your presentation should consist of five slides and include:

Slide 1:

- Title, author(s), and aim of your experiment. Your title should identify the specific compound you have produced and examined in your study.

Slide 2:

- A reaction scheme explaining how the Grignard reaction works.
- A description of the appearance of your product.
- The yield (g) and percentage yield of your product as well as an assessment of the purity of your product. *
- How does your yield compare to the theoretical yield? Account for your yield. <u>If you haven't been able to get a product, please explain possible reasons in your presentation. How would you do it differently next time around?</u>

Slide 3:

- Figures (with appropriate captions) showing pH vs volume of NaOH for the second titration with benzoic acid, and of the first and second derivatives.
- Your calculated pK_a values for your substituted benzoic acids.

Slide 4:

- A table of all the pK_a values from the different acids used in the group.
- You should compare your experimental pK_a with a value from the scientific literature. (In oral presentations, references are presented as a footnote at the bottom of the slide where the information appears.)
- A discussion tying together the various results reported.

Slide 5:

- Your summary and conclusions from this experiment.

**Make sure that you pay attention to the number of significant figures which you use.*