Microwave-assisted Hydrolysis of Benzonitrile

**Required Pre-Lab Readings:** McMurry Sections 15.7 & 16.7.

**Techniques you must be prepared to perform:** Reflux (pp 59-63) and Recrystallization (pp 183-197).

**Introduction**

Microwaves are a type of electromagnetic radiation with wavelengths ranging from 0.1 cm – 100 cm. As an alternative to traditional thermal heating, microwave irradiation has been used increasingly in recent years to heat reaction mixtures. Due to the dipolar polarization heating mechanism between microwave irradiation and polar molecules, microwave-assisted organic reactions have many advantages. It is energy efficient and allows accurate control over several reaction parameters. Shorter reaction times are often possible because higher than normal temperatures can be achieved if the reaction is performed in sealed vessels. The products of microwave reactions provide purer products due to the homogenous *in situ* heating.

Nitriles are derivatives of carboxylic acids and, as is the case of all derivatives of carboxylic acids, they can be hydrolyzed (literally, “to break with water”) to form a carboxylic acid. The hydrolysis of carboxylic acid derivatives is of particular importance in biology. In prebiotic chemistry, -amino nitriles, such as the one below, are thought to be precursors to the -amino acids found in biological systems. The reactions below give the -amino acid glycine as the product. The hydrolysis of fats (esters) and proteins (amides) are just two of many examples of hydrolysis reactions that occur in animals.



In this lab you will complete a base promoted conversion of benzonitrile to benzoic acid under microwave irradiation (below). Because of their stability, nitriles require the presence of an acid or base, and elevated temperatures for efficient hydrolysis. The mechanism involves initial attack of the nucleophilic hydroxide on the electrophilic carbon. Proton transfer from the solvent (water) results in an intermediate that tautomerizes to the corresponding amide. The amide proceeds on to the carboxylate by a mechanism analogous to the base hydrolysis of esters.



This will be the first “microscale” experiment that you will be performing this semester. It is important that you understand and feel comfortable working with materials on a small scale. Microscale experiments have the advantages of being less expensive, less polluting, and using less equipment than larger scale reactions. They also go faster, so if anything goes wrong, you will often have time to repeat the experiment.

Working on microscale has the disadvantages that you must measure reagents and products more carefully and work a little more carefully since losses in transferring materials make a greater difference in yield. Be aware that even though a few flakes of product may look like a lot, they may weigh less than 1‑2 mg, and you can still afford that kind of loss

**Procedure**

Into a microwave reaction vial (pictured on the right; Standard Wheaton® glass vials 13-425, 15x46 mm, Type I borosilicate glass) add 1 mmol of benzonitrile (\_\_\_\_ g; \_\_\_\_ mL) and 1 mL of 2.5 M NaOH solution. Use the **capping tool** to carefully put a microwave reaction seal (polytetrafluoroethylene, PTFE) on your vial. The capping tool will ensure the seal evenly lines-up with the top of the vial avoiding seal damage. Place a microwave reaction cap (polyether ether ketone, PEEK) on the vial and screw it on finger tight. Place the properly sealed and capped reaction vial in the transport box. Once the whole class finish preparing the samples, all the vials will be transferred to the microwave reactor. There are four black silicon carbide (SiC) plates in the microwave and each of them may hold up to 24 vials. Evenly distribute the vials on these plates for even irradiation. The hydrolysis of acetonitrile will be assisted by microwave irradiation at 150 oC for 10 min.

Once the microwave irradiation is finished, remove the vials from the microwave to the transport box. Then chill the sealed vials in an ice/water bath for several minutes. Open the caps and seals with caution and return the caps and seals to the designated beaker on the instructor’s desk. Transfer the reaction mixture to a small beaker and add cold 6 M HCl (with stirring) until the solution is acidic and precipitation of the product is complete (approximately how much HCl solution will you need?). Do not add the acid one or two drops at a time (think about what you should see). Collect the product by vacuum filtration and wash with cold water. Once the product is isolated, recrystallize the material from water using a scintillation vial. Allow the product to air dry for a week in the lab drawer. Once dried record the weight and melting point of the benzoic acid recovered.

Cautions and Reminder:

1. This reaction generates gas (which gas?), so it is necessary to chill the vial before you open it.
2. The reaction scale is only 1 mmol (~ 0.1 g), so handle it with care to avoid product loss, especially for the recrystallization. Do not use too much solvent to transfer or wash your crystals.
3. A stirring bar is not necessary because of the very small volume used under microwave irradiation.

**The microwave reaction caps ($40 each) and seals ($4 each) are specially designed for the microwave reactor and will be reused.**

 **Please return them to the designated beaker once you open your vials.**

The microwave reaction vials are disposable. Please put them in the designated beaker once you are done with your reaction.

Hydrolysis of Benzonitrile

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| **Name:** |  |  | **Section Number:** |  |

Overall Reaction: (use chemical drawing software)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Volume of benzonitirle: |  |  | Theo mmol benzoic acid: |  |
|  |  |  |  |  |
| mmol of benzonitirle: |  |  | Theo mass benzoic acid: |  |
|  |  |  |  |  |
| Volume of NaOH: |  |  | Mass recovered benzoic acid: |  |
|  |  |  |  |  |
| mmol of NaOH: |  |  | mmol recovered benzoic acid: |  |
|  |  |  |  |  |
|  |  |  | % yield of benzoic acid: |  |

Observed melting point of recovered benzoic acid:

Literature melting point:

Literature source:

Show complete calculations: (notebook)

**Post Lab Questions:**

1. Using four molecules of benzoic acid (draw the structure) and as many molecules of water as you like show what benzoic acid looks like in cold water and hot water.

|  |  |
| --- | --- |
|  |  |
| Benzoic acid in ***cold*** water | Benzoic acid in ***hot*** water |

2. Explain why benzoic acid is soluble in hot water and not soluble in cold water. Answer your question at the molecular level discussing the specific molecular interactions involved. Be sure your answer is consistent with your drawings in question 1.

3. Write out a complete mechanism for the base-catalyzed hydrolysis of benzonitrile. Be sure to indicate the formation of the amide intermediate amide by circling it.

4. Use ChemDraw to complete the hydrolysis reactions below.

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