Experiment 6 – Synthesis of *t*-Pentyl Chloride

Learning Objectives

- Observe liquid-liquid interface of two immiscible, clear liquids
- Perform a liquid-liquid extraction in a basic reaction "workup"
- Use gas chromatography (GC) to determine percent composition of products
- Apply infrared (IR) spectroscopy to determine reaction success
- Interpret chemical tests to determine presence or absence of alkyl halide

Alcohols are versatile starting materials in organic synthesis. They can act as an acid, base, nucleophile, or electrophile, depending on the reagent that they are paired! In the dehydration lab, students observed the acid-catalyzed elimination of alcohols at an elevated temperature (**Figure 1**). Elimination was the only product possible because the conjugate base of the acid (H_3PO_4 → HPO_4^-) is not a nucleophile. The addition of heat also promotes elimination over substitution.

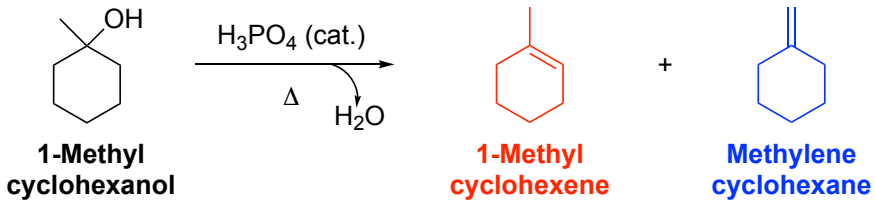

Figure 1. Dehydration of 1-methylcyclohexanol (Experiment 5)

When a haloacid (HX) like HCl is used, however, the reaction favors the substitution route (**Figure 2**). When the alcohol is protonated by HCl, a chloride ion (Cl^-) is formed as the conjugate base. The reaction in this lab occurs by an **S_N1 mechanism** because *t*-pentanol is a **tertiary alcohol**. An S_N2 reaction could *never* occur at a tertiary center due to steric hindrance. Alcohol protonation creates water as the **leaving group**. The C-O bond breaks spontaneously in a rate-limiting (slow) step to form a tertiary carbocation. Cl^- is the **nucleophile** carbocation to form a new C-Cl bond.

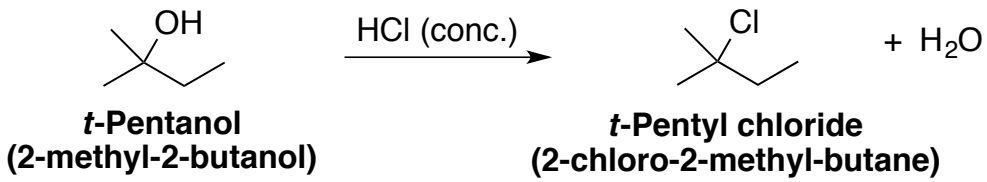

Figure 1. Synthesis of *t*-pentyl chloride

Competition with elimination is not an issue and alkene side-products are not formed because the reaction occurs at room temperature. The isolation of the product from solvent and by-products is called the **reaction work-up**. The crude reaction mixture is washed with water to dilute and remove excess HCl. Aqueous sodium bicarbonate neutralizes any remaining, unreacted HCl. These washes should be done relatively quickly to prevent hydrolysis of the product back to alcohol. If left to sit for 15+ minutes, the weakly basic $NaHCO_3$ solution begins to react with water to form ^-OH ions. Use of a stronger base would facilitate a much more rapid hydrolysis back to the alcohol so the weak base is preferred.

After work-up, the crude reaction mixture is analyzed by gas chromatography (GC), infrared (IR) spectroscopy, and chemical tests for alkyl halides (silver nitrate test and sodium iodide test). Time permitting, the product can be further purified by distillation. GC provides conclusive determination of reaction completion or percent composition if alcohol remains. IR is used to determine the presence or absence of the O-H and C-Cl bonds. The chemical tests determine the presence of an alkyl halide as evidenced by formation of a white precipitate, but cannot detect whether any alcohol or other impurity is present (**Table 1**).

Table 1. Reactions for positive chemical tests

Silver Nitrate in Ethanol Test	**Sodium Iodide in Acetone Test**
$RX_{(l)} + EtOH_{(l)} \rightarrow ROEt_{(l)} + HX_{(sol'n)}$ $AgNO_{3\,(sol'n)} + HX_{(sol'n)} \rightarrow HNO_{3\,(sol'n)} + AgX_{(s)}$	$RX_{(l)} + NaI_{(sol'n)} \rightarrow RI_{(l)} + NaX_{(s)}$
R = alkyl chain; X = Cl, Br, I	

The 'tails - Follow Exp 6 Canvas module

Before Lab

- Read this **PDF** or listen to **podcast** and watch the **pre-lab videos** on the Exp 6 Overview page
- Attend and/or watch **lab lecture** with **Exp 6 notes templates**
- Preview the lab on the **Slugs@home** platform!
- **Pre-lab questions** incorporated into **Pre-lab Quiz** – check Canvas for due date

Lab Notebook Preparation – *Required before lab;* Use the **worksheet** to prepare your **lab notebook** …

- **Purpose:** brief summary of the main lab goals and substitution reaction scheme
- **Reagent Table** – add chemical properties; Wikipedia is a reliable source for chemical info
- **Procedure with Diagrams** – hand-drawn using procedure in this PDF, Slugs@home, & class notes
  - Instructions, sketches, & labels for all **equipment, chemical names** with **amounts**, & **transfers**
  - Format: Break it up with flow charts, bullet-points, comic strip, and/or whatever works for you!

During Lab

- Check the **safety rules** to dress for lab and arrive a few minutes early to **Thimann Labs**
- **Pre-lab talk:** tips for success and open Q&A; Show your **lab notebook pages** to your TA
- Perform the experiment with a partner, fill out data & observations in **lab notebook**

After Lab

- Individual: Upload **Notebook Pages** to Canvas by midnight on lab day – completeness / participation
- *Option* to work individually or with ONE partner to complete the **Lab Report** – due date on Canvas
  - One student uploads the complete report to GradeScope (GS)
  - "**Select Pages**" then "**Add Group Members**" to include your partner's name

PROCEDURE

Reaction set-up: Check the provided conical vial for leaks by adding a little water, closing, and inverting. Discard the water and dry the vial with a paper towel. Use a Pasteur pipet and pluringe to carefully transfer 1.00 mL of *t*-pentanol (2-methyl-2-butanol) and 2.5 mL of concentrated HCl (37% w/w, density = 1.2 g/mL) directly into a 5-mL conical vial.** Record the least count of the pluringe and determine the ILE. Cap the vial and let the mixture stand for a minute. Then carefully shake the mixture with occasional venting in the fume hood (partially unscrew the cap to vent, then close). None of the mixture should leak from the vial but do not tighten so much that you can't unscrew it later. When pressure builds, it will be harder to open.

** Change gloves after getting reagents, whether or not you think your gloves are contaminated!
** Do not cross-contaminate pipets and be extra careful not to spill HCl (corrosive).
** Keep all reagent bottles in the fume hoods.
** Recap reagent bottles immediately, even if someone is right behind you about to use it.

Reaction work-up: Allow 10-15 minutes for the two phases to completely separate. Remove the water using a pipet and save the layer containing alkyl halide. **Use the densities to determine which layer is aqueous.** Quench and wash the reaction mixture with water as follows: Add 1 mL of water, mix, allow the layers to separate, then remove the water. Add 1 mL of 5% $NaHCO_3$ solution. Carefully agitate and vent. **What gas is formed in this step?** Allow the layers to separate and remove the aqueous layer. Add 1 mL of brine (saturated NaCl), mix, then remove as much water as possible on this last wash.

Add a small amount of anhydrous sodium sulfate (Na_2SO_4) using a micro-spatula. Allow this drying agent to absorb water for at least 5 minutes. Make a filter pipet with a tiny piece of loosely packed cotton and weigh a labeled vial for product. Use a second pipet to filter the product mixture through the filter pipet to remove the (Na_2SO_4) hydrate and collect the product in the pre-weighed vial.

Analysis: **Weigh the product** and **calculate % yield**. Inject and analyze GC chromatograms of standards (*t*-pentyl alcohol and *t*-pentyl chloride) and the reaction mixture. Analyze the provided IR spectra of *t*-pentyl alcohol and obtain the IR spectrum of the reaction mixture to determine the absence of *t*-pentyl alcohol and presence of *t*-pentyl chloride.

Perform *either* the Silver Nitrate *or* Sodium Iodide chemical tests (not both) as described below. Chemical tests are performed in the fume hood. Obtain four clean, dry medium test tubes and label with #1-4 using the following designations. **Which do you expect to give positive vs. negative tests for alkyl halides?**

1. *t*-Pentanol (starting material)	**2.** Product mixture	**3.** Bromobenzene	**4.** Butylbromide

Silver Nitrate Test: Add 0.5 mL of 0.1 M silver nitrate in ethanol to each test tube and one drop of compounds 1-4 to the appropriate test tube. Gently agitate (tap) the test tubes and patiently wait 5 minutes to observe precipitation. If no solid forms, bring the solutions to a boil in the community water bath in the fume hood set to around 80 °C. Wait another 5 minutes to see if precipitation occurs. Record your observations. The formation of a precipitate is a positive test for alkyl halides.

Sodium Iodide Test: Add 0.5 mL of the provided sodium iodide solution (15% w/v in acetone) to each test tube followed by one drop of compounds 1-4 to the appropriate tube and gently agitate. If no precipitate is observed after 3 minutes, transfer the test tubes to a water bath set to about 50 °C and heat for 5 minutes. Record your observations. The formation of a precipitate is a positive test for alkyl halides.

Table 2. Clean-up & Safety

Liquid waste: For all the liquids, including product, after you're sure you're done with them! *Rinse the test tubes with a small amount of ethanol into the liquid waste before washing in the sink.	Concentrated HCl is very corrosive. It will burn through your clothes and/or skin. Take only what you need and keep the bottle in the reagent hood. *t*-Pentyl alcohol, butylbromide, bromobenzene, and acetone are flammable.
Solid waste: pipets	

Adapted from Palleros, D. "Synthesis of *n*-Butyl Bromide and 2-Chloro-2-Methylbutane" in *Experimental Organic Chemistry*. Wiley: New York, **2000**, p. 280 - 291.

Pre-lab Questions - incorporated into pre-lab quiz due before lab – see date on Canvas

1. What type of reaction mechanism is exemplified in this lab? Why is this mechanism favored and why is no elimination product observed?

2. What is the by-product of the substitution reaction of t-pentyl alcohol with HCl?

3. Reaction Calculations - Show your work!

- Calculate the mmoles of both starting materials (*t*-pentyl alcohol and HCl) using the amounts given in procedure.
- Indicate the limiting reagent in this 1:1 reaction.
- Calculate the theoretical yield of product in mmol and mg.

4. Why is the product washed with sodium bicarbonate after the reaction is complete? Show the chemical equation for the reaction of sodium bicarbonate with HCl.

5. Explain why sodium bicarbonate is used instead of NaOH in the extraction.

6. Show the chemical equation for the substitution reaction of *t*-pentyl chloride with sodium iodide in acetone. What compound precipitates as a white solid?

7. Show the chemical equation for the substitution reaction of *t*-pentyl chloride that occurs in a positive silver nitrate in ethanol test. What compound precipitates as a white solid?

EXP 6 LAB REPORT

- *Option* to work individually or with ONE partner to complete the **Lab Report** – due date on Canvas
  - One student uploads the complete report to GradeScope (GS)
  - "**Select Pages**" then "**Add Group Members**" to include your partner's name

In-lab Questions (no abstract for Exp 6)

1. Draw the full arrow-pushing mechanism for the reaction of *t*-pentanol with HCl. *Hint: this mechanism has three steps with two reaction intermediates.*

2. Restate the theoretical yield (mmol and mg) from the given volume of alcohol. Report the actual yield and calculate the percent yield. Show your work.

3. The reaction work-up involved a liquid-liquid extraction with an organic (ORG) and aqueous (AQ) layer. What molecule makes up the ORG layer and was it on the top or bottom? Explain which layer was which and why they are not miscible (created separate layers). *Hint: comment on the polarity of the two layers and include the density values for t-pentyl chloride and water.*

4. What was the purpose of adding aqueous sodium bicarbonate ($NaHCO_3$, baking soda) in the reaction work-up? Show the balanced chemical equation for the reaction of sodium bicarbonate with HCl and indicate the gas formed at this step. *Yes, this is very similar to a pre-lab question … revisit yo quiz* ☺

5. Report which chemical test was performed. Tabulate all chemical test results with observations and brief interpretation of each. Was the reaction successful based on these results alone? Explain why or why not, including comparison to standard test results.

Table x. Chemical Test Results – sodium iodide in acetone or silver nitrate in ethanol

Sample	Observation	Interpretation
1. *t*-Pentanol		
2. Product Mixture		
3. Bromobenzene		
4. Butyl bromide		

6. Draw the two chemical reactions that occurred in the two positive chemical tests reported in #5 above: starting material, reagent & solvent (either sodium iodide in acetone or silver nitrate in ethanol), and product. *Revisit your Exp 6 pre-lab quiz for related questions* ☺

7. Interpret the IR spectra of the starting material and product in table format (see worksheet). Which band(s) of the IR spectra are used to determine conversion of alcohol to alkyl halide and was the reaction successful based on IR data alone?

8. Interpret the GC charts of starting material and product. Calculate retention times and integration (area) to determine percent composition of products. Report your results in table format. Show your work for each calculation. Conclude with a statement about reaction success based on GC results in combination with chemical test and IR data above, including presence of by-products in your product mixture.