Chemistry 211-212

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**TOTAL** | (170 points)

**SCORE** | (percent)

This is your report cover. Please fill this form out and attach it to your prelab.
Experiment 20
Esterification: Synthesis of Isoamyl Acetate Using
Azeotrophic Distillation and a Water Trap

General Safety Considerations

1. Isoamyl acetate, isoamyl alcohol and cyclohexane are toxic and irritants. They are also very flammable.

2. Acetic acid and p-toluene sulfonic acid are both very corrosive. p-Toluene sulfonic acid is also toxic and an irritant. The fumes from glacial acetic acid are particularly obnoxious.

3. In handling all the above chemicals take all the normal precautions. Continuously wear gloves and goggles. Work only in the hoods. As always, flames are prohibited.

4. If contact with any of the above chemicals occurs, flush the exposed area for fifteen minutes with cold water. Alert your instructor if any accidents or large spills occur.
Experiment 20
Flow Chart

Build Special Apparatus

1. Add to 100 mL r.b.
   a. 0.125 mole acetic acid
   b. 0.10 mole isoamyl alcohol
   c. 10 mL cyclohexane
   d. 0.075 g p-toluensulfonic acid
   e. boiling stones
2. Add to Claisen arm 25 mL cyclohexane
3. Reflux ~30 mins until all water is collected
4. Pour Claisen liquids into 125mL sep. funnel. Separate layers (measure volume water)

aqueous

Discard - hood drain

organic

aqueous

Discard - hood drain

organic

1. Add organics (cool!) from 100 mL r.b.
2. Extract with 40 mL sat. sodium bicarb. carefully!!

aqueous

Discard - hood drain

organic

Extract with 40 mL water

aqueous

Discard - hood drain

organic

NEXT SLIDE
Flow Chart (Experiment 20)
(continued)

Organic

Extract with 40 mL sat NaCl

aqueous organic

Discard - hood drain

Fraction A pot residue

25° - 82°C

Discard Non-halogenated waste

Simple Distillation

Fraction B

25° - 136°C

Discard Non-halogenated waste

Fraction C

136° - 146°C

1. weigh
2. % yield
3. GC
4. IR

pure isoamyl acetate
Stay away from honey bees!!
Experiment 20
Fischer Esterification: Synthesis of Isoamyl Acetate Using
Azeotropic Distillation and a Water Trap*

The synthesis of an ester (RCOO\textsuperscript{1}R\textsuperscript{2}) requires the putting together of two parts, a
carboxylic acid part (RCO\textsuperscript{1}-) and an alcohol part (-OR\textsuperscript{2}). One way of doing this is to react
an alcohol with a reactive derivative of a carboxylic acid, such as an acid chloride or an
anhydride. The high reactivity of the acid derivative pushes the reaction to completion.
Another method, which avoids the high costs, hazards, and complications of reactive
molecules, is to react the alcohol directly with a carboxylic acid in the presence of a
catalyst. Using this method, you will carry out the synthesis of isoamyl acetate from
isoamyl alcohol (3-methyl-1-butanol) and acetic acid:

\[
\text{CH}_3\text{COOH} + \text{CH}_3\text{CH(CH}_2\text{CH}_2\text{CH}_2\text{OH} \xrightarrow{\text{acid}} \text{CH}_3\text{C(OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3} + \text{H}_2\text{O}
\]

(As a catalyst we will use p-toluenesulfonic acid, CH\textsubscript{3}-C\textsubscript{6}H\textsubscript{4}-SO\textsubscript{2}OH, a convenient
solid.)

Isoamyl acetate is the major aroma constituent of bananas and pears, and is
known in the food industry as banana oil or pear oil.

This general method is known as the Fischer Esterification. (For the mechanism,
see Loudon, pp 913-916.) In this method, the challenge to be overcome is that the
reaction is subject to an equilibrium, in which some of the starting materials remain. In a
typical esterification, for example, if the equilibrium constant \( K = 3.0 \), the maximum
theoretical yield would be 63\%. (Do you remember how to calculate this?) Considering
that there are always losses during work-up, your final yield would be unacceptably low.
Therefore, some way has to be found to shift the equilibrium in favor of the desired
product. Some methods include: 1) using a large excess of one of the reagents, if it is
inexpensive; 2) using a large excess of strong acid catalyst.
This will convert the product water to H\textsuperscript{3}O\textsuperscript{+}, the conjugate acid of water, which is non-
nucleophilic and therefore unreactive in this reaction; 3) using a solvent in which the
water is not soluble; 4) using a substance like alumina to absorb the water; 5) removing
the water as it is formed, by distillation or some other method.

We will use the last approach, removing the water as it is formed. This is not,
however, as simple as it may seem. The boiling points of the various components of
the reaction mixture are as follows:

- iso-amyl alcohol 130°
- acetic acid 118°
- iso-amyl 142°
- acetate water 100°

Water has the lowest boiling point of all the components of the mixture, and it should be theoretically possible, therefore, to carry out the reaction in a distillation set-up and remove the water by distillation as it is formed. However, the boiling point of water is not enough lower than those of the other components to allow a good removal of water without losing some of the other components as well, unless a sophisticated and expensive set-up is used. Therefore, we must use a trick called azeotropic distillation. We will include, in the reaction flask, a compound which is unreactive with any of these reactants, and which forms an azeotrope with water, lowering its boiling point.

Briefly, an azeotrope results when two components of a mixture behave as a non-ideal solution. In an ideal solution, the attractive forces between unlike molecules are of the same strength as those between like molecules. In one type of non-ideal solution, the attractive forces between unlike molecules are weaker than those between like molecules, with the result that the total vapor pressure is greater than the vapor pressure expected of an ideal solution (since the molecules are held to one another less strongly, they vaporize more easily). If a mixture of these two liquids, having a certain definite composition, has a lower boiling point than either of the two pure components, it will boil as a single component without any change of composition. Such a mixture is called an azeotrope (or minimum-boiling azeotrope), and behaves as if it were a single component. During the boiling of this azeotrope the composition of the vapor stays fixed.

In a reaction such as esterification, an inert solvent can be added which forms an azeotrope with water. This azeotrope will have a lower boiling point than water itself. For the system under discussion, the addition of cyclohexane (B.P. 81.4°C) to the reaction mixture results in the formation of an azeotrope consisting of 91.5% cyclohexane and 8.5% water, and having a boiling point of 69.8°C. This boiling point is sufficiently below those of the other components of the mixture that an efficient separation of water can take place without a complicated distillation apparatus.

One further complication of this: If the reaction were done in an ordinary distillation apparatus, an enormous volume of cyclohexane would be necessary, since the azeotrope contains only 8.5% water. A device which enables the cyclohexane to be recycled is called a Dean-Stark trap, and is pictured below. The reactants and inert solvent (e.g. cyclohexane) are placed in the round-bottom flask, and the inert solvent is placed in the trap, shown as the device with a stopcock below. As the reaction proceeds, the azeotrope, having the lowest boiling point of any component in the flask, vaporizes, then condenses in the condenser and runs down into the trap. The components of the azeotrope (for example cyclohexane and water) are immiscible with one another in the liquid state, and, since water is denser than cyclohexane, the water falls to the bottom of the trap. The cyclohexane overflows back into the reaction flask. The water, however, stays at the bottom of the trap. Thus a small volume of cyclohexane is recycled many times. Clever, eh?
A simpler and, for our purposes, just as effective water trap can be assembled from ordinary glassware as in the diagram shown below. The whole apparatus is clamped at a 45-degree angle. The azeotrope collects in the sidearm of the Claisen adapter, the water sinks to the bottom of this sidearm, and the cyclohexane runs back into the flask.

![Diagram of water trap](image)

After the reaction is over, the volume of water collected can be measured and compared to the calculated theoretical yield of water, in order to confirm that the reaction has gone to completion. It is, however, common to obtain more than the theoretical volume of water because a) there is some water present in the reagents used; and b) some alcohol and acetic acid gets trapped in the water phase.

Since a portion of your product distills into the sidearm of the water trap, you will combine the organic phase of the material in the trap with the material in the reaction flask after the reaction is complete. The reaction mixture is worked up by first extracting with a base, aqueous sodium bicarbonate, to neutralize and remove the acid catalyst and unreacted acetic acid, then washing with water and salt solutions. Lower-boiling components are removed by fractional distillation, followed by a simple distillation to recover the product.

**General Guidelines for Lab Write-up**

**Main Reaction and Mechanisms**

Covered in lecture, textbook and Lab Manual.

**Side Reactions**

What do alcohols do in the presence of acid catalyst? How does a carboxylic acid react with another molecule like itself?

**Purification**

Straight forward - all steps have been carried out in previous experiments.
Table of Reagents

You should be able to figure this out.

Table of Products

Only include the major organic product.

Observations and Data

This section is up to you to some extent. Include important observations made during lab and raw data recorded during lab.

Results

For most of this section, please refer to page 20-11 of the lab manual. The only sections that might give you trouble are the IR and $^1$H NMR interpretations.

IR Interpretation

Here you are interpreting your own IR. You should include some discussion. Rigorously assign the functional group region and compare the general "topography" of the spectrum with the literature spectrum.

$^1$H NMR Interpretations

The spectra are not in the Aldrich Library. They can be found on reserve in the spectral file in Collier. The two spectra are quite similar so use one as a model for the other. Watch out for the hydroxyl hydrogen! For both spectra, the easiest groups to initially assign are the methyl groups and the methylene adjacent to the oxygen. Be prepared for some overlap in the spectrum.

Conclusion/Discussion

See page 20-13 of this lab manual.

Post-lab Problems

a) This problem always causes trouble even though it is fundamentally a freshman chemistry equilibrium problem. The key is to realize that $K = 3.0$ and $3.0$ is a relatively large value for an equilibrium constant. You can’t make the typical simplifying approximations made when solving an equilibrium problem involving a weak acid or base ($K << 1$). The other point to be aware of is the fact that all products and reactants are in the same pot so the volume is the same for each.

b) This synthesis can be carried out using reactions studied in the laboratory exclusively. Realize that this is strictly a paper synthesis. Just write equations for each step. No procedure is required. Give this a good shot before you ask about it.
Pre-Lab Questions: answer these in your laboratory notebook

1. From the equation for the reaction and the amounts of reagents used, calculate the theoretical yield of water expected, in mL, assuming the reaction goes to completion. Assume also that the density of water is 1.0. Enter this answer in your notebook as well.

2. Write the equation for the reaction that occurs when the acid in the flask is neutralized by sodium bicarbonate. What is responsible for the build-up of pressure in the separatory funnel at this stage?

3. What do you expect to be the major component(s) of Fraction A in the distillation?

4. Isoamyl acetate also functions as an insect pheromone. To learn more about this, read *Nature* 195, 1018 (1962). Briefly summarize this short paper.

Procedure

1. Into a 50 ml round bottom flask, supported in a beaker, measure out 0.163 mole of acetic acid, 0.05 mole of iso-amyl alcohol (you calculate the volumes; glacial acetic acid is 17.4 M), and 10 ml of cyclohexane. Weigh out 0.04 g of p-toluensulfonic acid, break up any lumps with a spatula, add it to the flask, and swirl to dissolve. Add boiling chips.

2. Attach the flask to an apparatus like that shown in the previous drawing. (A sample will be set up in the lab.) The flask is to be heated with a flask heater, not shown in the drawing. Note the following: The entire apparatus is supported by just one clamp, tightly secured about the neck of the flask. It may seem ridiculous, but it really works! The apparatus is tilted about 45 degrees. A special 14/20 stopper is used to close off the end of the sidearm. Both joints must be greased, and the stopper as well.

3. Remove the stopper on the sidearm of the Claisen adapter and carefully add enough cyclohexane to fill the sidearm. This should fill the sidearm until it is almost overflowing into the flask. Replace the stopper securely.

4. Start the water in the condenser and turn on the heater to a moderate setting (50-70 volts). After reflux begins, check to make sure that the condensate is dripping into the sidearm and not directly back into the flask. If the angle of the apparatus needs to be adjusted, be careful not to tip it in such a way that the lower water layer runs into the flask.

5. After a while you should observe a separate water layer form in the sidearm. If you look closely at the place where the drops from the condenser are running into the liquid in the sidearm, you should be able to see droplets of water separating and running down to the bottom of the sidearm. If, after 30 minutes of heating, it appears that there is very little, if any, water still entering the sidearm, turn the heat off and swing the heater out of the way. If not, heat for an additional 5 to 10 minutes.
6. After the flask has cooled and all the liquid has run back into the flask (cold water under the flask may hasten this), remove the condenser, then **CAREFULLY** remove the stopper from the sidearm and tip the contents of the sidearm into a 100 ml graduated cylinder. Record the volume of the lower, aqueous, phase. How does the volume compare to the theoretical volume you calculated in pre-lab question #1?

7. Transfer the material in the graduated cylinder to a 125 ml separatory funnel. Drain off and discard the lower aqueous layer. Transfer the contents of the 100 ml round bottom reaction flask to this same separatory funnel. Carefully extract with 20 ml of saturated NaHCO₃, in the following way: Add 20 ml of bicarbonate solution to the funnel BUT DO NOT SHAKE. Attach the cap, hold the stopcock securely and turn the funnel over. DO NOT SHAKE. Vent the funnel. Now shake it ONCE and VENT. Repeat these single shakes and vents until you no longer hear a lot of pressure being released upon opening the stopcock. Then shake a little more vigorously. Gradually increase the vigor and length of your shaking until the pressure is all released. Separate the layers and discard the lower aqueous layer.

8. Extract the organic phase with 20 ml of water, then 20 ml of saturated aqueous NaCl. This last wash pulls virtually all of the water and water-soluble compounds out of the aqueous phase.

9. Transfer the organic phase to a 25 or 50 ml round bottom flask and perform a careful fractional distillation through a column packed with steel or copper (review Experiment 2 if necessary). The heating control should be set between 70-90 volts. [Be sure to use a 260° thermometer, not 360°, so that the temperature range of interest is not covered by the rubber adapter.] Collect everything in this fractional distillation in one fraction labeled A. You will probably observe a temperature plateau at about 70° (what is this?), and another at about 81-82° (what is this?). After this second plateau, the distillation will slow down and the temperature may fall. At this point, turn the heat off, lower the heater and swing it out of the way. Allow the vapors to condense and run back into the flask.

10. **CAREFULLY** remove the fractionating column (REMEMBER, IT'S HOT), raise the flask and heater, and continue with a simple distillation. The heating control should be set between 80-110 volts. Distill fairly slowly, collecting the following fractions: B: Ambient to 136°; C (preweighed flask): 135 to 146° or until the pot is almost dry (but leave enough in the pot to just cover the boiling chips.) Collect the last remaining liquid which is held up in the top of the condenser by carefully tipping the condenser toward the receiving flask.

11. Carry out a GC analysis of your Fraction C. Instructions will be posted. You should expect to find a major peak corresponding to the ester, a minor peak for iso-amyl alcohol, and perhaps a trace of cyclohexane. Verify these contaminants by injecting standards and comparing retention times. Calculate the percentage of ester in your Fraction C.

12. Obtain an IR spectrum of your product (Fraction C). Compare it to those of the starting alcohol and product.
13. In your lab report, analyze the NMR spectra of iso-amyl alcohol and iso-amyl acetate. Assign each peak or set of peaks to a particular proton or set of protons, and explain the observed splitting patterns.

14. Answer the following questions:

a. If the equilibrium constant for this esterification reactions is 3.0, calculate the maximum theoretical yield that could have been obtained, based on the molar amounts of starting materials we actually used, if we had not removed the water from the reaction flask as it formed (i.e., if the reaction had been allowed to come to equilibrium).

b. Based on your knowledge of organic reactions, outline a synthesis of sec-butylacetate from acetic acid and ethanol.

+++

Music, when soft voices die,
Vibrates in the memory -
Odours, when sweet violets sicken,
Live within the sense they quicken.

*Shelly*
Specific Point Breakdown

Experiment 20: Esterification: Synthesis of Isoamyl Acetate
Using Azeotropic Distillation and a Water Trap

Notes for Grading Lab Reports

I. Pre-lab Exercises - 20 points total
   1. 6 points
   2. 3 points
   3. 3 points
   4. 8 points

II. Pre-lab write-up - 60 points total

Point breakdown:

8 points for introduction
4 points for balanced main reaction
12 points for writing mechanisms for the synthesis. The students should use the
   arrow formalism and show all intermediates.
8 points for the side reactions
10 points for purification
10 points for the completed table of reagents
8 points for the completed table of products

III. Completed Lab Report - 50 points total

4 points for observations and data
26 points for results

Breakdown:

1 point for yield in grams
2 points for yield in moles
2 points for percent yield calculation
2 points for product appearance
3 points for GC trace with product and contaminant retention times
2 points for percent isoamylacetate in fraction C based on GC
4 points for the IR with interpretation
5 points NMR interpretation isoamyl alcohol
5 points NMR interpretation isoamyl acetate

20-12
20 points for conclusion

Breakdown:

- 4 points for summary of evidence supporting product identity (B.P., GC, IR)
- 8 points for explanation of deviation of yield from 100%
- 8 points for discussion of purity of product and possible sources of contamination

IV. Answers to Assigned Problems - 20 points total

2a. **10** points
b. **10** points

V. Products - (Quality) - 20 points total

- 8 points for quality of product yield
- 8 points for purity of product (use GC and IR in this determination)
- 4 points for appearance of product