Introduction

The bromination reaction is a very useful electrophilic aromatic substitution reaction because brominated arene rings can be used to undergo carbon-carbon bond-forming reactions to build up chemical structures (e.g., Grignard reaction). Traditionally, a solution of acetic acid and molecular bromine (Br₂) has been used to brominate aromatic systems. This is a hazardous concoction to handle, so a novel “green” way of performing the same reaction was devised. This new method involves the reaction of sodium hypochlorite (NaClO) under acidic conditions with sodium bromide to generate molecular bromine. This is much safer than handling acidic solutions of Br₂ since most of the bromine made is consumed immediately by the electrophilic aromatic substitution reaction.

In this experiment, bromoacetanilide is the desired product and we want to use aniline as a starting material. To synthesize bromoacetanilide from aniline, two routes are proposed in Scheme 1. When there is more than one-step in the synthesis, the overall reactions are collectively called “multistep synthesis”.

![Scheme 1. Proposed routes to bromoacetanilide.](image)

Notice that the bromine is not directly connected to a carbon atom on the benzene ring in Scheme 1, but instead the bond bridges over another bond; this is the notation used to show that the Br is attached to a carbon of the aromatic ring, but its location on the ring has yet to be determined.

Most of the time in multistep syntheses, only one or two of the proposed routes will make practical sense. In this case, of the two proposed routes, only Route 1 (acetylation followed by bromination) makes sense for reasons discussed below.
Protection

It is known that if aniline was reacted with bromine (Route 2), a variety of products will form (mainly di- and tri-bromo substituted products). As well, under the new “green” bromination conditions, the mixing of an amine with bleach (strong oxidizer) will generate a dangerous (possibly violently explosive) mixture (1). To prevent multi-substitution on the aromatic ring and the formation of hazardous compounds, the aniline nitrogen is “protected” before undergoing the green bromination reaction. Functional group protection is a common synthetic strategy used in organic synthesis to prevent the production of unwanted products and uncontrollable side reactions.

Bromination

The proposed series of equilibria involved to generate the electrophilic bromine in the bromination reaction will be discussed in the report’s discussion section. One of the key reagents used for the bromination is sodium hypochlorite (NaClO) found in household bleach. Most bleach bottles will state that the NaClO concentration is about 5-6%. Unfortunately, the NaClO concentration in bleach depletes over time and therefore one of the tasks in this experiment is to determine that concentration. To determine its concentration, all of the NaClO is reduced in an acidic solution of iodide (I\textsuperscript{−}) to yield the distinctively brown-coloured iodine (I\textsubscript{2}). As the titrant standard, sodium thiosulfate (Na\textsubscript{2}S\textsubscript{2}O\textsubscript{3}), is added, iodine is reduced to I\textsuperscript{−} by the thiosulfate ion (Scheme 2).

\[
\text{NaClO} + 2\text{NaI} + 2\text{CH}_3\text{CO}_2\text{H} \rightarrow \text{I}_2 + \text{NaCl} + \text{H}_2\text{O} + 2\text{CH}_3\text{CO}_2\text{Na}
\]
\[
2\text{S}_2\text{O}_3^{2−} + \text{I}_2 \text{(brown)} \rightarrow \text{S}_4\text{O}_6^{2−} + 2\text{I}^{−} \text{(colourless)}
\]

Scheme 2. The redox reaction for NaClO concentration determination.

Therefore, the endpoint of the titration has been reached when the analyte solution becomes colourless.

References


Scenario

The overall task is to synthesize and confirm the isomer identity of bromoacetanilide. Data will need to be presented as evidence to support any conclusions and assertions made.
DAY 1 NOVEMBER 7, 2012

Part 1: Synthesis of Acetanilide
1. Measure 1 mL of aniline using a 1 mL syringe and add it to a 125 mL Erlenmeyer flask.
2. Measure 2 mL of acetic anhydride via syringe and add it to the same flask.
3. Add a stirbar, and let the reaction stir while cooling.
4. Cool the mixture in an ice bath to 5 oC and let it continue stirring for 5 minutes.
5. After 5 minutes, add 30 mL of an 0.5 M NaOH solution.
6. Warm the mixture to dissolve the solids, adding more water as necessary.
7. Once the solution is fully dissolved, slowly cool the solution to encourage crystals to form.
8. The crystals that form should be filtered via vacuum filtration.
9. Allow the crystals to dry in your drawer until the next lab period.

Part 2: Standardization of Sodium Hypochlorite in Bleach
Students should work in groups for this part of the experiment – we should have 4 groups – two groups of four students and two groups of three students.
1. Prepare a 0.1 M sodium thiosulfate pentahydrate (Na2SO3•5H2O) solution by placing 2.5 g of sodium thiosulfate pentahydrate into a 100 mL volumetric flask and then filling with water to the mark.
2. Transfer this solution to a burette. Clean the burette first with a little bit of the titrant before committing the rest of the solution to the burette. This will be your standard solution.
3. Prepare an acidic iodide solution by mixing 8 mmole NaI and 4 mL acetic acid in a 100 mL volumetric flask and then diluting to the mark with water.
4. Now you are ready to do a titration. Perform three trials. For each trial, do the following:
   A. Measure 25 mL of the acidic iodide solution into a flask.
   B. Add 1 mL of the bleach solution via pipette.
   C. Pipette the standard solution carefully into the flask and record how much standard solution you add until the color of the iodine solution disappears.
   D. Record the amounts used for each trial and show the necessary calculations in the report.
   E. Calculate the concentration of sodium hypochlorite in bleach using the data collected.

DAY 2 NOVEMBER 8, 2012

Synthesis of Bromoacetanilide
1. Determine a mass for your acetanilide product from day 1 and calculate a % yield.
2. Add the following chemicals to a 125 mL Erlenmeyer flask: (a) 7.4 mmol of acetanilide; (b) 1.8 grams of NaBr; (c) 6 mL of 95% ethanol; and (d) 5 mL of acetic acid. Use a graduated cylinder to measure the solvents.
3. Cool the solution in an ice bath to 5 oC.
4. In the fume hood, add enough bleach to deliver 7.8 mmol of NaClO (sodium hypochlorite), based on your calculations from Day 1 of the experiment.
5. Let the reaction stir for about 1 minute, and then remove the ice bath and let the reaction warm to room temperature over approximately 15 minutes.
6. After 15 minutes, cool the reaction down in an ice bath and then quench the unreacted bromine by adding 1 gram of sodium thiosulfate and 1 gram of sodium hydroxide. Stir vigorously for a few minutes.
7. Collect your crude precipitate via vacuum filtration.
8. Recrystallize the crude product from a 1:1 mixture of ethanol: water.
9. Let the product dry in your drawer until the next lab period.