21. Synthesis of Cyclohexanone Oxime

This experiment is the second step in a two-step synthesis. The cyclohexanone synthesized in the previous week will be transformed into cyclohexanone oxime by the addition of hydroxyl amine. This synthesis is an important commercial step in the manufacture of Nylon-6.

Cyclohexanone oxime will be synthesized, isolated, and analyzed by melting point. This reaction is one example of the many derivatives which can be formed from carbonyl containing molecules. The mechanism begins with a nucleophilic attack on the carbon of the carbonyl by the nitrogen of the hydroxylamine. This forms a tetrahedral intermediate which then undergoes a series of proton transfers. The sp² carbon is reformed and the oxygen eliminated.

PRE-EXPERIMENT ASSIGNMENT

Study this chapter of the manual and the notes on the Organic Chemistry departmental web site. Review lecture notes concerning nucleophilic attack on carbonyls. Complete the first seven sections of your notebook write up.

A student who has prepared for the oxime synthesis experiment should be able to:
1. Draw the reaction including all starting materials and products.
2. Define or explain the role of sodium hydroxide.
3. Draw the mechanism of sodium hydroxide reacting with hydroxyl amine hydrochloride.
4. Explain the value or application of this chemistry.
5. Explain how the identity and purity of the product will be assessed.
6. Identify and explain safety considerations for the day’s experiment.
7. Perform the day’s experiment safely and successfully.

Quizzes given after the experiment has been performed may also include:

8. Draw the complete mechanism.
9. Explain observations that lead one to believe product was being formed.
10. Predict the impact on percent yield and purity based on changes in procedures such as temperature, reaction time, and changing amounts of reactants.
11. Calculate the percent yield for the single step and both steps in the multi-step synthesis.

**Safety Considerations**

Sodium hydroxide aqueous solution is corrosive and will cause burns. This may be diluted or neutralized and disposed of down the drain. Hydroxylamine and hydroxylamine hydrochloride aqueous solution is toxic to aquatic organisms. Do not dispose of down drain, but instead place in the Aqueous Waste container. Cyclohexanone has a rather low negative health effects but is flammable. Excess cyclohexanone should be disposed of in the Liquid Non-Halogenated Organic Waste container.

**EXPERIMENT**

Place a 250 mL beaker having about 2 inches of water and one boiling stone on a hot plate in the hood. Adjust the setting to 3 or 4 to just get the water to form bubbles.

If the cyclohexanone quality from last week is suspect, use fresh reagent cyclohexanone to begin this synthesis.

Measure your cyclohexanone. If beginning with fresh cyclohexanone, measure out some volume between 0.5 and 1.0 mL. Read and record volume accurately and precisely. Place in clean 50 mL Erlenmeyer flask. Multiply the starting volume of cyclohexanone by 5 to determine the target starting volume each of aqueous hydroxyl amine hydrochloride and sodium hydroxide solution. (For example, if you begin with 0.60 mL (0.48 g) of cyclohexanone, you will have a target amount of ~3.0 mL of aqueous hydroxyl amine (2.5 M) and ~3.0 mL sodium hydroxide (2.5 M)).

Using 10mL graduated cylinders, measure the 2.5 M aqueous hydroxylamine hydrochloride and 2.5 M aqueous sodium hydroxide solutions. Record exact volume used. Add these materials and one boiling stone to the 50mL Erlenmeyer flask containing the cyclohexanone.

Swirl the flask to mix and gently place the flask into the beaker of hot water. Be careful not to allow Erlenmeyer flask to tip over into the water and flood. Write your observations directly into lab notebook.

Heat for 15 minutes in slowly bubbling water. If water cools, heat for longer time. Remove from water bath. Let cool slowly and undisturbed to room temperature. Observe flask as it cools. Record observations in notebook. After flask has reached room temperature, immerse in a beaker approximately half full of ice water. Allow to cool for a minimum of 5 minutes. Be sure Erlenmeyer flask cannot tip over within beaker.

Collect crystals using vacuum filtration and a Hirsch funnel. The crystals may be rinsed in the Hirsch funnel (with vacuum on) with a small amount of cold acetone. Do not use too much acetone or solid
product will dissolve. Run the vacuum for a MINIMUM of 5 minutes. Water is difficult to remove completely. Record mass collected. Obtain melting point.

**CLEANUP**

Discard used pipettes in broken glass container. Dispose of aqueous hydroxyl amine and filtrate (from vacuum flask) in the aqueous waste container. Hydroxylamine is toxic to aquatic animals so DO NOT dispose of it down the drain. Sodium Hydroxide is used in Draino ® and can be disposed of down drain. Place organic product in the non-halogenated organic solid waste container. Wipe up work area with damp sponge.

**POST-EXPERIMENT ASSIGNMENT**

Write lab report and turn in at beginning of next lab period. Note your lab report will be over **both cyclohexanol to cyclohexanone and cyclohexanone to Cyclohexanone oxime.** Even if you obtained pure Cyclohexanone for the beginning of the second step of the two-step synthesis, discuss the overall synthesis and calculate an overall percent yield for the two steps together. Prepare for Synthesis of Cyclohexanone Oxime portion of next quiz.

**REFERENCES**


**Revised:** February 22, 2018, S.L. Weaver