Chemistry 360

Organic Chemistry II

Laboratory Manual 2009/12

Athabasca University

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CHEM 360 Lab Manual Contents

CHEM 360 Lab Manual Contents (cont.)

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The following sources are also hereby respectfully acknowledged:

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The experiments described in this laboratory manual are mainly variations of similar experiments that may be found described in the laboratory manuals of other universities or in commercially produced lab texts. Each experiment has been modified and rewritten, keeping the particular needs of Athabasca University students in mind.

Ross Witherell, Jason Norman, Nina Vo, James Sochan, Scott McGavin, Nyron Jaleel, Klaus Thomson, Robert Carmichael, Jerry Pyrozko, Roger Klemm, and Glen Conlin, have all checked the procedures described in this manual. The continued comments and suggestions for improvement received from all the individuals mentioned above have been and always will be greatly appreciated by the Course Professor and Course Co-ordinator.

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Introduction

Welcome to the laboratory component of Athabasca University's *Chemistry 360*. The series of experiments performed in this course are a logical extension of those performed in *Chemistry 350*. Although the laboratory component of this course is very intensive, we hope that you will find the experience intellectually stimulating and memorable. We also hope you are able to take advantage of every opportunity to meet and discuss organic chemistry with your tutor and other Athabasca University students.

If you were to take a course such as *Chemistry 360* in a traditional college or university, you would probably be expected to attend a three-hour laboratory session every week for 10-12 weeks. During this time you would receive somewhere in the order of 30-36 hours of laboratory instruction. In our course, you will receive approximately 32 hours of instruction, spread over four days.

Although we feel that our method of providing the laboratory component of this course is the best that we can achieve, given the circumstances under which we operate, there are undoubtedly some disadvantages to the system. We bring these disadvantages to your attention so that you can adjust your work habits accordingly, and minimize any potential problems.

a. **Hours of work.** At each day-long laboratory session, you will be working for approximately eight to eight and one-half hours. Your instructor will ensure that you take a proper lunch break, but we also recommend that you take both a morning and an afternoon refreshment break. Regular breaks make it easier for you to concentrate while you are working, and will decrease the likelihood of an accident. As the level of fumes in the laboratory will increase during the day, we also recommend that you take a brief walk outside during one or more of your breaks.

b. **Feedback.** Many laboratory courses operate on the principle that a student submits his or her laboratory report shortly after having completed an experiment, and that the report is returned a few days later, before the student attempts the next experiment. In the Athabasca system this is clearly not possible. After completing each day of laboratory work you will have to write up a number of reports, submit them by mail to your tutor, and then wait for feedback. We hope that some response can be provided before your next laboratory session, but if your sessions are scheduled close together, or if it takes you a long time to write your reports, this may not be possible.

Remember to **keep a duplicate copy** of all your laboratory experiment reports before you send them to your tutor. Your tutor will give you feedback and your grades on each report, but will not return your submitted lab reports.

Remember, if you have difficulty in writing your laboratory report, contact your tutor, or the Science Lab Co-ordinator (780-675-6276).

Also remember to keep a duplicate copy of all your experimental results; we will suggest a method for doing so in the section titled "Writing Laboratory Reports".

c. **Preparation.** Whereas the student in a traditional institution needs to prepare only one experiment at a time, Athabasca students must prepare several experiments for each day of laboratory work. For example, before attending the first laboratory session, you must read through Experiments 10-12, making sure that you understand exactly what you will be doing, noting possible problems, and so on. The following two sections on "Lab Registration" and "Organization" (including a suggested schedule for completing the labs) will, we hope, help you prepare for your laboratory sessions.

Lab Registration

To arrange to attend a laboratory session, please contact the Science Lab Co-ordinator at:

1-800-788-9041, ext.-**6729** or 780-675-6729 (Athabasca),
or **780-481-3704** (Edmonton home office),
or by E-mail at **robertc@athabascau.ca**.

The Lab Coordinator will help you to sort through a list of upcoming supervised lab dates, from which you may select the ones you find most convenient to attend. You may also consult our online Chemistry Lab Schedule (see below) and then fill out our online lab booking form at: https://secure3.athabascau.ca/Labs/booking.php/

There is no lab registration fee, and students may change the dates they have selected right up to the day of the labs. We only ask that if you have a change of plans that you notify us, so that we do not worry unnecessarily over your whereabouts.

Please note that the Organic Chemistry Lab Instructor has the right to refuse any walk-ins (students who have not registered) by phone or E-mail.

For an up to date listing of the **Chemistry Lab Schedule**, students may also consult our web site at:

http://science.athabascau.ca/Labs/schedules/

Other information about the labs (location, food and lodging, lab safety, table of reagents) is also provided via the above web page.

Lab Organization

The laboratory component of *Chemistry 360* comprises approximately 32 hours of laboratory work. During this time you will be expected to complete all of the experiments listed below. You will notice a number in parentheses following the title of each experiment. This number indicates the maximum number of marks that can be obtained for each experiment. In addition, the instructors' continuous assessment will be worth a further 10 marks, giving a total of 100 marks.

10. Fischer Esterification Reaction (10)

11. Reactions of the common functional groups—
Part II: Alcohols and alkyl halides (5)

12. Reduction of benzophenone using sodium borohydride (10)

13. An aldol condensation (10)

14. Infrared-NMR Spectroscopy Exercise (15)

15. Reactions of the common functional groups—Part III: Aldehydes and ketones (5)

16. Triphenylmethanol via a Grignard reagent (15)

17. Multi-step synthesis: Benzocaine (20)

(Total = 90 marks)

As you can see, a total of eight experiments are listed, and we may add others as we find it necessary to modify the course.

The *Chemistry 360* laboratory sessions may differ from other laboratory classes that you have attended, in that not all of the students present will be working on the same experiment at any given time. The main reason is that some experiments require the use of an expensive instrument, and it is not feasible for Athabasca University to provide every individual student with such an instrument. Thus, at any given time during the first laboratory session, you may observe three students working on Experiment 10 and two others working on 12, while the rest of the class is working on 13. The course is organized in such a way that many of the experiments can be completed in any order; (unlike *Chemistry 350* where all students completed Experiments 1 through 5 before proceeding to any other experiment.)

Suggested Schedule for Completing the Labs

Schedule 1

	8:30am	9am	10am	11am	12noon	1pm	2pm	3pm	4pm	5pm	
Day 1	Orientat'n	Start Ex.10		Start 11	BREAK		Start Ex.12/13			Cleanup	**Day 1**
			Start Ex.11.....						Start Ex.15		
Day 2	Complete Ex. 12		Complete Ex.13		BREAK					Cleanup	**Day 2**
				Compl.Ex.14 and 15							
Day 3	Start Exp 16				BREAK					Cleanup	**Day 3**
								Analyses			
Day 4	Start Exp.17				BREAK					Cleanup	**Day 4**
			Complete all analyses								

The lab instructor has total discretion on deciding order the experiments that will be done during each of the lab days. Our lab instructors are very experienced and it would be wise to listen to their suggestions and directions on how best to complete all the lab work in the allotted time.

Materials to be Provided by the Student

When attending a *Chemistry 360* laboratory session, each student must provide herself or himself with the following items:

1. **a lab coat**. Lab coats can usually be purchased at college or university bookstores, at army surplus stores, and similar establishments. In case of difficulty, see "Uniforms—Retail" in the "yellow pages" of your telephone directory.

2. **safety glasses**. Safety glasses can usually be purchased at college or university bookstores, or at safety supply stores.

3. **an electronic calculator**.

4. **a lab notebook**. A lab notebook should be bound. The preferred size is approx. 23.5 cm × 18.4 cm.

5. **a pen**, a pencil and a ruler.

Optional Materials to be Obtained by the Student

1. students may request a set of important reference pages from the *Organic Chem Lab Survival Guide* from the Athabasca University library. The survival guide you obtain may be the first or third edition. The relevant pages in the first or third edition of the survival guide worth reading are noted in each of the experiments. Please note a copy of the guide will be available in the lab.

2. a black 'Sharpie' marking pen for making labels.

Evaluation

All students must work individually, except where otherwise indicated in the lab manual; pairing up and the pooling of data, solutions, etc., is not permitted.

Note that the penalties for plagiarizing laboratory reports are identical to those incurred for other types of plagiarism.

Your lab reports must be legible and preferably typed.

You must attain an average of 60% for laboratory work in order to pass the course. The grade for laboratory work, which is worth 20% of the overall *Chemistry 360* mark, is determined as follows:

Performance on assigned experiments	90 marks
Instructors' continuous assessment*	10 marks
Total	100 marks

* The instructors will assess each student for such things as preparedness, ability to solve unexpected problems, efficiency, competence in handling glassware and chemicals, etc.

Experiment Products

Products prepared in the lab are to be submitted to the lab instructor for evaluation. The product should be weighed and submitted in a labelled vial (your name, product name, weight, melting point or boiling point, and date submitted).

Marking of Laboratory Reports

Your laboratory reports must be mailed to your tutor within 1 month of completing your last supervised laboratory session. Late lab reports will be penalized 10% for every month they are late. Thus sending in your lab reports **four months late will mean that you fail** the lab component, since you need an overall average of 60% to pass the lab component and course.

Laboratory Examination

Currently, there is no written lab exam for the *Chemistry 360* laboratory component.

Writing Laboratory Reports

The first key to obtaining good marks on laboratory experiment reports is to keep a neat and organized lab notebook. Prepare your notebook in advance by setting out the purpose and main reactions of the experiment, certain properties of the reagents and expected products (plus calculations), and a table to receive your results and observations. The second key is to understand the type of experiment you are being asked to perform. In this course, it will be either an investigative or preparative experiment. This knowledge should help you to prepare your lab notebook in an appropriate way, and will obviously dictate the format of the report you will write and submit for marking. The final key is to always remember to be concise in your writing, no matter what the type of report.

Standard Report Formats

Investigative	**Preparative**
Title, date and references	Title, date and references
Purpose	Purpose and Introduction
Procedure	Procedure
-Table of Reagents	-Table of Reagents
Results	Results
-Observations	-Observations
-Table of Products/Inferences	-Table of Products
Questions	Discussion
Conclusion	Questions
	Conclusion

In *Chemistry 360*, you are expected to prepare a report on each experiment, as soon as possible after you have completed it and to submit the report to your instructor for grading. Some hints designed to assist you in writing your reports are given below, although you should also take into account any specific instructions given to you by the instructor.

Some general comments on laboratory reports may be found in Chapter 4 of *The Organic Chem Lab Survival Manual* (or Chapter 2 in 3rd ed.). In addition, each experiment in the *Chemistry 360 Laboratory Manual* contains a section discussing the approach to be used when writing-up that particular experiment. In general, each report should include the sections outlined below.

[Please be aware of the optional use of the downloadable CHEM360 Lab Report Book for writing all your lab reports.]

Organic Chemistry 360 Lab Report Writing Hints

1. **Title, date, name and student ID number.**

2. **Purpose/Objective of experiment**

   Example: To prepare cyclohexene from purified cyclohexanol by acid catalyzed dehydration reaction. Also the technique of …
   Note: Have a main purpose and several minor purposes.

   Try to be as specific as possible.

   e.g., The main objective of this experiment is to synthesize the alkene, cyclohexene, from cyclohexanol, using an acid catalyzed dehydration mechanism. The product formed is stabilized by 'salting out' of the water using brine, neutralizing any trace acid present with sodium carbonate, and drying using a drying agent anhydrous calcium chloride. Purified cylclohexene is obtained by distillation and the final product is characterized by bp, density, infrared spectroscopy and refractometry. A minor objective is to become familiar with infrared spectroscopy sample preparation.

3. **Introduction**

   Give a brief introduction to the purpose of the experiment and the approach to be used for this for **all lab reports**, whether they be investigative or synthetic style reports. Do not copy directly from the laboratory manual. Usually, one or two paragraphs will be adequate, i.e., should be kept to less than a page long and demonstrate that you understand the objective and the key concepts of the experiment. You may include relevant balanced and fully labelled chemical equations at this point. Use only the third person, present tense, passive voice when writing the introduction. For example,

   Correct: In this experiment, cyclohexanol is converted to cyclohexene using.....

   Incorrect: In this experiment, I will be performing an acid catalyzed dehydration…

   do not just write the General Reaction equation, e.g., ROH (alcohol) + $H^+ \leftrightarrow$ R-C = C-R (alkene)

4. **Procedure**

   You may simply refer to the relevant pages in the lab manual (referenced properly). Whatever you do, do not regurgitate the laboratory manual. If the procedure has been modified, or changed in any way, note the changes here. Remember that the procedure section should be sufficiently detailed for another student to be able to

repeat the whole experiment based on your report. Prepare a simple flow chart of the procedure, and record any observations alongside., Finally, keep the following points in mind:

i. use the third person, the passive voice, and the past tense.

Correct: The solution was heated on a hot-plate for 30 minutes.
Incorrect: I heated the solution on a hot-plate for 30 minutes.
Incorrect: The solution is heated on a hot plate for 30 minutes.

ii. avoid the "recipe format".

Incorrect: Heat the solution on a hot-plate for 30 minutes.

iii. incorporate your observations into the procedure.

Example: The solution was heated on a hot-plate for 30 minutes, during which time the colour of the solution changed from red to green.

iv. avoid unnecessary detail.

Acceptable: 20 mL of hydrochloric acid (3 mol· L^{-1}) was added to the solution with constant stirring.
Unnecessary detail: 20 mL of 22.5 °C hydrochloric acid (3 mol· L^{-1}) was poured from a graduated cylinder into a 100-mL beaker containing the solution. During this process the solution in the beaker was stirred with a 15-cm long glass rod having a diameter of 5 mm.

v. Remember to include a table of reagents.

Experiment X Table of Reagents

Reagent	Solid or Liquid	FW (g/mol)	Volume Used (mL)	Density (g/mL)	Weight Used (g)	moles used (g/mol)	MP/BP (°C)	Hazardous Properties
Cyclohexanol	L	100.16	21.0	0.963	20.22	0.202	161.1	Irritant, hygroscopic
Acetone	L	58.08	10.0	0.818	8.18	0.14	56.5	Flammable, irritant
…								

Reference: _____

Note: By filling out the amount and moles used, you will have determined your limiting reagent. The limiting reagent must be calculated in preparative type experiments in order to determine your % yield.

vi. It is perfectly acceptable to record your observations along side a flow chart of the procedure.

Procedure	Observations
Equipment and Glassware Preparation	All clean and dried with acetone, then placed in 110°C oven for 30 min.
Reaction Mixt. Preparation (perform in fume-hood)	
1. Add 11.2 mL bromobenzene to 50 mL diethyl ether	-solution clear and colourless
2. Add 2.4 g of Mg (s) to 250mL round bottom flask	-…
3.	-
4.	-
5.	-
Reaction Workup	
1.	-
2.	-
3.	-
Analysis	-shiny sl. translucent needles, mass of prod=2.5 g

5. References:

Use an acceptable scientific journal sytle/format for your objectives. Be consistent. Do not use one format in one report and a different one in the next.

Author name (surname, inititals.), year published. Title, publisher name, publisher location (e.g. AB for Alberta), page numbers.

6. Results

This is most important section of your report. Wherever possible, **tabulate your data**. A summary of observations is also acceptable here. Show your calculations for the % yield. The discussion portion gives you an opportunity to discuss the significance of your results, to assess the validity of the method, to indicate possible reasons for a poor yield, and so on. Do not over-comment on IR spectra, just pick out and comment on the spectral peaks of importance.

Show sample calculations. Remember there is a difference between % Recovery yield calculations and % Yield calculations where you must determine limiting reagents and a theoretical yield (Exp. 10, 12, 13, 16 and 17).

Label and title all attached flowcharts, spectra etc.

7. Discussion

First, your discussion should state what you've made (draw the structure and name it) and what it appears like (was it as expected, compared to standard or literature) e.g., white shiny crystalline solid.

Next discuss the **yield and purity** of the product(s) you recovery/synthesized. Qualitatively assess the performance (e.g., very good >80%, good 60-80%, fair 40-60%, poor <40%). [Note: This scale might not be appropriate for all experiments. You may have to adjust it accordingly.]

A discussion should **quote actual experimental values** and not talk in vague terms. e.g., "The product obtained was found to be pure." (too vague)

"The product obtained was found to be fairly pure because it had a mp of 110-112° C, a map range of only 2° C. This result was 3 degrees below the literature value of 115° C for 'compound X', and this also shows that the product was not completely pure."

or

"The infrared spectrum of the alkene product (see page xx of the report) had the absorption bands of the expected alkene, 3050 cm^{-1} sp^2 C-H stretch and 1650 cm^{-1} C=C sharp absorption. No broad alcohol band was observed at 3300 cm^{-1}, indicating no reagent alcohol remains and that the reaction resulted in the conversion of the alcohol to the alkene product."

The next section of your discussion covers sources of error and loss. Try to think of at least 2 of each for every experiment.

Sources of error -**theoretical** (assuming reaction goes to 100% completion), and **practical** (the 'instrument' used was not calibrated, or the 'glassware' used to measure my reagent was not calibrated)

Sources of loss - -**theoretical** (e.g., reaction byproduct formation if any (be specific), and **practical** (surface adhesion loss on glassware (be specific), mechanical transfer loss (spilt product when transferring to vial at the end of the experiment!).

Finally, mention at least one way to improve the experiment (should you get to do it again!).

Example Discussion of Product Formed

A clear colorless liquid with a slight alcohol odor, corrected bp 196-201° C, and refractive index of 1.5262 (at 20° C), was obtained from the reaction of…[also draw and name structure of product here]…

Example Discussion of Product Yield

The yield of 1-phenylethanol was 13.2 g of clear, colorless liquid, and the % yield was 56%. The theoretical yield for the reaction was calculated to be 23.57 g, but this assumes that all the limiting reagent (acetophenone) reacted and that no byproducts formed (styrene) Thus, this a fairly good yield for this reaction, which normally gives yields of product around 85% (ref: textbook pp#).

Example Discussion of Product Purity

The product appears to be pure. According to the CRC Handbook the product should be a clear, colorless liquid, with a bp of 203° C. The product obtained was clear and colorless with a (barometric pressure corrected) bp of 195-201° C. The boiling point of the product was 2 C below the literature value, indicating some impurity and/or error, and boiled over a range of 6° C, which definitely means some impurities are still present.

The refractive index of the product was 0.0010 below the literature value of 1.5272, indicating again that some slight impurities are present.

The infrared spectrum for the product shows good purity. All the absorbance bands for an aromatic/aliphatic alcohol were present; O-H stretch @ 3350 cm^{-1}, aromatic C-H stretch @ 3080 cm^{-1} and alkane C-H stretch @ 2850-2950 cm^{-1}, C=C stretching @ 1600, 1500 and 1450 cm^{-1}, and C-O stretch for a alcohol @ 1077 cm^{-1}. No absorbance bands due to reasonable impurities were observed in the infrared spectrum.

The HPLC chromatogram showed high purity, 99.54%, with only traces of acetophenone and styrene being present.

Example Discussion of Sources of Loss and Error

The boiling point of the product was 2° C below the literature value, however an uncalibrated thermometer was used to take this reading. This may account for why the temperature reading was low, but does not explain why the product boiled over a range of 6° C.

The refractometer used in this experiment was uncalibrated. This is a practical source of error for the experiment. And might partly account for why the RI was 0.0010 below the literature value of 1.5272.

8. Answers to post lab questions

The post lab questions are in the lab manual at the end of each experiment.

9. **Conclusion**

You would usually include a sentence or short paragraph that summarizes your results and puts them into some kind of context. If you have made a product, it would be wise to draw its structure again here.

Note: A good concluding statement is sometimes very hard to write. You have to address the objectives you've mentioned at the start of the experiment (do not repeat your objectives word for word!!), mention your key result and say something about the success/failure of the experiment, all in one or two (max.) sentences.

Note: that in some cases the format given above may be completely inappropriate. In such situations, you will be advised as to the most suitable form in which to submit your report.

Submitting Laboratory Reports

[Your lab reports are submitted to your tutor for marking.]

Finally, in most laboratory courses, a student is expected to submit her or his laboratory reports in a bound notebook. With the Athabasca University system this is not practical. Mailing costs would be too high, and there might be a problem with getting notebooks returned before the next scheduled laboratory session. Thus, you should adopt the procedure outlined below.

1. All your results, observations, etc. should be recorded directly in a bound laboratory notebook (preferred size ca. 23.5 cm × 18.4 cm). This notebook is your permanent record of work carried out in the laboratory. (**Note:** your results will also be recorded and initialled on a Product Evaluation Form kept by the lab instructor.) How you choose to organize this notebook is up to you, as it will not normally be submitted to your instructor. However, in the event of some future discrepancy, you may be asked to produce the notebook for inspection.

2. Write your reports on loose-leaf paper (21.5 cm × 28 cm) and submit by mail to your tutor. Be sure to number the pages, and write your name and the number of the experiment on each page. Should your report get lost in the mail, you will still have your results recorded in your notebook and the report can be re-submitted. Please include your address and telephone number with your reports.
Hint: Remember to photocopy your experiment report(s) before mailing them to your tutor.

Weights, Volumes, Measurements and Calculations

SI units and the metric system are used in chemistry.

Measurement	SI Unit	Conversion Factors
Length	Meter (m)	1 m = 100 cm 1 cm = 10 mm 1000 mm = 1 m 1 cm = 0.3937 inches (in) 1 in. = 2.54 cm 1 angstrom (A) = 10^{-8} cm 1 mile = 1.6093 km
Mass	Kilogram (kg)	1 kg = 1000 g 1000 mg = 1 g 1000 mg = 1 μg 1 kg = 2.205 pounds (lbs) 1 lb = 453.6 g 1 amu* = $1.6605402 \times 10^{-24}$ g electron rest mass = 9.10939×10^{-28} g proton rest mass = 1.672623×10^{-24} g neutron rest mass = 1.67495×10^{-24} g
Volume	Cubic meter (m^3)	1 cm^3 = 1 mL 1000 mL = 1 L 1 liter (L) = 10^{-3} m^3 1 in^3 = 16.4 m^3 1 liter (L) = 1.057 quarts (qt)
Density	d	Density = g/mL or kg/L
Mole	m	6.0221367×10^{23} atoms/mol**
Temperature	Kelvin (K)	0 °K = -273.15 °Celsius (C) 0 °K = -459.67 °Fahrenheit (F) °F = (9/5)C + 32° °C = (5/9)(°F - 32)
Molar Mass Molecular Weight Formula Weight	MM MW (Σ of atomic weights of a molecular formula) FW (Σ of atomic weights of a chemical formula)	MM = g/mole MW = g/mole FW = g/mole
Time	Second (s or sec)	1 minute (min) = 60 s 1 hour (hr) = 60 min 1 day (d) = 24 hr 1 day (d) = 86,400 s

* 1 atomic mass unit is derived by assigning the value of 12 amu to a single atom of ^{12}C isotope of carbon.

** the number of atoms in exactly 12 g of ^{12}C.

Prefixes used to indicate decimal fractions and multiples in the SI system

Prefix	Symbol	Number Unit	Example
mega-	M	10^6	1 megabyte (Mb) = 10^6 bytes
kilo-	k	10^3	1 kilogram (kg) = 10^3 g
deci-	d	10^{-1}	1 decimeter (dm) = 0.1 m
centi-	c	10^{-2}	1 centimeter (cm) = 0.01 m
milli-	m	10^{-3}	1 milligram (mg) = 10^{-3} g
micro-	μ	10^{-6}	1 microgram (μg) = 10^{-6} g
nano-	n	10^{-9}	1 nanometer (nm) = 10^{-9} m
pico-	p	10^{-12}	1 picogram (pg) = 10^{-12} g
femto-	f	10^{-15}	1 femotometer (fm) = 10^{-15} m

Other Important Concepts in Organic Chemistry

Yield

The yield is the weight or quantity (in grams) of dried*, pure product that is actually recovered in an experiment. This number is used to calculate the percentage yield (see below).

*The product should always be air dried to a constant weight. Do not heat organic compounds to dry them as they often will decompose, melt or oxidize. Instead use vacuum drying when trying to remove moisture/solvents from an organic solid.

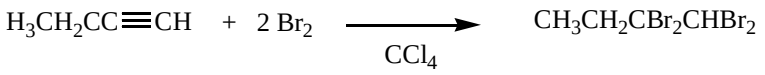
Theoretical Yield

The theoretical yield is the maximum weight or quantity (in grams) of product that can be expected to be formed from a reaction. This number is also used to calculate the percentage yield (see below). The theoretical yield cannot be calculated until the limiting reagent for a reaction has been determined.

Limiting Reagent

The limiting reagent in a reaction is the reactant added to the reaction vessel in the fewest number of moles, after taking into account the stoichiometry of the reaction equation. Consider the following example, where 0.01 g of 1-butyne are reacted with 3 mL of a 1% solution of bromine in carbon tetrachloride, yielding 0.35 g of tetrabromonated product.

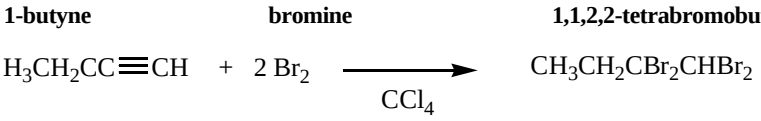
To determine the limiting reagent, the first step is to write out the molecular/chemical formula, and then calculate the molecular or formula weights for the reactants.



1-butyne	bromine	1,1,2,2-tetrabromobutane
C_4H_6	Br_2	
Mwt = 54.09 g/mol	FW = 159.81 g/mol	
Moles = ?	Moles = ?	
Molar Equiv = ?	Molar Equiv = ?	

The second step is to then calculate the # of moles of each reactant added to the reaction vessel. To calculate the number of moles of each reactant, divide the quantity of the reactant (g) by the molecular or formula weight. This procedure is made slightly more complicated for bromine, since we are not given a gram amount but rather a weight percentage. (2% solution = 2 g/100 mL) therefore 3mL will contain 0.06 g (2g /100 mL = ? g/3 mL, ? = (2 g × 3 mL)/100 mL).

The third step is to look at the stoichiometry of the reaction. Notice that 2 moles of bromine react with 1 mole of 1-butyne. To take this fact into account, the moles of reactant are converted into molar equivalents (since it takes 2 moles of bromine for every mole of 1-butyne, divide the bromine moles by 2 to get the molar equivalent).



C_4H_6	Br_2	$C_4H_6Br_4$
Mwt = 54.09 g/mol	FW = 159.81 g/mol	Mwt = 213.9 g/mol
Amt. Used = 0.01 g	Amt. Used = 3 mL	Yield = 0.035 g
	%wt. = 1%	
Moles = 0.000185 mol	Moles = 0.000375	Moles =?
Molar Equiv **= 1.85 × 10^{-4}**	Molar Equiv = 1.88 × 10^{-4}	

Therefore, **1 butyne is the limiting reagent** since there are fewer molar equivalents present of 1-butyne than of bromine.

% Yield Calculation

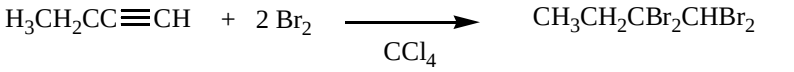
The percentage yield is one of the most important calculations to learn in organic chemistry. It is a measure of the efficiency of the reaction procedure, and is determined by comparing the actual yield to the theoretical yield:

$$\%\ \text{yield} = \left(\frac{\text{actual yield}}{\text{theoretical yield}} \right) \times 100\%$$

There are six steps in the calculation of the % Yield for a reaction. **Note:** The first four steps were illustrated in the calculation of the moles of the limiting reagent.

Step 1 Write the molecular formulas and determine molecular weights for reactants and products.
Step 2 Determine the number of moles of each of the reactants.
Step 3 Convert moles to molar equivalents if necessary by looking at stoichiometry of reaction.
Step 4 Determine the limiting reagent = maximum number of moles of product formed.
Step 5 Convert moles of product to grams of product = theoretical yield.
Step 6 Solve for % yield using the equation given above.

To illustrate the % Yield calculation, we will carry on with the same example as above,



1-butyne	**bromine**	**1,1,2,2-tetrabromobutane**
C_4H_6	Br_2	$C_4H_6Br_4$
Mwt = 54.09 g/mol	FW = 159.81 g/mol	Mwt = 213.9 g/mol
Amt. Used = 0.01 g	Amt Used = 3 mL	Yield = 0.035 g
	%wt. = 1% soln	
Moles = 0.000185 mol	Moles = 0.000375 mol	Moles = 0.000185 mol
Molar Equiv **= 1.85×10^{-4}**	Molar Equiv = 1.88×10^{-4}	Theor. Yield = 0.04 g

Therefore the % Yield for the above reaction is:

$$\%\ \text{yield} = \left(\frac{\text{actual yield}}{\text{theoretical yield}} \right) \times 100\% = \left(\frac{0.035\ \text{g}}{0.04\ \text{g}} \right) \times 100\% = 87.5\%\ \text{yield}$$

% Recovery Yield

The percentage recovery is used when compounds are extracted from natural sources, or when a reagent hasn't been changed during a procedural step, such as a recrystallization. The % recovery calculation is used to measure either (1) the % content of the starting material that is the compound of interest or (2) the efficiency by determining the amount of loss during a procedural step. It is often confused with % yield:

$$\%\ \text{recovery yield} = \left(\frac{\text{actual yield}}{\text{amount of starting material}} \right) \times 100\ \%$$

% Error

The percentage error calculation is used to measure the % difference between the actual experimentally derived value and the theoretical expected value. It too is often confused with % yield:

$$\%\ \text{error} = \left(\frac{|\ \text{actual value - theoretical value}\ |}{\text{theoretical value}} \right) \times 100\ \%$$

Safety

General

In 1975, a survey carried out by Her Majesty's Inspectors of Schools showed that of the 70,000 accidents reported in British schools, only two per cent occurred in a science laboratory. Although Athabasca University students are not attending laboratory sessions in Britain, and are more mature than most school-children, this statistic is relevant to the laboratory component of *Chemistry 360*. The figures suggest that, although a laboratory is a potentially dangerous place to work, the chances of an injury-causing accident are relatively low. This situation exists because of the strict safety rules that are applied to students working in laboratories, and because of a willingness of both students and instructors to look out for unsafe practices and possible hazards at all times.

Some people will approach the laboratory component of their Athabasca University chemistry course with a certain amount of trepidation. In a sense, this is a good thing—no one can afford to adopt a complacent attitude towards laboratory safety. However, you should realize that you could well face a greater chance of being killed or injured as you drive to the laboratory session than you will while you are working in the laboratory. Most of the hazards that you are likely to face while performing the experiments in this laboratory are relatively minor and easily avoided. They include:

minor cuts—most cuts can be avoided if a student never uses broken or cracked glassware, and is particularly careful when carrying out potentially dangerous operations, such as inserting glass tubing into a rubber stopper.

burns—burns usually occur when a student forgets that something which has just been heated on a hot-plate or in a heating mantle may be very hot.

chemical spills—spills can usually be avoided if students pay particular attention to the technique used when pouring chemicals from a container, and injury caused by spills can be minimized if students wear the appropriate protective clothing: safety glasses, gloves, and lab coat or apron.

Another possible danger is the presence of hazardous gases or vapours in the air. In this course, we have kept the use (or production) of such materials to a minimum. Where eliminating such materials is not practical, you will be advised to work in a fume hood, which will protect both you and your co-workers from exposure to undesirable concentrations of toxic or otherwise unpleasant vapours.

When designing the laboratory component of this course, we found it necessary to strike a balance between minimizing possible hazards and exposing you to a full range of techniques. By its very nature, chemistry often necessitates the handling of dangerous substances; if chemistry students are never exposed to such situations, we would never have any fully trained chemists. Having said this, perhaps we should reassure you that, provided you follow the safety rules that follow, we do not anticipate that any problems will arise.

Safety Rules

1. **Safety glasses must be worn in the laboratory at all times.** Wearers of prescription glasses may wear their own spectacles, but should be aware of the possibility that chemicals or flying glass could enter the eye through the gap between the temple and the frames of the glasses. Thus, in potentially hazardous situations, wearers of spectacles are advised to wear safety goggles or a safety mask over their prescription glasses. Contact lenses must *not* be worn in the laboratory.

   Note 1: Safety glasses will be provided by Athabasca University and must be worn at all times—even when you are not actively using chemicals and glassware. Remember that injury could result through carelessness on the part of one of your fellow students.

Note 2: Contact lenses are not permitted for two reasons.

a) If a chemical is splashed into the eye of a person wearing contact lenses, neither the normal tearing mechanism nor external irrigation (with water) is effective in removing chemicals from under the contact. The contact must first be removed before tearing and irrigation is effective; however, the contact may be difficult to remove because of the tight squeezing shut of the eye that occurs in response to the chemical in the eye. Since time is of the essence with a chemical burn, a delay caused by the necessity of removing a contact lens could have serious consequences.

b) Soft contact lenses present an additional hazard. Any chemical (including vapours) that comes into contact with such a lens can diffuse into the interior of the lens, which then acts as a reservoir that can create additional exposure, even if the lens is removed and rinsed.

Note 3: The correct emergency treatment for chemicals that enter the eye is to wash the injured eye thoroughly with plain water for 15 minutes. Medical attention should be sought for all eye injuries. An eye-wash fountain should be available in the laboratory; make sure that you are aware of its location.

2. **A lab coat should be worn at all times.** You must purchase a lab coat in order to participate in the laboratory component of this course. A lab coat will not only make you look and feel like a chemist, but will also protect you and your clothes in the event that you inadvertently spill a chemical.

   While we are on the subject of clothes, dress sensibly. It can become very hot in the laboratory and you will not be comfortable working all day with a three-piece suit worn underneath your lab coat. Similarly, clothes worn in the laboratory tend to acquire a "chemical odour", and it may be advisable to leave your more expensive shirts and sweaters at home.

3. **Protect your feet by wearing "sensible" shoes.** Bare feet, open-toed sandals, etc., are not permitted. Spilling concentrated sulfuric acid on your big toe, or cutting your foot on a piece of broken glass would result in a trip to the hospital. Avoid high-heeled shoes; remember that you will be "on your feet" for up to eight and one-half hours on any given lab day.

4. **Tie back long hair.** Long hair can be a fire hazard. Also, when you bend over to inspect the contents of a beaker containing a chemical, long hair can easily fall into that chemical. Not only could this damage your hair, but it could also ruin your experiment!

5. **Never run in the laboratory, and never be tempted to become involved in practical jokes or other horseplay.**

6. **On no account attempt an unauthorized experiment.**

7. **Never work in the laboratory when the supervisor is not in attendance.** Our regulations require that at least one qualified supervisor be present in the laboratory whenever a student is working there.

8. **Eating, drinking and smoking are not permitted in the laboratory.** Food and drink may become contaminated by toxic substances. Smoking is a fire hazard. When you leave the laboratory, wash your hands, particularly before eating.

9. **In the event of fire:**

   a. do not panic; many small fires can be extinguished without the use of a fire extinguisher, simply by cutting off the air supply. For example, when a flammable liquid 'catches' fire in a beaker, the fire can quickly be put out by placing an asbestos pad or watch-glass over the beaker.

   b. if the use of a fire extinguisher is necessary, leave it to the supervisor and concentrate on getting yourself to the nearest exit.

   c. in the event that your instructor is incapacitated (e.g., through injury), be prepared to extinguish a fire, especially if human life is in danger. To do so, you must know the location of the nearest fire extinguisher and how to use it. Most of the extinguishers that you will encounter are of the ABC type, which means they are effective on fires involving trash, wood or paper (Class A), liquids and grease (Class B), and electrical equipment (Class C). These extinguishers are not effective on Class D fires. (i.e. those involving active metals such as sodium and potassium). Fires involving the latter substances are unlikely to occur during a *Chemistry 360* lab, but you should be aware of the special problems that these materials can cause. When using a fire extinguisher, aim at the base of the fire and use a sweeping motion. Note that you should never attempt to extinguish a laboratory fire using water. (A possible exception might be to extinguish a burning paper towel by placing it in a sink and turning on the tap.)

d. if your clothing catches fire, wrap yourself in a fire blanket (or a coat if no fire blanket is available) and roll on the ground.

10. **Report all accidents.** All accidents, however minor, must be reported to your supervisor and the details entered in the accident book. If you are involved in an accident, do not resume work until you have received the appropriate first aid or medical attention. Never work with open cuts on your hands; cover all small cuts and scratches with 'band-aids'.

11. **Always dispose of chemical wastes in the correct manner.** In general, you would never dispose of chemicals, particularly organic solvents, by pouring them down the drain. Throughout the *Chemistry 360* laboratory manual you will find that you are told repeatedly to "pour excess reagents into the waste container provided". Ensure that waste chemicals are placed in the correct container—putting the wrong material into a container is potentially dangerous. Never attempt to return "used" chemicals to their original containers. Note that certain substances, such as dilute acids or solutions of "harmless" compounds (e.g., sodium chloride), etc., *may* be washed down the drain with copious amounts of water. When in doubt, check with your instructor. Be particularly careful to place any chlorinated hydrocarbons in the waste container designated for such substances.

12. **Never pour concentrated inorganic acid (e.g., H_2SO_4) or base into a bottle marked 'Organic Waste only'.** Violent exothermic reactions can occur between potential reagents, causing a splatter of toxic and corrosive material.

13. **Never over fill a waste bottle.** Keep an eye on the volume level in the waste bottle and let the instructor know when it is ¾ full.

Some General Advice About Laboratory Work

1. People with clean and tidy benches are less likely to be involved in accidents. Communal areas, such as balance rooms and fume hoods, should also be kept tidy. Clean up all spills. Any glassware containing chemicals that is left in a communal area should be clearly labelled with the owner's name and details of the contents (e.g., L. Worker, concentrated nitric acid).

2. Do not rummage through a cupboard or communal glassware/supply drawer or box without care and attention. Sharp object may be present. Discard sharp objects (needles, razor blades, broken glass) in the appropriate sharps discard receptacle.

3. Wear your lab coat at all times when working in the lab, and wear protective latex gloves whenever handling corrosives and solvent. Do not store sharp objects (e.g., Pasteur pipettes) in your coat pocket.

4. When assembling apparatus or glassware, always check with the instructor before proceeding with the experiment.

5. Handle all organic solvents (e.g., acetone, dichloromethane) with care. Most are flammable, and many have a long-term, cumulative effect on the body.

6. If a fire starts, or the fire alarm sounds, unplug any electrical apparatus and vacate the laboratory in an orderly manner.

7. When diluting a concentrated acid, always **add the acid to the water**. Do so slowly, with stirring.

7. If you get acid on your clothing, neutralize it with **dilute** ammonia solution ($1\ mol \cdot L^{-1}$) and wash well with water.

9. If you get alkali on your clothing, wash it off with large quantities of water.

10. If you get any corrosive chemical on your skin, wash it off immediately with water and consult your instructor. Pay special attention to the safety notes given in bold type in the "Procedure" sections of the lab manual. These notes will inform you of any special precautions that you might need to take, and will also inform you if the "wash well with water" maxim does not apply.

11. If you spill a large quantity of acid on the bench or floor, use crude sodium bicarbonate (available from the instructor) to neutralize the acid and then wash well with water.

12. Mercury from broken thermometers presents a special kind of hazard. The vapour from the spilled mercury represents a long-term hazard and so the liquid mercury should be cleaned up very carefully. If you break the thermometer, ask your instructor for assistance in cleaning up the mercury. Do not touch the mercury globules with your hands.

13. Always check for any possible hazards associated with using a given chemical. The quickest way of doing so is to make certain that you read the label on the container from which the chemical is removed. Some chemical manufacturers use symbols or codes on the labels of their chemical containers to indicate possible hazards. When in doubt, consult your instructor.

14. In the event of a real emergency, it could be important for medical personnel to know certain facts about you, facts that they could not obtain if you were unconscious or in a severe state of shock. On the next page is a copy of a *Medical Information Form* that you should have received either with this laboratory manual, or separately in the mail. We advise you to fill out the form that you received, and paste it inside the front cover of your lab notebook. You might regard some of this information as being rather personal. However, keep in mind that normally we do not expect you to show us your lab notebook (see "Writing Laboratory Reports") so confidentiality of your medical history should be maintained. If you still have doubts, keep in mind that, in the event of an accident, your instructor has been asked to put your lab notebook on your stretcher as they carry you off to the hospital.

15. As mentioned in the safety rules, all accidents that result in injury must be reported and recorded in the accident book. In addition, an "Accident Report Form" must be completed and returned to the course co-ordinator. A sample form is shown on the page after next.

Note: The *Medical Information Form* on the next page is adapted from one suggested by Ben Ruekberg and David W. Ball, *Journal of Chemical Education*, 63, **A247** (1986).

Sample Medical Information Form: *Chemistry 360*

Name: A. Student

Social Insurance Number: 123 456 789

Address: 4812, 43rd Street, Small Town, Alberta

Phone: 675-6111

Alberta Health Care Number: 987.65.432.123

Age: 35

Sex: M

Height: 173 cm

Weight: 68 kg

Chronic medical problems: Epilepsy

Current medical problems: None

Do you normally wear contact lenses? No

Physical disabilities: Partially deaf

Allergies to medication: Allergic to penicillin

Current medication being used: None

Personal physician: Dr. V. Rich

In case of emergency, please contact: Susan Student (wife) 675-6111

Special information: My religious beliefs prevent me from accepting a blood transfusion.

Chemistry Laboratory Accident Form (Student Labs)

Name of injured student: Alan Student

Date of incident: April 1, 1987

Time of incident: 2:06 p.m.

Course: *Chemistry 360*

Instructor: A. Tutor

Nature of injury: Glass tubing penetrated palm of right hand.

How injury incurred: Student was attempting to insert glass tubing into rubber stopper without using recommended lubricant.

First aid rendered: Wound was washed thoroughly, a piece of glass appeared to be embedded in the hand. Pressure applied around the wound using a ring pad. Covered with built-up dressing.

First aid rendered by: A. Tutor (instructor), G. Help (student)

Further medical treatment sought? (if yes give details). Patient was driven to outpatients at the nearest hospital where the wound was examined and the embedded glass removed.

Instructor's comments: Student returned to lab at 4 p.m. to collect belongings. His wife had been contacted and she came to drive him home.

Was instructor in the room when the incident occured? Yes

Student's signature: A. Student

Follow up (course co-ordinator): Contacted student by phone (April 3), his condition is now being monitored by his family physician.

WHMIS

On October 31, 1988, the Workplace Hazardous Materials Information System (*WHMIS*) went into effect. This is a national system intended to provide laboratory personnel with uniform information on chemicals used in the workplace. There are three main features of WHMIS:

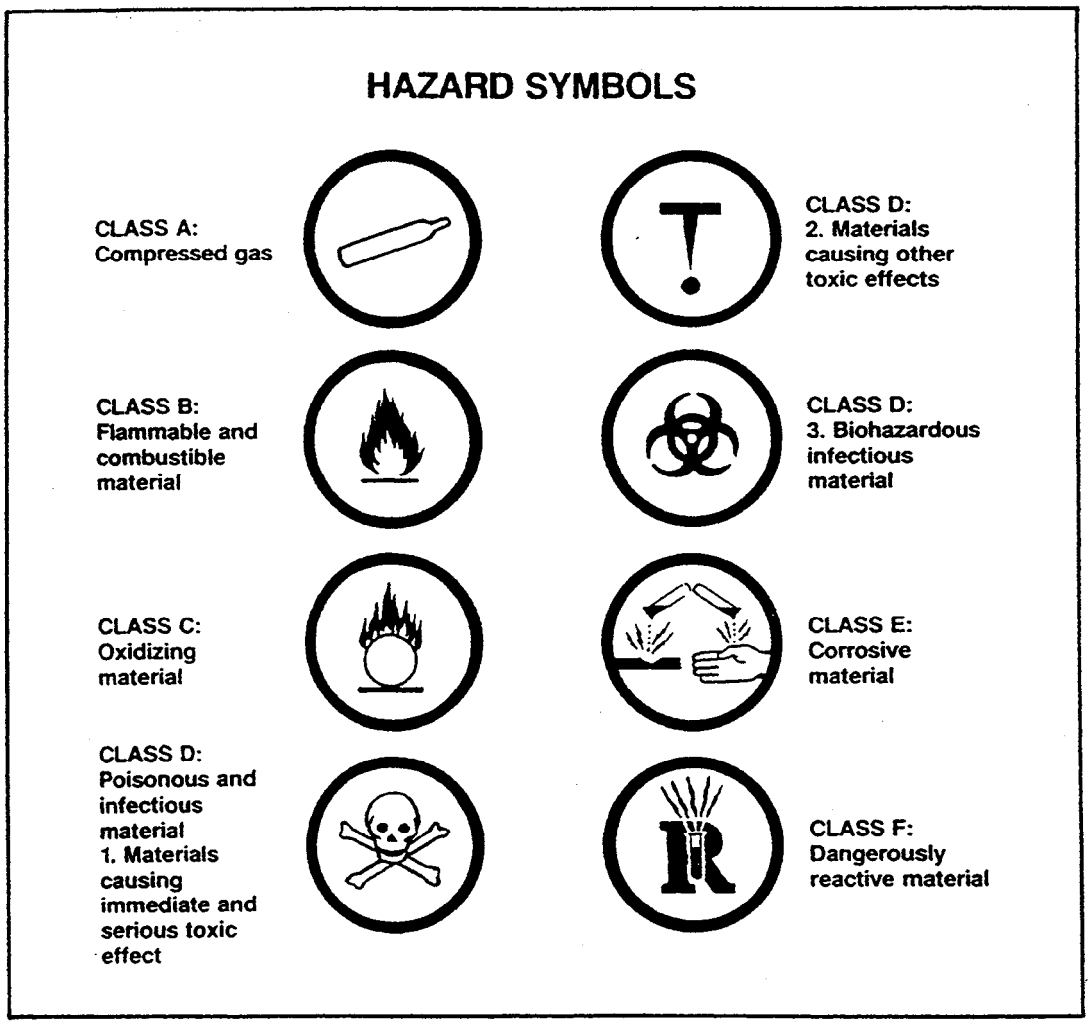
1. Chemical manufacturers are now obliged to label each container of hazardous material, giving details on the product's hazards and what action to take in an emergency.

2. The manufacturer must provide the consumer with a Material Safety Data Sheet (*MSDS*) for each hazardous product. These sheets give complete details on the possible health effects that exposure to the product can produce, preventive measures that should be taken, etc.

3. Employers must provide an appropriate education program for all workers whose work may bring them into contact with hazardous products.

The WHMIS regulations do not affect you as a student, although if you are involved in a chemistry-related job you should be familiar with them. Most of the chemicals that you will handle in this course are no longer in their original containers. Under the WHMIS regulations, such chemicals do not require detailed labels. However, you should read all labels carefully, and pay special attention to the hazard warnings that appear throughout the laboratory manual. The hazard symbols that you may observe on certain chemical containers are reproduced on the following page. A file containing up-to-date MSDSs for all the chemicals used in *Chemistry 360* is maintained at each of the locations where laboratory sessions for these courses are held. Additional information on WHMIS may be obtained from Alberta Community and Occupational Health, Occupational Health and Safety Division.

Hazard Symbols



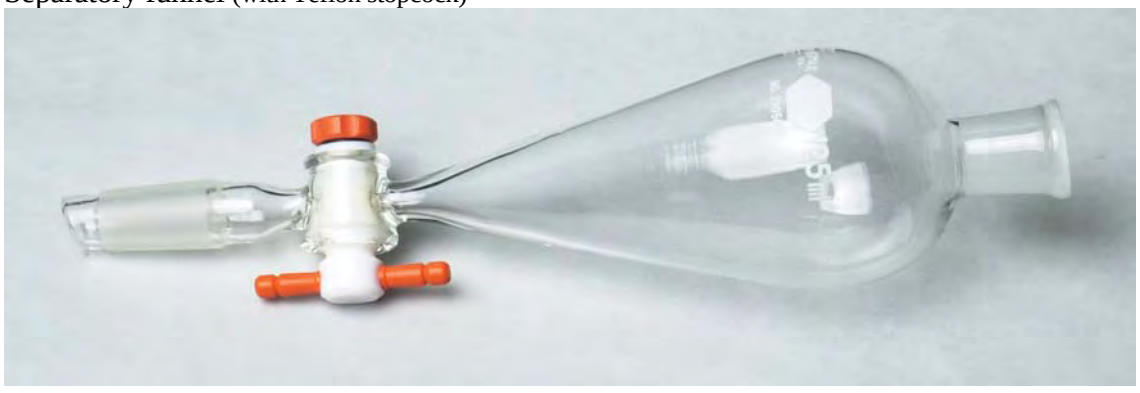
Common Apparatus

We assume that you are already familiar with the common apparatus found in a general-chemistry laboratory; however, you may not recognize some of the items of glassware that are used in organic chemistry. The following pages illustrate the glassware that is included in the kit that you will be given. Please endeavour to familiarize yourself with the name of each item **before** you attend your first laboratory session.

Condensor (West)

Distilling Column (Fractionation Column – without and with fractionating material, glass beads, inside)

Separatory funnel (with Teflon stopcock)



Connecting Adapter (three way adapter, still head)

Claisen Adapter

Pennyhead Stoppers

Vacuum Adapter

Flat bottom dish

Round bottom flasks

Lab jack

Thermometer Outlet Adapter

Before Starting *Chemistry 360* Experiments:

Chemistry 360 laboratory experiments are essentially a continuation of *Chemistry 350* laboratory experiments. It is therefore essential for you review the principles and techniques learned in the *Chemistry 350* laboratory experiments **before** proceeding with the experiments outlined in this manual.

For Your Safety:

Remember at all times that you are working with dangerous (flammable, corrosive, toxic, carcinogenic, etc.) compounds, and that you must take steps to protect yourself and other students present in the lab. You can do this by always thinking before you act! Find out the hazards of each chemical **before** you use them, and then take the appropriate precautionary steps.

Some Major Does and Don'ts:

1. Never leave a reagent stock bottle open and unattended. Securely close and put the bottle away immediately after obtaining your aliquot/sample.
2. Use a clean metal spatula (not a glass rod) to break up clumps of solids in bottles.
3. Think ahead as to where you are going to set aside or discard any wastes or contaminated glassware.
4. Never work hastily. Always be in control and know the next procedural step(s).
5. Label your glassware/reaction vessels. If you don't you will lose marks!
6. Some reagents require special handling, even in discarding. For instance aluminum trichloride, sodium metal, and acetyl chloride react violently with water.
7. Never discard an organic compound or rinse out dirty glassware in the sink. Discard (and rinse out with acetone) all organics (halogenated or non-halogenated) in the appropriate waste container in the fumehood.
8. Never discard concentrated acid or base or rinse out acid or base contaminated glassware in the sink. All concentrated acids and bases MUST FIRST BE DILUTED (note original volume and concentration of solution!) AND THEN NEUTRALIZED before discarding. Get your instructor to assist you with this!!
9. Do not assemble an apparatus over a sink.
10. Avoid skin contact with unknown compounds or reagents. Do not breathe vapours.
11. Before using flammable organic liquids, check that there are no flames in the vicinity. **NEVER heat flammable liquids over a flame**!
12. Never heat a closed system. A closed system will explode. Do not heat an Erlenmeyer flask that is more than 2/3^{rds} full. Always use boiling stones.
12. Use gloves when handling heated glassware.
13. For recrystallizations, use an Erlenmeyer flask, not a beaker. Beakers tip over easy.
14. Do not hold chemicals near your face, ever!
15. Keep your work area clean and tidy at all times.

Chemistry 360 Technique Review:

In *Chemistry 350*, Organic Chemistry I, the student learned the following techniques:

	Solid Organic	**Liquid Organic**
Purification Method	Recrystallization	Distillation (simple or fractional)
Assessment of Purity	Melting point, TLC, Polarimetry	Boiling point, Refractive index, Polarimetry
Identification	Mixed Melting Point, *(Co-Spot TLC)**, Qualitative Organic Analysis, IR Spectroscopy	Qualitative Organic Analysis, IR Spectroscopy, Derivative Formation
Separation of Mixtures	Liquid-Liquid Extraction Solid-Liquid Extraction	Distillation (simple or fractional)
Drying of Organic Compounds	Air Drying, Vacuum Drying	Pre-drying-'salting out' Drying Agents (e.g. anhydr. $CaCl_2$)

*not done in this course.

Please review these techniques before attending the CHEM360 Supervised Labs.

1. Melting Point Determinations

Four stages of melting may be observed:

1. First signs of change (for example, shrivelling).
2. First signs of liquid formation. -RECORD the lower limit at this point
3. Formation of a meniscus.
4. Formation of a completely clear liquid. -RECORD the upper limit.

Pure compounds have sharp melting points. Impure compounds have broad ranges.

2. Recrystallizations

Five steps of single solvent recrystallization:

1. Select the solvent (soluble in hot, insoluble in cold).
2. Dissolve in a minimum of hot solvent.
3. Decision Time? Hot gravity filtration if solid impurities (particulates) present. Add charcoal if coloured impurities present.
4. Slow cool to room temp. Allow crystals to form. Place crystals on ice.
5. Collect product by vacuum filtration. Save filtrate for possible second crop. Wash crystals with **ice cold** solvent and allow to air dry to a constant weight.

Six steps of a two solvent recrystallization:

1. Determine the solvents (one soluble at all temps. (A), one insoluble all temps.(B), both must be miscible).
2. Dissolve in a minimum of hot solvent A.
3. Decision Time? Hot gravity filtration if solid impurities (particulates) present. Add charcoal if coloured impurities present.
4. Add solvent B until the solution clouds. Heat to clear solution.
5. Slow cool to room temp. Allow crystals to form. Place crystals on ice.
6. Collect product by vacuum filtration. Save filtrate for possible second crop. Wash crystals with **ice cold** solvent, and allow to air dry to a constant weight.

3. Distillation Procedure:

Six steps are required to perform a distillation

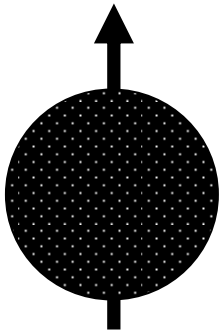
1. Select the heat source (heating mantle, Bünsen burner, steam bath, or water bath).
2. Clean, dry and assemble the distillation apparatus. Use joint grease?-No.
   i) Start assembling the apparatus from the bottom up.
   ii) Place heat source in position. Use lab jack to adjust height.
   iii) Clamp distillation flask in position.
   iv) Place three-way connector into distillation flask.
   v) Place thermometer adapter into the top of three-way connector.
   vi) Approximately set height of receiving flask using a utility clamp.
   vii) Place condenser into position and secure with joint clamps.
   viii) Attach tubing to water inlet and water outlet to the condenser.
   ix) Adjust height of thermometer.
   x) Inspect to ensure no joint is under stress and that the system can be safely heated (i.e. it is open to the air via the vacuum take-off adapter and it is not a BOMB.)
3. Turn on the cold water supply to the condenser. Check for water leaks.
4. Add the liquid to be distilled to the distillation pot. Add boiling stones.
5. Heat the liquid and collect the product in the receiving flask.
6. Allow the apparatus to cool and disassemble it. Clean all glassware parts thoroughly with acetone (discard in organic wastes) before washing with soapy water.

4. Extractions

Five steps to performing a extraction using a separatory funnel. They are:

1. Dissolve the unknown compound in a solvent. Place the mixture in the separatory funnel supported with a ring clamp on a retort stand.
2. Add the extraction solvent to the separatory funnel.
3. Stopper the funnel, invert the funnel, vent, shake gently and vent again. Continue shaking/venting until no further pressure is released and then gently shake the funnel for 30 sec.
4. Return the separatory funnel to the ring clamp and allow the layers to separate.
5. Remove the stopper, drain the lower layer through the stopcock (out the bottom). Remove the upper layer by pouring it out of the top of the separatory funnel.

CHEM360 Infrared Spectra Analysis Review:



To be done before attending the CHEM360 Supervised Labs:

1. Review the Theory on Infrared Spectroscopy
2. Review the Listing of Organic Functional Groups and their corresponding Infrared Spectra.
3. Perform the Sample Infrared Spectrum Problems.
4. Answer the Unknown Spectra (to be analyzed at home).

Introduction to Infrared Spectroscopy- Theory and Practice

Electromagnetic radiation

As you read this page, uncountable numbers of photons or 'light particles' are reflecting off its surface and are being absorbed by pigments (re., complex organic molecules) in the rod and cone cells in the retina of your eye. Where the ink (re., complex organic dye) has absorbed the photons you perceive a dark area (i.e., letters) due to the lack of photons from that point on the paper.

On a deeper level, photons (and electrons) are actually wave/particle dualities (re. quantum physics). For instance, photons carry only a discrete amount of energy, called quanta, but the amount of energy of a quanta is defined by the equation, $e = h \upsilon = h c/l$ where:

- e = the energy of 1 photon (quanta)
- h = Planck's constant (6.62×10^{-27} erg sec)
- υ = Frequency in hertz (cycles or l per sec)
- c = Speed of light (3×10^{10} cm per sec)
- l = Wavelength in cm

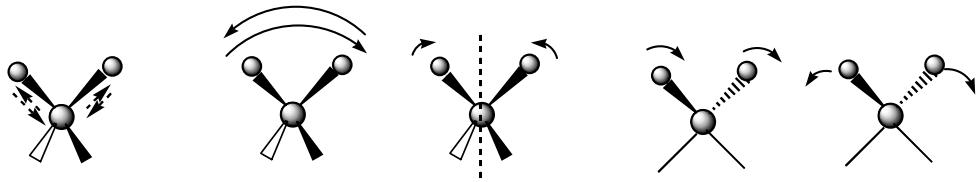
Thus the amount of energy carried by a photon varies directly with its frequency, and because of the relationship between frequency and wavelength, varies inversely with its wavelength. i.e. Photons also behave like waves of electromagnetic energy traveling at the speed of light.

Practically speaking however, you need only understand that photons are the messengers that carry the electromagnetic force between electrons and other elementary particles. Electrons, whether free or bound in a covalent bond, are capable of absorbing (or emitting) photons and changing their energy state. This leads to different types of excitation (nuclear transformations, electronic, rotational, nuclear spin changes, bond deformation) depending on the amount of energy carried by the photon. High-energy photons (x-ray, gamma ray, and cosmic ray) can cause ionization of the molecule, while UV photons are involved in electronic interactions. Remember it is the interaction of electrons (via photons) in the outer cloud surrounding atoms that forms the foundation of all chemical reactions.

Infrared radiation

Infrared radiation is composed of photons with a specific range of wavelengths (7.8×10^{-5} cm to 10^{-2} cm) and frequencies ($\sim10^{14}$-10^{12} Hz). This range includes the near infrared, the infrared and far-infrared regions. The actual wavelengths of interest to most organic chemists are 1.667×10^{-3} cm to 2.5×10^{-4} cm (the 'infrared' region). These wavelengths (λ) are most often expressed as there corresponding wave number (n) where $n = 1/\lambda$, with n measured in cm^{-1}. (e.g. l2.5-16.6 μm = 4000-600 cm^{-1}).

Infrared carries relatively low levels of energy (e.g. ~1-10 kcal/mol) which, when absorbed, result in only bond vibrations - stretching, rotating, bending and scissoring (i.e. deformation).



Stretching Vibration (symmetric or antisymmetric) (rocking vibration scissoring vibration wagging vibration twisting vibration)

SomeTypes of Bending Vibrations

Every molecule, depending on its make up, is capable of absorbing infrared photons and increasing the intensity of its molecular motions. Different functional groups within the molecule will absorb photons at different infrared wavelengths. Thus when a spectroscopic wavelength scan is performed on an organic molecule certain λ will be absorbed while other λ will pass through. Once we have the infrared spectrum of a compound, the spectrum can be analyzed and compared with known infrared absorptions for particular functional groups (see Table 8.1).

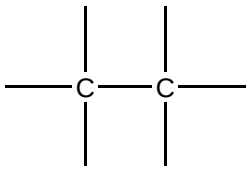
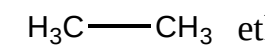
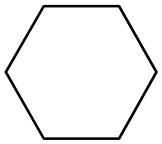
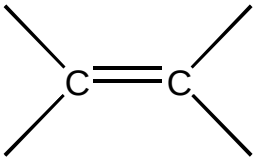
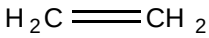
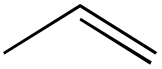
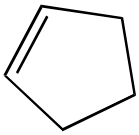
The infrared spectrum for a particular molecule can be very complex consisting of many absorption bands. This is due to the many possible motions each atom can undergo (a non-linear molecule has 3N-6 normal modes of vibration where N = the number of atoms in the molecule). When analyzing a spectrum, it is important to look at 4 different regions of the spectrum for the presence or absence of specific absorption peaks. Note: you are not required to analyze the fingerprint region.

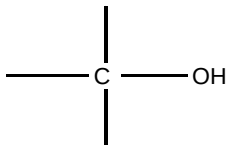
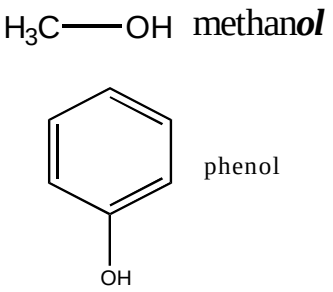
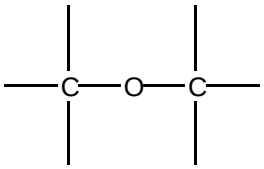
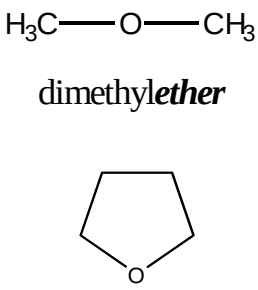
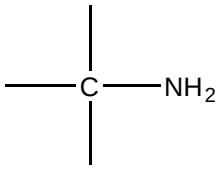
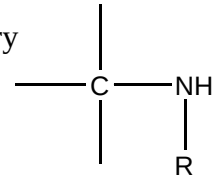
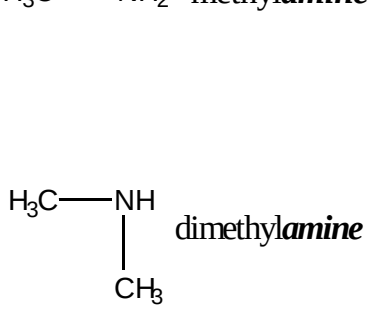
Wavenumber cm^{-1}

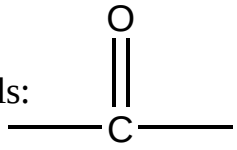
4000	3000	2000	1400	600
N-H O-H	CH	C≡N C≡C	C=C C=O C=N	fingerprint region

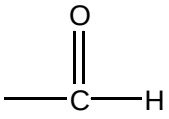
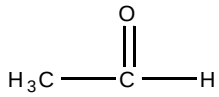
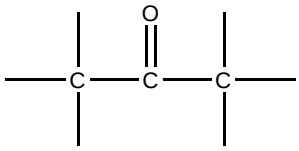
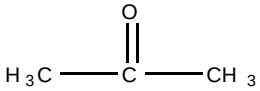
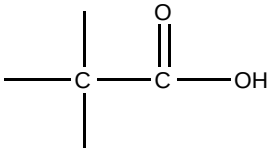
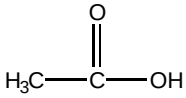
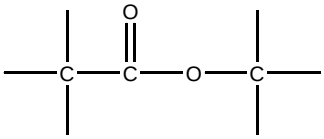
The following pages contain useful information to help you understand and interpret infrared spectra.

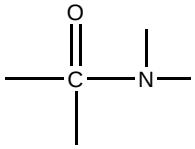
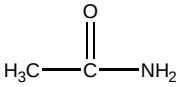
1. Included is a chart showing the structures of various functional groups, which you need to know.
2. The wavenumber of the functional groups is also included to help you locate pertinent absorption bands on an infrared spectrum.
3. Diagrams of the shapes and intensities of various infrared absorption bands will help in your interpretation of infrared spectra.
4. Finally, your instructor will lead you through the interpretation of sample infrared spectra representative of various functional groups. Unknown spectra are included to allow you to practice on your own. There is a great deal of information to learn, but the more you practice, the easier it becomes to interpret infrared spectra.

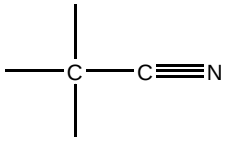
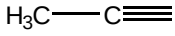
FAMILY NAME	FUNCTIONAL **GROUP STRUCTURE**	**EXAMPLES AND NOMENCLATURE**
Alkane	 sp^3 orbitals	 eth***ane***  pent***ane***  cyclohex***ane***
Alkene	 sp^2 orbitals	 eth***ene***  prop***ene***  cyclopent***ene***
Alkyne	 sp orbitals	 eth***yne*** (Acetylene)

Alcohol		
Ether		
Amines	Primary  Secondary 	

Carbonyls: 

Aldehyde		 ethan***al*** (Acetaldehyde)
Ketone		 propan***one*** (Acetone)
Carboxylic Acid		 ethan***oic acid*** (Acetic acid)
Ester		 methyl ethan***oate*** (Methyl acetate)

Amides		 ethan***amide*** (Acetamide)

Nitriles		 ethane***nitrile*** (Acetonitrile)

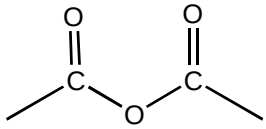
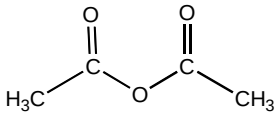
Anhydride		 acetic **anhydride**

Table 1 Correlation Table of Infrared Absorption and Functional Group.

Type of Absorption	Wavenumber (cm^{-1})	Intensity of Absorption	Absorption of:
O-H stretch	3400-3640	strong, broad	alcohol
	2500-3300	strong, very broad	carboxylic acid
N-H stretch	3310-3350	medium ('W' shape)	amine (1^o)
C-H stretch	3300	strong	sp C-H of alkyne
	3030	medium	aromatic
	3020-3100	medium	sp^2 C-H of alkene
	2850-2960	medium to strong	sp^3 C-H of alkane
	2750 & 2850	weak-medium ('W' shape)	O=C-H of aldehyde
C≡N stretch	2210-2260	medium, sharp	nitrile
C≡C stretch	2100-2260	medium, sharp	alkyne
C=O stretch	1670-1780	strong, sharp	carbonyl
	1730-1750		ester
	1720-1740		aldehyde
	1705-1725		ketone
	1700-1725		carboxylic acid
	1640-1700		amide
	ca 1800 and 1760		anhydride
C=C stretch	1650-1670	weak-medium, sharp	alkene
	1600, 1500, 1450	strong sharp	aromatic
C=N stretch	1640-1670	medium, sharp	imine
N-H bend	1500-1650	medium to strong, sharp	amine and amide
N=O stretch	1500-1600 (1540) and 1320-1390	strong, sharp	nitro-compound
C-N stretch	1030, 1230	medium	amine
C-O stretch	1050-1150	strong	alcohol
	1250-1310	strong broad	ester-conjugated
	1240	strong, broad	ester-acetates
	1175	strong, broad	ester-unconjugated
C-Cl stretch (terminal)	600-800	strong	alkyl halide
Ar-Cl stretch	1000-1175	medium-strong	aryl halide
C-Br stretch (terminal)	500-760	strong	alkyl halide
C-I (terminal)	500	strong	alkyl halide

Note: when a C=C bond is in conjugation with a carbonyl, the observed carbonyl absorption frequency will be < ~ 30 cm^{-1}.

Calculation of the # Degrees of Unsaturation in a Compound

(*See also Alkenes: 'Structure and Reactivity' in McMurry's 4th ed., pp. 180-182, 5th ed. pp. 190-192).

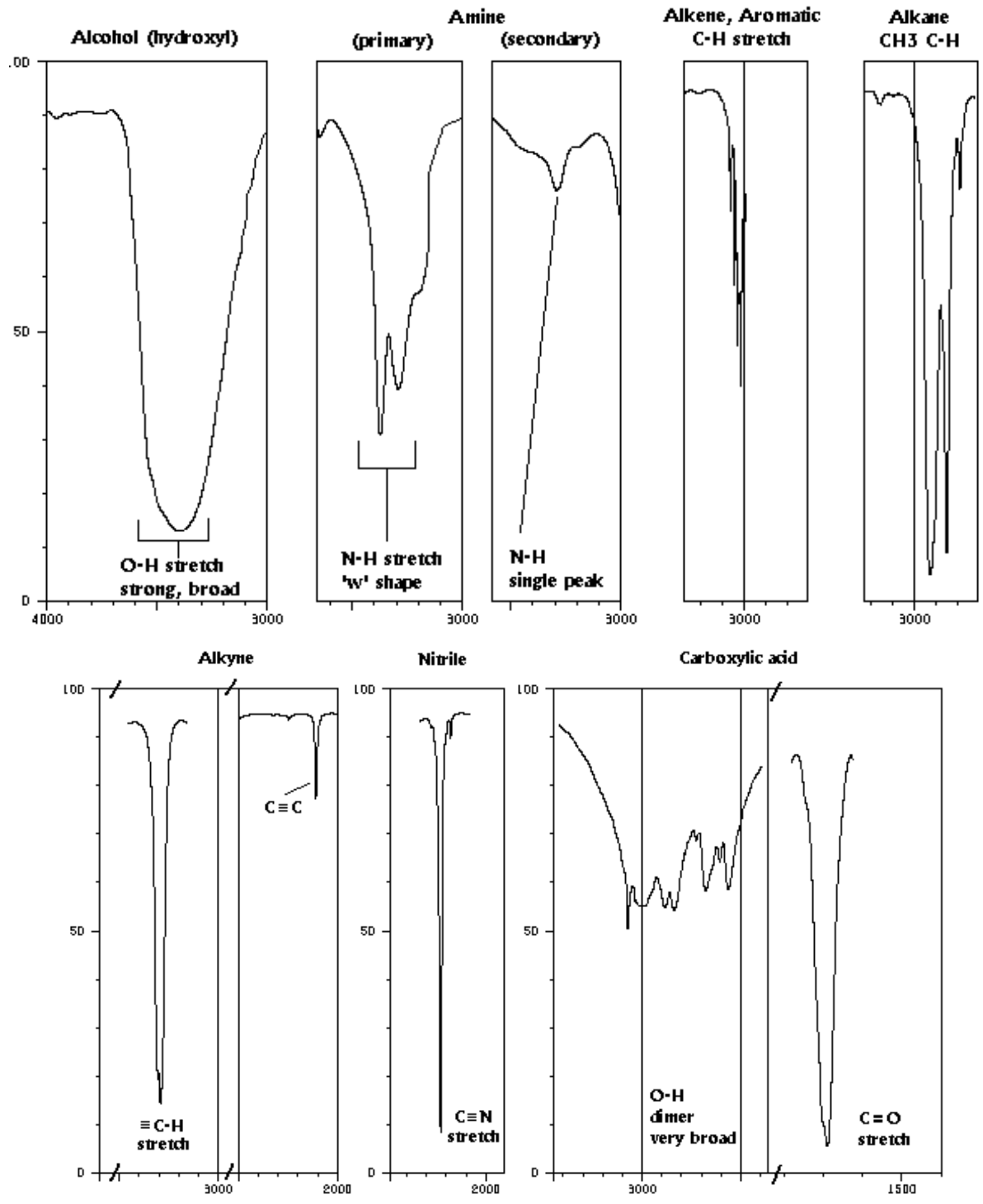
Number of Degrees of Unsaturation = nC +1 + 1/2N - 1/2 nH - 1/2 nX

e.g., Therefore, for Compound A, C_7H_{12} = (7) +1 + 1/2(0) - 1/2 (12) - 1/2(0)

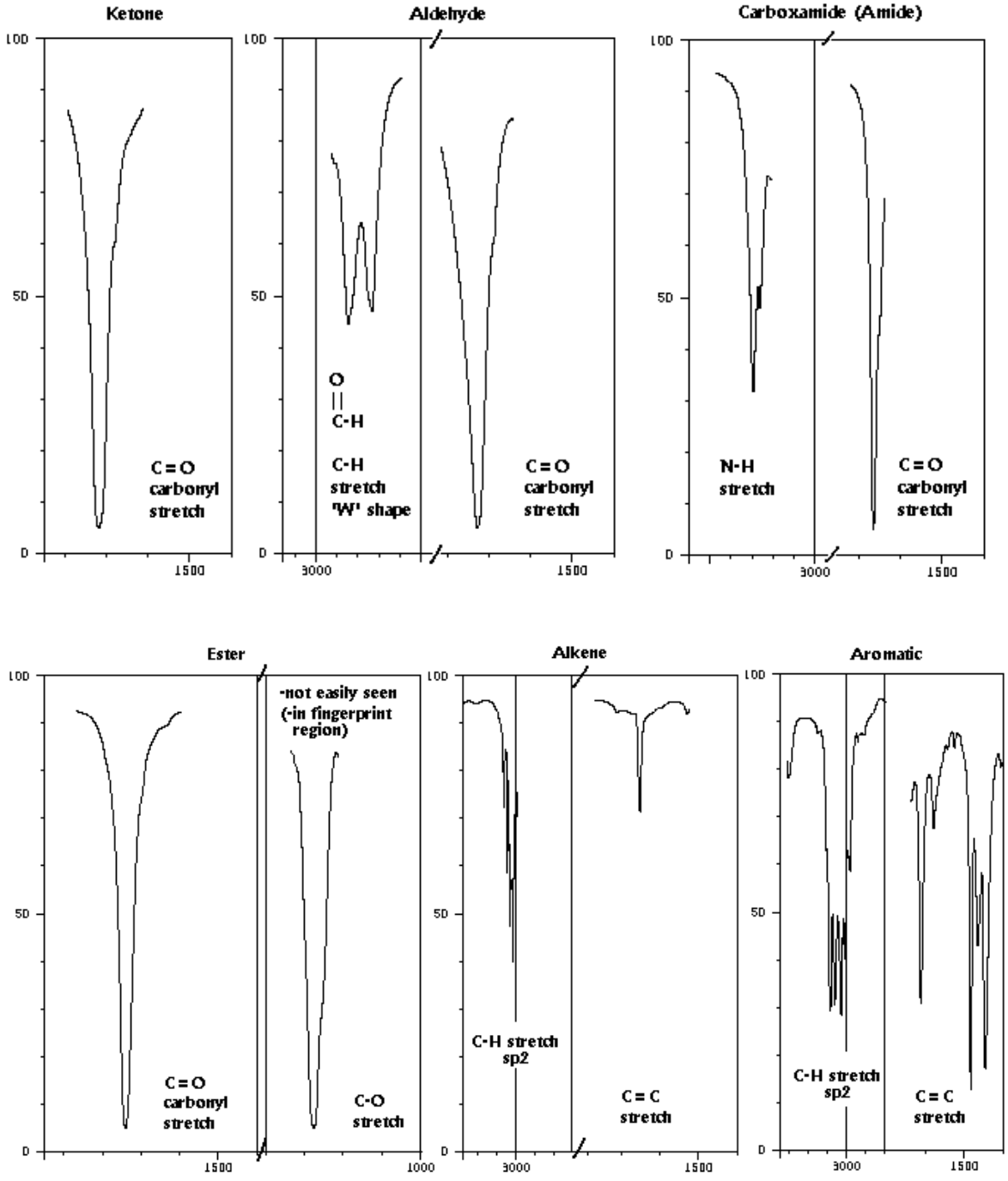
= 7 + 1 - 6 = **2** degrees of unsaturation in Compound A.

Note: an aromatic ring = 4 degrees of unsaturation, 1 for the ring + 3 for the 3 double bonds = 4

Shapes of Infrared Absorption Bands Observed for Different Functional Groups



Typical Absorption Band Shapes (cont.)



How to Interpret an Infrared Spectrum

Step 1 Divide the infrared spectrum into four main areas (use pencil and ruler and take into account any off-shift in the spectrum's wavenumbers).

i) Above 3000 cm^{-1}
ii) Between 3000 and 2000 cm^{-1}
iii) Between 2000 and 1400 cm^{-1}
iv) Below 1400 cm^{-1} (fingerprint region)

Step 2 Starting at the left of the spectrum, examine the area **above 3000 cm^{-1}**, first looking in the region near 3300 cm^{-1} and record in tabular format the presence/absence of:

i) a broad, very strong absorption band of an **'O-H'**. If present, it means you know that your molecule is at least an **alcohol**.
ii) A broad, weak to medium strength, double or single absorption band of **'N-H'**. If present it means you have an **amine** (1° or 2°) or possibly an **amide**.
iii) A sharp, medium to strong, single absorption band of **'≡C-H'** of a **terminal alkyne**. Note: If present, it means you should also see a 'C≡C' absorption near 2250 cm^{-1}.

After examining the region around 3300 cm^{-1}, look for any sharp, weak to medium absorption just above 3000 cm^{-1} (e.g. 3050 cm^{-1}) resulting from the 'C-H' stretch of a sp^2 hybridized carbon. If present, it means you have a **'C=C-H'** of an alkene or aromatic compound.

Step 3 Next examine the area between **3000 and 2000 cm^{-1}** and record the presence/absence of absorption bands or peaks.

i) First look just below 3000 cm^{-1} (e.g. 2850-2950 cm^{-1}) resulting from the 'C-H' stretch of a sp^3 hybridized carbon. If present, it means you are seeing the **'C-H'** stretch of an **-CH_2 or -CH_3** group. Note: This absorption is not very informative as most organic compounds have -CH_2 or -CH_3 groups.
ii) Then look for the extremely broad peak, actually starting at 3300 cm^{-1} and extending all the way to ~2500 cm^{-1}, caused by the **O-H dimer** between two **carboxylic acid** molecules (COOH). This absorption is probably the most difficult to see as other absorption peaks may be overlapping the broad peak.
iii) Finally look for a sharp, weak to medium peak caused by either **'C≡C'** or **'C≡N'**.
iv) If present, then the compound is an alkyne (might also have the 'C-H' of a terminal alkyne, see step 2 above) or a nitrile.

Step 4 Next examine the area between **2000 and 1400 cm^{-1}** and record the presence/absence of absorption bands or peaks.

i) First look near 1700 cm^{-1} (e.g. 1680-1750 cm^{-1}) for a sharp, strong peak resulting from the **'C=O'** stretch of a **carbonyl**. Note: <u>This absorption is very informative</u> and will be present if your compound is an aldehyde, ketone, ester, amide, or carboxylic acid.
ii) Next look near 1650 cm^{-1} (e.g. 1600-1670 cm^{-1}) for a sharp, weak peak resulting from the **'C=C'** stretch of an **alkene**.

iii) Finally look near 1600 cm^{-1} and 1500 cm^{-1} for a sharp, double peak resulting from the **'C=C'** stretch of an **aromatic ring**.

Step 5 If you dare, you may look in the **fingerprint region** (**area below 1400 cm^{-1}**) and record the presence of absorption bands or peaks.

i) First look near 1200 (1160-1310) cm^{-1} for a sharp, strong peak resulting from the **'C-O'** stretch of an **ester**.

Note: This absorption is very difficult to see and may or may not be present, i.e. conclusive if present, inconclusive if not present.

ii) If you suspect you have an aromatic ring (absorption bands at ~3030 and 1600 and 1500 cm^{-1} present), you may try to discern the substitution pattern of the benzene ring by looking at the strong absorption bands of the **ring 'C-H'** out-of-plane bending vibrations in the region 680-900 cm^{-1}.

Benzene Substitution Pattern	**Ring 'C-H' Absorption Bands Present (cm^{-1})**
monosubstituted	2 sharp peaks, 730-770, 690-710
ortho disubstituted	1 sharp peak, 735-770
meta disubstituted	3 sharp peaks, 860-900, 750-810, 680-725
para disubstituted	1 sharp peak, 800-860
1,2,3 trisubstituted	2 sharp peaks, 760-780, 705-745
1,3,5 trisubstituted	2 sharp peaks, 810-865, 675-730
1,2,4 trisubstituted	2 sharp peaks, 870-885, 805-825

Ref: McMurry, J., 2000. Organic Chemistry, 5th ed., Brooks/Cole, p.578-579, (4th ed, p.559)
Nakanishi, K., 1964. Infrared Absorption Spectroscopy, Holden Day p.27.

iii) Again, if you have an aromatic, you may also try to discern the ring substitution pattern of the benzene ring by looking at the very weak overtone-combination absorption bands of the **ring 'C-H'** stretch vibrations in the region 1670-2000 cm^{-1}.

Benzene Substitution Pattern	**Ring 'C-H' Overtone Bands Present (cm^{-1})**
monosubstituted	4 weak equally spaced and shaped sharp peaks
ortho disubstituted	3 weak irregularly spaced/shaped sharp peaks
meta disubstituted	2 weak sharp peaks + one weak broad peak
para disubstituted	2 weak sharp peaks

iv) If you suspect you have a long straight chain (>4 C) alkane, (absorption bands at 2850-2950 cm^{-1} present but not much else), you may try to see the sharp, weak absorption due to the concerted rocking of >4 $-CH_2$ in a chain. It lies in the region 720 ± 10 cm^{-1}.

Step 6 Finally, you will summarize your results by making a statement about what functional groups you suspect to be present in the molecule or perhaps you will be asked to select from a list of suggested structures, which molecule most likely would generate the spectrum just analyzed.

Infrared Analysis Practice Problems:

Use the tables below to record your results for the Infrared Spectral Analyses of the provided practice spectra on pages 47-50.

phenylacetylene	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}					
Between 3000 and 2000 cm^{-1}					
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent:

benzonitrile	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}					
Between 3000 and 2000 cm^{-1}					
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent:

styrene	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}					
Between 3000 and 2000 cm^{-1}					
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent:

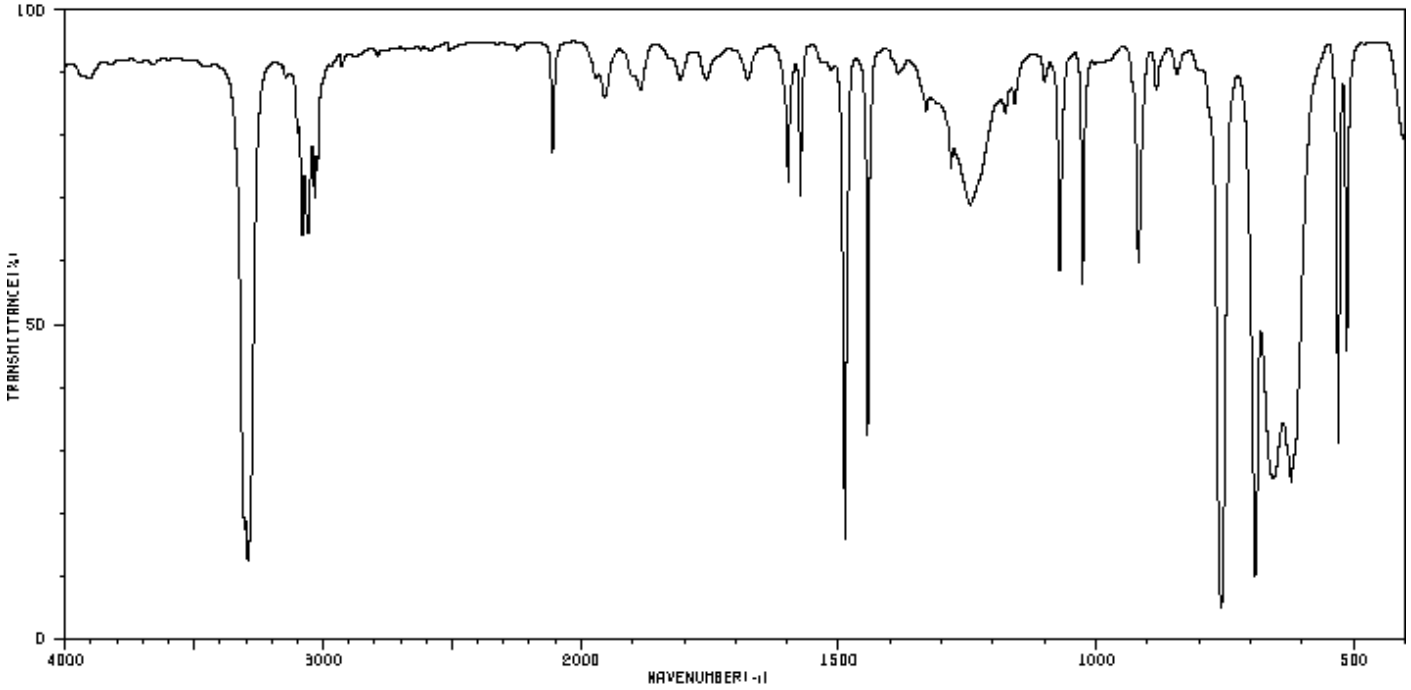
diethyl ether	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}					
Between 3000 and 2000 cm^{-1}					
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent:

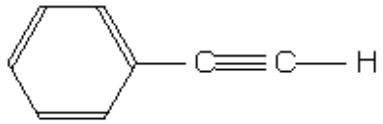
HIT-NO=1445	SCORE= ( )	SDBS-NO=1444	IR-NIDA-63379 : LIQUID FILM

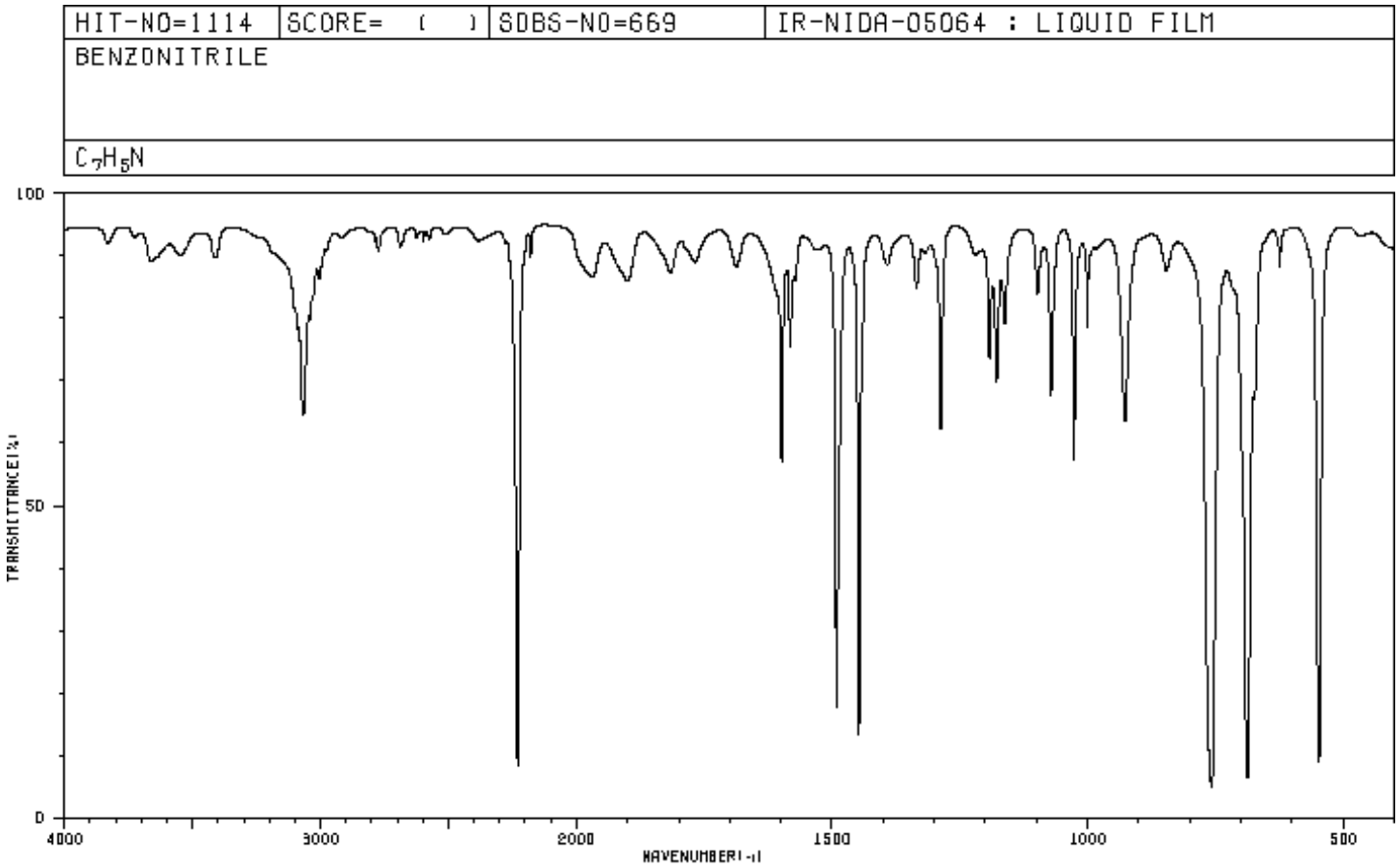
PHENYLACETYLENE

C_8H_6

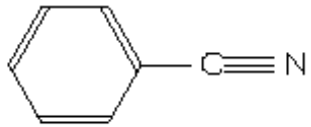


3906	86	2110	74	1674	68	1176	81	843	86
3306	16	1954	84	1488	15	1159	81	757	4
3291	12	1900	86	1444	31	1100	84	692	9
3081	62	1886	84	1386	86	1071	67	666	24
3058	62	1808	86	1331	81	1026	53	621	23
3034	66	1757	86	1282	72	918	57	530	30
3022	72	1698	70	1245	66	883	84	514	43





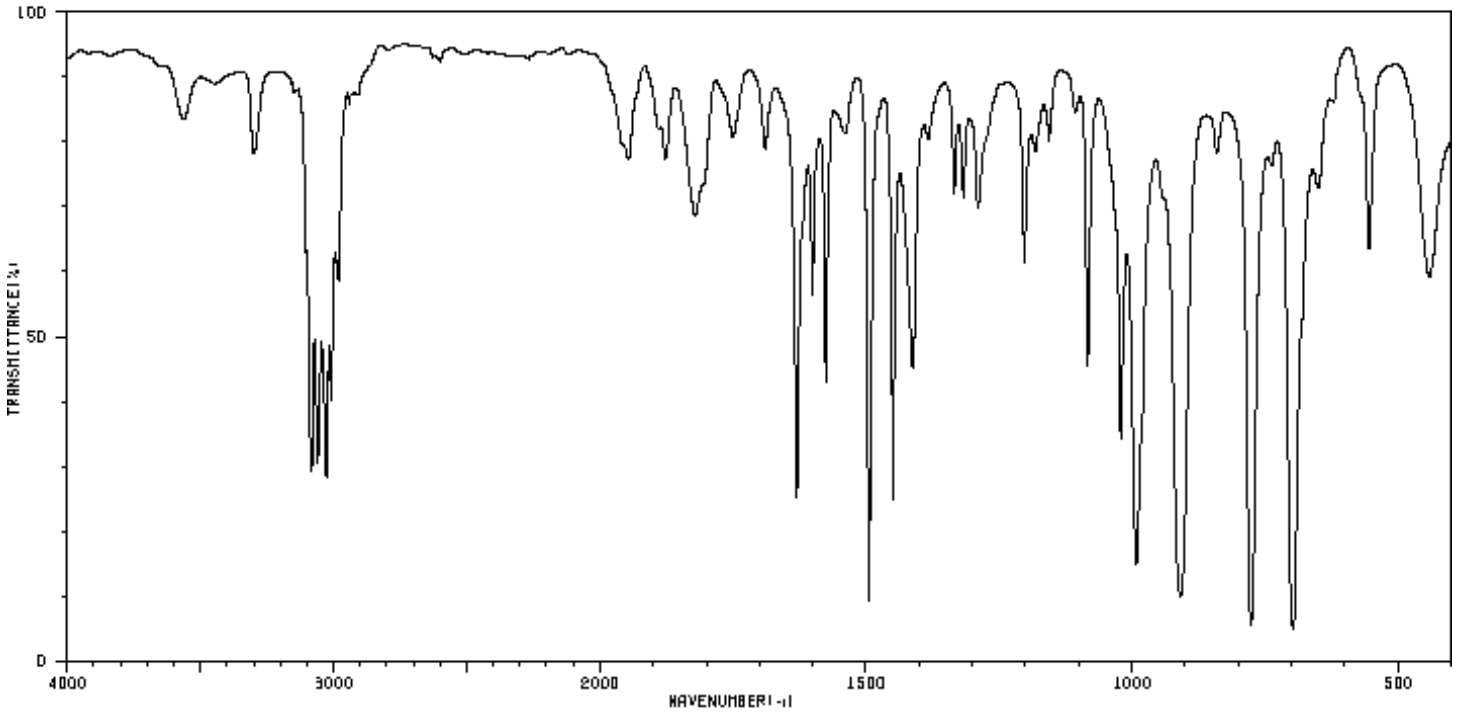
3646	86	2178	86	1582	72	1288	60	1001	74
3412	86	1969	84	1572	81	1193	70	927	60
3088	74	1899	81	1492	17	1178	66	846	64
3066	62	1816	84	1448	12	1163	77	758	4
3004	84	1768	86	1441	72	1098	81	688	6
2256	84	1688	84	1392	84	1072	64	625	64
2230	8	1599	66	1335	81	1027	66	548	8



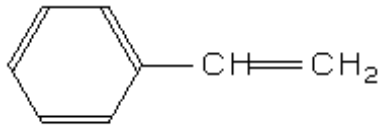
HIT-NO=2170	SCORE= ( )	SDBS-NO=3044	IR-NIDA-10290 : LIQUID FILM

STYRENE

C_8H_8



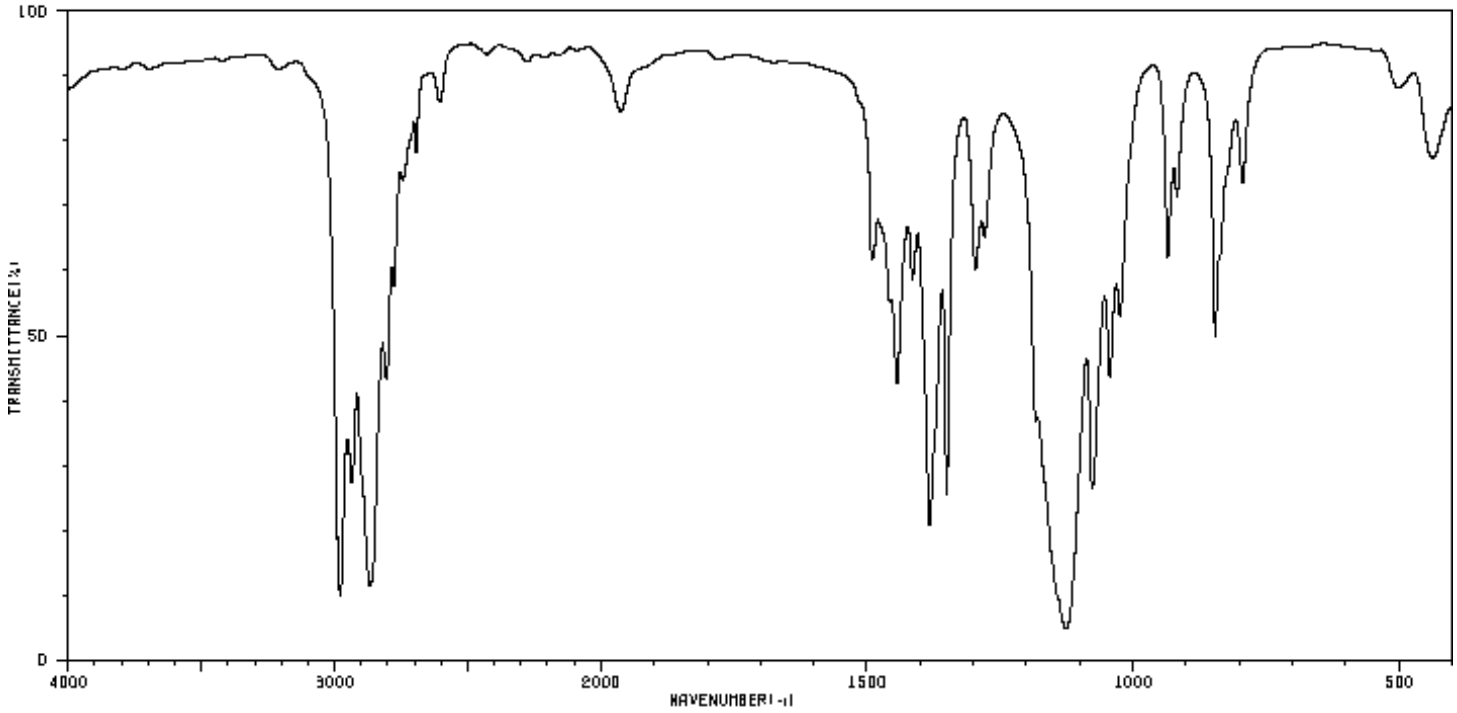
3299	74	1946	74	1496	9	1202	68	841	74
3082	28	1876	74	1449	23	1182	74	777	5
3060	29	1821	66	1412	43	1156	77	736	72
3027	27	1689	77	1383	77	1083	43	698	4
3009	38	1630	24	1334	70	1021	33	650	70
2980	57	1601	59	1317	66	992	14	555	60
1955	77	1576	41	1290	66	909	8	442	67



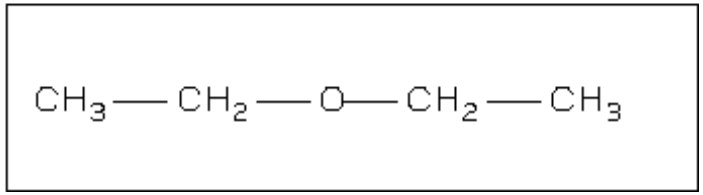
HIT-NO=1756	SCORE= ( )	SDBS-NO=2150	IR-NIDA-03139 : LIQUID FILM

DIETHYL ETHER

$C_4H_{10}O$



2989	17	2693	74	1383	20	1024	60
2979	9	2604	81	1351	24	935	58
2935	26	1962	81	1297	58	917	68
2868	10	1490	68	1279	62	846	47
2804	41	1457	53	1126	4	794	70
2777	55	1444	41	1077	25	501	84
2743	70	1416	67	1043	42	438	74



Experiment 10
Fischer Esterification: An ester from a carboxylic acid and an alcohol

Emil Fischer (1852-1919). After discovering phenylhydrazine as a graduate student, he is best known for all his research on stereochemistry of carbohydrates (stereochemistry of (+)-glucose in 1888; Fischer projections for depicting the 3D structure of tetrahedral carbon atoms in 2 dimensions in 1891), as well as many additional studies on amino acids, proteins, purines, and indoles. He won the second Nobel Prize (for Chemistry) in 1902, for his work on sugar and purine synthesis.

Preparation

Before beginning this experiment, you should have read through the details of this experiment and prepared a flow chart for the procedure to be followed, and

1. studied "Carboxylic Acid Derivatives and Nucleophilic Acyl Substitutions" of the theory component of the course,

2. completed the equivalent of Experiments 1 through 9, CHEM350

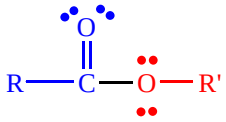
You may also wish to read, Chapter 19 of *The Organic Chem Lab Survival Manual* (Chapter 26 in 3rd ed.).

Objectives

The purpose of this experiment is to provide a practical example of the synthesis of an ester, using the Fischer esterification method. The product is formed during reflux, and will be purified by distillation, and assessed by refractive index. Also further practice in obtaining and interpreting infrared spectra and ^{1}H-NMR will be provided.

Introduction

Esters are naturally abundant and readily synthesized, but all have the same following structure,



Every day fragrances, such as the 'rich smell' of fresh ground coffee, are a combination of esters (>200 identifiable esters found so far in coffee!!). However, some esters are readily recognized by their very characteristic flavour or odour.

Esters are derivatives of carboxylic acids, and are mainly prepared by one of four methods:

1. Direct esterification of a carboxylic acid with an alcohol (Fischer Esterification).
2. Alcoholysis of acid chlorides, anhydrides, or nitriles.
3. Reaction of a carboxylic acid salt with an alkyl halide or sulfate.
4. Via the trans-esterification reaction.

In Table 10.1 below, several examples of Fischer esterification products are given.

Table 10.1. Combinations of carboxylic acids and alcohols resulting in 'familiar' esters

Ester	Structure	Fragrance/Flavour	Carboxylic acid	Alcohol
iso-butyl formate	$HCO_2CH_2CH(CH_3)_2$	Raspberry essence	formic acid	*iso*-butanol
Propyl acetate	$CH_3CO_2CH_2CH_2CH_3$	Pear essence	acetic acid	1-propanol
iso-amyl acetate	$CH_3CO_2(CH_2)_2CH(CH_3)_2$	Banana essence	acetic acid	*iso*-amyl alcohol
Octyl acetate	$CH_3CO_2CH_2(CH_2)_6CH_3$	Orange essence	acetic acid	octanol
Benzyl acetate	$CH_3CO_2CH_2C_6H_5$	Peach essence	acetic acid	benzyl alcohol
iso-butyl propionate	$CH_3CH_2CO_2CH_2CH(CH_3)_2$	Rum essence	propionic acid	*iso*-butyl alcohol
Ethyl butyrate	$CH_3CH_2CH_2CO_2CH_2CH_3$	Pineapple essence	butyric acid	ethanol
Methyl butyrate	$CH_3CH_2CH_2CO_2CH_3$	'Apple like' essence	butyric acid	methanol
iso-amyl butyrate	$CH_3CH_2CH_2CO_2(CH_2)_2CH(CH_3)_2$	Apricot essence	butyric acid	*iso*-amyl alcohol
iso-amyl valerate	$CH_3(CH_2)_3CO_2(CH_2)_2CH(CH_3)_2$	'real' Apple essence	valeric acid	*iso*-amyl alcohol
Methyl anthranilate	$H_2NC_6H_4CO_2CH_3$	Grape essence	anthranilic acid	methanol
Ethyl laurate	$CH_3(CH_2)_{10}CO_2CH_2CH_3$	Tuberose essence	lauric acid	ethanol
Methyl salicylate	$HOC_6H_4CO_2CH_3$	Oil of wintergreen	salicylic acid	methanol

iso-butanol = 2-methyl-1-propanol,
iso-amyl alcohol = 2-methyl-1-butanol
Tuberose is the fragrance of a tropical flowering plant with 'funnel' shaped flowers (Tuber + Rose).

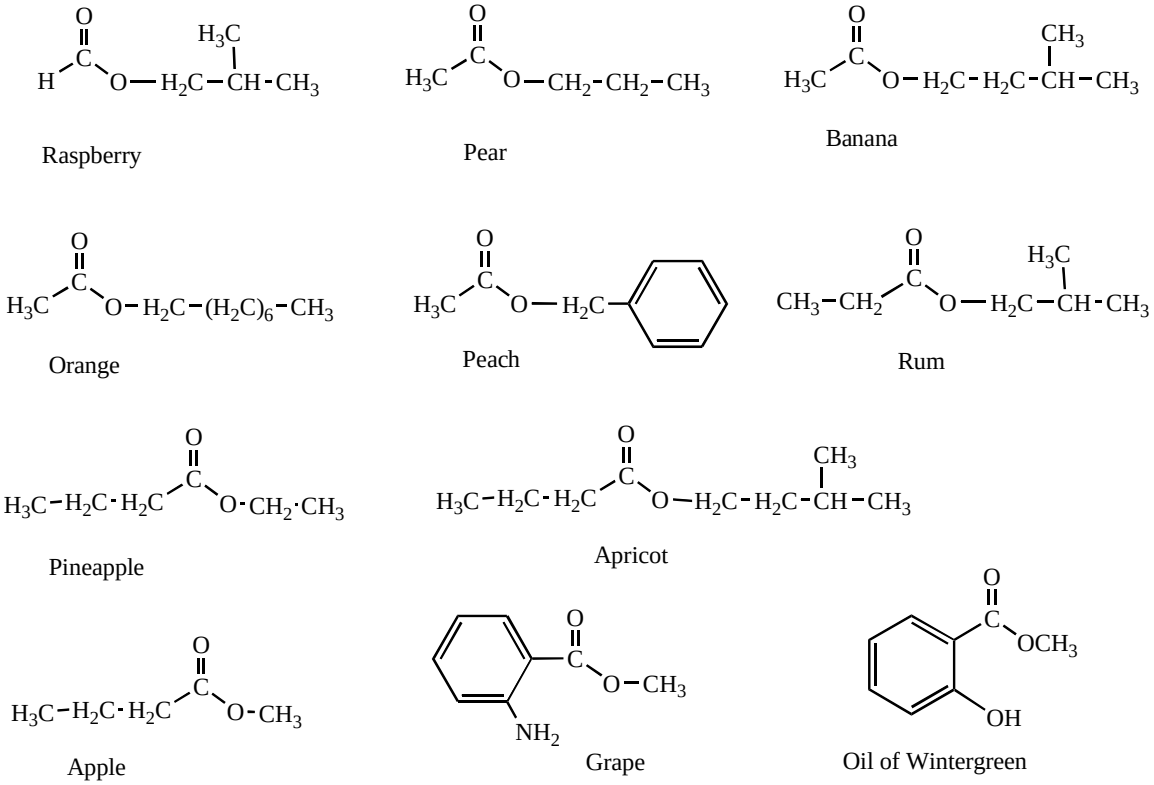
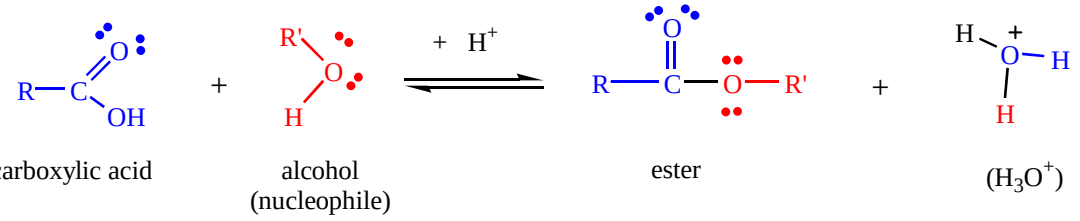


Figure 10.1. Structures of some familiar esters

In the Fischer esterification reaction, esters can be prepared by the **reversible**, acid-catalysed, combination of a carboxylic acid with an alcohol. Because it is reversible, the reaction must be shifted to the product side by using excess reagent, or removing one of the products. This reaction is also limited by any steric hindrance in the carboxylic acid or the alcohol. The general equation for a Fischer esterification is summarized below in Fig. 10.2.



carboxylic acid | alcohol (nucleophile) | ester | (H_3O^+)

Figure 10.2 Fischer esterification reaction for ester formation from a carboxylic acid.

The acid catalysed mechanism for a Fischer esterification is shown on the next page in Figure 10.3. Equilibrium is reached at every step in the reaction's multi-step mechanism. The reaction is driven to the right, towards the desired end product (i.e., Le Châtelier's Principle). In this experiment, a large excess of one of the reactants is used. The acids used in this experiment have a strong dehydrating capability and help 'soak up' the reaction water, also assisting in pulling the reaction to the right.

Fischer Esterification Reaction Mechanism (nucleophilic acyl substitution)

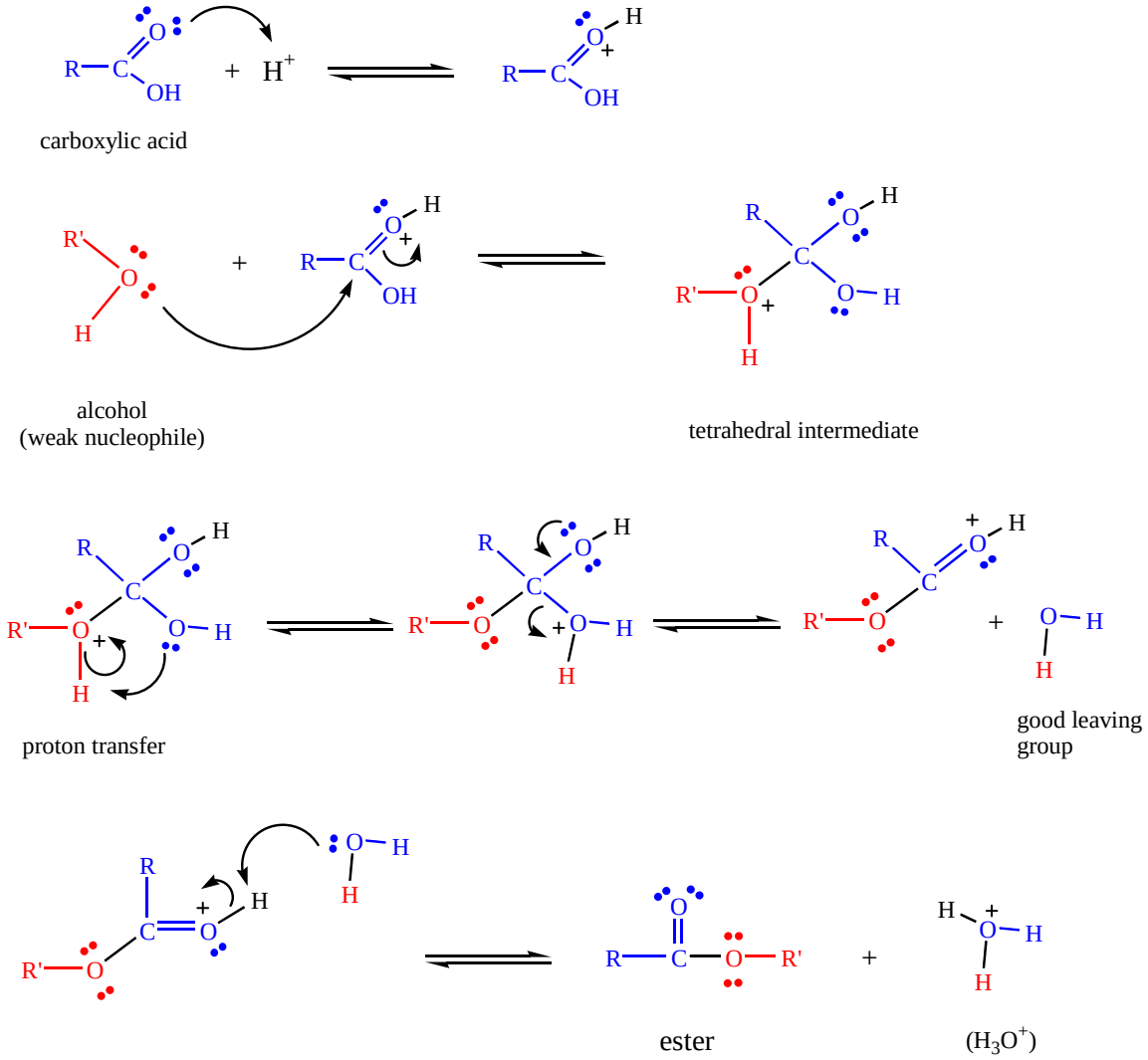
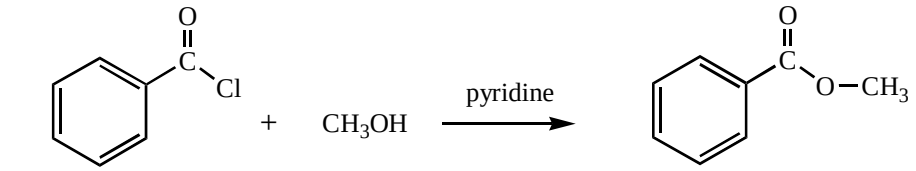


Figure 10.3 Reaction mechanism for the Fischer esterification (under acidic conditions)

Additional Information on the Synthesis of Esters

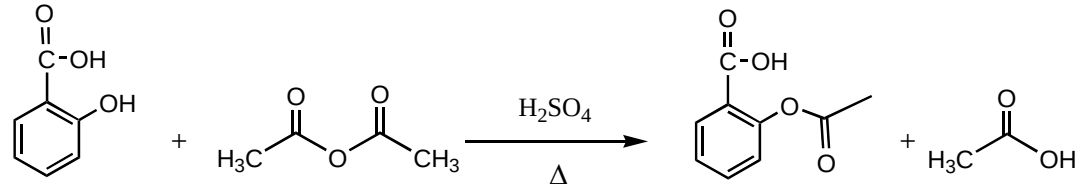
The best and most efficient way to synthesize an ester is to convert an acid chloride via alcoholysis (Fig. 10.4a). For more information, see 'Chemistry of Acid Halides' and 'Chemistry of Esters' in your textbook.



acid chloride (benzoyl chloride) | alcohol (methanol) | ester (methyl benzoate)

Figure 10.4a Esters from acid chlorides.

Another example of alcoholysis is when alcohols and phenols react with acetic anhydride (Figure 10.4b), in the presence of an acid catalyst, to yield esters. However, there are serious limitations to the formation of esters by this method, some of which are discussed in your text under 'Chemistry of Ester'; i.e., please note that half the acetic anhydride molecule is 'wasted' by this method.



salicylic acid
(2-hydroxybenzoic acid)
mp= 159° C
Mwt= 138.12 g/mol
amt used = ?
moles = ?

acetic anhydride
mp = -73.1° C
d=1.08 g/mL
Mwt = 102.09 g/mol
amt used = ?
moles = ?

aspirin
(acetylsalicylic acid)
mp=135° C
Mwt = 180.17 g/mol
max. moles = ?
Theor.Yield = ?

acetic acid
(ethanoic acid)
mp=16.6° C
Mwt = 60.05 g/mol

Figure 10.4b Salicylic acid's reaction with acetic anhydride to form an ester.

Final Additional Background Information

About Boiling Points

To correct for barometric pressure (**BP**) effects on the boiling point (bp) of a liquid, use the following formula to approximate the effect, or use a nomograph.

Corrected bp = observed bp + ((760 mm Hg – **BP** mm Hg)/10 mmHg)* 0.5 °C

where **BP** is the observed barometric pressure.

About Refractive Indexes

To correct for temperature effects on the refractive index (n_D) of a liquid, use the following formula, assuming that the sample temperature is equal to room temperature:

Corrected Refractive Index = observed n_D + (Room Temp – **20° C**)* 0.00045.
(to 20° C**)**

Procedure

Part A: Preparation of reagents and equipment.

1. The procedure is given for a 4:1 molar ratio when excess of an alcohol is used. Reverse the ratio if you synthesize an acetate ester. See Table 10.2 below.

Table 10.2 Choose one pair of carboxylic acid and alcohol.

Ester Name	Carboxylic acid	Moles used	Alcohol	Moles used
Isoamyl acetate	acetic acid	0.48	isoamyl alcohol	0.12
Methyl butanoate	butyric acid	0.12	methanol	0.48
Isoamyl butanoate	butyric acid	0.12	isoamyl alcohol	0.48
Isobutyl propionate	propionic acid	0.12	isobutyl alcohol	0.48
Propyl ethanoate	acetic acid	0.48	1-propanol	0.12
Methyl salicylate	*salicylic acid*	*0.05*	*methanol*	*0.10*

**Note: the combination of salicylic acid and methanol requires special workup procedures.*

2. Set up a reflux apparatus as shown in Figure 10.5, using a clean and dry condenser and a appropriately sized round-bottomed flask.

3. Measure out 0.12 mol of an isoamyl alcohol and add it to the round-bottomed flask.

4. Measure out 0.48 mol of acetic acid, and add it to the round-bottomed flask already containing the alcohol.

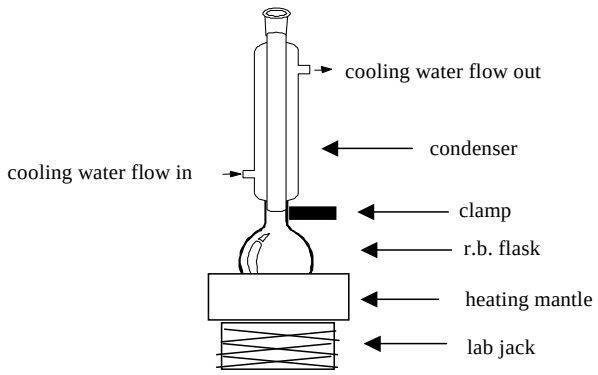


Figure 10.5 Reflux apparatus

Part B: Synthesis of the ester

1. Add several boiling stones to the round-bottomed flask containing the alcohol and carboxylic acid.

2. Very slowly and carefully add 0.05 moles of concentrated sulphuric acid, while swirling and cooling the flask.

3. Quickly reassemble the reflux apparatus, and heat the reaction for **45min to 1 hour,** while maintaining a steady reflux. (during the 1 hour reflux period, please start your next experiment).

Part C: Reaction Workup-recovery and purification of the ester

1. Remove the heating mantle and cool the reaction mixture to room temperature. You may speed the cooling up by placing the stoppered round-bottomed flask into a lukewarm water bath. Do not use an ice bath!

2. Pour the cooled mixture into a small separatory funnel containing 20 mL of water ice. Rinse the round-bottomed flask with a further 5 mL of cold distilled water, and add this also to the separatory funnel. Stopper the separatory funnel and invert it several times.

3. Extract your ester with 25 mL of diethyl ether and separate the layers. Keep the aqueous layer. Do not discard anything yet.

4. Wash the crude ester (in the diethyl ether) with 25 mL cold distilled water. [The purpose of this step is to wash away the water soluble impurities].

5. Wash the crude ester (in diethyl ether) with 25 mL of 5% M sodium carbonate. Be extra careful to frequently vent the separatory funnel, as you gently swirl the contents of the funnel. Do not invert the funnel at first. Carbon dioxide gas is formed during this step, and significant pressure builds up inside the funnel. When the amount of gas has declined, then invert and periodically vent the funnel.

6. Repeat the wash of the crude ester with another 25 mL of 5% sodium carbonate. Less CO_2 gas should be produced in this step than the previous.

7. Check the pH of the solution. It should be close to pH = 7.0.

8. Wash the crude ester with 25 mL of saturated sodium chloride. Draw the aqueous salt solution out the bottom of the funnel and pour the ester out the top of the separatory funnel into a small, clean, dry Erlenmeyer flask.

9. Dry the crude ester with anhydrous calcium chloride. Stopper and swirl the flask periodically for 15 min. Be sure to add enough of the anhydrous drying agent so that some of it is still freely moving in the liquid. When the ester is dry, the crude ester should be clear and transparent; cloudiness indicates that water is still present.

10. Decant the dry ester (or use a Pasteur pipette), and if time permits, set up an apparatus for a simple distillation.

11. Distil the crude ester, and collect the product in an appropriate sized, preweighed, clean, dry, round-bottom flask.

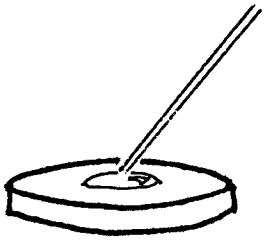
Part D: Characterization of the ester

1. Determine the yield, boiling point, refractive index, and % yield of the crude/purified ester. Store your ester in a suitably labelled glass vial, and hand it to your instructor for grading.

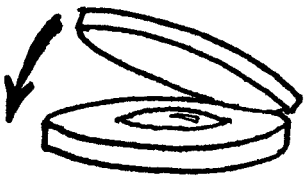
Part E: Infrared spectroscopy

1. With the assistance of your instructor, obtain an infrared spectrum of your pure product, and compare it to your starting reagents spectra. Submit these spectra with your data tables with your laboratory report.

   Preparation of the sample for infrared spectroscopy is done by 'thin film' in a salt (NaCl or KBr) disk 'sandwich' (see diagram below).



Place drop of liquid sample on disk using a Pasteur pipette.



Place another salt disk on top of the liquid, and gently press into a thin film.

Remember to only handle the salt disks by their edges. Clean the disks with chloroform. Do <u>not</u> use water or acetone.

Safety

Methanol is poisonous if swallowed. Its vapour is harmful to the eyes, lungs and skin and other organs. Highly flammable.

Ethanol is poisonous and its toxicity is increased by the presence of the denaturing substances that are added to laboratory ethanol in order to reduce its illegal consumption. High concentrations of ethanol vapour can be dangerous. Highly flammable.

1-Propanol is harmful to the lungs, skin, eyes and other organs. Poisonous if swallowed. Highly flammable. Use in a fume hood.

2-Methyl-1-propanol (isobutyl alcohol) is a flammable liquid, and an irritant.

3-Methyl-1-butanol (isoamyl alcohol) is an irritant. Avoid breathing vapors.

Butyric acid is corrosive and toxic.

Propionic acid (propanoic acid) is corrosive and toxic.

Glacial acetic acid is poisonous if swallowed. Both the liquid and vapour are irritating to the skin and eyes and can cause burns and ulcers. Flammable.

Concentrated sulfuric acid is highly corrosive. Wear gloves and proper eye protection when using this substance. Avoid contact with skin or clothes. Use only in a fume hood.

Sodium carbonate is basic, but does not pose any specific safety problems. Will decompose on the addition of acid to form carbon dioxide gas.

Saturated sodium chloride is an irritant and hygroscopic.

Sodium sulfate is an irritant and is hygroscopic.

Chloroform (trichloromethane) is poisonous if swallowed. Its vapour is an anaesthetic and causes nausea, headaches, vomiting and unconsciousness.

Additional information regarding the potential hazards in handling these chemicals may be obtained from the Material Safety Data Sheets that are available in the laboratory.

Waste disposal

The aqueous washes from the reaction workup may be washed down the drain with plenty of water.

All organic wastes should be placed into the appropriate non-halogentated waste container.

Write-up

This experiment should be written up using the standard format for "preparative type" experiments. Do not forget to report the mass of alcohol and carboxylic acid used, the mass of crude ester obtained, and the mass, percentage yield and boiling point plus refractive index data of the product. Your report should also include an assessment of the success of the experiment based on your analysis of the infrared spectra.

Remember to photocopy you lab report before mailing it to your tutor for marking.

Questions

Answers to be submitted with report.

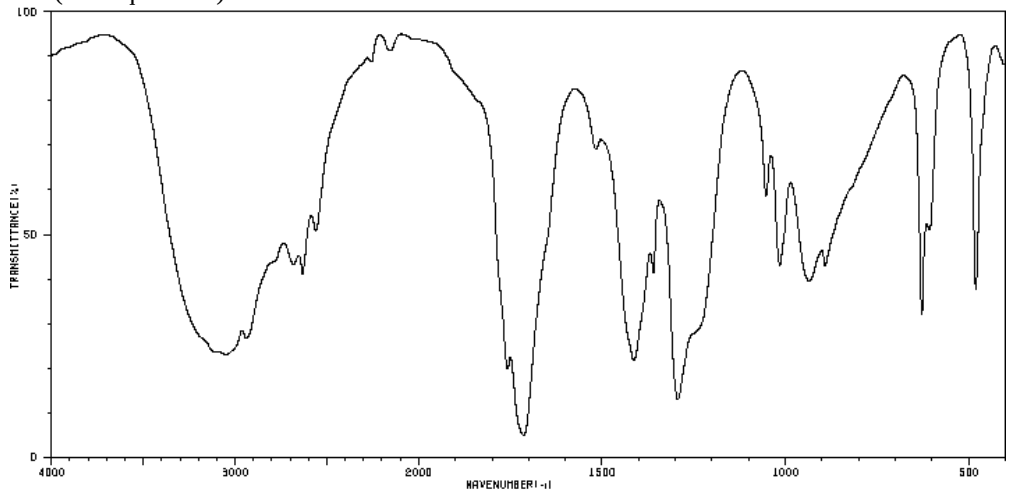
1. If the cost of **both** the alcohol and carboxylic acid were prohibitive, how would you maximize the yield of your Fischer esterification product while keeping costs down?

2. Why did you wash your product with water (3X), before washing it with the solution of sodium hydrogen carbonate? What was the purpose of washing with sodium hydrogen carbonate?

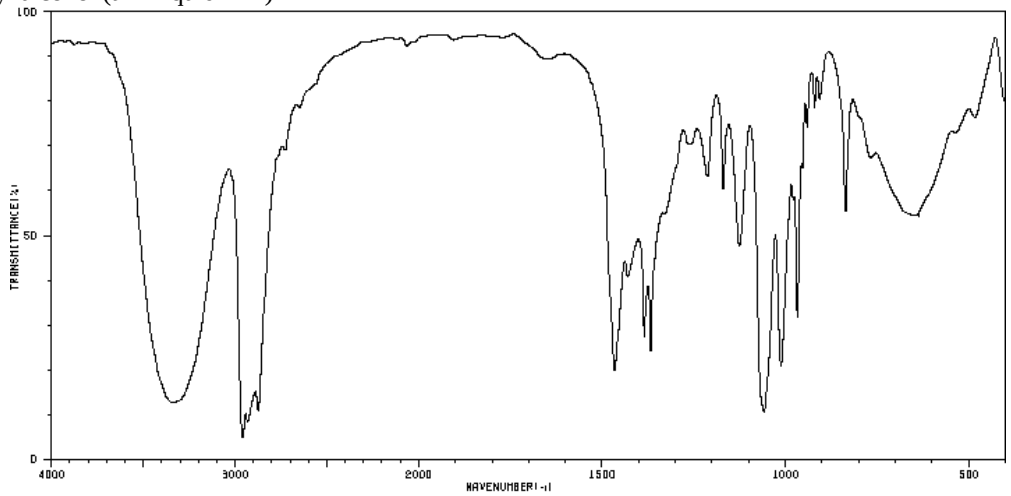
3. Explain the function of the acid catalyst in a Fisher esterification reaction.

4. What would the reactants be to produce isoamyl valerate via Fischer esterification reaction?

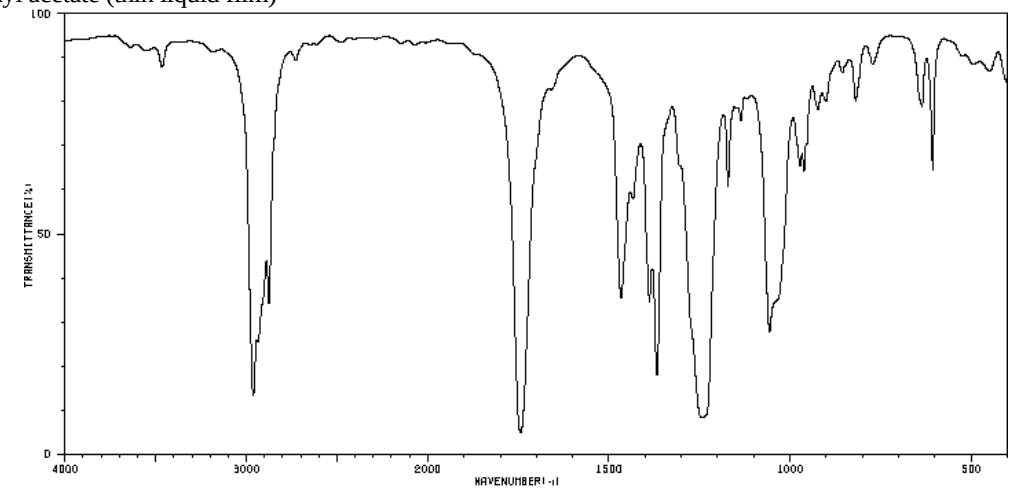
Acetic acid (thin liquid film)



Isoamyl alcohol (thin liquid film)



Isoamyl acetate (thin liquid film)



Experiment 11
Reactions of the common functional groups-- Part 2: Alcohols and alkyl halides

"I haven't touched a drop of alcohol since the invention of the funnel". Malachy McCourt (1931-)

On the abundance of alkyl halides: Edible Hawaiian algae, *Asparagopsis taxiformis* contains more than 100 different halogenated compounds, and 5 million tons of chloromethane are formed from natural sources every year (Ref: Chapter 10: 'Alkyl Halides' in McMurry 5th ed., p.355-384, and in McMurry's 4th ed. p. 342).

Preparation

None. However, in order to obtain the maximum benefit from this experiment you should have completed:

1. 'Reactions of Alkyl Halides', in the theory component of the *Chemistry 350* course, and
2. 'Alcohols and Phenols' in the theory component of this course.

Objectives

The purpose of this experiment is to illustrate to the student a selection of those reactions that are typical of two important classes of organic compounds: **alcohols and alkyl halides**. In this experiment, a variety of tests will be performed on a selection of known compounds. In a later experiment, the student will be expected to use the same tests plus Infrared and NMR analysis in order to identify assigned unknown compounds.

Theory

As we have previously stated in the introduction to *Chemistry 350's* Experiment 6, spectroscopic techniques have replaced many of the "wet" techniques that were formerly used by organic chemists to determine the identity of an unknown compound. However, many of the older techniques do illustrate the chemical differences between the various chemical families, thus there is much to be said for studying these techniques in an introductory organic chemistry course.

In this experiment you will study two reactions that enable organic chemists to distinguish between primary, secondary and tertiary alcohols. You will also examine the behaviour of a number of alkyl halides and some related compounds under both S_N1 and S_N2 conditions.

Reactions of Alcohols

Primary and secondary alcohols can be oxidized by a variety of reagents, whereas tertiary alcohols are not oxidized under normal conditions (see Figure 11.1). Depending on the conditions and the reagents used, primary alcohols can be oxidized to aldehydes or carboxylic acids. Secondary alcohols are oxidized to ketones:

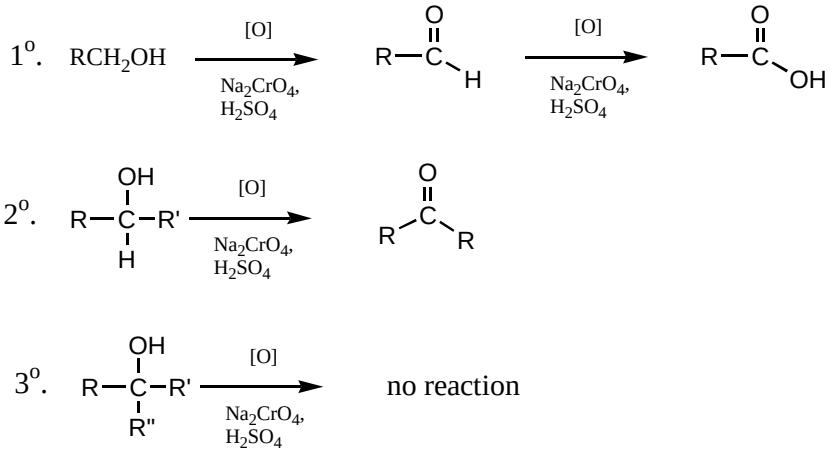


Figure 11.1 Oxidation reactions of primary, secondary and tertiary alcohols.

The oxidizing agent used in this experiment is a mixture of sodium dichromate and sulfuric acid. If a reaction occurs, the yellow-orange colour of the oxidizing agent changes to green, due to the formation of chromium(III) ions.

When the reaction can proceed via the formation of a stable carbocation, an alcohol will react with a mixture of hydrochloric acid and zinc chloride (known as Lucas reagent) to form an alkyl halide (see Fig. 11.2). The alkyl halide that forms is insoluble in the aqueous reaction mixture and thus the solution becomes cloudy if a reaction occurs. In general, tertiary alcohols react immediately, secondary alcohols produce 'cloudiness' within a few minutes, and primary alcohols do not react even after being allowed to stand for an hour or more:

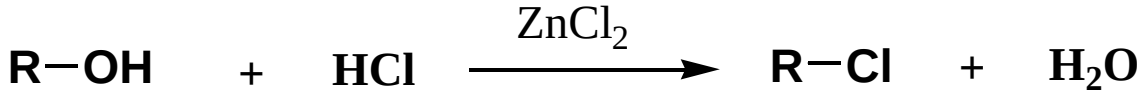


Figure 11.2 Lucas reagent reactions of alcohols.

Reactions of Alkyl Halides

Alkyl halides can react with nucleophiles by either an S_N1 or S_N2 mechanism. By studying the behaviour of an unknown alkyl halide under conditions that are known to favour either one of these two mechanisms, it may be possible to make certain deductions regarding the structure of the unknown compound. In this experiment, you will use known compounds in order to observe how structural variations influence the rate at which a compound reacts in an S_N1 or S_N2 reaction.

Silver nitrate dissolved in ethanol is a useful reagent for assessing the reactivity of an alkyl halide in an S_N1 reaction (see Fig. 11.3). The nitrate ion is a poor nucleophile, thus reaction by an S_N2 mechanism is unlikely to occur. In addition, ethanol is a moderately powerful ionizing solvent and will favour reaction by the S_N1 route. The formation of an insoluble silver halide also serves to enhance the forward reaction. (**Note:** products other than ROEt are formed, e.g., alkene addition products).

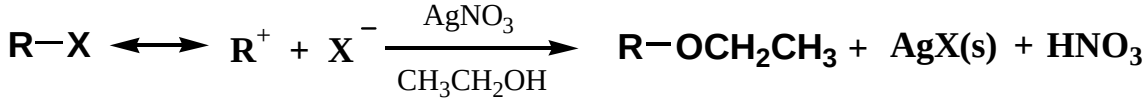


Figure 11.3 Silver nitrate S_N1 reactions of alkyl halides.

Acetone is a solvent of low polarity, which makes it a useful solvent for S_N2 reactions. Iodide ion is an excellent nucleophile, thus if a chemist wishes to study the S_N2 reactions of an alkyl halide, the reaction of the alkyl halide with potassium (or sodium) iodide dissolved in acetone is a good choice; a.k.a. Finkelstein reaction.

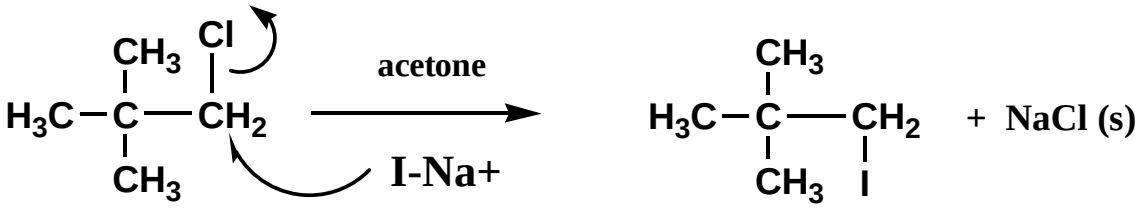


Figure 11.4 Sodium iodide S_N2 reactions of alkyl halides.

Although potassium and sodium iodide are soluble in acetone, the corresponding chlorides and bromides are insoluble, and the formation of a precipitate increases the tendency of the reaction to proceed to the right. Remember that an S_N2 mechanism goes through a bimolecular transition state.

Summary Table of Chemical Diagnostic Functional Group Tests:

Chemical Family	Solubility Class	Function Group Tests	Comment
Alkane	Neutral	Bromine Test, Sulfuric acid Test	Slow reaction, unreactive to Baeyer and sulfuric acid tests
Alkene	Neutral	Baeyer Test Bromine Test	Fast reaction. Color of reagent fades. No HBr formed in Bromine Test.
Alkyne	Neutral	Ammoniacal Silver Test	Terminal triple bond detected. Pptte formed
Alcohol	Neutral	1. Acetyl chloride treatment to form ester, then Ferric Hydroxamate Test 2**. Chromate Oxidtion** 3. **Lucas's test ($ZnCl_2$ in HCl)** Derivative Formation 1. 3-5-dinitrobenzoates 2. α-naphthylurethanes	-Forms the hydroxamate ester, then a Fe^{3+} colored complex **-Test for 1° and 2° alcohols. 3° alcohols do not react** **-Test for 2° or 3° alcohols. Solution turns cloudy.** -must be performed in a fumehood. -alcohol and glassware must be absolutely dry.
Alkyl Halides	Neutral (Acid/Base Insoluble)	**1. Silver Nitrate/Ethanol** **2. Sodium iodide/Acetone** 3. Beilstein Test Derivative Formation 1. S-alkylthiuronium picarates 2. Nitro compounds	-Ag nitrate test negative for vinyl and aryl halides. -both tests classify as 1°, 2° or 3°halogenated hydrocarbons -green to blue green flame indicates halogen cmpd.-test unreliable -Tertiary alkyl halides do not form this derivative. -may form mono-, di- or tri-nitro compounds
Ester	Neutral	1. Hydrolysis to carboxylic acid 2. Ferric hydroxamate Test	-Saponification with 30% NaOH then acidification. -Deep red-purple complexes formed with Fe^{3+}
Aldehyde	Neutral	1. 2,4-dinitrophenylhydrazine (2,4-DNP) 2. Tollen's Test	-Forms the 2,4-DNP derivative, a highly coloured precipitate. -Silver mirror formed in Tollen's Test
Ketone	Neutral	1. 2,4-dinitrophenylhydrazine (2,4-DNP) 2. Tollen's Test 3. Iodoform Test	-Forms the 2,4-DNP derivative, a highly coloured precipitate. -No silver mirror formed in Tollen's Test -detects methyl ketones. Yellow pptte & medicinal odor
Amide	Neutral	1. Amide Hydrolysis, 2. Ferric hydroxamate Test	-Saponification with 30% NaOH and detection of NH_3 in vapors. -See esters. Required more drastic reaction (>150º C)
Carbohydrate	Neutral	1. Benedict's Reagent 2. Tollen's Test	-Detects reducing sugars. Brick red pptte of Cu2O formed. -silver mirror formed by reducing sugars (aldehydes and α-hydroxy ketones)
Phenol	Weak Acid	1. Ferric Chloride Test, 2. Pauly Test	-Blue or purple complex for simple phenols. Red or green complexes with polysubstituted phenols -Red, orange, yellow-green or blue azo compounds formed when treated with diazonium salt of sulfanilic acid
Carboxylic acid	'Strong' Acid	Solubility	Soluble in 5% NaOH and sat. $KHCO_3$
Amine	'Strong' Base	1. Hinsberg Test, 2. Pauly Test for aromatic amines	-Forms the sulfonamide of 1º and 2º amines -Red, orange, yellow-green or blue azo compounds formed when treated with diazonium salt of sulfanilic acid

Procedure

Make sure that your test tubes are clean and dry. The presence of acetone in your test tubes may affect your results.

For each test carried out, record your observations, explain what the observations infer, and write an equation.

Part A: Reactions of alcohols

Perform the tests described below on each of the following alcohols:

1-butanol, 2-butanol, 2-methyl-2-propanol and cyclohexanol (use the sample obtained in Experiment 3, if you still have some).

1. **Oxidation of Alcohols**
   Place about 3 mL of the sodium dichromate solution (0.04 mol· L^{-1}) in a small test tube and add one drop of concentrated sulfuric acid. **(Caution: Concentrated sulfuric acid can cause serious skin and eye injuries. Wear gloves and proper eye protection.)** Shake the test tube and then add three drops of the alcohol being tested. Warm the test tube and its contents by placing it in a beaker of warm water for several minutes. Record your observations.

2. **Lucas Reagent Test for Stable Carbocations**
   Place 10 drops of Lucas reagent in a small test tube. **(Caution: Lucas reagent contains concentrated hydrochloric acid. Use in a fume hood, wear gloves and protect your eyes.)** Add one drop of the alcohol being tested. Mix the contents by vigorously swirling the test tube for about 3 to 5 seconds, place it in a test tube rack, and allow it to stand, without additional mixing, until a cloudiness develops. If the solution has not turned cloudy within one hour, you may assume that no reaction has occurred.

Part B: Reactions of alkyl halides

Perform the tests described below on each of the following compounds:

1-chlorobutane, 2-chlorobutane, 2-chloro-2-methylpropane, 1-bromobutane, 2-bromobutane, chlorobenzene, benzyl chloride, 3-chloro-1-butene (i.e., crotyl chloride), bromocyclohexane, bromocyclopentane, and β-bromostyrene (i.e.,C_6H_5-CH=CHBr).

1. **Ethanolic Silver Nitrate Test for S_N1 mechanism**
   Label a series of eleven clean dry test tubes from 1 to 11. Into each test tube place four (4) drops of the halide being tested (i.e., a different compound in each test tube). Add 2 mL of the 1% (~0.1 M) ethanolic silver nitrate solution to each test tube, making a careful note of the time at which each addition was made. Record the time taken for any precipitates to appear. For those solutions, which are still clear after 5 minutes, heat the test tube in a beaker of hot water and again note the time taken for any precipitates to appear.

2. **Sodium Iodide/Acetone Test for S_N2 mechanism**
   Label a series of eleven clean dry test tubes from 1 to 11. Into each test tube place four (4) drops of the halide being tested (as before, a different compound in each tube). Add 2 mL of the 15% sodium iodide in acetone solution, making a careful note of the time at which each addition was made. Record the time taken for any precipitates to appear. For those solutions, which are still clear after 5 minutes, heat the test tube in a beaker of hot (50^o C) water for six minutes, taking care not to boil off the acetone. Again, make a note of the time taken for any precipitates to appear.

Safety

In addition to the dangers involved when using concentrated sulfuric acid and Lucas reagent, you should also be aware of the potential dangers presented in handling the following substances:

1-butanol is harmful to the skin and can cause internal injury through skin absorption. It is highly flammable and has a harmful vapour.

2-butanol presents the same safety hazards as 1-butanol.

2-methyl-2-propanol can cause irritation to the skin and eyes. It is flammable and its vapour can cause drowsiness.

cyclohexanol is flammable, irritating to the skin and eyes, and is harmful if inhaled or ingested.

sodium dichromate is carcinogenic. Avoid contact with skin. Harmful if swallowed.

1-chlorobutane is flammable. Use only in a fume hood. Wear gloves and eye protection.

2-chlorobutane is flammable. Use only in a fume hood. Wear gloves and eye protection.

2-chloro-2-methylpropane is flammable. Use only in a fume hood. Wear gloves and eye protection.

1-bromobutane is harmful to the eyes and lungs. Toxic if swallowed. Highly flammable. Use only in a fume hood and wear gloves and eye protection.

2-bromobutane presents the same safety hazards as 1-bromobutane.

chlorobenzene is poisonous by swallowing, inhaling and skin absorption. It is also highly flammable. Use only in a fume hood.

benzyl chloride is poisonous if swallowed. The vapour irritates the respiratory system, eyes and skin. Use only in a fume hood. Wear gloves and eye protection.

1-chloro-2-butene (i.e., crotyl chloride) may be fatal if inhaled! It is harmful if ingested, inhaled or absorbed through the skin. Exposure can cause headache, wheezing and nausea. It is very flammable and may flashback. Do not use near an ignition source or open flame. Use in fumehood.

bromocyclohexane is poisonous and inhalation can cause headache and vomiting. Flammable.

bromocyclopentane is poisonous and an irritant to eyes and skin. Flammable.

β-bromostyrene is harmful when swallowed and may cause some skin irritation. Flammable.

silver nitrate is corrosive as a solid. Avoid contact with eyes and skin.

sodium iodide does not present any specific safety hazards. However, the ingestion of large amounts of this substance could be hazardous.

acetone (2-propanone) is an irritant to the eyes, skin and lungs. It is a narcotic and is harmful to the liver and kidneys if it is swallowed. Highly flammable. Use only in a fume hood or other well-ventilated area.

ethanol is highly flammable. The toxicity of this liquid is increased by the presence of denaturing substances. Avoid ingestion.

Waste disposal

Separate containers will be available for the disposal of each of the following materials:

alcohol/acidic dichromate mixtures

alcohol/Lucas reagent mixtures, alkyl halide/silver nitrate mixtures, alkyl halide/sodium iodide mixtures

Write-up

Use the investigative 'short style' format for writing this laboratory report. Be very brief for the purpose and nature of the tests and present the procedure in tabular format (i.e., Table of Reagents). Present your results in the form of a four-column table (test, observation, inference, equation). You should attempt to form a conclusion as to the reaction mechanism and to its relative rate/favourability.

Remember to photocopy you lab report before mailing it to your tutor for marking.

Questions

1. There are four isomeric alcohols having the formula $C_4H_{10}O$, and in this experiment you investigated the properties of three of them. How would you expect the fourth isomer to behave when treated with (i) acidic sodium dichromate, and (ii) Lucas reagent?

2. On the basis of your results, arrange the eleven halogen-containing compounds in order of *decreasing* reactivity in (i) S_N1 reactions and (ii) S_N2 reactions.

3. a. What results would you expect to observe when benzyl alcohol, $C_6H_5CH_2OH$, is treated with (i) acidic sodium dichromate, and (ii) Lucas reagent?

   b. What results would you expect to obtain when 1-chloro-2,2-dimethylpropane is treated with (i) ethanolic silver nitrate, and (ii) sodium iodide in acetone?

Experiment 12
The reduction of benzophenone with sodium borohydride

"To reduce or be reduced, that is the question." –Carbon Compound, since life began.

Preparation

Before beginning this experiment, you should have read through the details of this experiment and prepared a flow chart for the procedure to be followed, and

1. studied 'A Preview of Carbonyl Compounds' of the theory component of the course,

2. read 'Alcohols from Reduction of Carbonyl Compounds', and

You may also wish to read, Chapter 19 of *The Organic Chem Lab Survival Manual* (Chapter 26 in 3rd ed.).

Objectives

The purpose of this experiment is to provide a practical example of the reduction of a carbonyl group using sodium borohydride. Thin-layer chromatography will be used to assess the purity of the product, and further practice in obtaining and interpreting infrared spectra will be provided.

Introduction

The two most common reducing agents used to reduce carbonyl compounds to alcohols are sodium borohydride ($NaBH_4$) and lithium aluminum hydride ($LiAlH_4$). Both of these reagents are capable of transferring hydride ions to aldehydes and ketones to form complexes, which can then be hydrolyzed to the corresponding alcohols. If an aldehyde is used in the reaction, a primary alcohol is produced; if a ketone is used, the product is a secondary alcohol.

Sodium borohydride is a weaker reducing agent than lithium aluminum hydride. Reductions using the former may be carried out in aqueous or alcoholic solutions, while those involving the latter require the use of an inert solvent (e.g., tetrahydrofuran). However, there are certain limitations to the use of sodium borohydride and these are discussed in your textbook near the topic 'Alcohols from Reduction of Carbonyl Compounds'.

The general equation for a sodium borohydride reduction is summarized below in Fig. 12.1:

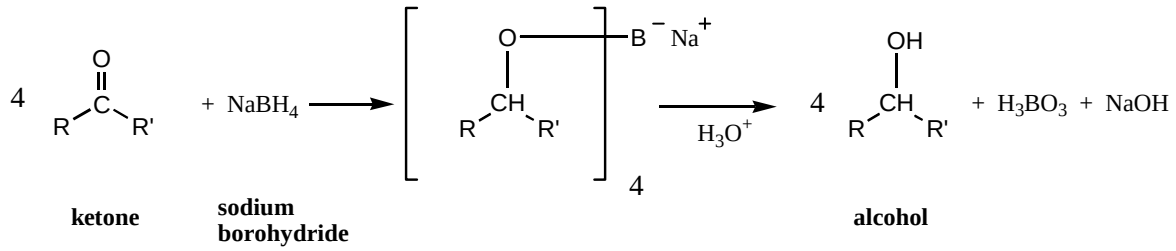


Figure 12.1 General reaction for sodium borohydride reduction of a ketone.

In the present experiment, you will reduce benzophenone to diphenylmethanol (see Fig.12.2):

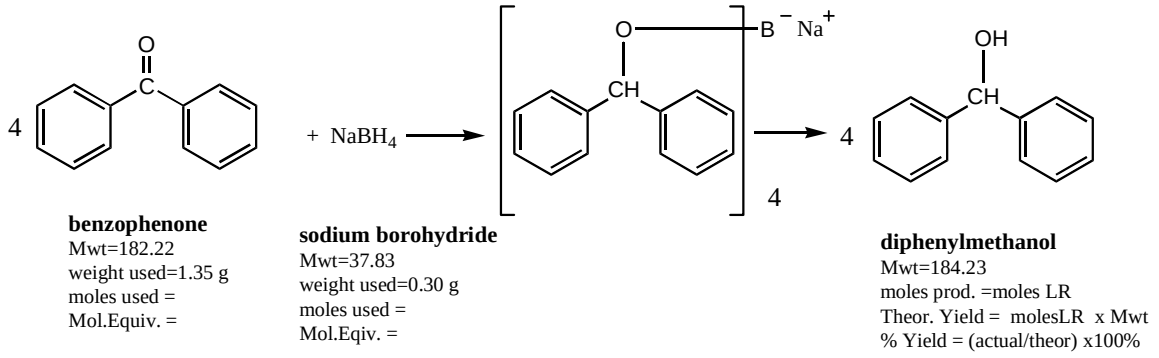


Figure 12.2 Benzophenone reaction with sodium borohydride.

In this experiment you will compare the purity of crude diphenylmethanol with that of recrystallized diphenylmethanol by spotting both samples on a single TLC plate. A sample of benzophenone will also be spotted on the same plate so that you can determine whether any of this starting material is present in either the crude or recrystallized product. Visualization will be achieved using an iodine tank as described in paragraph 2 of the "Visualization" section on page 145 of *The Organic Chem Lab Survival Manual* (p.249 in 3rd ed.).

Note: As an additional check on the purity of your product, an infrared spectrum will be run on the crude product, the recrystallized product, and the benzophenone starting material.

Thin-Layer Chromatography

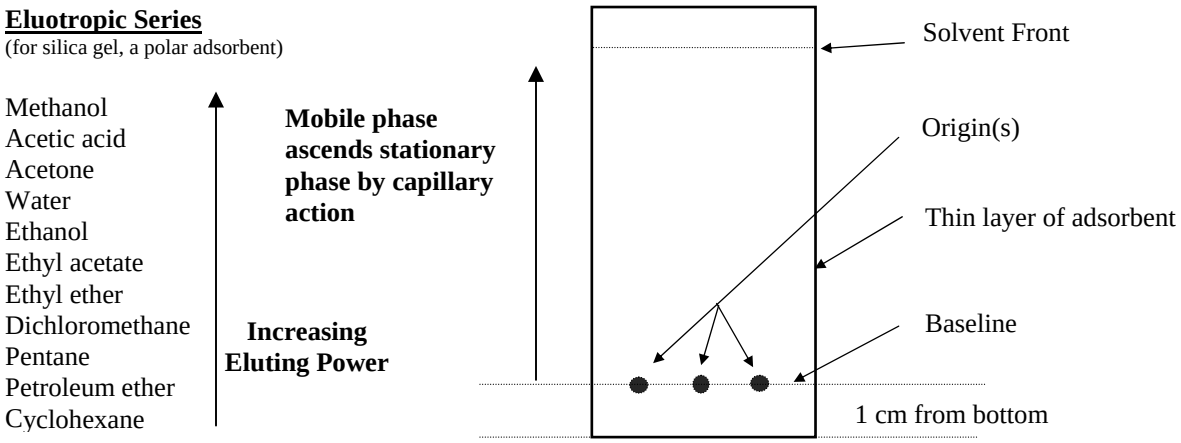
A discussion of this technique can be found in Chapter 19 *The Organic Chem Lab Survival Manual*, and in in your textbook under the topic 'Chromatography: Purifying Organic Compounds', hence the discussion here will be very brief. Please note that you will be provided with pre-prepared plates; i.e., you need not concern yourself with the details given in section titled "Preparation of TLC Plates" (pp. 140-141, or 244-245 in 3rd ed. of the *The Organic Chem Lab Survival Manual*. Similarly, you will be provided with an adequate supply of spotters.

Thin-layer chromatography is an indispensable analytical and preparative tool in organic chemistry. Chemists use it to check the purity of and identify compounds, check reaction mixtures, and follow the progress of reactions.

There are essentially **7 steps** to performing Thin Layer Chromatography:

1. Prepare the chromatogram (draw baseline and assign origins).
2. Dissolve compound in a spotting solvent (low bp, cmpd. highly soluble, make 1% solution).
3. Place 'spot(s)' on chromatogram (use capillary tube to keep the spot to a small diameter).
4. Prepare the development chamber/tank (allow to equilibrate).
5. Develop the chromatogram (to within ~2cm of top).
6. Stop development. Visualize the chromatogram (iodine tank, UV light)
7. Analyze the chromatogram. Determine R_f's.

Thin Layer Chromatorgraphy uses a thin layer of solid adsorbent (usually silica gel) on either a plastic or metal backing. The mobile phase is/are solvent(s) chosen carefully to move the compound from the point of origin to about 1/2 way up the chromatogram (R_f=0.5). Note: a pure compound will only show a single 'spot' on the chromatogram after development.



Perhaps the most difficult concept in TLC is the choice of the developing solvent (mobile phase or eluent). If the compound spotted is highly polar, it will bind more tightly to the polar absorbent, thus requiring a more powerful eluting solvent to 'mobilize' it and move it up the chromatogram.). If the compound spotted is non-polar, it will bind less to the polar absorbent, thus requiring a less powerful eluting solvent to 'mobilize' it and move it up the chromatogram. Sometimes a mixture of solvents (they must be miscible) is required to get the compound to move just right.

For instance, suppose a student was asked to check the purity of an unknown solid. At first she/he tried pentane:ethyl acetate (1:1) and found that the unknown barely moved from the baseline. To readjust the solvent system to get an R_f = 0.5, should the student increase the concentration of pentane (to 3:1) or increase the concentration of ethyl acetate (to 1:3)?

In this case, the student should prepare a more polar solvent in order to 'mobilize' the tightly bound compound on the silica gel (it stuck to the origin!). Therefore, the student should increase the concentration of the ethyl acetate, so that the solvent system is pentane:ethyl acetate (1:3).

Finally, what if you have a chromatogram of an amine (polar) and an ether (fairly non-polar). Would the **amine have a higher R_f than the ether if a polar mobile phase like ethanol→methanol was used** as the developing solvent? (Answer = Yes).

Procedure

Part A: The reduction of benzophenone

1. In a 25-mL Erlenmeyer flask, dissolve 1.35 g of benzophenone in 9 mL of methanol. If available, place a magnetic stir bar into the flask, and place the flask on a stir plate.

2. In a second 25-mL Erlenmeyer flask, dissolve 0.3 g of sodium borohydride in 4.5 mL of cold distilled water.

3. Use a Pasteur pipette to add the aqueous solution of sodium borohydride *one drop at a time* to the solution of benzophenone. Swirl the reaction mixture between the addition of each drop in order to disperse any cloudiness. Do not add more sodium borohydride until the cloudiness caused by the previous drop has disappeared.

4. When all the sodium borohydride has been added, use a magnetic stirrer to stir the reaction mixture until a heavy slurry of diphenylmethanol crystals has formed.

5. Decompose the excess sodium borohydride by *slowly* adding the slurry of crystals and solvent to a mixture of 30 g of crushed ice and 3 mL of concentrated hydrochloric acid in a 250 mL beaker. **(CAUTION: Prepare the latter by adding the concentrated hydrochloric acid to the crushed ice, not vice versa. Do this step in a fume hood. Wear gloves and protect your eyes.)**

6. Collect the diphenylmethanol by suction filtration. Wash the crystals with two 15-mL portions of water. Leave the aspirator (or vacuum pump) running for about 30 minutes in order to dry the crystals as best you can.

7. Place about 0.1 g of the crude diphenylmethanol in each of two *clean, dry* test tubes (13 × 75 mm) and stopper the tubes with corks. Save these samples for thin-layer chromatography and infrared spectroscopy.

8. Recrystallize the remainder of the diphenylmethanol using hexane as the solvent. (**Hint:** About 25-30 mL of solvent will be required, use 50^{o} C water bath to warm solvent.) After the crystals have been dried and weighed, place about 0.1 g of the diphenylmethanol in each of two *clean, dry* test tubes (13 × 75 mm) and stopper the tubes with corks. These small samples will be used in Parts B and C.

9. Determine the yield, melting point, mixed melting point with authentic standard (if available), and %yield of the pure diphenylmethanol. Store your crystals in a suitably labelled glass vial and hand it to your instructor for grading.

Part B: Thin-Layer Chromatography (TLC)

1. Prepare solutions of benzophenone, crude diphenylmethanol and recrystallized diphenylmethanol by dissolving each solid in about 1 mL of chloroform. (For the two diphenylmethanol samples, use the first of the two test tubes set aside in each of steps 7 and 8 of Part A. In the case of benzophenone, use about 0.1 g so that all of the solutions are of approximately the same concentration.) Stopper the test tubes.

2. Prepare a solution consisting of 1 mL of ethyl acetate dissolved in 5 mL of ligroin (or petroleum ether bp 60-80^{o} C) for use as the eluent.

3. Pour the eluent into a 150-mL beaker lined with filter paper as shown below. Cover with a watch glass and allow the beaker to stand undisturbed until it is needed.

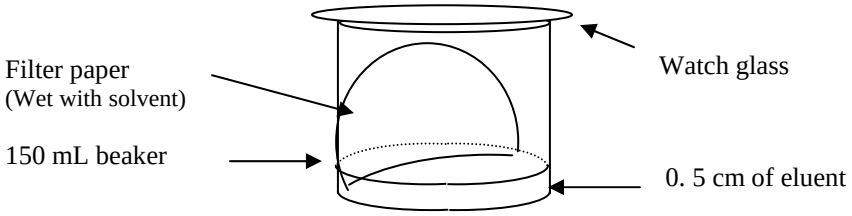


Figure 12.1 Development Chamber.

4. Use the supplied capillary tube to spot the pre-prepared TLC plate with each of three solutions prepared in step 1, above, as shown Figure 12.2).

(See "Spotting the Plates" on pages 142-143 of *The Organic Chem Lab Survival Manual*, pp.246-247 in 3rd ed

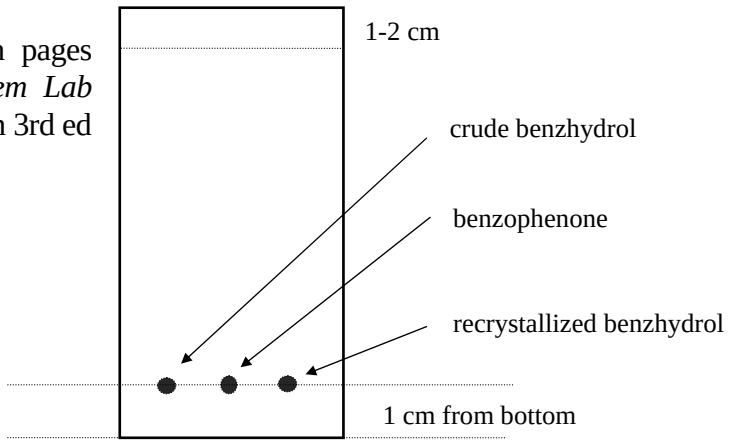


Figure 12.2 Appearance of the freshly spotted TLC plate

5. Place the TLC plate in the developing chamber. Make sure that the solvent level is **not** higher that the baseline on the TLC. Cover the beaker with a watch glass and wait for the solvent to travel up the plate until it reaches the line that you have marked about 1 cm from the top of the plate.

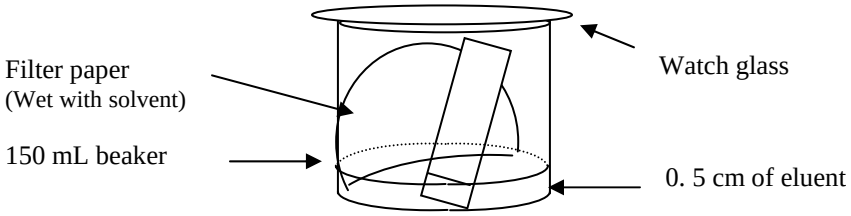


Figure 12.3 Developing the chromatogram

6. Allow the plate to dry.

7. Use tweezers to place the plate in the iodine tank (or UV light box) that will be provided. Allow the plate to remain in the tank until the spots on the plate are clearly visible. Use tweezers to remove the plate from the iodine tank and mark the spots with a pencil. Calculate the value for benzophenone and diphenylmethanol.

8. Keep the plate in a safe place so that you can submit it to your instructor when you have completed the experiment.

Part C: Infrared spectroscopy

1. With the assistance of your instructor, obtain an infrared spectrum of benzophenone, your crude diphenylmethanol and your recrystallized diphenylmethanol. Submit these spectra with your laboratory report.

Safety

Benzophenone is harmful if swallowed, inhaled or absorbed through the skin. Flammable.

Methanol is harmful to the lungs, skin, eyes and other organs. Poisonous if swallowed. Highly flammable. Use in a fume hood.

Sodium borohydride is toxic if ingested. Avoid contact with skin and take precautions against inhaling its dust.

Diphenylmethanol is an irritant and is poisonous when ingested.

Concentrated hydrochloric acid is extremely corrosive to the skin and eyes. Its vapour is irritating to the eyes, lungs and skin. Wear gloves and eye protection. Use only in a fume hood.

Hexane is highly flammable. Its vapour is irritating and can have a narcotic effect.

Chloroform (trichloromethane) is poisonous if swallowed. Its vapour is an anaesthetic and causes nausea, headaches, vomiting and unconsciousness.

Ethyl acetate is harmful if swallowed. Prolonged exposure to its vapour can cause corneal cloudiness and anaemia. Highly flammable.

Ligroin (or petroleum ether bp. 60-80^{o} C) is harmful if inhaled or swallowed. Can cause skin irritation and exposure may produce a burning sensation, headache and vomiting. Very flammable!

Iodine causes internal irritation if swallowed. Its vapour is harmful to the respiratory system. Contact with the skin or eyes is dangerous.

Additional information regarding the potential hazards in handling these chemicals may be obtained from the Material Safety Data Sheets that are available in the laboratory.

Waste disposal

The aqueous filtrate obtained when the crude product is isolated by suction filtration may be washed down the drain with plenty of water.

The filtrate from the recrystallization (hexane) should be placed in the container provided for non-halogenated organic wastes, as should the TLC eluent (ethyl acetate/ligroin).

The solutions of benzophenone and diphenylmethanol that were prepared for TLC should be placed in the container for halogenated organic wastes as the solvent used was chloroform, $CHCl_3$.

Write-up

This experiment should be written up using the standard format for "preparative type" experiments. Do not forget to report the mass of benzophenone used, the mass of crude diphenylmethanol obtained, and the mass, percentage yield and melting point plus mixed melting point data of the recrystallized product. Your report should also include an assessment of the purity of both the crude and recrystallized product based on your analysis of the thin-layer chromatogram and the infrared spectra.

Remember to photocopy you lab report before mailing it to your tutor for marking.

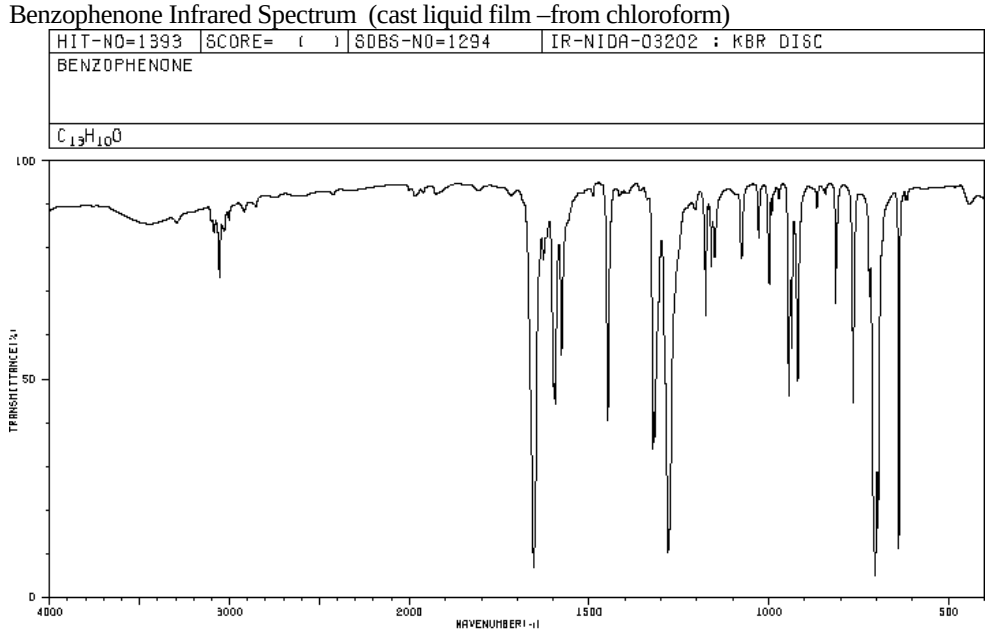
Questions

Answers to be submitted with report.

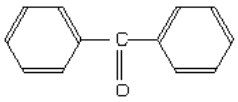
1. Aldehydes and ketones can be reduced to alcohols using hydrogen gas and a metal catalyst. Suggest two reasons why the use of sodium borohydride is preferred over the catalytic hydrogenation in order to prepare diphenylmethanol from benzophenone.

2. In this experiment, you destroyed the excess sodium borohydride by reacting it with hydrochloric acid (Part A, Step 5). What gas was evolved during the process? Write a balanced equation for the reaction that occurred. (**Hint:** one of the products was boric acid).

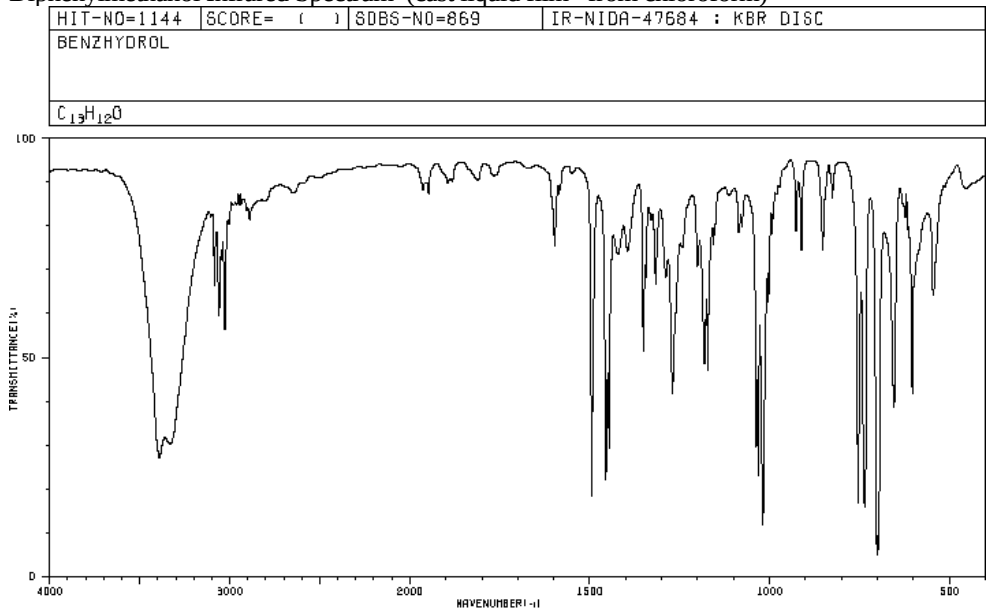
Benzophenone Infrared Spectrum (cast liquid film –from chloroform)



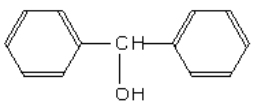
3291	81	1666	8	1206	86	992	84	720	66
3088	81	1627	74	1176	82	945	44	705	4
3067	79	1595	42	1162	72	936	55	697	15
3057	70	1577	69	1151	74	919	47	639	10
3030	81	1449	38	1076	74	867	86		
3003	84	1323	32	1028	79	814	64		
2919	84	1281	10	999	68	765	42		



Diphenylmethanol Infrared Spectrum (cast liquid film –from chloroform)



3392	26	1598	72	1345	66	1172	44	863	72
3359	30	1495	17	1317	64	1156	72	754	16
3331	29	1458	21	1289	66	1037	28	735	15
3085	64	1446	27	1271	39	1032	22	702	4
3059	57	1422	70	1244	72	1019	11	654	37
3049	70	1385	72	1201	68	1003	60	604	39
3027	63	1361	49	1182	46	912	72	545	62



Experiment 13
An aldol condensation

Preparation

Before beginning this experiment, you should have read through the details of this experiment, prepared a flow chart for the procedure to be followed, and

1. studied 'Carbonyl Condensation Reactions' of the theory component of the course,

2. read 'Mixed Aldol Reactions', and

3. completed Experiments 10 through 12.

Objectives

The purpose of this experiment is to provide an illustration of how an aldol condensation can be used in organic synthesis. Further practice in obtaining and interpreting infrared spectra is also provided.

Introduction

(Aldol = **ald**ehyde + alcoh**ol** = β-hydroxy aldehyde)

The aldol condensation (or carbonyl condensation) is a common organic reaction and is of great use to the synthetic chemist because it provides a convenient method of forming a new carbon-carbon bond. In its simplest form, the aldol condensation involves the reaction (via a combination of nucleophilic addition and α-substitution steps) of two molecules of an aldehyde (See Fig. 13.1 below) or ketone. The major requirement of the reaction is that the aldehyde or ketone concerned has at least one hydrogen atom attached to the **α-carbon** atom (in boldface). For example,

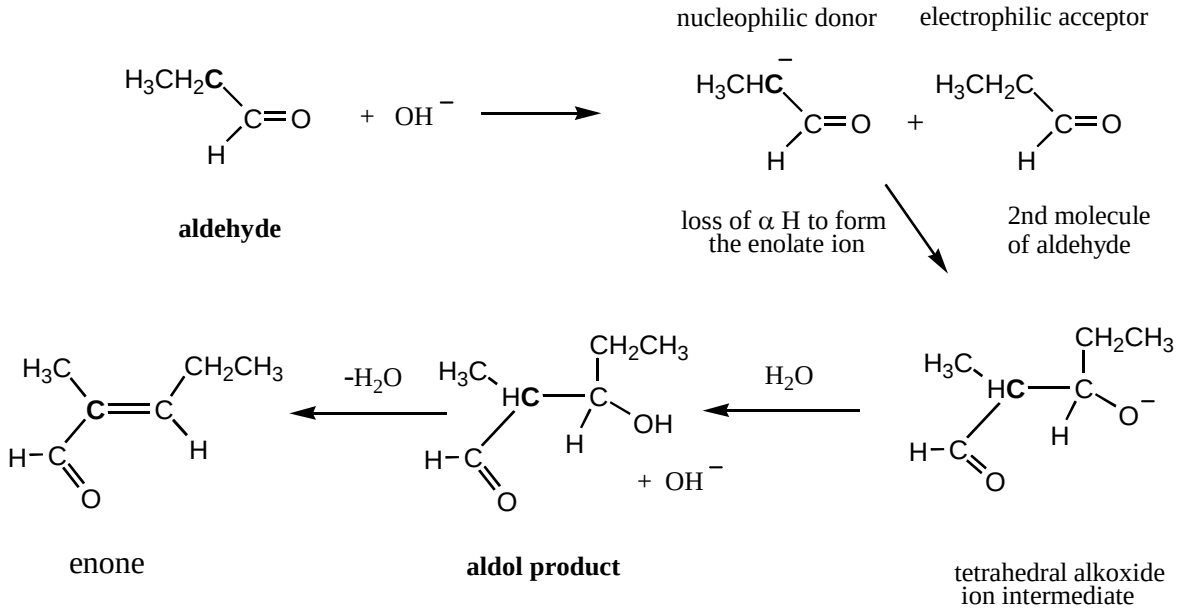


Figure 13.1 Base catalyzed aldol condenstation of two aldehyde molecules

Note that the last step shown above results in the formation of a conjugated enone (a dehydrated aldol)

In a mixed (or crossed) aldol condensation, two different carbonyl compounds are used. For instance, in the reaction between acetaldehyde and propanal, this leads to a mixture of four products (2 symmetrical, and 2 mixed aldol products). Not a very useful reaction!

Therefore it is usual to use an aldehyde that has **no** α-hydrogen atoms (e.g., an aromatic aldehyde) and a ketone that is either symmetrical (e.g., acetone, C**H**$_3$-CO-C**H**$_3$) or only has α-hydrogens on one side of the carbonyl group (e.g., acetophenone, C_6H_5-CO-C**H**$_3$). By using such combinations, the number of possible products is kept to a minimum. For example,

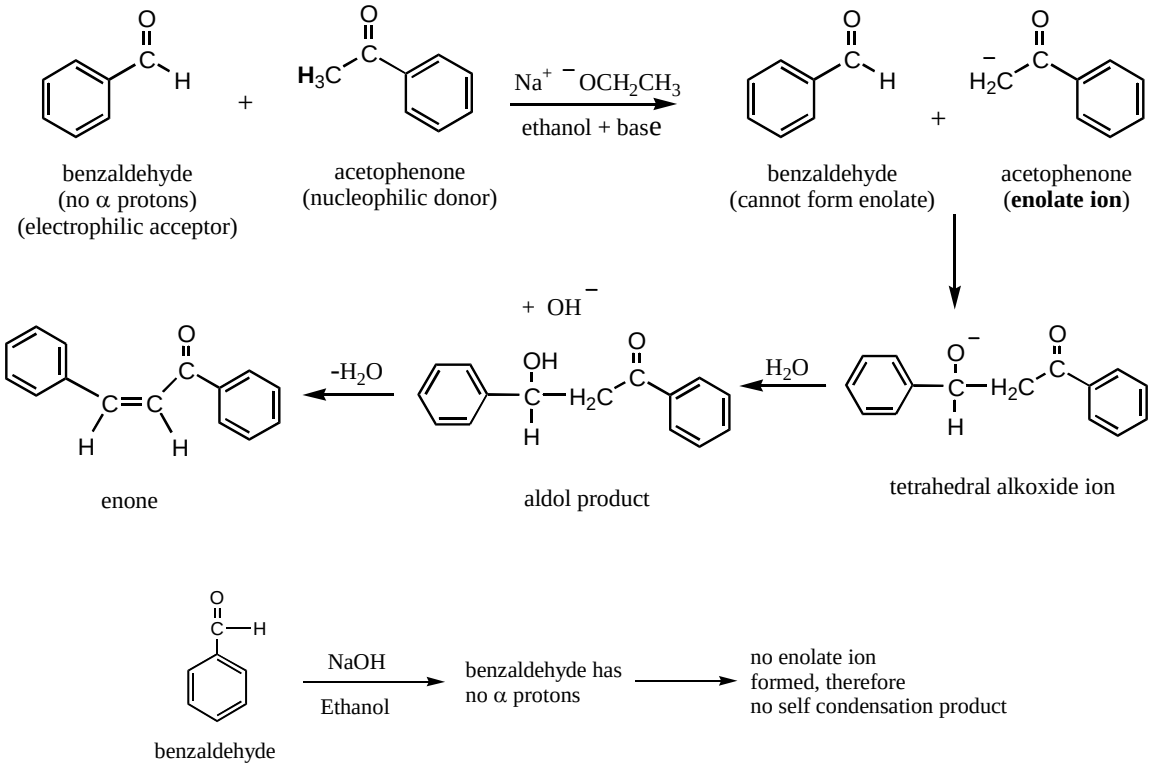


Figure 13.2 Mixed aldol condensation between benzaldehyde and acetophenone.

When a compound such as acetone is used in an aldol condensation (see Fig. 13.3), the presence of two sets of α-hydrogen atoms means that two moles of aldehyde can react with each mole of acetone. It is a reaction of this type that you will perform in this experiment.

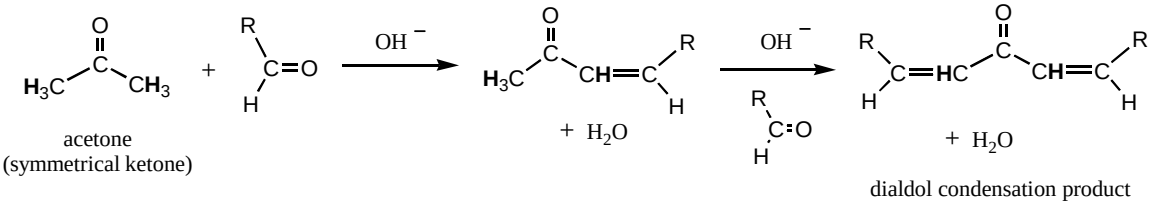


Figure 13.3 Dialdol condensation reaction

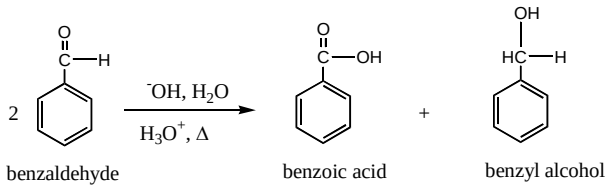
You will be assigned one of four aromatic aldehydes and one of four ketones, thus the instructions given in the "Procedure" section are fairly general in nature and may need to be modified depending on which combination you are given.

The four aldehydes that will be available are benzaldehyde, 4-methylbenzaldehyde, 4-methoxybenzaldehyde and cinnamaldehyde (3-phenylpropenal).

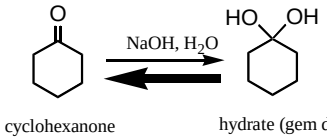
The four ketones that will be available are acetone, cyclopentanone, cyclohexanone and 4-methylcyclohexanone. Your instructor may add other aldehydes or ketones to this list of his/her discretion.

Other base initiated reactions to be aware of:

1. Cannizaro Reaction



2. Formation of Hydrates



Before coming to the laboratory

1. You may contact your laboratory instructor in order to find out which aldehyde and ketone have been assigned to you. Otherwise be prepared to perform your calculations for the amount of ketone and aldehyde required in the lab (see below).

2. Determine the mass of the aldehyde and ketone that you will need. If either substance is a liquid, determine the volume that you should use as it is easier to measure out a given volume of liquid than a given mass. The necessary densities are given in the table below.

Compound	**Density ($g \cdot mL^{-1}$)**
benzaldehyde	1.0415
4-methylbenzaldehyde	1.0194
4-methoxybenzaldehyde	1.1191
cinnamaldehyde [(E)–3-phenylpropenal]	1.0497
acetone	0.7899
cyclopentanone	0.9487
cyclohexanone	0.9478
4-methylcyclohexanone	0.9138

3. Draw a flow chart of the procedure to be followed.

Procedure

1. Into a 125-mL Erlenmeyer flask, place **0.020 mol of the ketone, plus 0.040 mol of the aldehyde**, 25 mL of 95% ethanol, and 30 mL of 1 mol· L^{-1} sodium hydroxide solution. A precipitate may begin to form immediately. Add a magnetic stir-bar to the reaction mixture and stir on a stirrer/hot-plate until no more precipitate forms. (If no precipitate forms during this time, warm the reaction mixture on the hot-plate for an additional 15–30 minutes.)

2. Cool the Erlenmeyer flask in ice and then collect the condensation product by suction filtration.

3. Wash the crude product (must be kept ice-cold at all times!) with:
   (a) 10 mL of ice-cold 95% ethanol,
   (b) 10 mL of ice-cold 95% ethanol containing 4% acetic acid, and
   (c) 10 mL of ice-cold 95% ethanol.

4. In the hood, recrystallize the product from 95% ethanol or toluene. (You may have to determine for yourself which of these two solvents is the more appropriate. See Chapter 10 in *The Organic Chem Lab Survival Manual* pp. 48-50, and 59-61 or Chapter 13 pp. 118-120 and 129-131 in 3rd ed.). Please see your instructor before trying to recrystallize all of your product. This might take several liters of solvent!

5. Determine the yield, melting point, and percent yield of your recrystallized product.

6. Obtain an infrared spectrum of your starting aldehyde, your starting ketone and your recrystallized product. **Note:** Spectra of solids should be obtained using Nujol mulls; liquids should be run "neat." Consult your instructor if you require assistance.

Safety

Benzaldehyde is harmful to the eyes, lungs and skin. Poisonous by swallowing and skin absorption. Contact may cause dermatitis. Flammable.

4-Methylbenzaldehyde no M.S.D.S. information available. Handle the same as benzaldehyde.

4-Methoxybenzaldehyde is harmful if swallowed, inhaled or absorbed through the skin. It is an irritant to both skin and eyes. Flammable.

3-Phenylpropenal (cinnamaldehyde) may be harmful by inhalation, ingestion or skin absorption. Vapor or mist irritating to the eyes and upper respiratory tract. Flammable.

Acetone (2-propanone) is an irritant to the eyes, skin and lungs. Harmful to the liver and kidneys if swallowed. Highly flammable. Use only in a well-ventilated area.

Cyclopentanone is poisonous by inhalation, ingestion or skin absorption. Causes **severe** eye irritation! Flammable.

Cyclohexanone may be **fatal** if inhaled. Mild exposure may cause wheezing, headache, nausea and vomiting. Target organs: liver, kidneys, central nervous system and lungs.

4-Methylcyclohexanone is harmful when swallowed and causes eye and skin irritation. Flammable.

Ethanol (95%) may contain denaturing substances that enhance its toxicity.

Sodium hydroxide solution is corrosive to the skin, harmful if swallowed, and extremely dangerous to the eyes.

Acetic acid (ethanoic acid) can be irritating to the skin and eyes, particularly if concentrated. Dilute solutions of ethanoic acid are relatively harmless.

Toluene is poisonous by skin absorption. Its vapour irritates the eyes and respiratory system and can cause dizziness, headaches and nausea.

Additional information regarding the potential hazards in handling these chemicals may be obtained from the Material Safety Data Sheets that are available in the laboratory.

Waste disposal

The filtrate from the suction filtration and washings should be placed in the container provided. If 95% ethanol was used in the recrystallization, the filtrate from this process may be placed in the same bottle.

If toluene was used in the recrystallization, the filtrate should be placed in the container provided for non-halogenated hydrocarbons.

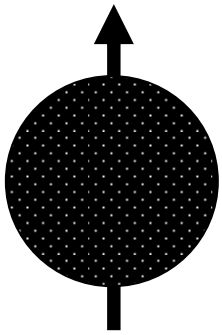
Write-up

This experiment should be written up using the standard format for "preparative type" experiments.

Question

Answer to be submitted with report.

1. The product obtained in this experiment results from a crossed condensation between an aldehyde and a ketone. Identify two other base-initiated reactions that could conceivably occur involving either or both of these reactants. Suggest reasons why these reactions do not result in the formation of large quantities of by-products.



Experiment 14
IR-NMR Exercise (to be done at home)

Preparation

Before beginning this experiment, you should have

1. studied 'Structure Determination: Mass and Infrared Spectroscopy'.

2. studied 'Structure Determination: Nuclear Magnetic Resonance'.

You may also wish to read Chapter 29 in J.W. Zubrick's 'The Organic Chem Lab Survival Manual: A Students Guide to Techniques' pp.201-222, and Chapter 30 in J.W. Zubrick's 'The Organic Chem Lab Survival Manual: A Students Guide to Techniques' pp.223-233.

Objectives

Throughout the course, you have been exposed to the technique of 'Infrared Spectroscopy'. This has allowed you to correctly predict or confirm the presence or absence of certain functional groups in organic compounds. The purpose of this experiment is to test your ability to interpret and correlate IR and ^{1}H-NMR spectra data. From this information you will be able to identify functional groups and arrangements of hydrogen atoms within a molecule. Students are encouraged to discuss their approach to interpreting the spectra of the unknowns with their instructor and tutor.

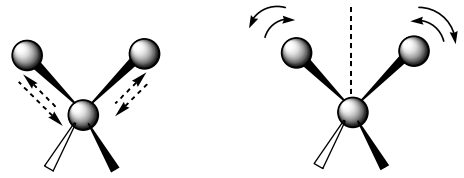
Introduction to Infrared Spectroscopy- Theory and Practice

Electromagnetic radiation

See 'Infrared Spectra Analysis Review' on pp.35-50 of the CHEM360 Lab Manual 2009/12

Infrared radiation

Remember, infrared radiation carries relatively low levels of energy (e.g. ~1-10 kcal/mol) which, when absorbed, result in only bond vibrations - stretching, rotating, bending and scissoring (i.e. deformation).



stretching vibration bending vibration

Every molecule, depending on its make up, is capable of absorbing infrared photons and increasing the intensity of its molecular motions. Different functional groups within the molecule will absorb photons at different infrared wavelengths. Thus when a spectroscopic wavelength scan is performed on an organic molecule certain λ will be absorbed while other λ will pass through. Once we have the infrared spectrum of a compound, the spectrum can be analyzed and compared with known infrared absorptions for particular functional groups (see Table 14.1 and Table 14.2).

When analyzing a spectrum, it is important to look at four different regions of the spectrum for the presence or absence of specific absorption peaks. **Note:** you are not required to analyze the fingerprint region.

Wavenumber cm^{-1}

4000	3000	2000	1400	600
N-H O-H	CH	C≡N C≡C	C=C C=O C=N	fingerprint region

Table 14.1 Four Regions of the Infrared Spectrum

Table 14.2 Correlation Table of Infrared Absorption and Functional Group.

Type of Absorption	Wavenumber (cm^{-1})	Intensity of Absorption	Absorption of:
O-H stretch	3400-3640	strong, broad	alcohol
	2500-3300	strong, very broad	carboxylic acid
N-H stretch	3310-3350	medium ('W' shape)	amine (1^o)
C-H stretch	3300	strong	sp C-H of alkyne
	3030	medium	aromatic
	3020-3100	medium	sp^2 C-H of alkene
	2850-2960	medium to strong	sp^3 C-H of alkane
	2750 & 2850	weak-medium ('W' shape)	O=C-H of aldehyde
C≡N stretch	2210-2260	medium, sharp	nitrile
C≡C stretch	2100-2260	medium, sharp	alkyne
C=O stretch	1670-1780	strong, sharp	carbonyl
	1730-1750		ester
	1720-1740		aldehyde
	1705-1725		ketone
	1700-1725		carboxylic acid
	1640-1700		amide
	ca 1800 and 1760		anhydride
C=C stretch	1650-1670	weak-medium, sharp	alkene
	1600, 1500, 1450	strong sharp	aromatic
C=N stretch	1640-1670	medium, sharp	imine
N-H bend	1500-1650	medium to strong, sharp	amine and amide
N=O stretch	1500-1600 (1540) and 1320-1390	strong, sharp	nitro-compound
C-N stretch	1030, 1230	medium	amine
C-O stretch	1050-1150	strong	alcohol
	1250-1310	strong broad	ester-conjugated
	1240	strong, broad	ester-acetates
	1175	strong, broad	ester-unconjugated
C-Cl stretch (terminal)	600-800	strong	alkyl halide
Ar-Cl stretch	1000-1175	medium-strong	aryl halide
C-Br stretch (terminal)	500-760	strong	alkyl halide
C-I (terminal)	500	strong	alkyl halide

Note: when a C=C bond is in conjugation with a carbonyl, the observed carbonyl absorption frequency will be < ~ 30 cm^{-1}.

Calculation of the # Degrees of Unsaturation in a Compound

(*See also 'Alkenes: Structure and Reactivity, Calculating a Molecules Degree of Unsaturation' McMurry 5th ed., p.190-192.

Number of Degrees of Unsaturation = nC +1 + 1/2N - 1/2 nH - 1/2 nX

e.g., Therefore, for Compound A, C_7H_{12} = (7) +1 + 1/2(0) - 1/2 (12) - 1/2(0)

= 7 + 1 - 6 = **2** degrees of unsaturation in Compound A.

Note: an aromatic ring = 4 degrees of unsaturation, 1 for the ring + 3 for the 3 double bonds = 4

In this exercise, you will be provided with infrared spectra, and hints to the λ of interest.

NMR Spectroscopy—Theory and Practice

In physics courses you would learn about many properties of electrons including their mass, charge and spin. These properties may appear to be self evident, but really they are only conceptual models to help describe their complex behavior. Science trivia experts probably know the following properties of the electron:

diameter = $\sim 10^{-12}$ cm
rest mass= me=9.109534×10^{-31} kg or 0.5110041 MeV or 1/1837 of H nucleus
charge= 1.60219×10^{-19} C
specific charge= e/me = 1.7588047×10^{11} C kg^{-1}
magnetic moment= 9.284832×10^{-24} J T^{-1}
spin= 1/2

Note: The property of 'spin' is not exactly like the earth rotating on its axis or a merry-go-round. Rather it tells us what a particle looks like from different directions. A particle of spin =1/2 must go through two rotations to look the same! Remember 'spin' is a quantum number which explains the splitting of spectral lines and that the 'spin' of a particle can line up parallel or anti-parallel with the magnetic field of an atom.

Like the electron, many nuclei also have spin properties (e.g., ^{1}H, ^{13}C, ^{2}H, ^{14}N, ^{19}F, ^{31}P). Those that do are all with odd numbered masses or even numbered masses with odd atomic numbers. Those that do have spin properties are known as magnetic nuclei. Thus nuclei that have even masses and atomic numbers (e.g., ^{12}C, ^{16}O, ^{32}S) are non-magnetic.

Magnetic nuclei will have nuclear spins without a specific orientation, if not in a strong external magnetic field. However when placed into a magnetic field the nuclei will orient themselves parallel (favoured lower energy state) or anti-parallel (less favoured higher energy state) with the field. Then if the nuclei are exposed to radio waves of the right frequency, energy absorption can occur and the parallel spin will convert to anti-parallel spin (spin-flip). This spin-flipping between energy states of the two spin orientations of the nucleus is what is meant by 'nuclear magnetic resonance'.

(For a more detailed discussion of the theory behind NMR, please refer to your textbook).

Nuclear magnetic resonance (NMR) spectroscopy is a very useful tool for organic chemists. Used in conjunction with mass and IR spectroscopy, it allows you to form a framework of the carbon-hydrogen and carbon-carbon bonds in a molecule from which you are able to infer the structure and identity of a compound.

When you look at a ^{1}H-NMR spectrum you are trying to decipher and correlate four different kinds of information. Because the information in NMR spectra sometimes is very complex, you must develop a systematic approach to analyzing NMR spectra.

1-First the spectrum contains **chemical shift (δ) information** (i.e. the position of the peak) which tells you about the structural grouping to which the H is bound (analogous to relationship between infrared λ and functional groups). Chemical shifts (δ) are measured in **hertz (Hz) or ppm** and are the distance from the center of the signal to a reference signal, usually tetramethylsilane (TMS). Refer to the chemical shifts shown in Table 14.3.

2-Second, the size of or area under a peak (determined by **integration**) tells you about number of identical H in a particular electronic environment.

Table 14.3 ^{1}H NMR Chemical Shifts (σ, ppm) for Various Functional Groups

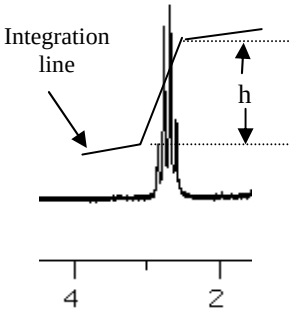
	σ, ppm		σ, ppm
TMS $(CH_3)_4Si$	0	TMS is used as reference for both ^{1}H and ^{13}C-NMR. It gives rise to a single peak that occurs upfield (farther right) of other absorptions normally found in organic cmpds.	
Cyclopropane	0.0-0.4		
Alkanes			
RCH_3	0.7-1.3		
R_2CH_2	1.2-1.4		
R_3CH	1.4-1.7		
Alkenes		Vinylic protons are strongly deshielded by the neighbouring pi bond and therefore absorb in this characteristc downfield position.	
$-C=C-H$ (vinyl)	4.6-5.9		
$-C=C-CH_3$ (allyl)	1.6-1.9	protons on C next to unsaturated (allylic, benzylic, next to carbonyl) show charact. absorptions in this region, just downfield from other alkane resonance.	
Alkynes			
$-C\equiv C-H$ (alkynyl)	2.5-2.7		
$-C\equiv C-CH_3$	1.8		
Aromatic		protons on aromatic rings (aryl protons) are strongly deshielded by the pi orbitals of the ring and show charact. absorptionsin this lower-field range.	
$Ar-H$ (aryl)	6.5-8.0		
$Ar-CH$ (benzyl)	2.5-2.7		
Fluorides, $F-CH$	4.0-4.5	protons on C next to electronegative atoms (X, O, N) are deshielded because of the electron-withdrawing ability of these atoms. Thus the protons absorb in this midfield range.	
Chlorides, $Cl-CH$	3.0-4.0		
Cl_2CH	5.8		
Bromides, $Br-CH$	2.5-4.0	protons on oxygen bearing C atoms are deshielded by the electron-withdrawing effect of the nearby O. Splitting of OH proton not usually observed, therefore usually seen as a broad singlet.	
Iodides, $I-CH$	2.0-4.0		
Nitroalkanes, O_2N-CH	4.2-5.6		
Alcohols, ethers			
$HO-CH$	3.3-4.0		
$RO-CH$	3.3-4.0		
Esters			
$R-C(=O)-O-CH$	3.7-4.1		
$RO-C(=O)-CH$	2.0-2.6		
Carboxylic acids			
$HO-C(=O)-CH$	2.0-2.6		
$R-C(=O)-O-H$	10.5-12		
Ketones			
$R-C(=O)-CH$	2.1-2.4		
Aldehydes			
$R-C(=O)-H$	9.7-10.0		
Amides			
$R-C(=O)-N-H$	5.0-8.0		
Alcohols $R-O-H$	2.5-5.0		
Phenols $Ar-O-H$	4.0-12.0		
Amines $R-NH_2$	1.0-5.0		

The integration data may be in the form of **'peak areas'** or an **'integration line'** on the NMR spectrum. If the integration data is in the form of peak areas, the number of protons responsible for signal is easily obtained from the integration by looking at the molecular formula for the unknown and using the following equation:

$$\#\text{ of Protons Responsible for Signal} = \text{total \# of protons in molecule} \times \frac{\text{area under signal}}{\sum \text{area under all signals}}$$

e.g., If the molecular formula of the unknown is C_6H_{11}, and has 3 signals with areas of 31, 6, and 20 (sum = 57), then the number of protons responsible for the first signal is $11 \times 31/57 = 5.98 = 6$; and $11 \times 6/57 = 1.15 = 1$ for the second signal; and $11 \times 20/57 = 3.86 = 4$ for the third signal ($6 + 1 + 4 = 11$).

If the integration data is in the form of an 'integration line' on the NMR spectrum, the number of protons responsible for signal is obtained by measuring the height (h) of each of the integration lines for each of the signals. The **ratio of the signals heights** are then compared with the molecular formula to determine the number of protons responsible for each signal.



Note: in this experiment, the integration data has been analyzed and given to you.

3-The third type of information you are looking for is called **signal splitting or multiplicity**. This information tells you about the number of neighbouring H and is calculated using the 'n+ 1 Rule'.

$$\mathbf{N = n + 1}$$

where N = number of peaks observed, and n = number of equivalent adjacent H (see Table 14.4 for calculating signal splitting).

Table 14.4 Signal Splitting Calculation Using Pascal's Triangle (N=*n*+1)

N = number of peaks observed for absorbing protons.
n = number of equivalent adjacent hydrogens.

	n+1	*n*	splitting
1	**1**	**0**	**singlet**
1 1	**2**	**1**	**doublet**
1 2 1	**3**	**2**	**triplet**
1 3 3 1	**4**	**3**	**quartet**
1 4 6 4 1	**5**	**4**	**quintet**
1 5 10 10 5 1	**6**	**5**	**sextet**
1 6 15 20 15 6 1	**7**	**6**	**septet**
Pascal's Triangle			

4-The last type of information to seek has to do with **coupling constants (J)**. This is the distance between two adjacent peaks in the signal and is measured in hertz. For ideal triplets and quartets, their signal peaks should be symmetrical with relative peaks areas of 1:2:1 and 1:3:3:1 respectively. In actual spectra this is rarely the case and the peak ratios are distorted.

In Figure 14.5, the peaks of two sets of protons are interacting with each other, i.e., they share the **same** coupling constant (J_{ab}), they are leaning towards each other, and the peaks on the side nearest the other set of signals are higher than predicted.

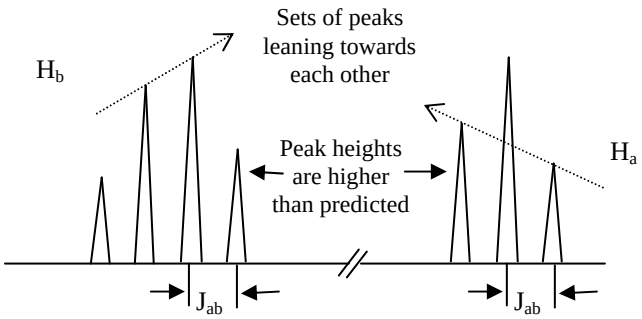


Figure 14.5 Coupling constant (J) for nearest neighbouring H's.

The protons of 'set H_a' have split the protons of 'set H_b' into a quartet and the protons of 'set H_b' have split the protons of 'set H_a' into a triplet. The interacting triplet-quartet peaks of this kind are evidence of the presence of an ethyl group (CH_3CH_2-) in the molecule.

In summary, you must systematically analyze a ^{1}H-NMR and correlate four different kinds of information: the chemical shift, the integration, the multiplicity or signal splitting pattern, and the coupling constants.

Finally, as a chemistry student, is essential that you have a good understanding of the concepts and practice of ^{1}H-NMR. Unfortunately modern NMR spectrometers are very expensive to own and require a great deal of technical experience to operate. Therefore in this course you will only be able to gain experience in the theory, interpretation and analyses of ^{1}H-NMR spectra. This exercise, where you are provided with unknown ^{1}H-NMR spectra plus integration data, will allow you learn and practice this important area of chemistry.

Procedure

1. Do the instructor led and practice problems.

2. Obtain __4__ unknown samples of organic compounds, and perform melting points or boiling points, and mass, infrared, and ^{1}H-NMR spectroscopy on each of them (This may have been already done for you!).

3. Analyze the provided spectral data, and determine the identity and structure of each unknown. (Your instructor will provide you with a handout for each unknown).

4. Calculate the 'Degrees of Unsaturation' present in the molecule.
   Number of Degrees of Unsaturation = nC +1 + 1/2nN - 1/2 nH - 1/2 nX

5. Then analyze the infrared spectrum. (see pp. 99-100 of this lab manual for instructions)

6. It is suggested you analyze your ^{1}H-NMR spectra as follows (see also pp. 99-101 of this lab manual for instructions):
   a) Always survey the spectrum from left (downfield) to right (upfield). As a rule, the further the H signal is shifted downfield, the more electronegative the group to which the H is bound.
   b) Number/code the signals, furthest downfield being #1 or A.
   c) Ask yourself how many hydrogens are giving rise to each signal?
   d) Determine the chemical shift of the signal (δ), in PPM.
   e) Next determine the multiplicity of the signal. Is it a singlet, doublet, triplet, quartet, sextet, septet, multiplet? From this you will be able to say how many H are on the neighbouring carbon.
   f) Now begin to build the framework of C, H, O, and N, which is also supported by the information obtained from the mass and infrared spectra. From this you will eventually obtain the complete structure or the molecule.
   g) Once you have arrived at a structure, confirm the presence (or absence) or the expected peaks such a molecule would give in the Infrared and ^{1}H-NMR spectra. Check to see if the other physical data matches your conclusion (mp or bp, and chemical formula).

7. Submit your answers, along with your reasoning and spectra, in a brief lab report (see 'Write-up Instructions'). If you have any questions about the data, please call your instructor or tutor.

How to Interpret an Infrared Spectrum

Step 1 Divide the infrared spectrum into four main areas (use pencil and ruler and take into account any off-shift in the spectrum's wavenumbers).

v) Above 3000 cm^{-1}
vi) Between 3000 and 2000 cm^{-1}
vii) Between 2000 and 1400 cm^{-1}
viii) Below 1400 cm^{-1} (fingerprint region)

Step 2 Starting at the left of the spectrum, examine the area **above 3000 cm^{-1}**, first looking in the region near 3300 cm^{-1} and record in tabular format the presence/absence of:

iv) A broad, very strong absorption band of an **'O-H'**. If present, it means you know that your molecule is at least an **alcohol**.
v) A broad, weak to medium strength, double or single absorption band of **'N-H'**. If present it means you have an **amine** (1° or 2°) or possibly an **amide**.
vi) A sharp, medium to strong, single absorption band of **'≡C-H'** of a **terminal alkyne**.
Note: If present, it means you should also see a 'C≡C' absorption near 2250 cm^{-1}.

After examining the region around 3300 cm^{-1}, look for any sharp, weak to medium absorption just above 3000 cm^{-1} (e.g. 3050 cm^{-1}) resulting from the 'C-H' stretch of a sp^2 hybridized carbon. If present, it means you have a **'C=C-H'** of an alkene or aromatic compound.

Step 3 Next examine the area between **3000 and 2000 cm^{-1}** and record the presence/absence of absorption bands or peaks.

v) First look just below 3000 cm^{-1} (e.g. 2850-2950 cm^{-1}) resulting from the 'C-H' stretch of a sp^3 hybridized carbon. If present, it means you are seeing the **'C-H'** stretch of an **-CH_2 or -CH_3** group. Note: This absorption is not very informative as most organic compounds have -CH_2 or -CH_3 groups.
vi) Then look for the extremely broad peak, actually starting at 3300 cm^{-1} and extending all the way to ~2500 cm^{-1}, caused by the **O-H dimer** between two **carboxylic acid** molecules (COOH). This absorption is probably the most difficult to see as other absorption peaks may be overlapping the broad peak.
vii) Finally look for a sharp, weak to medium peak caused by either **'C≡C'** or **'C≡N'**.
viii) If present, then the compound is an alkyne (might also have the 'C-H' of a terminal alkyne, see step 2 above) or a nitrile.

Step 4 Next examine the area between **2000 and 1400 cm^{-1}** and record the presence/absence of absorption bands or peaks.

iv) First look near 1700 cm^{-1} (e.g. 1680-1750 cm^{-1}) for a sharp, strong peak resulting from the **'C=O'** stretch of a **carbonyl**. Note: <u>This absorption is very informative</u> and will be present if your compound is an aldehyde, ketone, ester, amide, or carboxylic acid.
v) Next look near 1650 cm^{-1} (e.g. 1600-1670 cm^{-1}) for a sharp, weak peak resulting from the **'C=C'** stretch of an **alkene**.
vi) Finally look near 1600 cm^{-1} and 1500 cm^{-1} for a sharp, double peak resulting from the **'C=C'** stretch of an **aromatic ring**.

Step 5 If you dare, you may look in the **fingerprint region** (**area below 1400 cm^{-1}**) and record the presence of absorption bands or peaks.

v) First look near 1200 cm^{-1} for a sharp, strong peak resulting from the **'C-O'** stretch of an **ester**.
Note: <u>This absorption is very difficult to see and may or may not be present</u>, i.e. conclusive if present, inconclusive if not present.

vi) If you suspect you have an aromatic ring (absorption bands at ~3030 and 1600 and 1500 cm^{-1} present), you may try to discern the substitution pattern of the benzene ring by looking at the strong absorption bands of the **ring 'C-H'** out-of-plane bending vibrations in the region 680-900 cm^{-1}.

Benzene Substitution Pattern	Ring 'C-H' Absorption Bands Present (cm^{-1})
monosubstituted	2 sharp peaks, 730-770, 690-710
ortho disubstituted	1 sharp peak, 735-770
meta disubstituted	3 sharp peaks, 860-900, 750-810, 680-725
para disubstituted	1 sharp peak, 800-860
1,2,3 trisubstituted	2 sharp peaks, 760-780, 705-745
1,3,5 trisubstituted	2 sharp peaks, 810-865, 675-730
1,2,4 trisubstituted	2 sharp peaks, 870-885, 805-825

Ref: McMurry, J., 2000. Organic Chemistry, 5th ed, Brooks/Cole, p.578-579, (4th ed, p.559)
Nakanishi, K., 1964. Infrared Absorption Spectroscopy, Holden Day p.27.

vii) If you suspect you have a long straight chain (>4 C) alkane, (absorption bands at 28050-2950 cm^{-1} present but not much else), you may try to see the sharp, weak absorption due to the concerted rocking or >4 $-CH_2$ in a chain. It lies in the region 720 ± 10 cm^{-1}.

Step 6 Finally, you will summarize your results by making a statement as to what functional groups you suspect to be present in the molecule or perhaps you will be asked to select from a list of suggested structures, which molecule most likely would generate the spectrum just analyzed.

As tabular format that you might find useful for recording your findings is shown below:

Infrared Data:

	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}					
Between 3000 and 2000 cm^{-1}					
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent:

How to Interpret a ^{1}H-NMR Spectrum

Step 1 Survey the ^{1}H-NMR spectrum from left (downfield) to right (upfield). As a rule, the further the H signal is shifted downfield, the more electronegative the group to which the H is bound. Assign a code # for each signal or group of signals, furthest downfield being #1. Remember, each signal or group of signals represents a proton(s) in a different chemical environment.

Step 2 Determine the **chemical shift** (δ or delta scale, PPM) for each signal, or group of signals, by measuring the distance from the reference TMS peak to the center of the signal or group of signals.

Step 3 Determine the **number of hydrogens** giving rise to each signal or group of signals. This information may be provided (integration data), or you may have to measure the area under the peak(s) of each signal (see page 96 of the CHEM360 Lab Manual). It is important to check that the sum of the # of protons from each signal adds up to the total number of H indicated in the molecular formula.

Step 4 Determine the **multiplicity or splitting pattern** of the signal or group of signals by counting the number of distinguishable peaks. This may be difficult at times as very weak peaks may be overshadowed by background noise. Also note that you can have irregular signals, and signals that have been split by several other unequivalent protons. In this case, more advanced methods of analysis than shown here are then required to determine the multiplicity.

Step 5 Use the **N = n + 1** rule to determine the number of **neighbouring hydrogens** for each signal.
(N = number of peaks observed, and n = number of equivalent adjacent H.)

Splitting Pattern	# of Neighbouring Hydrogens
singlet	0
doublet	1
triplet	2
quartet	3
quintet	4
sextet	5
septet	6

see Table 14.4 for calculating signal splitting

Step 6 Make your **signal assignments** after consulting the Table 14.3 ^{1}H-NMR Shifts for Various Functional Groups.

Step 7 This is the most crucial step in the analysis, and the most difficult. Now you must begin to put together all your results, using the signal assignments, the infrared spectra data, the degrees of unsaturation, and molecular formula to piece together the structure of the unknown organic compound. The tabular format that you will find useful for recording your results is shown below:

Table #X. ^{1}H-NMR Spectral Data:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

In the following pages, we present sample spectrum interpretations for 2-propanol and for 1-propanol.

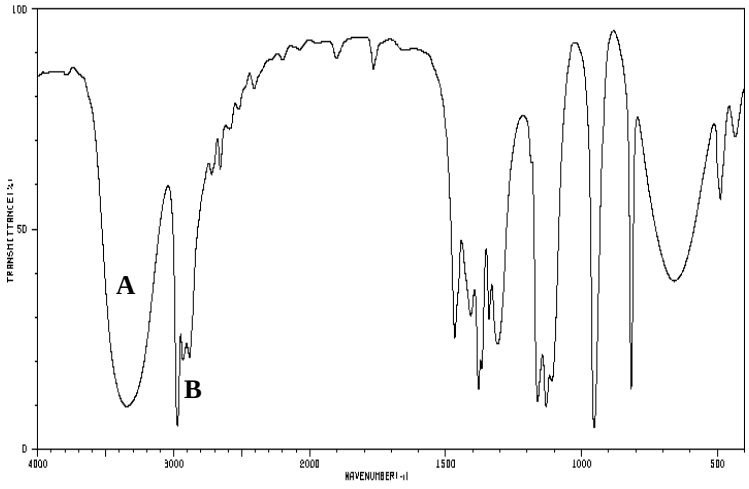
Sample Interpretation of a ^{1}H-NMR Spectrum

Use the following examples to understand the step by step approach of how to use a ^{1}H-NMR spectrum to identify an unknown. Please note that the 'degrees of unsaturation' has been calculated, and the infrared spectrum has already been analyzed.

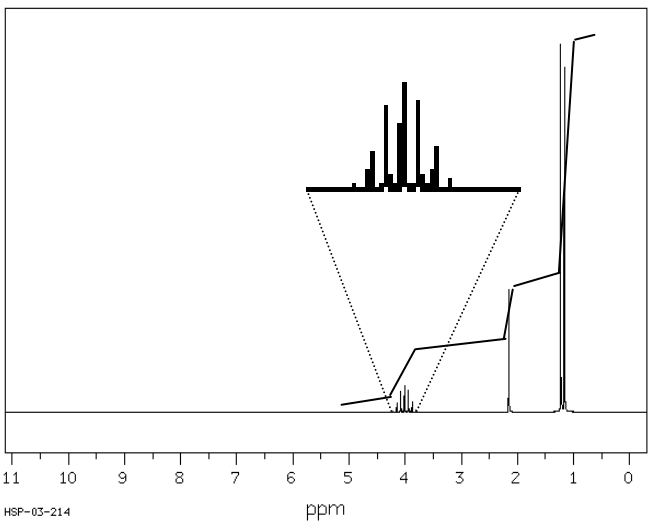
Experiment 14 Student Name**: Earle L. Mier** **AU ID#: 2550100**

Unknown #: 360-14-A Mol. Wt.: 60.1 g/mol Formula: C_3H_8O BP: 82.4° C

Infrared Spectrum of 360-14-B (thin film)



^{1}H-NMR Spectrum of 360-14-B (90 MHz in $CDCl_3$)



Number of Degrees of Unsaturation = **nC +1 + 1/2nN - 1/2 nH - 1/2 nX**

for Compound 360-14-A, C_3H_8O = (3) +1 + 1/2(0) - 1/2 (10) - 1/2(0)

= (3 + 1 + 0- 4 - 0) = **0** degrees of unsaturation

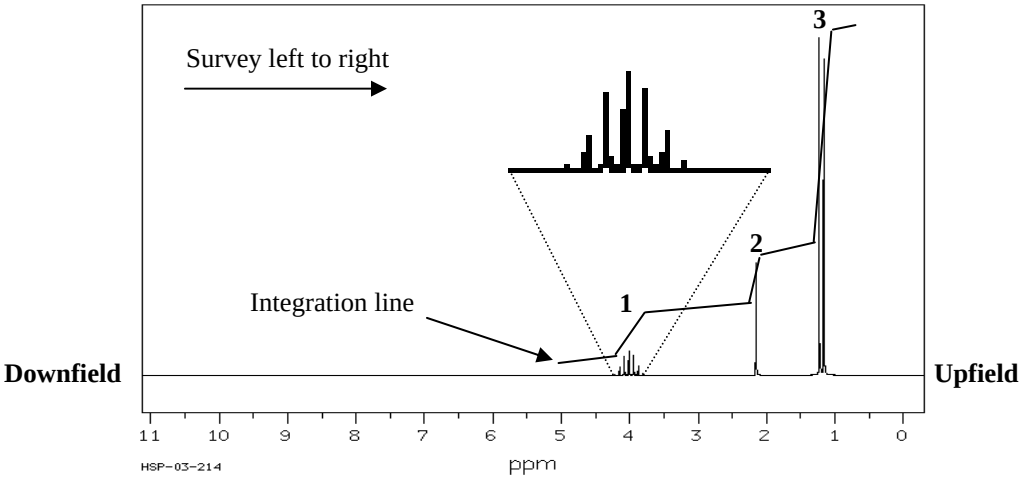
Infrared Spectrum Data for Unknown 360-14-A:

	Absorption Band	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}	A	3346	Broad	Strong	O-H stretch of alcohol
Between 3000 and 2000 cm^{-1}	B	2972, 2933, 2884	Multiple, Sharp	Strong	sp^3 C-H stretches of alkane
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent: no N-H, C≡C-H, sp^2 C-H, C≡C, C≡N, C=O, C=C alkene or aromatic

Interpretation of the ^{1}H-NMR Spectrum for Unknown 360-14-A

Step 1 Survey the ^{1}H-NMR spectrum from left (downfield) to right (upfield), assigning a code # for each signal or group of signals, furthest downfield being #1. Two proton signals are shifted downfield, indicating they are 'close' to an electronegative group (deshielded). The spectrum also indicates that there are proton(s) in a total of 3 different chemical environment. Note that Signal 1 has been

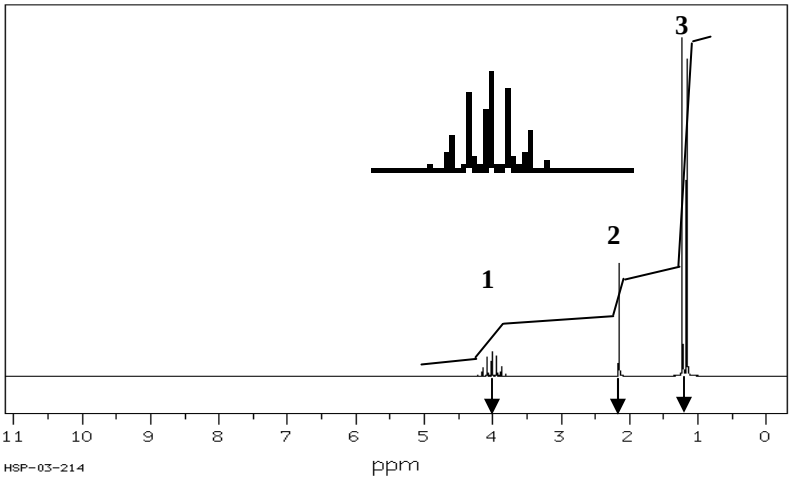


expanded for easier viewing.

^{1}H-NMR Spectral Data for Unknown 360-14-A:

Signal #	Shift	Integrat'n	Splitting	**Comment**	#Neighbour H	Signal Assignment
1				Shifted downfield		
2				Shifted downfield		
3						

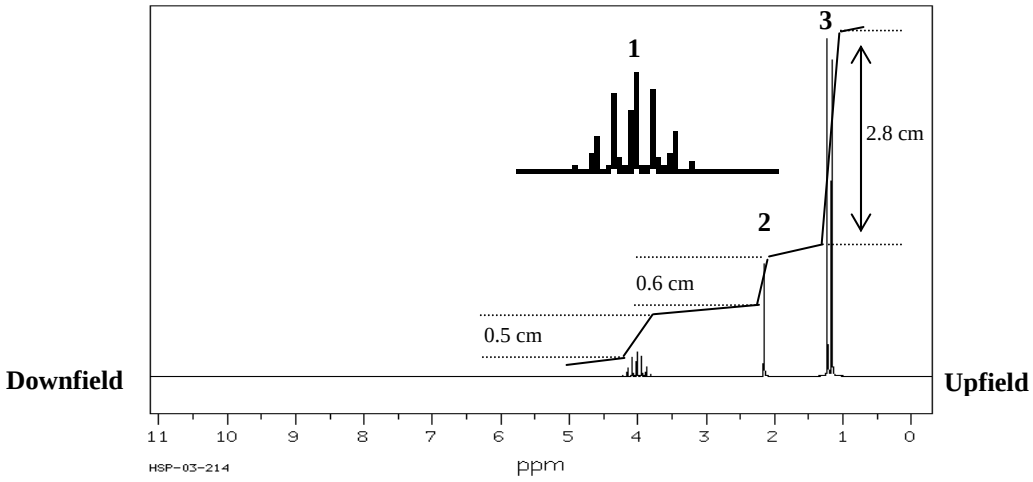
Step 2 Determine the **chemical shift** (δ or delta scale, PPM) for each signal, or group of signals, by measuring the distance from the reference TMS peak (0.0) to the center of the signal or group of signals.



^{1}H-NMR Spectral Data for Unknown 360-14-A:

Signal #	**Shift**	Integrat'n	Splitting	**Comment**	#Neighbour H	Signal Assignment
1	**4.0**			Shifted downfield		
2	**2.15**			Shifted downfield		
3	**1.2**					

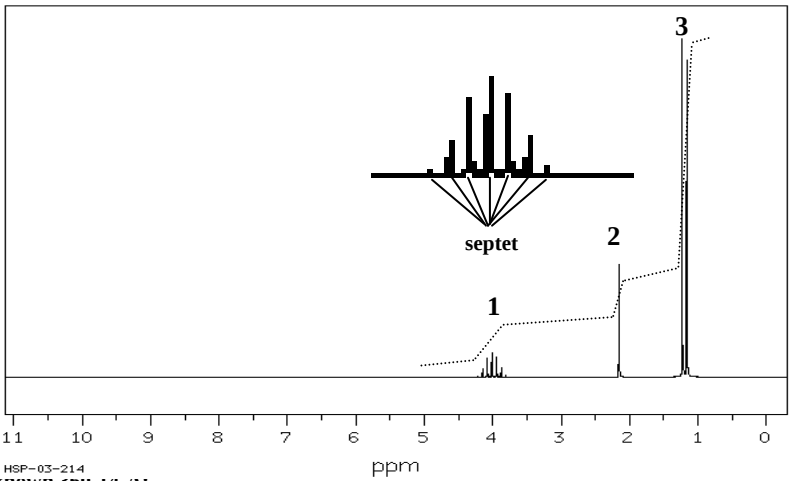
Step 3 The **number of hydrogens** giving rise to each signal or group of signals may be provided as integration data, or you may have to determine the ratio of the area under the peak(s) of each signal (see page 96 of the CHEM360 Lab Manual). Use a ruler to measure the height of each integration line (from left to right = 0.5 cm: 0.6 cm: 2.8 cm). The sum of the # of protons from all signals must add up 8 = the total number of H indicated in the molecular formula. In this case, this is accomplished by multiplying by 2 and rounding off the ratio of heights (from left to right = 1 : 1 : 6) = 8 H total.



^{1}H-NMR Spectral Data for Unknown 360-14-A:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	4.0	**1**		Shifted downfield		
2	2.15	**1**		Shifted downfield		
3	1.2	**6**				

Step 4 Determine the **multiplicity or splitting pattern** of the signal or group of signals by counting the number of distinguishable peaks in each signal. Signal 1 is a septet (as shown on the expanded area below). Signal 2 is a singlet. Signal 3 is a doublet.



^{1}H-NMR Spectral Data for Unknown 360-14-A:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	4.0	1	**septet**	Shifted downfield		
2	2.15	1	**singlet**	Shifted downfield		
3	1.2	6	**doublet**			

Interpretation of the ^{1}H-NMR Spectrum for Unknown 360-14-A (cont.)

Step 5 Use the **N = n + 1** rule to determine the number of **neighbouring hydrogens** for each signal. (N = number of peaks observed, and n = number of equivalent adjacent H.) For Signal 1, N = n + 1 = (7 = n + 1), so n = 6. Signals 2-4 # Neighbouring H are calculated the same way.

^{1}H-NMR Spectral Data for Unknown 360-14-A:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	4.0	1	septet	Shifted downfield	**6**	
2	2.15	1	singlet	Shifted downfield	**0**	
3	1.2	6	doublet		**1**	

Step 6 Make your **signal assignments**, consulting Table 14.3 ^{1}H-NMR Shifts for Various Functional Groups.
-According to Table 14.3, **Signal 1** (downfield 1H septet at δ 4.0) must be an alkyl halide, an ether, or an alcohol. It can't be an alkyl halide, because there is no halogen in the molecular formula, so it must be an ether, or an alcohol. It is therefore given the signal assignment of R-O-C**H**-R_2.
-We know that there is an alcohol in this unknown compound from the infrared analysis (absorption band A). Therefore we must look to find a decoupled (0 neighbours), deshielded (shifted downfield) signal due to a single proton bonded directly to an oxygen. Only **Signal 2** (singlet, 1H at δ 2.15) could be the H of the hydroxyl group of an alcohol. It is therefore given the signal assignment of R-O-**H**.
-Signal 3 (6H at δ 1.2) is due to an alkane R-C**H**$_3$ (δ 0.7-1.3), or R_2-C**H**$_2$ (δ 1.2-1.4), but not R_3-C**H** (δ 1.4-1.7). It is likely that Signal 3 is slightly shifted down field, and so it is more likely the signal assignment should be R-C**H**$_3$.

^{1}H-NMR Spectral Data for Unknown 360-14-A:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	4.0	1	septet	Shifted downfield	6	R-O-C**H**-R_2
2	2.15	1	singlet	Shifted downfield	0	R-O-**H** of an alcohol
3	1.2	6	doublet		1	R-(C**H**$_3$)$_2$

Your ^{1}H-NMR Spectral Data Table is now complete. Proceed to Step 7 on the next page.
Please note that you have not been asked to extract information from the spectrum regarding coupling constants (J).

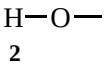
Interpretation of the ^{1}H-NMR Spectrum for Unknown 360-14-A (cont.)

Step 7 Again, this is the crucial step of the analysis. Let's begin to put together all your results by using the signal assignments, the infrared spectra data (O-H in molecule), the degrees of unsaturation (0), and molecular formula (C_3H_8O).

Rationale:

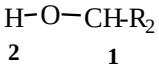
It was immediately apparent that unknown 360-14-A is an **alcohol**, -OH, due to the broad infrared absorption band O-H at 3346 cm^{-1}, and an downfield lone proton (Signal 2 singlet at δ 2.15).

(Note: 'Atomic Accounting' is now: C_3H_8O - OH = C_3H_7).



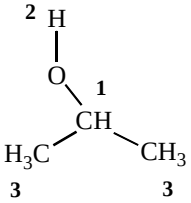
Signal 1 indicates there is a R-O-C**H**- (δ = 4.0, Integration = 1H, splitting pattern = septet) in the molecule. Also this O-C**H**- must have a neighbouring carbons with 6 H on it, so it must be O-CH-$(CH_3)_2$. This is confirmed by the presence of a R-**CH_3 group** (δ=1.2, Integration = 6H, splitting pattern = doublet). The last piece of the puzzle is that the CH_2 group is shifted downfield (δ=3.67) and so must be bonded to the only oxygen in the molecule, i.e. an **O-CH-$(CH_3)_2$- group**.

(Note: 'Atomic Accounting' is now: C_3H_7 - CH = C_2H_6).



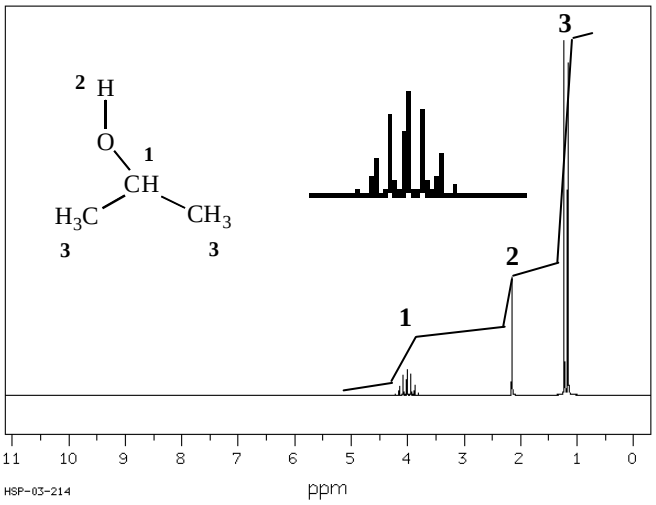
Signal 3 confirms that there is are 2 **methyl groups** R-CH_3 (δ=1.2, Integration = 6H, splitting pattern = doublet). Also these 2 -CH_3- both have the same neighbouring carbon with a single1 H, so Signal 3 must be due to $(CH_3)_2$-CH-.

(Note: 'Atomic Accounting' is now: C_2H_6 - 2(CH_3) = 0, all atoms accounted for!).



In summary unknown #360-14-A contains an alcohol, and 2 methyl groups. Therefore the **Unknown #360-14-A** must be **2-propanol**, which also has the correct/matching molecular weight/formula, and boiling point. Also the ^{1}H-NMR Spectrum shows there are 3 different types of H environments present in the molecule (and all 3 have been accounted for).

Note: The calculation for the 'degrees of unsaturation' in this problem also makes sense. There are 0 degrees of unsaturation present in the unknown.



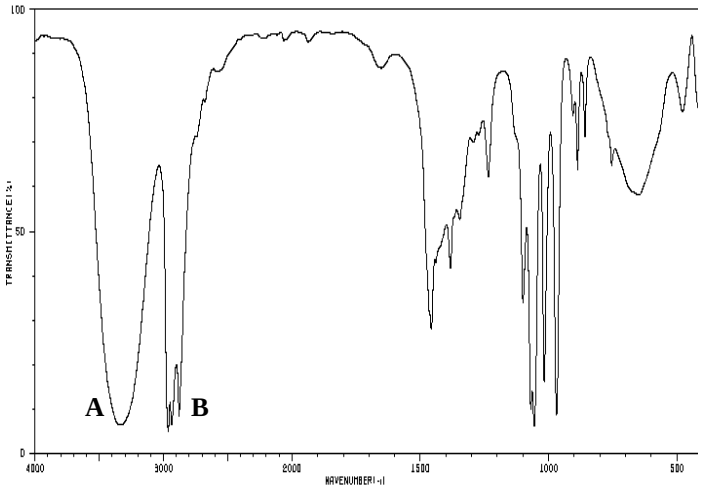
Another Sample Interpretation of a ^{1}H-NMR Spectrum

Use the following examples to understand the step by step approach of how to use a ^{1}H-NMR spectrum to identify an unknown. Please note that the 'degrees of unsaturation' has been calculated, and the infrared spectrum has already been analyzed.

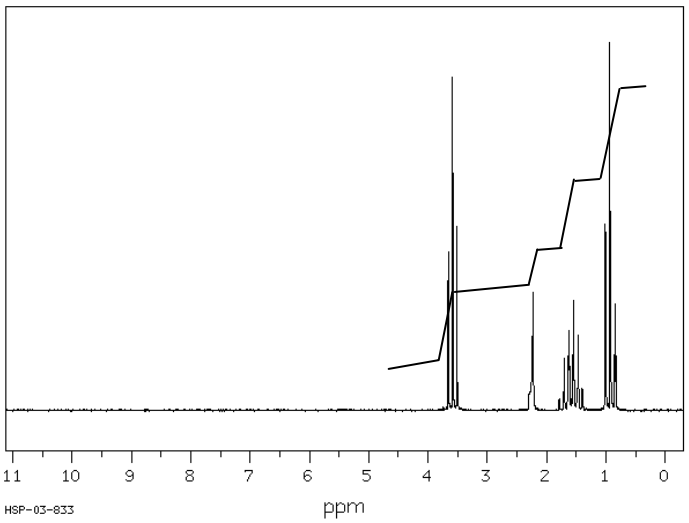
Experiment 14 Student Name**: R.B. Flask** **AU ID#: 2550100**

Unknown #: 360-14-B Mol. Wt.: 60.1 g/mol Formula: C_3H_8O BP: 97° C

Infrared Spectrum of 360-14-B (thin film)



^{1}H-NMR Spectrum of 360-14-B (90 MHz in $CDCl_3$)



Number of Degrees of Unsaturation = **nC +1 + 1/2nN - 1/2 nH - 1/2 nX**
for Compound 360-14-B, C_3H_8O = (3) +1 + 1/2(0) - 1/2 (10) - 1/2(0)
= (3 + 1 + 0- 4 - 0) = **0** degrees of unsaturation

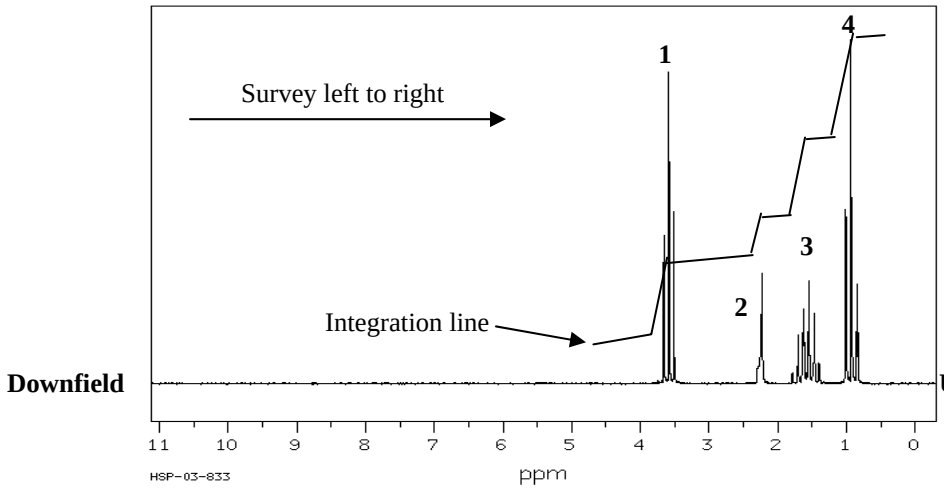
Infrared Spectrum Data for Unknown 360-14-B:

	Absorption Band	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}	A	3333	Broad	Strong	O-H stretch of alcohol
Between 3000 and 2000 cm^{-1}	B	2963, 2938, 2878	Multiple, Sharp	Strong	sp^3 C-H stretches of alkane
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent: no N-H, C≡C-H, sp^2 C-H, C≡C, C≡N, C=O, C=C alkene or aromatic

Interpretation of the ^{1}H-NMR Spectrum for Unknown 360-14-B

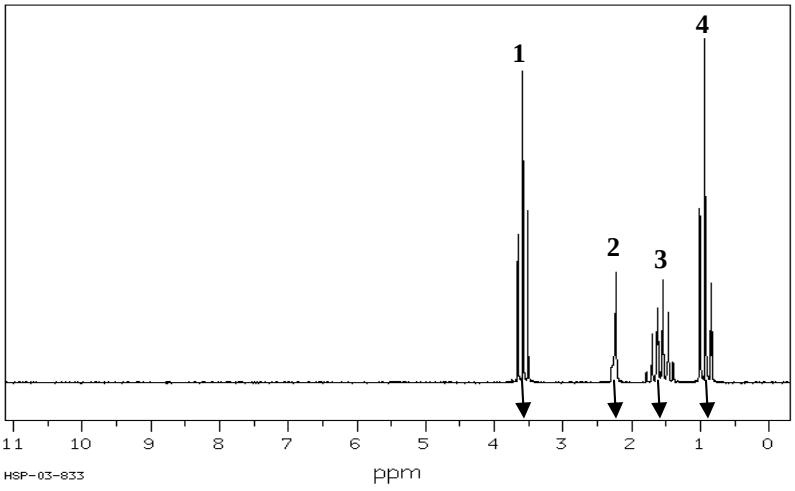
Step 1 Survey the ^{1}H-NMR spectrum from left (downfield) to right (upfield), assigning a code # for each signal or group of signals, furthest downfield being #1. Two proton signals are shifted downfield, indicating they are 'close' to an electronegative group (deshielded). The spectrum also indicates that there are proton(s) in a total of 4 different chemical environment.



^{1}H-NMR Spectral Data for Unknown 360-14-B:

Signal #	Shift	Integrat'n	Splitting	**Comment**	#Neighbour H	Signal Assignment
1				Shifted downfield		
2				Shifted downfield		
3						
4						

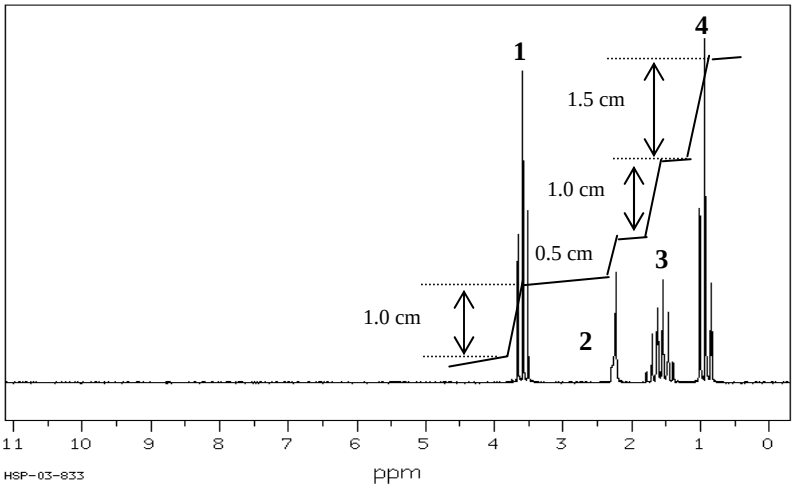
Step 2 Determine the **chemical shift** (δ or delta scale, PPM) for each signal, or group of signals, by measuring the distance from the reference TMS peak (0.0) to the center of the signal or group of signals.



^{1}H-NMR Spectral Data for Unknown 360-14-B:

Signal #	**Shift**	Integrat'n	Splitting	**Comment**	#Neighbour H	Signal Assignment
1	**3.6**			Shifted downfield		
2	**2.25**			Shifted downfield		
3	**1.6**					
4	**0.95**					

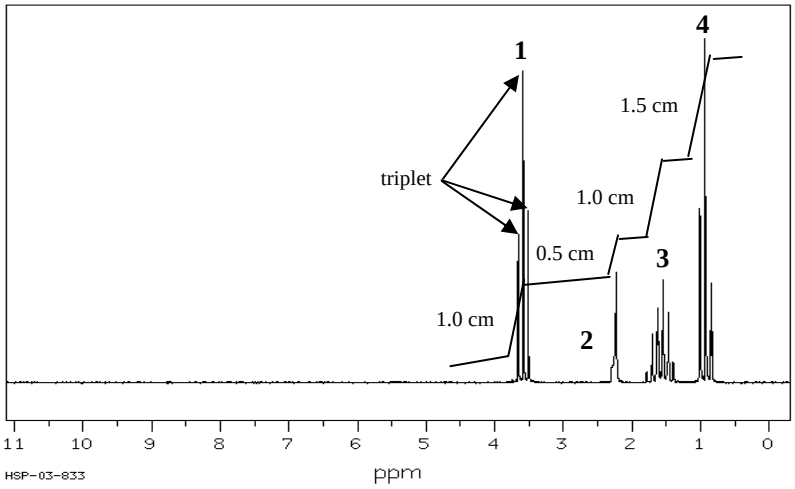
Step 3 The **number of hydrogens** giving rise to each signal or group of signals may be provided as integration data, or you may have to determine the ratio of the area under the peak(s) of each signal (see page 96 of the CHEM360 Lab Manual). Use a ruler to measure the height of each integration line (from left to right = 1cm: 0.5cm: 1cm: 1.5cm). The sum of the # of protons from all signals must add up 8 = the total number of H indicated in the molecular formula. This is accomplished by multiplying the ratio of heights by 2 (from left to right = 2 : 1 : 2 : 3) = 8 H total.



^{1}H-NMR Spectral Data for Unknown 360-14-B:

Signal #	**Shift**	**Integrat'n**	Splitting	**Comment**	#Neighbour H	Signal Assignment
1	3.6	**2**		Shifted downfield		
2	2.25	**1**		Shifted downfield		
3	1.6	**2**				
4	0.95	**3**				

Step 4 Determine the **multiplicity or splitting pattern** of the signal or group of signals by counting the number of distinguishable peaks in each signal. Signal 1 is a triplet (as shown on the spectrum below). Signal 2 is a singlet. Signal 3 is difficult to interpret, but it is a quintet. Signal 4 is clearly a triplet.



^{1}H-NMR Spectral Data for Unknown 360-14-B:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	3.6	2	**triplet**	Shifted downfield		
2	2.25	1	**singlet**	Shifted downfield		
3	1.6	2	**quintet**			
4	0.95	3	**triplet**			

Interpretation of the ^{1}H-NMR Spectrum for Unknown 360-14-B (cont.)

Step 5 Use the **N = n + 1** rule to determine the number of **neighbouring hydrogens** for each signal. (N = number of peaks observed, and n = number of equivalent adjacent H.) For Signal 1, N = n + 1 = (3 = n + 1), so n = 2. Signals 2-4 # Neighbouring H are calculated the same way.

^{1}H-NMR Spectral Data for Unknown 360-14-B:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	3.6	2	triplet	Shifted downfield	**2**	
2	2.25	1	singlet	Shifted downfield	**0**	
3	1.6	2	quintet		**4**	
4	0.95	3	triplet		**2**	

Step 6 Make your **signal assignments**, consulting Table 14.3 ^{1}H-NMR Shifts for Various Functional Groups.

-According to Table 14.3, **Signal 1** (2H at δ 3.6) must be an alkyl halide, an ether, or an alcohol. It can't be an alkyl halide, because there is no halogen in the molecular formula, so it must be an ether, or an alcohol. It is therefore given the signal assignment of R-O-C**H**$_2$-.

-We know that there is an alcohol in this unknown compound from the infrared analysis (absorption band A). Therefore we must look to find a decoupled (0 neighbours), deshielded (shifted downfield) signal due to a single proton bonded directly to an oxygen. Only **Signal 2** (singlet, 1H at δ 2.25) could be the H of the hydroxyl group of an alcohol. It is therefore given the signal assignment of R-O-**H**.

-According to Table 14.3, **Signal 3** (2H at δ 1.6) must be due to an alkane or alkene. Since there is no C=C in the molecule (see infrared data, and degrees of unsaturation = 0), it must be due to an alkane R-C**H**$_3$, R$_2$-C**H**$_2$ or R$_3$-C**H**. Of the three possibilities, the table suggests it could be R$_3$-C**H** (δ 1.4-1.7). But what if Signal 3 is near enough to be coupled with protons bonded to a carbon bonded to an oxygen. They might be slightly deshielded as well, due their 'close' proximity to the electron-withdrawing oxygen. So this signal could also be due to R$_2$-C**H**$_2$ (δ 1.2-1.4). This makes more sense, since we are dealing with a 2H signal (integration = 2). Thus Signal 3 is given the signal assignment R$_2$-C**H**$_2$.

-Signal 4 (3H at δ 0.95) must be due to an alkane R-C**H**$_3$ (δ 0.7-1.3).

^{1}H-NMR Spectral Data for Unknown 360-14-B:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	3.6	2	triplet	Shifted downfield	2	R-O-C**H**$_2$-
2	2.25	1	singlet	Shifted downfield	0	R-O-**H** of an alcohol
3	1.6	2	quintet		4	R$_2$-C**H**$_2$
4	0.95	3	triplet		2	R-C**H**$_3$

Your ^{1}H-NMR Spectral Data Table is now complete. Proceed to Step 7 on the next page.
Please note that you have not been asked to extract information from the spectrum regarding coupling constants (J).

Interpretation of the ^{1}H-NMR Spectrum for Unknown 360-14-B (cont.)

Step 7 This is the most crucial step in the analysis, and the most difficult. Now you must begin to put together all your results by using the signal assignments, the infrared spectra data (O-H in molecule), the degrees of unsaturation (0), and molecular formula (C_3H_8O).

Rationale:

It was immediately apparent that unknown 360-14-B is an **alcohol**, -OH, due to the broad infrared absorption band O-H at 3333 cm^{-1}, and an downfield lone proton (Signal 2 singlet at δ 2.25).

(Note: 'Atomic Accounting' is now: C_3H_8O - OH = C_3H_7).

H—O—
2

Signal 1 indicates there is a R-O-C**H**$_2$- (δ = 3.6, Integration = 2H, splitting pattern = triplet) in the molecule. Also this O-C**H**$_2$- must have a neighbouring carbon with 2 H on it, so it must be O-CH_2-CH_2. This is confirmed by the presence of another **-CH$_2$ group** (δ=1.6, Integration = 2H, splitting pattern = quintet). The last piece of the puzzle is that the CH_2 group is shifted downfield (δ=3.67) and so must be bonded to the only oxygen in the molecule, i.e. an **O-CH$_2$-CH$_2$- group**.

(Note: 'Atomic Accounting' is now: C_3H_7 - C_2H_4 = CH_3).

H—O—CH_2-CH_2-
2 **1** **3**

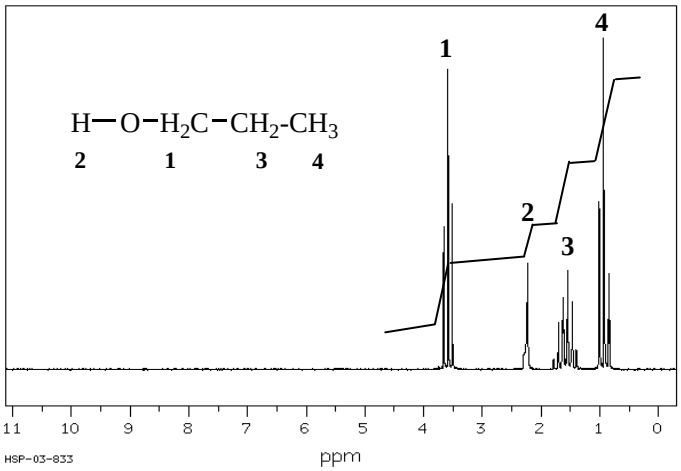
Signal 3 confirms that there is a **methylene group** R_2CH_2 (δ=1.6, Integration = 2H, splitting pattern = quintet). Also this -CH_2- has neighbouring carbons with 5 H on it so it must be CH_3-C**H**$_2$-CH_2. This is confirmed by the presence of a **CH$_3$ group** Signal 4 (δ=0.95, Integration = 3H, splitting pattern = triplet) thus the CH_2- also has as a neighbour, a carbon with 3 H on it so it must be -CH_2-CH_3.

(Note: 'Atomic Accounting' is now: CH_3 - CH_3 = 0, all atoms accounted for!).

H—O—H_2C—CH_2-CH_3
2 **1** **3** **4**

In summary unknown #360-14-B contains an alcohol, and an ethyl group. Therefore the **Unknown #360-14-B** must be **1-propanol**, which also has the correct/matching molecular weight/formula, and boiling point. Also the ^{1}H-NMR Spectrum shows there are 4 different types of H environments present in the molecule (and all 4 have been accounted for).

Note: The calculation for the 'degrees of unsaturation' in this problem also makes sense. There are 0 degrees of unsaturation present in the unknown.

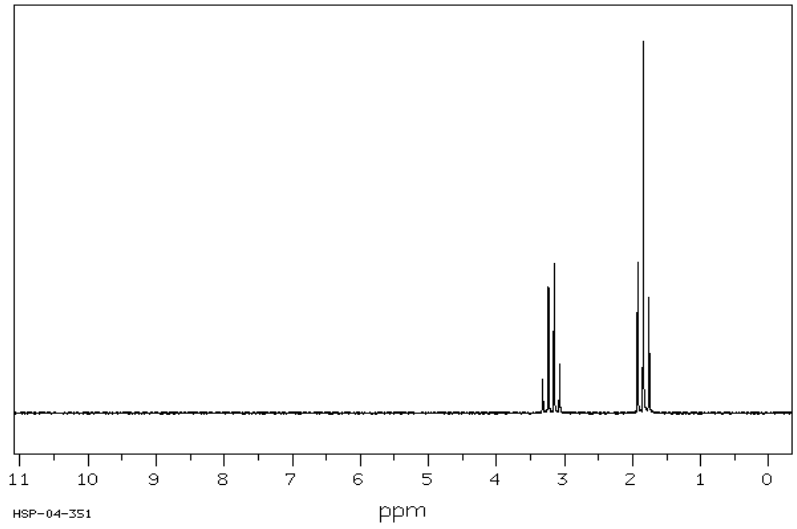


Instructor-Led Group ^{1}H-NMR Analysis Problems (answers on p.125)

Use the tables below to record your results of the '^{1}H-NMR Spectral Analyses' for the following compounds. Remember to label the signals on the spectrum, and assign signal codes to each 'H' in the structure.

Problem 1 **C_2H_5I** **Degrees of Unsaturation = _____**

Structure and name



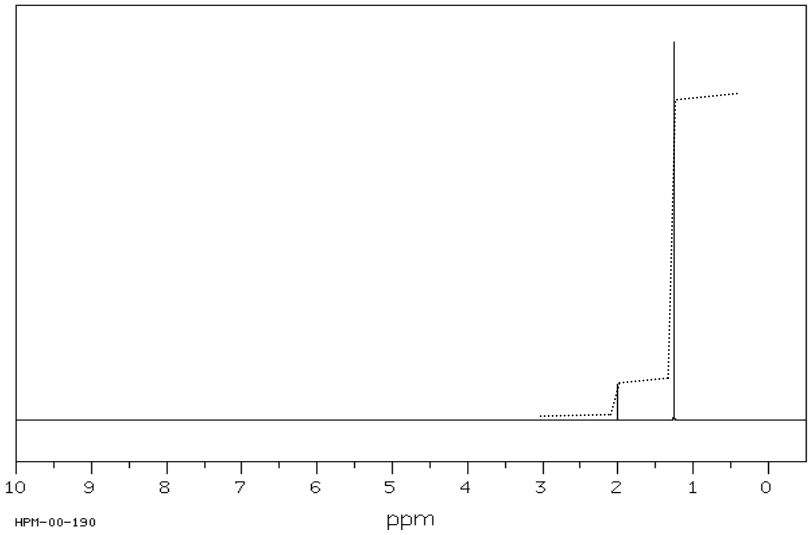
Structure Assembly Work Area

^{1}H-NMR Spectral Data for Instructor-Led Problem 1: **90 MHz (0.04 mL : 0.5 mL $CDCl_3$)**

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
	3.2	2				
	1.8	3				

Problem 2 **$C_4H_{10}O$** **Degrees of Unsaturation = _____**

Structure and name



Structure Assembly Work Area

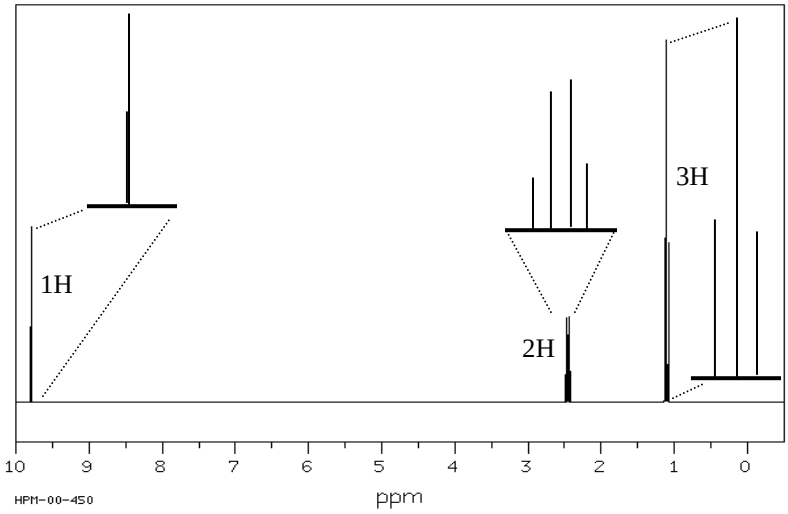
^{1}H-NMR Spectral Data for Instructor-Led Problem 2: **300 MHz (0.05 g : 0.5 mL $CDCl_3$**

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

Instructor-Led Group ^{1}H-NMR Analysis Problems (cont.)

Problem 3 **C_3H_6O** **Degrees of Unsaturation = _____**

Structure and name



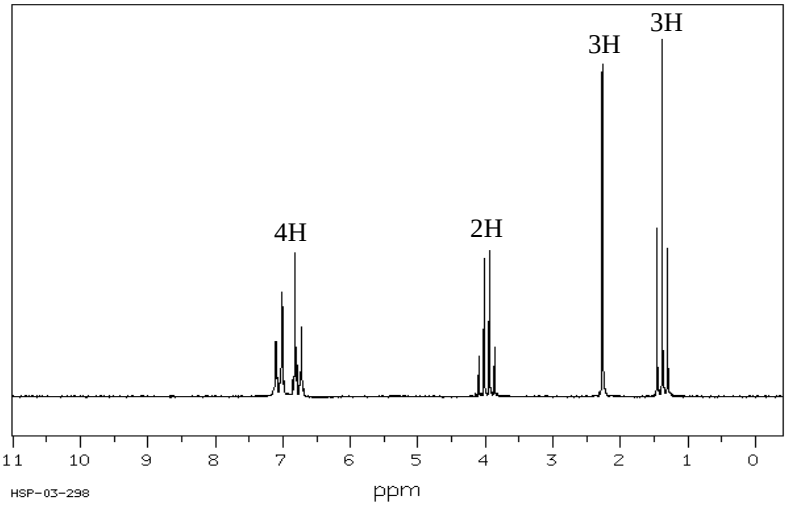
Structure Assembly Work Area

^{1}H-NMR Spectral Data for Instructor-Led Problem 3: **90 MHz (0.02 mL : 0.5 mL $CDCl_3$)**

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

Problem 4 **$C_9H_{12}O$** **Degrees of Unsaturation = _____**

Structure and name



Structure Assembly Work Area

^{1}H-NMR Spectral Data for Instructor-Led Problem 4: **90 MHz (0.04 mL : 0.5 mL $CDCl_3$)**

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

^{1}H-NMR Analysis Practice Problems

Use the tables below to record your results of the '^{1}H-NMR Spectral Analyses' of the provided known spectra on this page of the lab manual.

^{1}H-NMR Spectral Data for :

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

^{1}H-NMR Spectral Data for :

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

^{1}H-NMR Spectral Data for :

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

^{1}H-NMR Spectral Data for :

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

Write -up

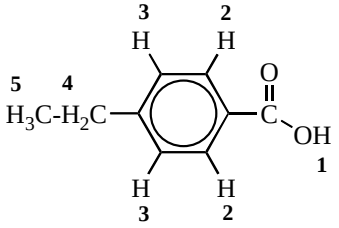
Use the following example as a guide for reporting your answer for each of the unknowns.

Experiment 14 Student Name**: Phil Terpaper** **AU ID#: 9876543**

Unknown #: 360-14-00 Mol. Wt.: 150.18 Formula: $C_9H_{10}O_2$ MP or BP: 112-113° C

Number of Degrees of Unsaturation = nC +1 + 1/2nN - 1/2 nH - 1/2 nX
for Compound 360-14-00, $C_9H_{10}O_2$ = (9) +1 + 1/2(0) - 1/2 (10) - 1/2(0)
= 9 + 1 - 5 = **5** degrees of unsaturation

Structure: (neatly draw the structure and be sure to indicate and label all the hydrogens)



p-ethylbenzoic acid

Name of Compound: *p*-ethylbenzoic acid

Table 1. Infrared Spectral Data:

***p*-ethylbenzoic acid**	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}	A B	2500-3300 3050	v.broad sharp	medium weak	broad carboxylic OH sp^2 C-H stretch
Between 3000 and 2000 cm^{-1}	C	2950	sharp	weak	sp^3 C-H stretch
Between 2000 and 1400 cm^{-1}	D E	1725 1600,1580,1500	sharp sharp	strong med	C = O carboxylic acid C=C aromatic
< 1400 cm^{-1}	F	840	sharp	med-strong	*para* subst.benzene

Functional Group(s) absent: C ≡N, C≡C, N-H

Table 2. ^{1}H-NMR Spectral Data:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	δ 12.1	1H	singlet	(exchanges with D_2O)	0	0-**H** of carboxylic acid
2	δ 8.0	2H	doublet	(Signals 2 and 3 could be referred to together as a multiplet, i,e., 4H)	1	Aromatic **H**, para substitution pattern
3	δ 7.3	2H	doublet			
4	δ 2.7	2H	quartet		3	Ar-C**H**$_2$- (shifted downfield)
5	δ 1.3	3H	triplet		2	CH_3-C (methyl group)

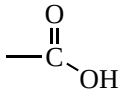
Discussion and Conclusions:

It was immediately apparent that Unknown # 360-14-00 was a carboxylic acid, -COOH (absorption bands A and D), and an extremely downfield (deshielded) proton (Signal 1 at δ 12.1). The next functional group indicated was an aromatic ring (absorption bands E and B), and downfield protons (Signals 3 and 4 at δ 7.3 and 8.0). Finally, the ^{1}H-NMR spectrum shows a methyl group (Signal 1). This -CH_3- has as neighbouring carbon with 2 H on it, so it must be CH_3-CH_2. This is confirmed by the presence of a -CH_2 group (Signal 2). The last piece of the puzzle is that the CH_2 group is shifted downfield (δ=2.7), so it is bonded to an aromatic ring, i.e. an Ar-CH_2-CH_3 group. In summary unknown #360-14-20 contains a carboxylic acid, an aromatic ring and an ethyl group. The substitution pattern appears to be *para*. Therefore the **Unknown #360-14-00** is ***p*-ethylbenzoic acid**, which also has the correct/matching molecular weight/formula, and boiling point.

Extra Detailed Answer for this Example:

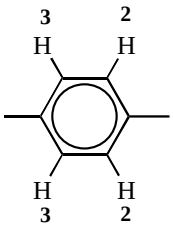
After analyzing and recording the infrared and ^{1}H-NMR data in Tables 1 and 2 above, and consulting the table of 'Chemical Shifts' on page 95 of the CHEM360 Lab Manual, the following can be deduced. It was immediately apparent that unknown 360-14-00 was a **carboxylic acid**, -COOH, (due to broad infrared absorption bands for C=O and O-H at 1725 and 3300-2500 cm^{-1} respectively), and an extremely downfield proton (δ 12.1).

(Note: 'Atomic Accounting' is now: $C_9H_{10}O_2$ - CO_2H = C_8H_9).



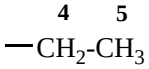
The next functional group apparent in the unknown was an **aromatic ring** (infrared absorption bands for C=C and sp^2 C-H at 1600/1500 and 3050 cm^{-1} respectively), and downfield (deshielded) protons (δ7.3, 8.0). It is also known that the aromatic ring is di-substituted, in a *para* orientation, hence $C_6H_{\mathbf{4}}$. This is due to the presence of a single infrared absorption at 840 cm^{-1} and the pattern of aromatic H δ at 7.3 and 8.0 (displays anisotropy).

(Note: 'Atomic Accounting' is now: C_8H_9 - $C_6H_{\mathbf{4}}$ = C_2H_5, an 'ethyl group' perhaps?!).

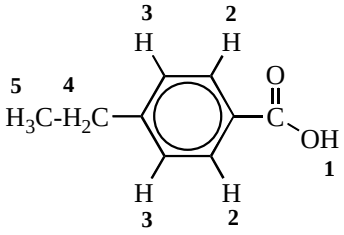


Finally, the spectrum shows a **methyl group** (δ=1.3, Integration = 3H, splitting pattern = triplet). Also this -CH_3- has as neighbouring carbon with 2 H on it so it must be CH_3-CH_2. This is confirmed by the presence of a **CH_2 group** (δ=2.7, Integration = 2H, splitting pattern = quartet) thus the CH_2- also has as a neighbour, a carbon with 3 H on it so it must be -CH_2-CH_3. The last piece of the puzzle is that the CH_2 group is shifted downfield (δ=2.7) and so must be bonded to an aromatic ring, i.e. an **Ar-CH_2-CH_3 group**.

(Note: 'Atomic Accounting' is now: C_2H_5 - C_2H_5 = 0, all atoms accounted for!).



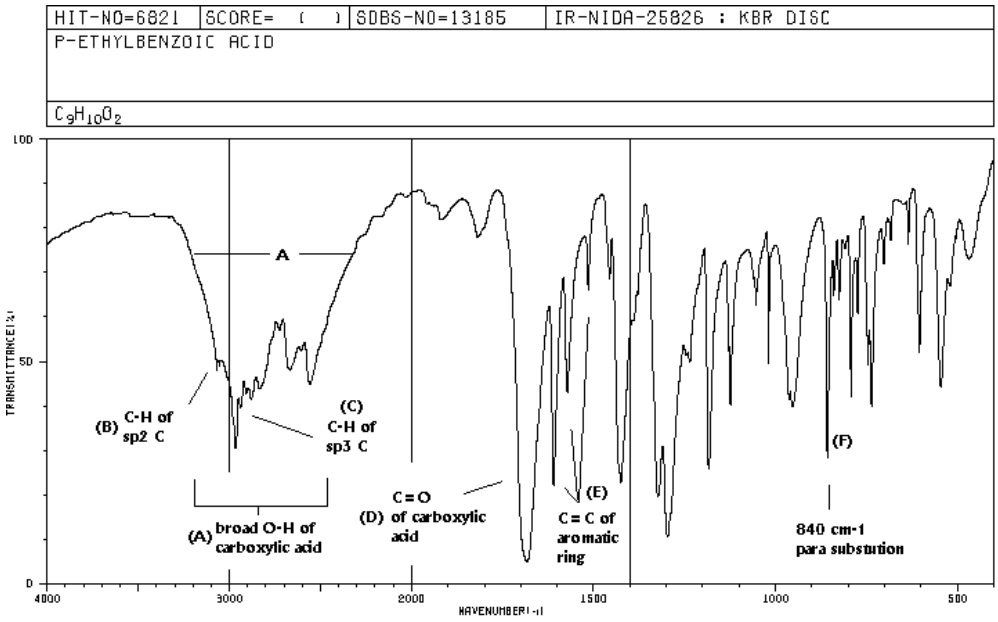
In summary unknown #360-14-00 contains a carboxylic acid, an aromatic ring and an ethyl group. The substitution pattern appears to be *para*. Therefore the **Unknown #360-14-00** must be ***p*-ethylbenzoic acid**, which also has the correct/matching molecular weight/formula, and boiling point. Also, in the ^{1}H-NMR Spectrum, there are 5 different types of H environments present in the molecule (and all 5 have been accounted for).



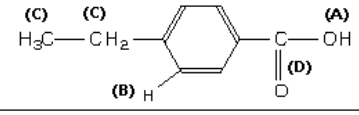
p-ethylbenzoic acid

Note: The calculation for the 'degrees of unsaturation' in this problem also makes sense (aromatic ring (4) + carbonyl (1) =5 degrees of unsaturation.

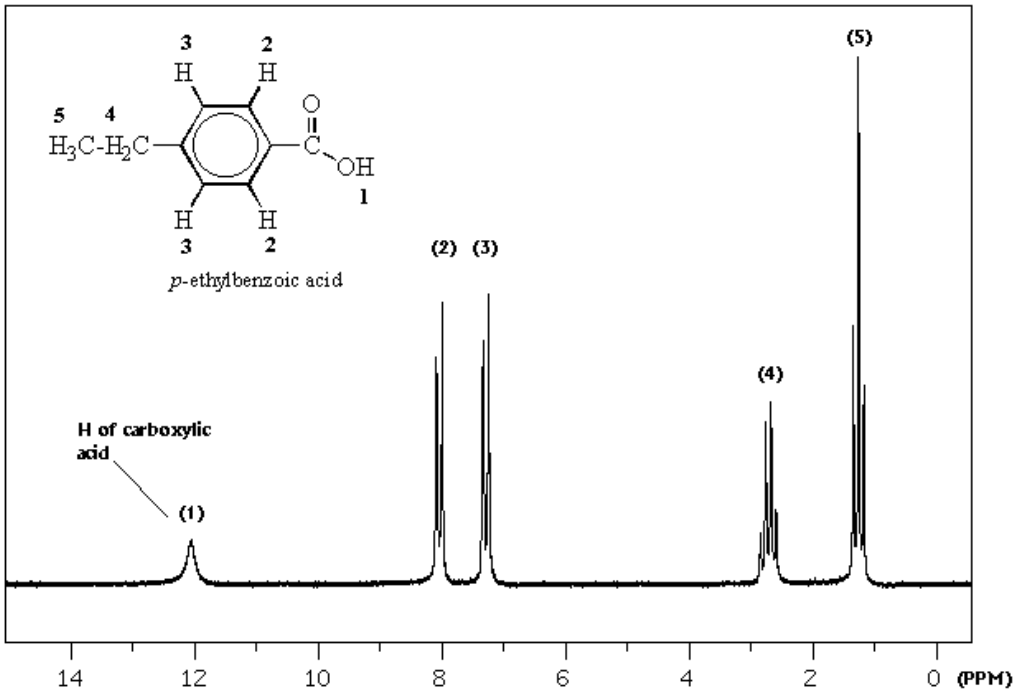
Infrared Spectrum of *p*-ethylbenzoic acid

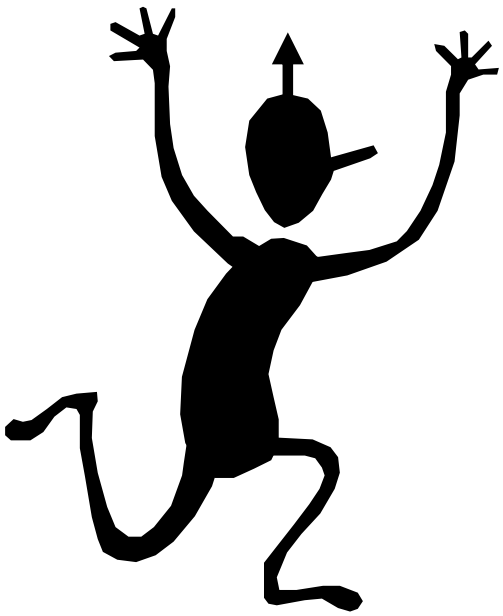


2977	35	2868	46	1425	21	1064	60	793	41
2966	29	2557	43	1322	18	1020	47	775	58
2940	37	1682	4	1297	10	963	38	747	47
2908	41	1610	21	1236	47	953	38	736	38
2878	39	1572	41	1184	25	858	26	605	50
2836	42	1515	64	1124	38	840	62	547	42
2723	55	1466	66	1061	66	825	60	522	64



^{1}H-NMR Spectrum of *p*-ethylbenzoic acid (90 MHz in $CDCl_3$)





I think I've done enough NMR study today.

References

1. J.W. Lehman. 1999. Operational Organic Chemistry, 3rd ed., Prentice Hall, Upper Saddle River, NJ.
2. N.A.J. Luff. 1972. DMS Working Atlas of Infrared Spectroscopy, Verlag Chemie, Butterworths & Co. Ltd., London.
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6. C.J. Pouchert and J.R. Campbell. 1974. The Aldrich Library of NMR Spectra, vols 1-11, Aldrich Chemical Company, Inc., Milwaukee, Wisconsin.
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Athabasca University wishes to thank Drs. K. Tanabe and T. Tamura and for all the IR/NMR Spectra used in this manual, obtained from the SDBS web site: http://www.aist.go.jp/RIODB/SDBS/ (04-Dec-1999).

Answers to Instructor led Group Problems:

Problem 1 iodoethane, 90 MHz (0.04 mL : 0.5 mL $CDCl_3$)

Problem 2 t-butyl alcohol, 300 MHz (0.05 g : 0.5 mL $CDCl_3$)

Problem 3 propanal, 90 MHz (0.02 mL : 0.5 mL $CDCl_3$)

Problem 4 p-ethoxytoluene, 90 MHz (0.04 mL : 0.5 mL $CDCl_3$)

Experiment 15
Reactions of the common functional groups — Part III: Aldehydes and ketones

Preparation

None: However, in order to obtain the maximum benefit from this experiment you should read:

1. 'Functional Groups, and
2. 'A Preview of Carbonyl Compounds' and 'Aldehydes and Ketones', and
3. 'Oxidation and Reduction in Organic Chemistry'.

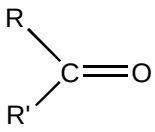
all in your textbook as part of the theory component of the course.

Objectives

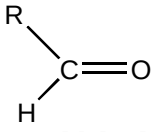
The purpose of this experiment is to illustrate a selection of reactions that are typical of two important classes of organic compounds: aldehydes and ketones. The reactions that have been chosen are intended to demonstrate similarities and differences between these two classes of compounds. A number of tests will be performed on a selection of known compounds. In a later experiment, the student will be expected to use the same tests in order to identify an assigned unknown compound.

Theory

As you should know, aldehydes and ketones both contain a carbonyl group (C=O). The difference between these two classes of compounds is that ketones have two alkyl (or aryl) groups bonded to the carbonyl-carbon atom, whereas aldehydes have one alkyl (or aryl) group and one hydrogen atom bonded to the carbonyl-carbon atom.



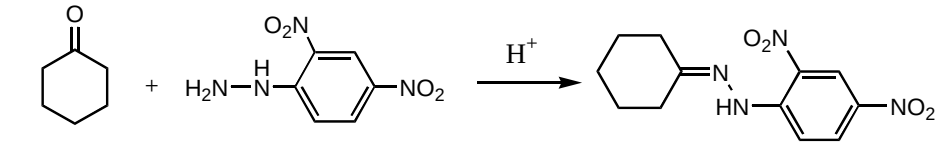
ketone



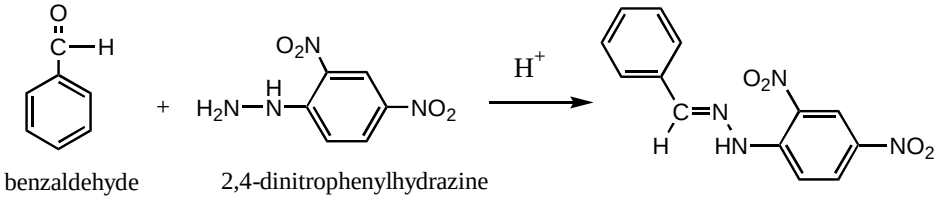
aldehyde

Brady's Reagent

The chemistry of these two classes of compounds is primarily that of the carbonyl group, thus there are a number of reactions that are common to both aldehydes and ketones. An example of a reaction that is common to both aldehydes and ketones is the reaction with 2,4-dinitrophenylhydrazine (**Brady's reagent**), a reaction that can be used in order to detect the presence of a carbonyl group.



cyclohexanone 2,4-dinitrophenylhydrazine 2,4-DNP derivative of cyclohexanone

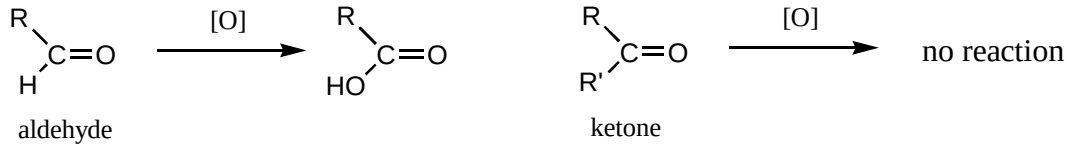


benzaldehyde 2,4-dinitrophenylhydrazine 2,4-DNP derivative of benzaldehyde

The 2,4-dinitrophenylhydrazones that are produced in this reaction are usually brightly coloured: unconjugated ketones give yellow precipitates, conjugated ketones give orange or red precipitates. This reagent is used to prepare derivatives of aldehydes and ketones (derivatives are used to help identify an unknown compound).

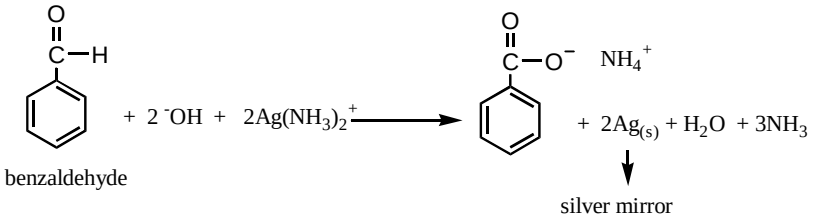
Tollens' Reagent

An important difference between aldehydes and ketones is the ease with which the latter can be oxidized.



aldehyde ketone

In the so-called "silver mirror test", an ammoniacal solution of silver nitrate **(Tollens' reagent)** is added to the carbonyl compound being investigated. If the latter is an aldehyde, the silver ions are reduced to metallic silver, which is then deposited as a mirror on the side of the test tube. Ketones do not react.

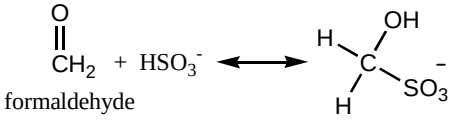


benzaldehyde

(NOTE: This equation has been balanced correctly)

Schiff's Reagent

A second method for distinguishing between aldehydes and ketones involves the use of **Schiff's reagent**. The usefulness of this test hinges on the ability of aldehydes to form addition compounds with solutions containing bisulfite ions:



formaldehyde

Schiff's reagent is a complex of fuchsin (rosaniline hydrochloride) and sulfur dioxide. Fuchsin itself is dark red, but the fuchsin-sulfur dioxide complex is colourless.

Equation 1

In an aqueous solution of Schiff's reagent, the sulfur dioxide that is present is also in equilibrium with sulfurous acid:

Equation 2 $SO_2\,(aq) + H_2O\,(l) \rightleftharpoons H_2SO_4\,(aq) \rightleftharpoons H^+(aq) + HSO_3^-(aq)$

aldehyde

aldehyde reacts with bisulfate ions present → $SO_{2\,(aq)}$ gets removed from system → This changes Fuchsin -Sulfur dioxide (colourless) to coloured (red)

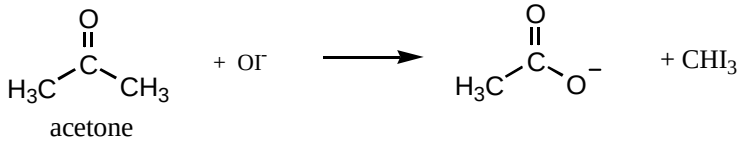
Thus, when an aldehyde is added to Schiff's reagent and reacts with the bisulfite ion present, equilibrium (2) shifts to the right and removes $SO_{2\,(aq)}$ from the system. This, in turn, causes equilibrium (1) to shift to the left, with the result that the solution changes from colourless to red.

Most ketones do not cause this colour change, although there are exceptions. The test is very sensitive, and traces of aldehyde impurities can give misleading results.

Iodoform Test

The final reaction that will be studied in this experiment enables us to determine whether a given ketone contains a CH_3-(C=O)-group, i.e., allows us to identify methyl ketones. However, care must be taken in using this test, as compounds containing a CH_3-CH(OH)-group also give positive results due to the case of oxidation of the latter to CH_3-(C=O)-.

When treated with a solution of iodine in sodium hydroxide (essentially sodium hypoiodite), methyl ketones react to form iodoform (CHI_3). Thus, this test is often called the iodoform test.



acetone

Procedure

Part A: Reaction with 2,4-dinitrophenylhydrazine

This test should be carried out on the aldehyde and ketone used in Experiment 13.

1. In a small test tube, dissolve one drop of the carbonyl compound in about 0.5 mL of methanol and add approximately an equal volume of Brady's reagent. Also prepare a positive and negative control tube. Shake all the solutions in for several minutes.

2. If no precipitate forms, warm the test tube in a beaker of hot water for 5 - 10 minutes and then allow the solution to cool. Record your observations.

Part B: Silver mirror test

As in Part A, this test should also be carried out on the aldehyde and ketone used in Experiment 13.

1. Add one drop of sodium hydroxide solution (3 mol·L^{-1}) to 2 mL of silver nitrate solution (0.3 mol· L^{-1}) in a small test tube.

2. To the solution prepared in Step 1, add ammonium hydroxide solution (1 mol·• L^{-1}) until the precipitate that first forms just redissolves.

3. Place 2 or 3 mL of the freshly prepared ammoniacal silver nitrate solution (from Step 2) in a **clean** test tube. To this solution add one or two drops of the carbonyl compound being investigated and allow the solution to stand at room temperature for several minutes. Also prepare a positive and negative control tube. Record your observations. Note: A dirty test tube often causes a finely divided black precipitate of silver to form instead of the expected silver mirror. Either result may be regarded as being positive.

CAUTION: Tollens' reagent decomposes on standing to form sodium fulminate, a very explosive substance. Decompose any excess of this reagent by adding concentrated nitric acid to your stock solution and your test solutions before washing them down the sink with plenty of water. Do not attempt to store Tollens' reagent and do not be tempted to give any excess reagent to a fellow student for use "later".

Part C: Schiff's test

1. Add 1 mL of Schiff's reagent to a few drops of each of the following:

    a. solution of formaldehyde

    b. the aldehyde that you used in Experiment 13

    c. the ketone that you used in Experiment 13

2. If no immediate reaction occurs, allow the solution to stand for 30 minutes. Record your observations.

Part D: Iodoform test

This test should be carried out on each of the following compounds: acetone, cyclohexanone, acetophenone, 1-butanol, and 2-butanol.

1. To one drop of the liquid being tested, add 3 mL of iodine in potassium iodide solution followed by enough sodium hydroxide solution (3 mol· L^{-1}) to make the iodine colour disappear. The formation of a yellow precipitate indicates that iodoform has been produced.

2. If no precipitate forms immediately, allow the reaction mixture to cool in an ice-water bath and add further iodine in potassium iodide solution until a permanent yellow colour persists. If a yellow precipitate still does not form, you can assume that no iodoform has been produced.

Safety

Sodium hydroxide solution is corrosive to the skin, harmful if swallowed, and extremely dangerous to the eyes.

Silver nitrate solution should not be allowed to come into contact with the skin or eyes.

Ammonium hydroxide (or **ammonia solution**) is basic, therefore care should be taken to prevent contact with skin or eyes. Inhalation of ammonia fumes should also be avoided. Use only in a fume hood.

Aldehydes and ketones used in Experiment 13 should be handled with care. See Experiment 13 for details of specific hazards.

Methanol is harmful to the eyes, lungs, skin, and other organs. Avoid inhaling the vapour or ingesting the liquid. Highly flammable.

Brady's reagent is a solution of 2,4-dinitrophenylhydrazine in methanol and sulfuric acid and should be handled accordingly. Protect your eyes and avoid contact with skin. Solid 2,4-dinitrophenylhydrazine is explosive and is harmful by inhalation of its dust and by skin absorption.

Tollens' reagent forms an explosive mixture on standing. See "Procedure" section for details of how to dispose of excess Tollens' reagent.

Formaldehyde solution is a skin irritant and is poisonous if swallowed. Its vapour is very irritating to the eyes and lungs.

Schiff's reagent contains sulfur dioxide in solution. Avoid contact with the skin or eyes. Vapour escaping from this solution may irritate the respiratory system, especially in individuals suffering from bronchitis and asthma.

Acetone (propanone) is an irritant to the eyes, skin and lungs. Harmful to the liver and kidneys if swallowed. Highly flammable. Use only in a fume hood or other well-ventilated area.

Acetophenone is harmful if swallowed, inhaled or absorbed through the skin. It causes **severe** eye irritation! Flammable.

Cyclohexanone: see Experiment 13 for specific hazards.

1-Butanol and 2-butanol: see Experiment 11 for specific hazards.

Iodine in potassium iodide solution may cause internal irritation if ingested. Avoid contact with skin.

Iodoform is harmful by inhaling, ingesting or skin contact.

Additional information regarding the potential hazards in handling these chemicals may be obtained from the Material Safety Data Sheets that are available in the laboratory.

Waste disposal

The test solutions from Parts A and C should be placed in the container marked "Non-halogenated organic wastes".

Instructions for dealing with excess Tollens' reagent and the test solutions from Part B are given in the "Procedure" section.

The test solutions from Part D should be placed in the container marked "Halogenated organic wastes".

Write-up

See Experiment 11 for a suggested way of writing up this type of experiment. Keep the introduction brief. Do not regurgitate all the theory. Simply define the tests used. You should not attempt to write equations for the Schiff's test.

Questions

Answers to be submitted with your report.

1. Write a balanced equation for the reaction of acetaldehyde (i.e. ethanal) with ammoniacal silver nitrate. Remember that this is a redox reaction.

2. Outline a systematic functional group test procedure that would enable you to distinguish among hexanal, 2-hexanone, 3-hexanone, 2-hexanol, and cyclohexanol.

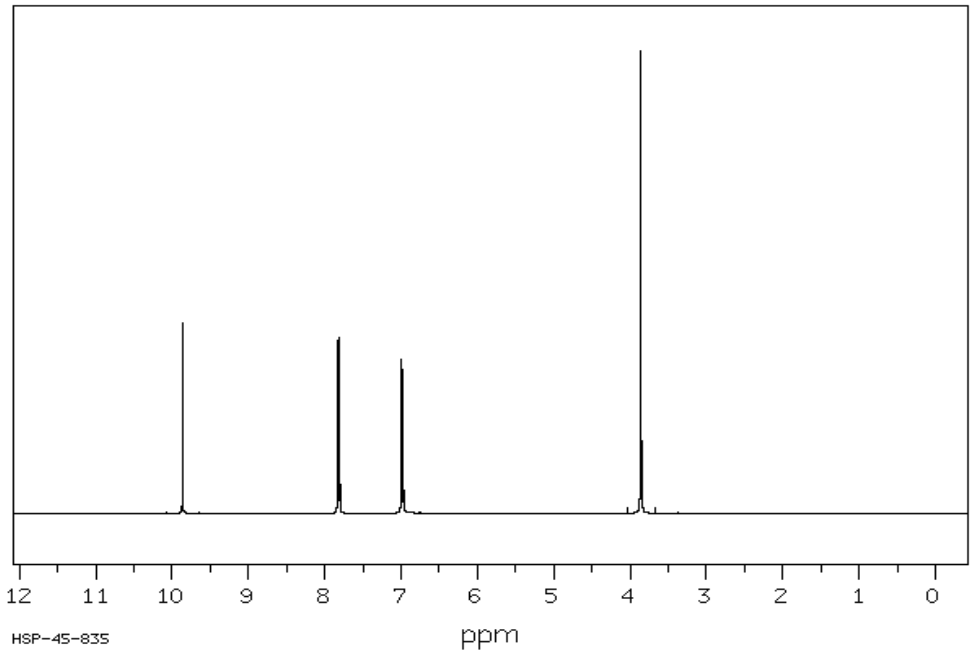
3. Aldehydes and ketones can also be easily distinguished by their infrared spectra and their identity deduced from their ^{1}H-NMR spectra. Explain why this is.

4. From the following results, identify the unknown compounds.

   a) Compound A: 2,4-DNPH positive, Tollens Test positive, Schiff's test positive, Iodoform negative (see Spectrum (A) next page).

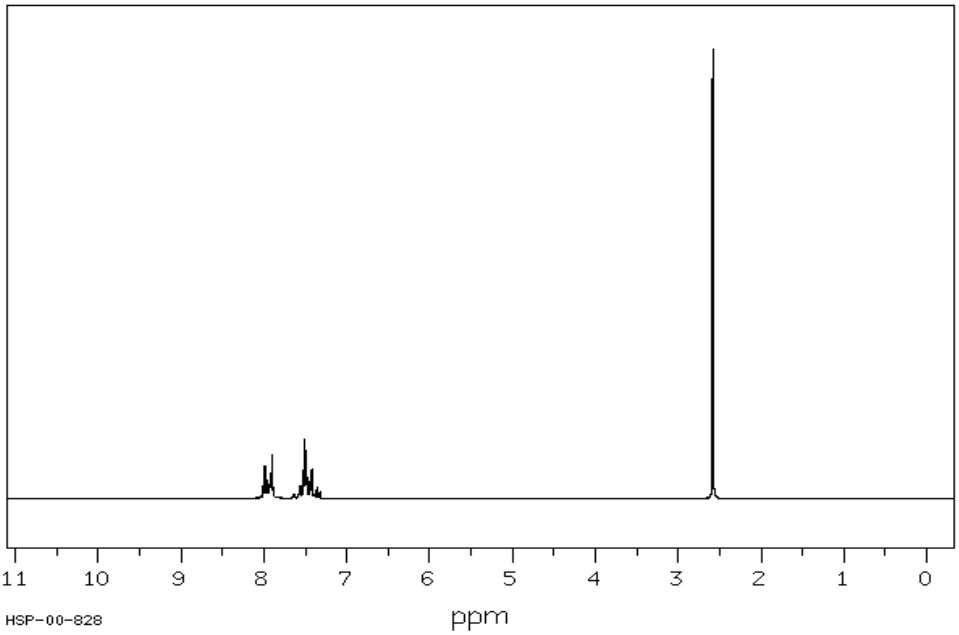
   b) Compound B: 2,4-DNPH positive, Tollens Test negative, Schiff's test negative, Iodoform positive (see Spectrum (B) next page).

Spectrum (A): ^{1}H-NMR, 400 MHz in $CDCl_3$



Molecular Formula $C_8H_8O_2$, δ 9.9 = 1H, δ 7.8 = 2H, δ 7.0 = 2H, δ 3.9 = 3H.

Spectrum (B): ^{1}H-NMR, 90 MHz in $CDCl_3$



Molecular Formula C_8H_8O , δ 7.9 = 2H, δ 7.3-7.7 = 3H, δ 2.6 = 3H.

Experiment 16
Triphenylmethanol by a Grignard reaction

"One never notices what has been done; one can only see what remains to be done".
Marie Curie, chemist (1867-1934)

Preparation

In order to begin this experiment, you should have read through the details of this experiment, and prepared a flow chart for the procedure to be followed, and

1. read 'Alcohols from reaction of Carbonyl Compounds with Grignard Reagents' in the chapter titled 'Alcohols from Reaction of Carbonyl Compounds' in the theory component of the course,

2. read 'Alcohols Nucleophilic addition of Grignard Reagents and Hydride Reagents: Alcohol Formation' in the chapter titled 'Aldehydes and Ketones: Neuclophilic Addition in the theory component of the course,

3. calculated the volume of bromobenzene (density = 1.4950 g· mL^{-1}), and ethyl benzoate (listed in CRC Handbook under 'benzoic acid, ethyl ester'; density = 1.0468 g· mL^{-1}) required for the reaction,

4. completed Experiment 12 (TLC), and

you may also wish to optional read pages 124-129 of *The Organic Chem Lab Survival Manual* (pp.221-226 in 3rd ed.).

Objectives

The purpose of this experiment is to provide the student with practical experience in the preparation of a Grignard reagent. It also illustrates how such reagents can be used to prepare a tertiary alcohol from an ester. The student will also obtain further experience in the use of thin-layer chromatography--a technique that was introduced in Experiment 12. The ease of formation of certain resonance-stabilized carbocations is also illustrated.

Introduction

Francois Auguste Victor Grignard (1871-1935). Professor of Chemistry at the University of Lyons and Nancy. Received Nobel Prize in 1912 for his work on organometallic compounds.

Although Grignard reagents can be used to synthesize a wide range of organic compounds, it is perhaps their reactions with carbonyl compounds (aldehydes, ketones and esters) to yield alcohols that are most utilized by organic chemists. In this experiment (see Fig. 16.1), you will react phenylmagnesium bromide with ethyl benzoate in order to obtain triphenylmethanol.

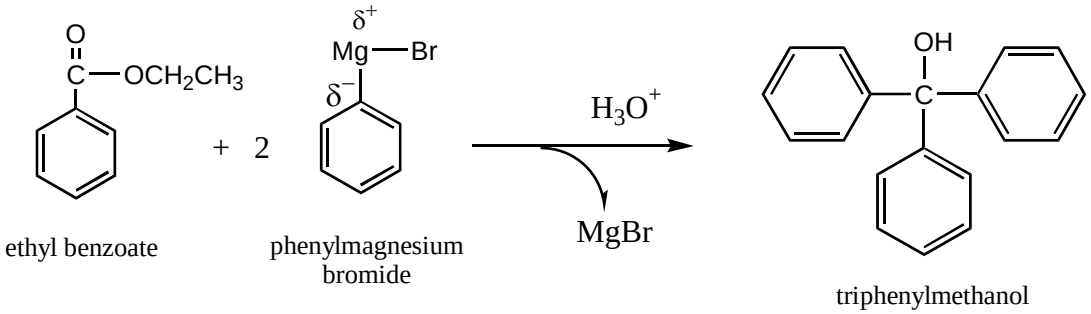


Figure 16.1 Overall reaction for formation of triphenylmethanol

The Grignard reagent (phenylmagnesium bromide) is prepared by the reaction of bromobenzene with magnesium as shown in Fig. 16.2:

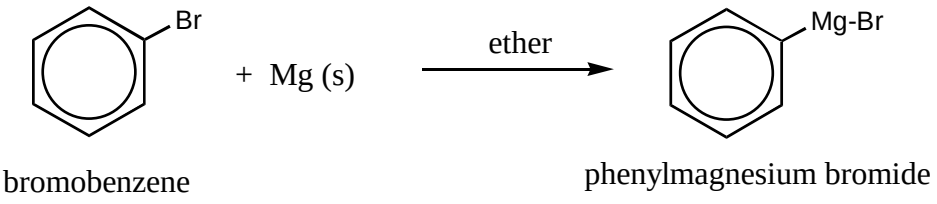


Figure 16.2 Formation of phenylmagnesium bromide from bromobenzene

This overall reaction to produce an alcohol is carried out in anhydrous diethyl ether and is sometimes difficult to initiate. Once the Grignard reagent has been formed, it behaves as a typical nucleophile and is capable of attacking a carbonyl group to form an intermediate magnesium salt (see Fig. 16.3). The latter may then be hydrolyzed to the desired alcohol.

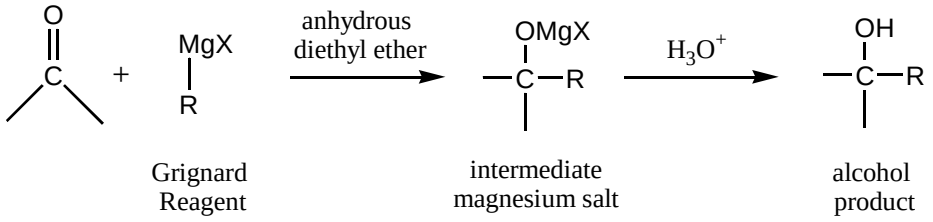


Figure 16.3 Formation of alcohols by hydrolysis of magnesium salt.
(**R** = 1º, 2º, or 3º alkyl, aryl or alkenyl; **X** = Cl, Br, or I)

Reaction of Grignard Reagents with Certain Functional Groups

Figure 16.4 below shows the type of products formed from the reaction of Grignard reagents with certain functional groups. Please note that **the reaction between an ester (see Fig. 16.1) and a Grignard reagent** is slightly more complicated than indicated in the above mechanism because of the ability of the **ester to react with two mole equivalents of Grignard reagent** rather than one.

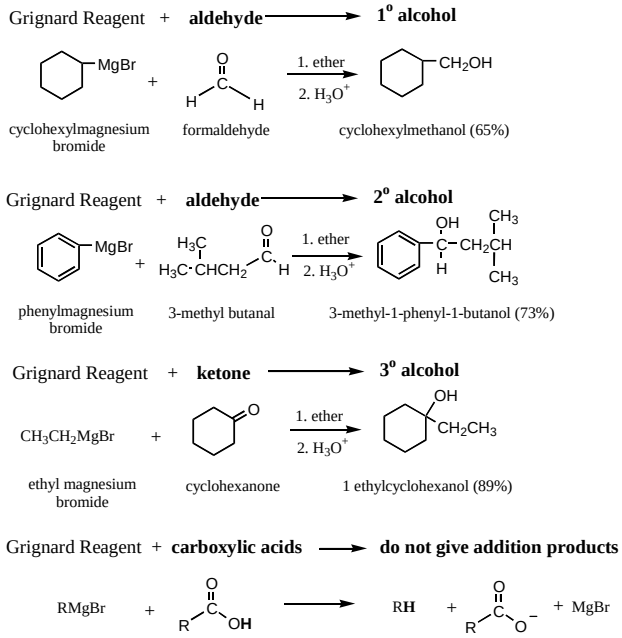
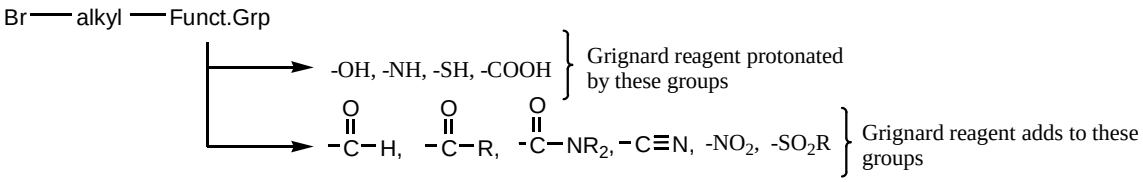


Figure 16.4 The reaction of Grignard reagents with certain functional groups

Severe Limitations of Grignard Reagents

1) The Grignard reagent cannot be prepared from an organohalide if there are other 'reactive' functional groups present in the molecule.

Alkyl halide with other functional groups



Note that bromobenzene is a suitable organohalide for preparation of a Grignard reagent.

2) Grignard reagents are very sensitive to moisture and can only be prepared under anhydrous conditions.

$$RMgX + H_2O \longrightarrow RH + Mg(OH)X$$

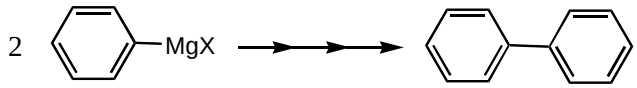
This is overcome in this experiment by thoroughly drying the glassware prior to use and the use of anhydrous reagents (they are more expensive!).

3) Grignard reagents are sensitive to the presence of oxygen

$$2RMgX + O_2 \longrightarrow 2ROMgX \xrightarrow{2H_2O} 2ROH + 2Mg(OH)X$$

This is mostly overcome in this experiment by keeping the solvent warm during preparation of the Grignard reagent. The diethyl ether forms a thick 'vapour barrier' above the reaction mixture thereby reducing the diffusion of oxygen gas into the solution.

4) Grignard reagents can, through a complex radical reaction, couple with themselves to form high molecular weight byproducts. It is the reason for biphenyl forming as the major byproduct in this experiment.



phenylmagnesium halide

biphenyl

Procedure

Part A: The preparation of phenylmagnesium bromide

CAUTION: Diethyl ether is highly flammable!!! There must be no flames in the laboratory while this experiment is in progress.

1. In this experiment, all glassware must be absolutely dry. Drain any water out of your condenser, wash it with acetone, and place it in the oven to dry (15 minutes at 110–120^{o} C). Similarly, carefully clean a 200–mL round-bottom flask (and if necessary a Claisen adapter and a 125 mL separatory funnel minus stopcock) and place it/them in the oven to dry.

2. Place 2.4 g of magnesium turnings in the clean, dry, 200-mL round-bottom flask. (Make sure that the magnesium turnings used are those supplied specifically for use in Grignard reactions.) Attach the condenser to the flask (do not forget the grease!) and then attach a (granular calcium chloride) drying tube (see Figure 16.5) to the top of the condenser.

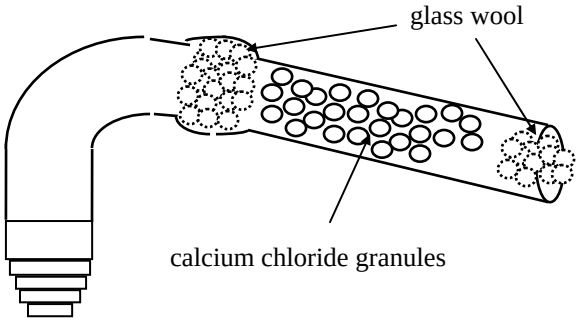


Figure 16.5. A calcium chloride (granular) drying tube

3. Clamp the round-bottom flask to a retort stand. Place a hot-plate/stirrer beneath the flask. Clamp condenser and begin to circulate water through the condenser. Use a Claisen adapter to attach the separatory funnel and condenser to the round bottom flask.

4. Dissolve 0.10 mol of bromobenzene in 50 mL of anhydrous diethyl ether and transfer the solution to an equalizing funnel. [An equalizing funnel, also called a

pressure-equalizing addition funnel, enables you to add reactant to a reaction mixture without opening up the system to air and atmospheric moisture (see Figure 60(c) on page 126 of *The Organic Chem Lab Survival Manual* or Fig.110(c) on p.227 of 3rd ed.).
If no equalizing funnels are available, you can achieve the same result by using a separatory funnel with a drying tube instead of a stopper. [If necessary, please consult your instructor.]

5. Add 10 mL of anhydrous ether to the round-bottom flask containing the magnesium and a magnetic stir-bar. Attach a Claisen adapter to the flask. Insert the condenser (with drying tube attached) into the mouth of the adapter and insert the equalizing funnel into the arm of the adapter (see also Figure 61, p. 128 of *The Organic Chem Lab Survival Manual*; Fig. 111 on p.228 in 3rd ed.).

6. Allow about 10 mL of the bromobenzene solution to run out of the equalizing funnel into the round-bottom flask. Stir the reaction mixture slowly and watch for signs that the reaction has begun. These signs include:

   a. the evolution of heat, i.e., the flask gets warm
   b. bubbles begin to appear from the magnesium metal
   c. a white precipitate begins to appear, i.e., the solution becomes cloudy
   d. the brown colour of the iodine disappears

Do not proceed with the next step
until your instructor has confirmed that the reaction is under way.
(a single crystal of iodine maybe added to help initiate the reaction)

7. When the reaction has begun, add the bromobenzene solution at such a rate that a steady reflux is maintained. (This usually means that the bromobenzene solution is added dropwise.) If the reaction becomes too vigorous, slow the rate at which the bromobenzene is being added and cool the round-bottom flask in an ice-water bath (i.e. remove the hot-plate/stirrer and replace with an ice-water bath supported by a lab jack).

8. After all the bromobenzene solution has been added and the reaction appears to have ceased, use a bath of warm (40–50^{o} C) water to heat the round-bottom flask for about 20–30 minutes. During this period, a steady reflux should be maintained and virtually all of the magnesium should dissolve. *Do not* attempt to accelerate this process by using a heating mantle or a Bunsen burner.

Part B: The reaction of phenylmagnesium bromide with ethyl benzoate

1. In a small, dry Erlenmeyer flask, dissolve 0.047 mol of ethyl benzoate in 15 mL of anhydrous diethyl ether. Transfer this solution to the equalizing funnel that previously contained the solution of bromobenzene.

2. Cool the round-bottom flask containing the Grignard reagent in an ice-water bath.

3. Slowly, and with constant stirring, allow the solution of ethyl benzoate to run into the flask containing the Grignard reagent. The formation of a coloured precipitate indicates that the intermediate magnesium salt is being formed. If the reaction appears to be too vigorous, continue to cool the flask in the ice-water bath.

4. When addition of the ethyl benzoate solution is complete, heat the reaction mixture to 40-50^{o} C for 30 minutes using a bath of warm water (as before). Again, a heating mantle or Bunsen burner must not be used.

Part C: The isolation of triphenylmethanol

Note: A precipitate may have formed. If so it will have to be redissolve by adding more diethyl ether than 5 mL indicated in Step C.2 below. Caution: the total volume of all the washes etc. must be kept < 250 mL (maximum size of separatory funnel available.

1. Place 50 g of ice and 50 mL of sulfuric acid (2 mol$\cdot$ L^{-1}) in a 400-mL beaker and decant the reaction mixture into the beaker leaving any solid, unreacted magnesium in the round-bottom flask. **CAUTION: An exothermic reaction will occur in the beaker!**

2. Rinse the round-bottom flask, first with 5 mL of diethyl ether and then *cautiously* with 5 mL of sulfuric acid (2 mol$\cdot$ L^{-1}). Add each of the washings to the 400-mL beaker containing the hydrolyzed reaction mixture and try to leave any unreacted magnesium in the round-bottom flask.

3. Pour all of the hydrolyzed mixture into a separatory funnel (250 mL) and add 75 mL of diethyl ether. Shake the funnel (carefully) and separate the layers.

4. Wash the organic layer with an equal volume of water. Separate the layers.

5. Wash the organic layer with an equal volume of sodium hydrogen carbonate solution (0.6 mol· L^{-1}). Separate the layers. Note: If a yellow solid develops, remove it, dissolve in ether, and then 're-separate'.

6. Wash the organic layer with an equal volume of water. Wash the organic layer with an equal volume of brine (saturated sodium chloride solution). Separate the layers and transfer the organic phase to an Erlenmeyer flask. Add about 1 g of anhydrous sodium sulfate, stopper the flask and allow the solution to dry for 10–15 minutes during which time the flask should be swirled frequently.

7. Filter the dried solution through a fluted filter paper, collecting the filtrate in a 200–mL round-bottom flask. Add about 25 mL of ligroin (high boiling point petroleum ether) to the filtrate.

8. Add a boiling chip to the solution in the flask and set up the apparatus for a simple distillation using a hot-water bath as the heat source.

9. Distil the diethyl ether into a receiver that is being cooled in an ice-water bath. When most of the diethyl ether has been removed, cool the flask in an ice-water bath and crystals of triphenylmethanol should begin to appear.

10. Collect the solid triphenylmethanol by suction filtration. If the yield appears to be very low, you may not have removed enough diethyl ether from the mother liquor. If this is the case, return the filtrate to the round-bottom flask and distil off some more diethyl ether and hence obtain a second crop of crystals.

11. Save samples of the filtrate and the crude triphenylmethanol for testing by thin-layer chromatography.

12. Recrystallize the bulk of your triphenylmethanol from absolute (100%) ethanol.

13. Determine the yield, melting point, mixed melting point with authentic standard (if available), and %yield of your recrystallized product. Transfer the product to a suitably labelled vial.

Part D: Observation of the triphenylmethyl carbocation

1. Dissolve a small amount (~0.05 g) of triphenylmethanol in a few drops of reagent grade methanol in a 'large test tube'. Place the test tube plus sample in a **small beaker of ice** in a fume hood. With the test tube point away from you, carefully add 1 mL of concentrated sulfuric acid using a Pasteur pipette, mixing frequently throughout the addition, and note any colour change.

   CAUTION: Concentrated sulfuric acid is extremely hazardous and causes serious chemical burns. **Wear latex gloves** and protect your eyes. The heat generated during this test can cause the liquid in the test tube to splatter out.

2. *Carefully* pour the solution obtained in step 1 into 10 mL of cold water. Note any changes that occur.

3. Repeat steps 1 & 2, using the diphenylmethanol that you prepared in Experiment#12.

	Observations	
After Procedure Step	**Triphenylmethanol (Exp.16)**	**Diphenylmethanol (Exp. 12)**
Appearance of dry crystals		
Addition of methanol		
Addition of 1 mL sulphuric acid		
Dilution into 10 mL water		

Part E: Analysis by Thin-Layer Chromatography

IMPORTANT: If you did not complete Experiment 12, you should review the sections pertaining to thin-layer chromatography provided in the instructions for that experiment. Also, you should read Chapter 19 of *The Organic Chem Lab Survival Manual* (Chapter 26 in 3rd ed.), omitting the sections on "Preparation of TLC Plates" and "Preparative TLC".

1. Prepare solutions of each of the following substances by dissolving about 50 mg of substance in 2 mL of dichloromethane (methylene chloride) in small test tubes: crude triphenylmethanol, recrystallized triphenylmethanol, and biphenyl. You will also need the small sample of the mother liquor obtained in step 11 of Part C.

2. Prepare a development chamber using a 9:1 mixture of ligroin and dichloromethane as the eluent. (See Experiment 12 and p. 144 of *The Organic Chem Lab Survival Manual*; p. 247 in 3rd ed.)

3. Spot the TLC plate with samples of the four solutions as shown in Figure 16.6.

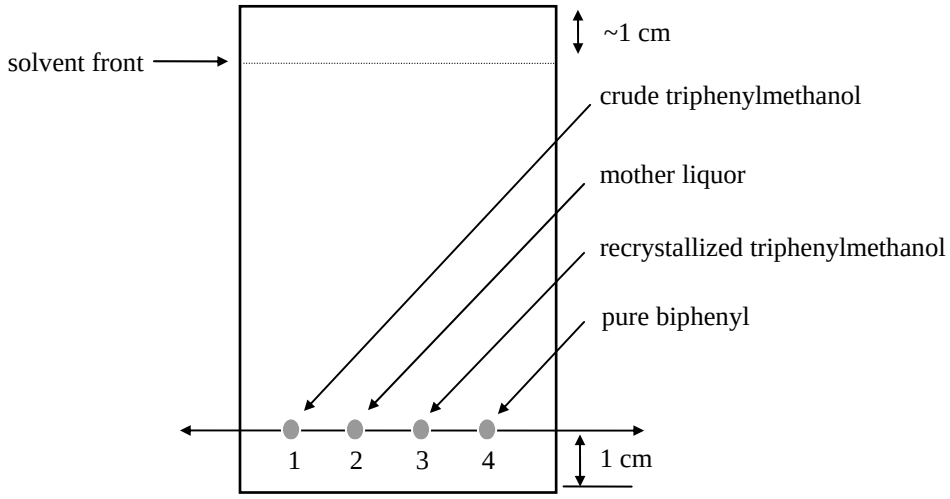


Figure 16.6. Thin-layer chromatography plate

4. As in Experiment 12, dip the lower end of the TLC place in the eluent contained in the development chamber. Observe the progress of the solvent up the plate. Remove the plate from the chamber when the solvent front reaches the line down at the top of the plate.

5. Dry the plate by shaking it in air and examine the dried plate under an ultraviolet lamp. Circle any spots with a pencil.

6. Calculate the R_f values of triphenylmethanol and biphenyl.

7. Submit your pure triphenylmethanol and your report, with a **sketch** of the TLC plate attached, to your tutor for marking.

Safety

Diethyl ether (ethoxyethane) is highly flammable. Inhalation of the vapour may result in intoxication, drowsiness and unconsciousness. Never attempt to evaporate an ether solution to dryness as this could result in the formation of highly explosive peroxides.

Ethyl benzoate is an irritant and is harmful when swallowed. Flammable.

Bromobenzene is poisonous if swallowed and is also poisonous by skin absorption. The vapours from this compound may be narcotic in high concentrations. In low concentrations it irritates the eyes. Flammable.

Concentrated sulfuric acid is highly corrosive. Wear gloves and proper eye protection when using this substance. Avoid contact with skin or clothes. Use only in a fume hood.

Petroleum ether (or ligroin bp. 60-80^{o} C) is harmful if inhaled or swallowed. Can cause skin irritation and exposure may produce a burning sensation, headache and vomiting. Very flammable!

Dichloromethane is harmful if inhaled, swallowed or absorbed through the skin. It is dangerous to the eyes and has strong narcotic powers.

Iodine can burn the skin. Causes internal irritation if swallowed. Its vapour is harmful to the respiratory system.

Magnesium metal is flammable. Magnesium fires should be extinguished only with sand or a Class D fire extinguisher. Do not attempt to extinguish a magnesium fire using water or ABC-type fire extinguishers.

Biphenyl is harmful if swallowed, inhaled or absorbed through the skin.

Methanol is poisonous if swallowed. Its vapour is harmful to the eyes, lungs and skin. Highly flammable.

Ethanol is poisonous and its toxicity is increased by the presence of the denaturing substances that are added to laboratory ethanol in order to reduce its illegal consumption. High concentrations of ethanol vapour can be dangerous. Highly flammable.

Additional information regarding the potential hazards in handling these chemicals may be obtained from the Material Safety Data Sheets that are available in the laboratory.

Waste disposal

Small quantities of unreacted magnesium (from Part C, step 1) should be dissolved in dilute hydrochloric acid and washed down the drain with plenty of water.

The aqueous layer from step 3 of Part C may be washed down the drain, as may the aqueous washings from subsequent steps in the procedure.

The sodium sulfate used to dry the ethereal solution of triphenylmethanol should be placed in a garbage can.

The diethyl ether that is removed from the triphenylmethanol by distillation should be placed in the container for "Non-halogenated Organic Wastes."

The diethyl ether/ligroin mixture from the suction filtration in step 10 of Part C should be placed in the container for "Non-halogenated Organic Wastes."

The (ethanol) filtrate from the recrystallization of triphenylmethanol should be placed in the container for container for "Non-halogenated Organic Wastes."

The solutions obtained in Part D may be washed down the drain with plenty of water.

The solutions used in the thin-layer chromatography section of the experiment, and the 9:1 mixture of ligroin and dichloromethane used as the eluent in this part of the experiment, should be placed in the container for "Halogenated Organic Wastes."

Write-up

This experiment may be written up using the standard approach for preparative-type experiments. Do not forget to include details such as the melting point and yield of the product. In addition, be sure to include a discussion of the results of your thin-layer chromatography analysis.

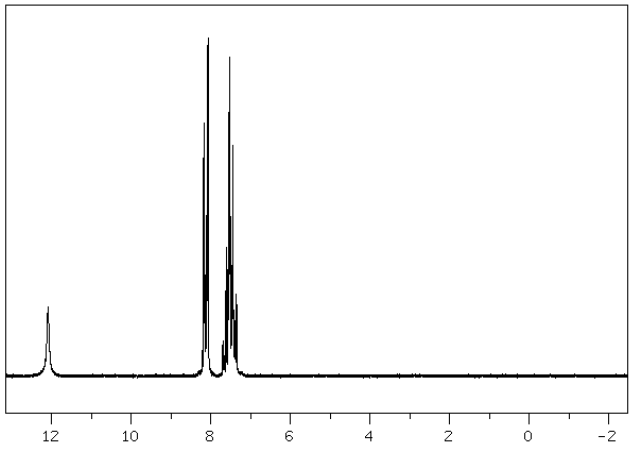
Questions

Answers to be submitted with your report.

1. How do you account for the fact that biphenyl is formed as a by-product in this reaction?

2. Why do you think that reactions involving Grignard reagents are sometimes carried out in an atmosphere of nitrogen or argon?

3. A Grignard reaction was performed and the following ^{1}H-NMR (90 MHz in $CDCl_3$) was obtained of the purified product. Deduce the product's structure (Molecular Formula = $C_7H_6O_2$). Also write the overall reaction for its formation from <u>any</u> organohalide and carbonyl compound.



^{1}H-NMR Spectral Data:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment
1	δ 7.5	3H				
2	δ 8.1	2H				
3	δ 12.1	1H		Xchngs with D_2O		

Experiment 17
Multi-step synthesis: Benzocaine

Preparation

Before beginning this experiment, you should have read through the details of this experiment, and prepared a flow chart for the procedure to be followed, and

1. read 'An Introduction to Organic Synthesis', and

2. studied the 'Oxidation of Aromatic Compounds'.

3. studied the 'Nucleophilic Acyl Substitution Reactions of Carboxylic acids' and 'Chemistry of Amides'.

4. studied the 'Synthesis of Amines'.

5. completed at least three "preparative type" experiments (e.g., Experiments 10, 12, 13, and 16)

You may also wish to read the section on "Steam Distillation" on pp. 117-119 of *The Organic Chem Lab Survival Manual* (Chapter 20 pp. 208-212 in 3rd ed.).

Objectives

The purpose of this experiment is to provide an example of how a multi-step synthesis can be used in order to prepare an organic compound, which is present in a number of consumer products.

Introduction

Benzocaine, ethyl 4-aminobenzoate, is found in medications used to ease the pain of wounds, burns and sunburn. It is also used in suppositories for hemorrhoid sufferers. A quick look around the shelves of any drug store would reveal the wide use of this compound in such products as Solarcainev ®, Lanacaine ® and Anivy ®. Benzocaine may be prepared from 4-nitrotoluene by the following five-step synthesis shown in Figure 17.1:

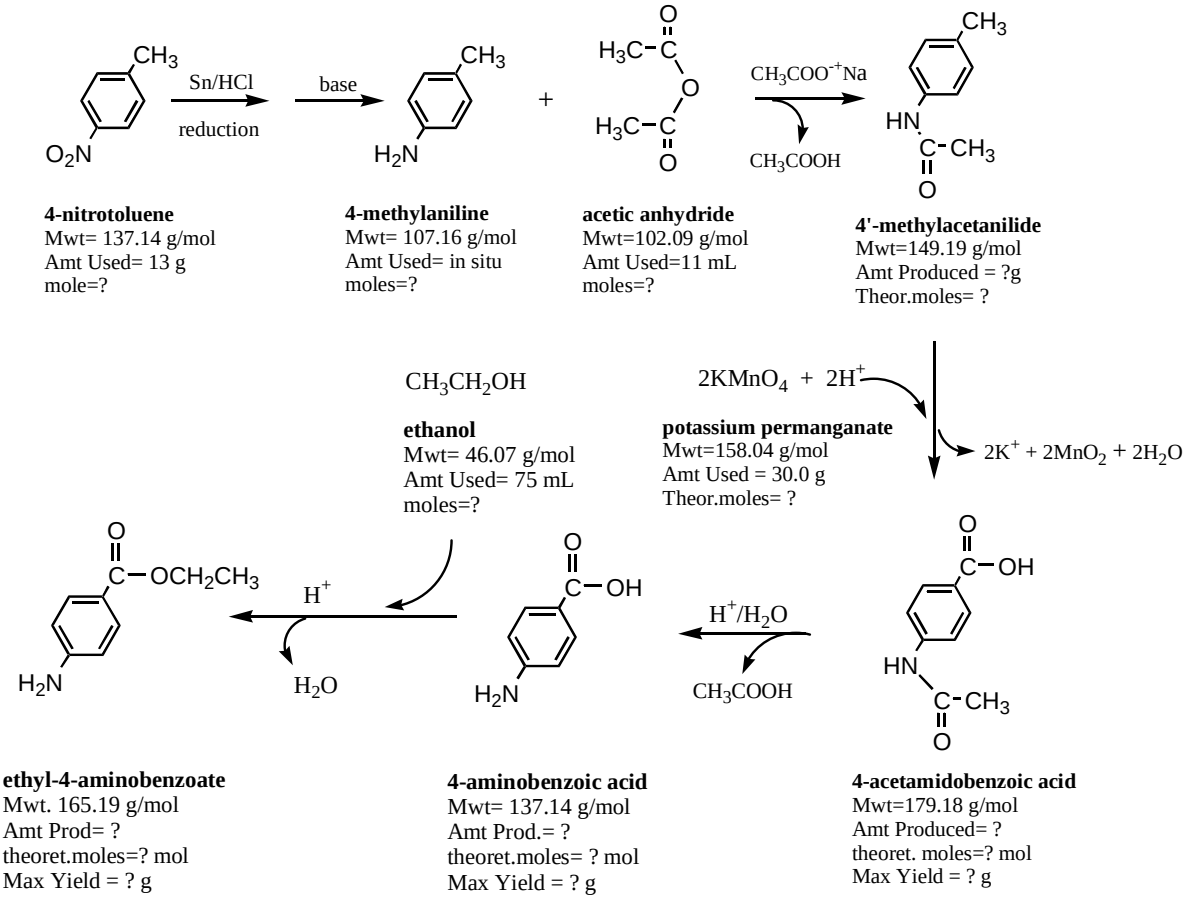


Figure 17.1 Overall reaction for the formation of benzocaine from *p*-nitrotoluene.

One problem with a synthesis of this type is that the overall yield of the final product is often quite low. For example, if a 50% yield is obtained in each of the five steps shown in the above reaction scheme, the overall yield will be 0.50 x 0.50 x 0.50 x 0.50 x 0.50 = 0.03125, or just over 3%. This should give you an indication of why synthetic organic chemists sometimes appear to be obsessed with obtaining the maximum percentage yield from a given reaction.

Let us now consider the overall strategy that we shall employ.

By comparing our starting material, 4-nitrotoluene, with our penultimate product, 4-aminobenzoic acid, we see that our goal will be to convert a methyl group into a carboxyl

group and to reduce a nitro group to an amino group. The final step in the synthesis will than be a simple esterification. However, it is important that the first four steps are carried out in the correct order. For example, if the methyl group is oxidized to a carboxyl group in the first step, the subsequent reduction of the nitro group to an amine would result in the formation of a product containing both an acidic and basic group (-CO_2H and -NH_2, respectively). Such a product would be soluble in the acidic reducing mixture (tin and hydrochloric acid) and would also be soluble in base. Thus, isolation of the product from the reaction mixture would be difficult to achieve. The problem cannot be solved by esterifying the carboxyl group before reducing the nitro group because the ester would simply hydrolyze back to a carboxylic acid under the conditions employed in the reduction.

The approach that you will use involves the reduction of the nitro group before the methyl group is oxidized. The reagent used to bring about the reduction is a mixture of tin and hydrochloric acid. After the reduction is complete, the reaction mixture is made basic and the product, 4-methylaniline, is extracted using a process called *steam distillation*. Because 4-methylaniline contains two activating groups, CH_3 and NH_2, it is very susceptible to oxidation. To prevent oxidation from occurring, the amine is immediately converted to a salt by dissolving it in aqueous acid.

Once 4-nitrotoluene has been converted to 4-methylaniline (in fact 4-methylanilinium chloride), the next step is to oxidize the methyl group. This cannot be done directly, however, as the highly activated aromatic ring would be destroyed under the conditions employed. Instead, the highly activating amino group is acetylated to give an acetamido group, CH_3-(C=O)-NH-, which is much less activating. The product of this reaction, 4'-methylacetanilide, is then oxidized to 4-acetamidobenzoic acid under approximately neutral conditions. The acetamido group is then hydrolyzed back to an amino group and the resulting 4-aminobenzoic acid is esterified to give the desired product.

Now that you understand the overall strategy to be employed, let us examine the details of each of the individual steps in the synthesis.

(i) The reduction of 4-nitrotoluene

The reduction of nitro compounds is the principal method of preparing primary aromatic amines. This reduction can be achieved through the use of hydrogen and a suitable catalyst, or by using a metal/acid combination such as tin and hydrochloric acid. A variety of nitrogen compounds is formed as the reduction proceeds, but under the conditions used in this experiment none of the intermediates can be isolated. The actual product of the reduction is the double salt, $(C_6H_5NH_3)_2SnCl_6$, and the free amine is liberated by treating this double salt with base. This treatment also has the added advantage that it renders any tin salts soluble through the formation of stannate ions (SnO_3^{2-}). The amine is extracted from the reaction mixture by steam distillation. (See "Steam Distillation" on pp. 117-119 of *The Organic Chem Lab Survival Manual* or pp.208-212 in 3rd ed.). You will employ a set-up similar to the one shown in Figure 57 (Fig.106 in 3rd ed.), except that, instead of a three-necked flask, you will use a single-necked flask and a Claisen adapter. As we have

previously explained, 4-methylaniline is very susceptible to air-oxidation, thus it is immediately converted to a salt through the addition of hydrochloric acid.

(ii) The acetylation of 4-methylaniline

This step is relatively straightforward and requires no detailed explanation.

(iii) The oxidation of 4'-methylacetanilide

Although alkanes and aromatic hydrocarbons are generally very resistant to oxidation, the carbon attached to the aromatic ring of an alkylaromatic hydrocarbon is sufficiently activated to be quite easily oxidized. While it is occasionally possible to obtain other oxidation products, an alkyl group is normally cleaved between the α- and β-carbons to give the corresponding aromatic carboxylic acid. In the oxidation of a methyl group, the partially oxidized intermediates, the alcohol and the aldehyde, are more easily oxidized than the methyl group, so that only under rather special conditions is it possible to stop the oxidation and isolate these intermediates. Thus, benzoic acid or some other aromatic acid is the usual product.

The use of chromium (VI) as an agent for oxidizing the side chain of an aromatic hydrocarbon requires elevated temperatures and acidic conditions. However, the permanganate ion can bring about such oxidations at about 80-90^{o} C in an almost neutral solution. The permanganate ion is reduced to manganese(IV) oxide and, as we see from the half-equation,

$$3e^{-} + MnO_4^{-}{}_{(aq)} + 2H_2O_{(l)} \longrightarrow MnO_{2\,(s)} + 4OH^{-}{}_{(aq)}$$

the reaction mixture becomes increasingly basic as the oxidation proceeds. In order to prevent the base-promoted hydrolysis of the acetamido group, magnesium sulfate is added to the reaction mixture so that the hydroxide ion is removed as the sparingly soluble magnesium hydroxide.

$$Mg^{2+}{}_{(aq)} + 2OH^{-}{}_{(aq)} \rightleftharpoons Mg(OH)_{2\,(s)}$$

The oxidation is slow; in part because the starting material is not very soluble, when the reaction is complete, a large amount of solid manganese(IV) oxide and some unreacted permanganate ions are present. These substances may be reduced to water-soluble manganese(II) ions through the addition of an acidic solution of sodium hydrogen sulfite.

The acidification also serves to convert the product from the soluble potassium salt to the less soluble carboxylic acid and the latter then crystallizes out of solution.

(iv) The hydrolysis of 4-acetamidobenzoic acid

The hydrolysis of an amide group is generally performed under acidic conditions. At elevated temperatures it is possible that, with the presence of the electron-withdrawing carboxyl group in the para position, some nucleophilic displacement could occur. Once produced, the free amine could also undergo some air oxidation.

The product of this reaction is an amino acid. In basic solutions, the amino acid will be converted to the water-soluble carboxylate salt, while in acidic solutions it will be present as the water-soluble amine salt (see Figure 17.2). Thus, care must be taken in adjusting the pH of the final solution so that 4-aminobenzoic acid itself is precipitated.

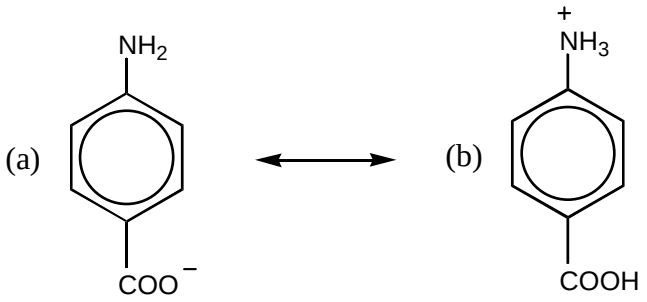
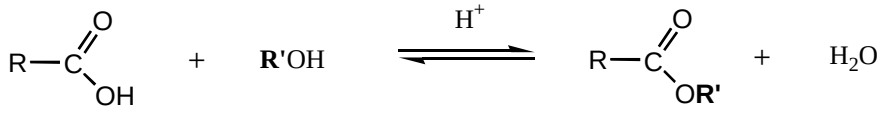


Figure 17.2 4-Aminobenzoic acid in its anionic form (a) and in its protonated form (b).

(v) The esterification of 4-aminobenzoic acid

The acid catalyzed esterification of a carboxylic acid is an equilibrium reaction that usually requires either a large excess of one of the reactants (usually the alcohol) or the removal of one of the products (usually water) in order for a good yield of ester to be obtained.



carboxylic acid alcohol ester

As the product of our reaction is quite soluble in ethanol, some of the latter must be removed from the reaction mixture before the product can be isolated.

Procedure

This experiment involves approximately twelve hours of work. We suggest that the various steps be spread over three days as outlined below.

DAY 1: Reduction of 4-nitrotoluene and the acetylation of 4-methylaniline. **[OPTIONAL]**
DAY 2: Oxidation of 4'-methylacetanilide.
DAY 3: Hydrolysis of 4-acetamidobenzoic acid and esterification of 4-aminobenzoic acid.

Part A: The reduction of 4-nitrotoluene to 4-methylaniline

Note: It is desirable to have dry starting material in Part C of this experiment, thus it is advantageous to complete Parts A and B during the same laboratory period.

1. Place 24.0 g of tin and 13.0 g of 4-nitrotoluene in a 500-mL round-bottom flask and attach a condenser and an acid-vapour trap (see Figure 17.3). Prepare about 100 mL of sodium hydroxide solution containing 10% more sodium hydroxide than the mass you calculated would be required to neutralize all the hydrogen chloride that will be liberated during this step.
   CAUTION: Sodium hydroxide will burn your skin and is particularly dangerous to the eyes. Wear gloves and safety glasses while preparing and working with this solution. Much heat is generated when dissolved in water.

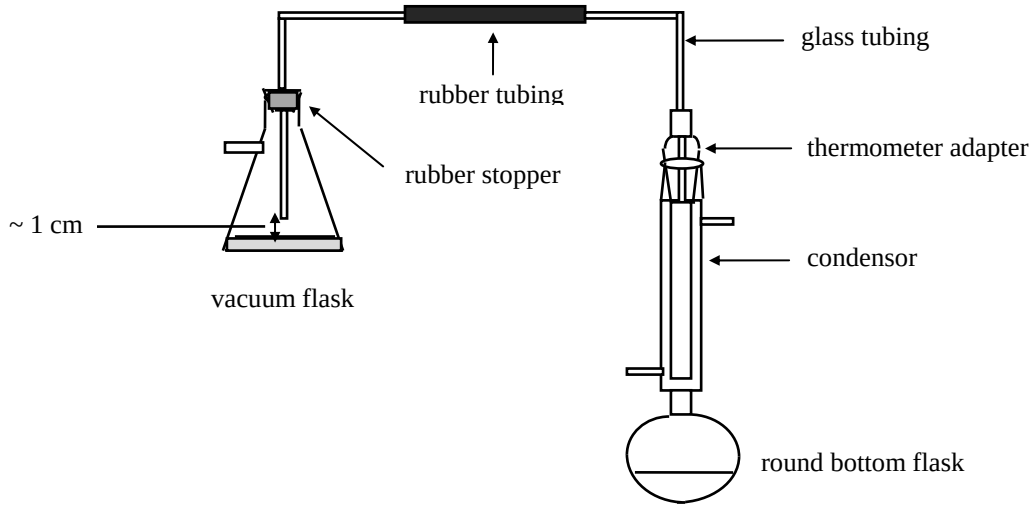


Figure 17.3 Acid-vapour trap

2. Briefly remove the acid-vapour trap and, through the top of the condenser, add 60mL of concentrated hydrochloric acid in six 10-mL portions. After each portion of hydrochloric acid is added, re-connect the acid-vapour trap and shake the flask gently to ensure that the reactants are thoroughly mixed. **CAUTION: Concentrated hydrochloric acid is highly corrosive and its fumes are harmful. Wear gloves, protect your eyes and work in a fume hood.**

   An exothermic reaction will begin to occur and the reaction mixture may begin to boil. Keep the mixture close to boiling, but cool the flask in a cold-water bath if the reaction becomes too vigorous. **CAUTION: Do not over-cool the mixture at the start of the reaction or else it may become too violent later on.**

3. When about half of the hydrochloric acid has been added, the rate of addition may be increased. The addition should be completed in about 30 minutes.

4. After all the acid has been added, heat the mixture for a further 30 minutes using a beaker of water on a hot plate as a heat source. Warm gently at first, and be prepared to quench the reaction by cooling the reaction vessel in cold water if the reaction becomes too violent. (Use heating mantle on setting 2).

5. In a 250-mL beaker, dissolve 38 g of sodium hydroxide in 60 mL of water. **CAUTION:** Sodium hydroxide is highly corrosive. Wear gloves and protect your eyes. Much heat is generated when sodium hydroxide dissolves in water. Be careful!

6. Remove the acid trap, raise the round-bottomed flask out of the heating mantle and cool the reaction mixture to room temperature and cautiously add the solution of sodium hydroxide that was prepared in step 5. Cool the reaction vessel during the addition and ensure that the contents of the flask are mixed thoroughly. When all the sodium hydroxide has been added, the reaction mixture should be strongly alkaline. Use red litmus paper to ensure that this is so.

7. Assemble the apparatus for steam distillation--the exact procedure may depend on the location at which the laboratory session is being conducted (see "Introduction" and pp. 117-119 of *The Organic Chem Lab Survival Manual* or pp. 208-212 in 3rd ed.). Remember to add fresh boiling stones.

8. Steam distil the product. Very cold water may cause the 4-methylaniline to solidify in the condenser. If this occurs, turn off the water supply to the condenser for a short while or, if necessary, briefly drain the water from the condenser jacket.

9. Cool the steam distillate and carefully add 8 mL of concentrated hydrochloric acid in order to dissolve all the 4-methylaniline. **CAUTION: Hydrochloric acid is extremely corrosive. Wear gloves and protect your eyes.**

10. If necessary, add water to the solution from step 9 so that the total volume of he solution is about 200 mL.

Part B: The acetylation of 4-methylaniline

1. In a 50-mL beaker, dissolve 13 g of sodium acetate trihydrate in 18 mL of water.

2. If you have not already done so, transfer the solution of 4-methylaniline (from Part A) to a 400-mL beaker and warm it to 50^{o} C on a hot plate.

3. **In a fume hood**, add 11 mL of acetic anhydride to the warm solution of 4-methylaniline and stir quickly. Immediately add the sodium acetate solution from step 1. Mix thoroughly and cool in an ice-water bath.

4. Isolate the crystals from the reaction mixture by suction filtration and wash three times with small quantities of cold water.

5. Allow the crystals to dry thoroughly and record their yield and melting point. Calculate the overall yield obtained from Parts A and B of this experiment.

6. Measure out 10.0 g of dry product for use in Part C of the experiment. Transfer the remainder to a sample vial and submit it to your instructor for grading.

Part C: The oxidation of 4'-methylacetanilide

1. Transfer 5.0 g of 4'-methylacetanilide and 51 g of magnesium sulfate heptahydrate to a 600mL beaker and add 350 mL of water. (**Note:** if you did not obtain 5.0 g of 4'methylacetanilide in Part B of the experiment, please ask your instructor to provide you with some of this material. Ensure that you retain a small sample of the 4'-methylacetanilide that you prepared so that you can hand it in to your instructor for grading. NO SAMPLE means NO GRADE!)

2. Heat the reaction mixture to 80—90^{o} C on a hot plate/stirrer.

3. Obtain 15.0 g of potassium permanganate and divide the sample into ten approximately-equal portions.

4. Add the first portion of potassium permanganate to the hot solution of 4'-methylacetanilide, with constant stirring. When the purple colour fades, add the second portion, and so on until all the potassium permanganate has been added. The addition should take about one hour. It is OK to occasionally rinse down sides of beaker with distilled water.

5. Keep stirring and heating for 10—15 minutes after the purple colour due to the final portion of potassium permanganate has faded.

6. Cool the solution and add 18.0 g of solid sodium hydrogen sulfite (sodium bisulfite). In a fume hood, cautiously acidify the reaction mixture with concentrated hydrochloric acid (~8 - 20 mL). **CAUTION:** Concentrated hydrochloric acid is highly corrosive; wear gloves and protect your eyes. Avoid inhaling the vapour.

7. Check that the reaction mixture is acidic by using congo red indicator paper. (NOTE: Congo red indicator paper turn blue in acid solutions--the exact opposite of litmus paper.) If all of the brown precipitate of manganese(IV) oxide has not dissolved and the solution is acidic, more sodium hydrogen sulfite should be added. An off-white precipitate of 4-acetamidobenzoic acid should remain.

8. Cool the reaction mixture thoroughly in an ice-water bath. Isolate the 4-acetamidobenzoic acid by suction filtration, wash the product with a small quantity of water, and dry thoroughly.

9. Determine the yield of 4-acetamidobenzoic acid obtained, but do not attempt to determine its melting point.

10. Measure out 4.0 g of dry 4-acetamidobenzoic acid for use in Part D of the experiment. Transfer the remainder to a sample vial and submit it to your instructor for grading.

Part D: The hydrolysis of 4-acetamidobenzoic acid

1. Transfer 4.0 g of 4-acetamidobenzoic acid and 25 mL of hydrochloric acid (HCl- 6 mol L^{-1}) to a 250-mL round-bottom flask with boiling stones and equipped with a reflux condenser.
   (**Note**: If you did not obtain 4.0 g of 4-acetamidobenzoic acid in Part C of the experiment, please ask your instructor to provide you with some of this material. Ensure that you retain a small sample of the 4-acetamidobenzoic acid that you prepared so that you can pass it in to your instructor for grading. NO SAMPLE means NO GRADE!)

2. **In a fume hood**, using a heating mantle as your heat source, reflux the reaction mixture gently for 30-40 minutes, cool in an ice-water bath, and add an equal volume of water.

3. Transfer the reaction mixture to a 400-mL beaker and, in a fume hood, use a Pasteur pipette to add concentrated ammonia solution until the mixture is just alkaline to litmus. **CAUTION: Concentrated ammonia is highly corrosive; wear gloves and protect your eyes. Avoid inhaling the vapour.**

4. Estimate the volume of the reaction mixture and add 1 mL of glacial acetic acid for each 30 mL of reaction mixture (see step D.3). **CAUTION: Glacial acetic acid is highly corrosive; wear gloves and protect your eyes. Avoid inhaling the vapour.**

5. Cool the reaction mixture in an ice-water bath and watch for crystals to begin to form. If necessary, scratch the inside wall of the beaker with a glass stirring rod to initiate the crystallization process.

6. Isolate the 4-aminobenzoic acid by suction filtration and allow it to dry thoroughly. Record the yield and melting point of the dry crystals.

7. Measure out 2.5 g of **dry** 4-aminobenzoic acid for use in Part E of the experiment. Transfer the remainder to a sample vial and submit it to your instructor for grading.

Part E: The esterification of 4-aminobenzoic acid

1. Transfer 2.5 g of dry 4-aminobenzoic acid to a 250-mL round-bottom flask. (Note: If you did not obtain 2.5 g of 4-aminobenzoic acid in Part D of the experiment, please ask your instructor to provide you with some of this material. Ensure that you retain a small sample of the 4-aminobenzoic acid that you prepared so that you can pass it in to your instructor for grading. NO SAMPLE means NO GRADE!)

2. Obtain 40 mL of absolute (100%) ethanol in a 250-mL beaker and to it add, carefully with stirring, 2.5 mL of concentrated sulfuric acid. **CAUTION: Concentrated sulfuric acid is highly corrosive; wear gloves and protect your eyes.**

3. Add the ethanol/sulfuric acid mixture to the 4-aminobenzoic acid in the 250-mL round-bottom flask. Attach a reflux condenser and, using a heating mantle (setting 4-5) as a heat source, reflux the mixture for ~one hour (or for 10 minutes after the last of the solid has dissolved; this may occur in as little as 20 min).

4. Rearrange the apparatus for a simple distillation, and distil off 25 mL of ethanol. This ethanol should be stored in a stoppered flask and used for the recrystallization in step 9.

5. Cool the residue that remains in the distilling flask and then pour the residue into a 600mL beaker.

6. Rinse the distilling flask with 85 mL of distilled water and add this rinse-water to the 600mL beaker containing the reaction mixture.

7. Add sodium carbonate solution (2 mol· L^{-1}) to the reaction mixture until the mixture is neutral to litmus. This addition should be carried out with care, because much foaming will occur. Stir the reaction mixture throughout the addition. Do not add excess sodium carbonate solution.

8. Cool the reaction mixture on ice and isolate the ethyl 4-aminobenzoate by suction filtration.

9. Recrystallize the product using a **two solvent** recrystallization method. Crush the solid thoroughly in a 125 or 250-mL Erlenmeyer flask and add the 'preheated' ethanol (recovered in step 4) until all the ethyl 4-aminobenzoate has dissolved. (Remember that any inorganic impurities that are present will not dissolve.)

10. Add a pinch of charcoal and heat the mixture to boiling on a hot plate.

11. Add an equal volume of water (pptte. should dissolve) and boil for two minutes. Filter through a fluted filter paper into a pre-heated Erlenmeyer flask.

12. Bring the filtrate to the boil once more and add small portions of water until the boiling solution appears to be slightly cloudy.

13. Allow the solution to cool to room temperature. Scratch the inside of the flask with a glass rod if no crystals have appeared after 30 minutes. When crystals have begun to form, cool the flask in an ice-water bath and then isolate the product by suction filtration.

14. Dry the crystals thoroughly and record the yield and melting point. Store your product in a suitably labelled vial and submit it to the instructor for grading.

Safety

Tin is harmful if inhaled, swallowed or absorbed through the skin.

4-Nitrotoluene is highly toxic! DANGER! May be fatal if swallowed or absorbed through the skin. It is readily absorbed through the skin. Chronic effects include cancer and genetic mutation. Use gloves!

Concentrated hydrochloric acid is extremely corrosive to the skin and eyes. Its vapour is irritating to the eyes, skin and lungs. Wear gloves and eye protection. Use in a fume hood.

Sodium hydroxide is highly corrosive, both as a solid and in solution. Very harmful if swallowed. Extremely dangerous to the eyes.

4-Methylaniline (p-toluidine) may be fatal if inhaled, swallowed or absorbed through the skin. Wear gloves and use in fumehood. Flammable.

Sodium acetate trihydrate is an irritant and may be harmful if swallowed or absorbed in the body.

Acetic anhydride is poisonous if swallowed, causing immediate irritation, pain and vomiting. The liquid irritates and may severely burn the skin and eyes. The vapour irritates the respiratory system and the eyes. Flammable.

4'-methylacetanilide (p-acetoluidide)

Magnesium sulfate heptahydrate is an irritant and may be harmful if swallowed or inhaled. It can cause central nervous system depression.

Potassium permangante is a skin irritant. Its' dust is harmful to the lungs. Can explode on sudden heating.

Sodium hydrogen sulfite (sodium bisulfite) causes severe irritation! It is harmful if swallowed or absorbed through the skin. It is also very destructive to the upper respiratory system.

4-Acetamidobenzoic acid is an irritant and may be harmful if ingested, inhaled or absorbed through the skin.

Concentrated ammonia solution has a pungent odour and is poisonous if inhaled or swallowed. Both the solution and vapour are irritating to the eyes. The solution burns the skin.

Glacial acetic acid is poisonous if swallowed. Both the liquid and vapour are irritating to the skin and eyes and can cause burns and ulcers. Flammable.

4-Aminobenzoic acid is used in preparations that are intended to prevent sunburn, thus it is not normally considered to be a safety hazard.

Ethanol is highly flammable. The toxicity of this liquid is increased by the presence of denaturing substances. Avoid ingestion.

Concentrated sulfuric acid is very corrosive to eyes, skin and other materials. Violent reaction possible when mixed with water. Wear gloves and eye protection when using this substance.

Sodium carbonate solution is slightly basic, but does not pose any specific safety problems.

Additional information regarding the potential hazards associated with handling the above chemicals may be obtained by consulting the Material Safety Data Sheets that are available in the laboratory.

Waste disposal

Please consult the laboratory instructor regarding the disposal of the various wastes produced in this experiment.

Write-up

This experiment may be written up using the standard format for "preparative type" experiments. Do not forget to calculate the individual step yields for each Part of the experiment and the overall percentage yield obtained for the complete 5-step sequence.

In addition, analyze the following Infrared and ^{1}H-NMR spectra and place the data in your results section. Use the following table formats for recording your analyses:

Infrared Data:

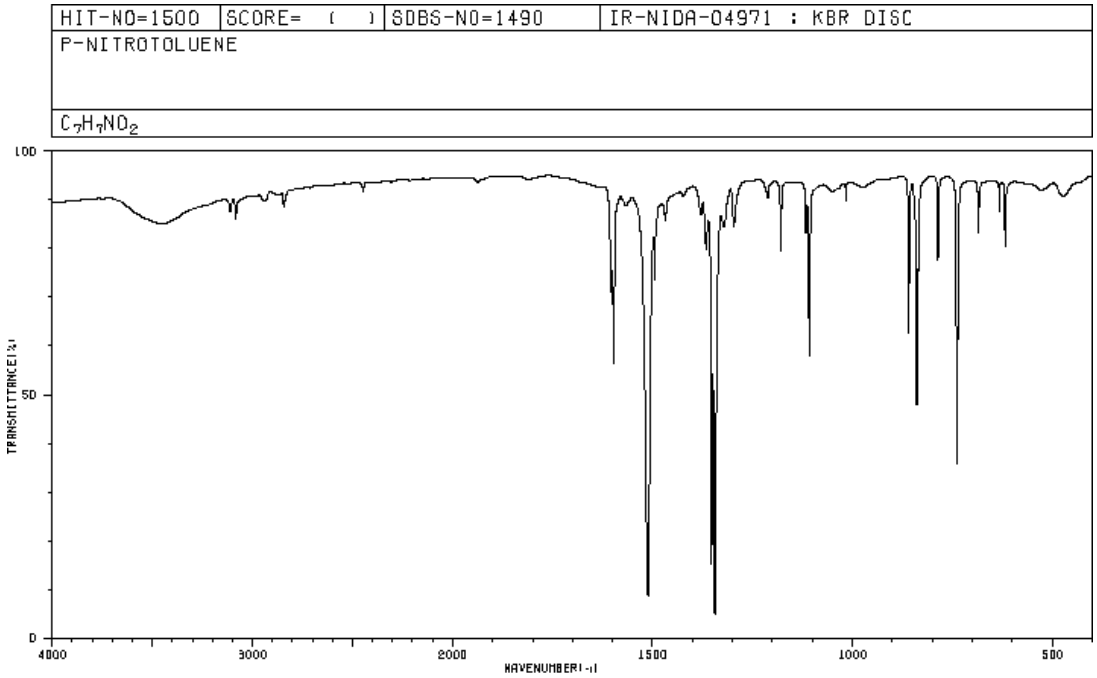
	Absorption Band#	Frequency (cm^{-1})	Peak Shape (sharp, broad)	Peak Intensity (strong, med. or weak)	Functional Group Indicated
> 3000 cm^{-1}					
Between 3000 and 2000 cm^{-1}					
Between 2000 and 1400 cm^{-1}					
< 1400 cm^{-1}					

Functional Group(s) absent:

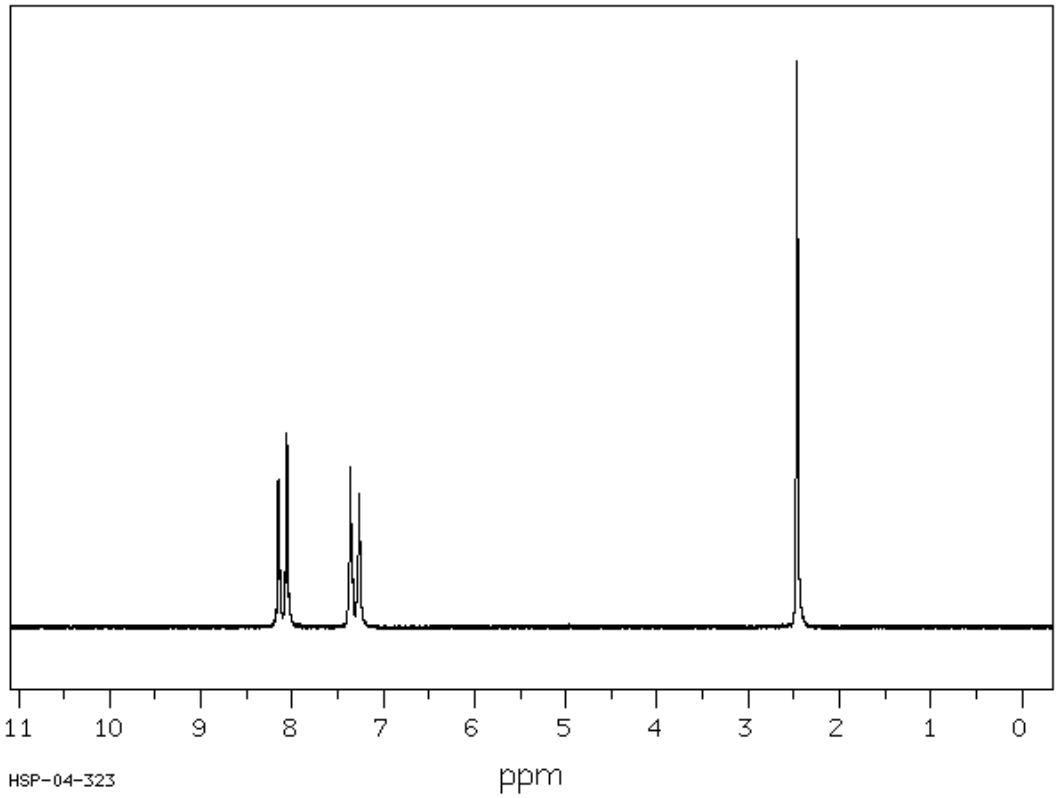
^{1}H-NMR Data:

Signal #	Shift	Integrat'n	Splitting	Comment	#Neighbour H	Signal Assignment

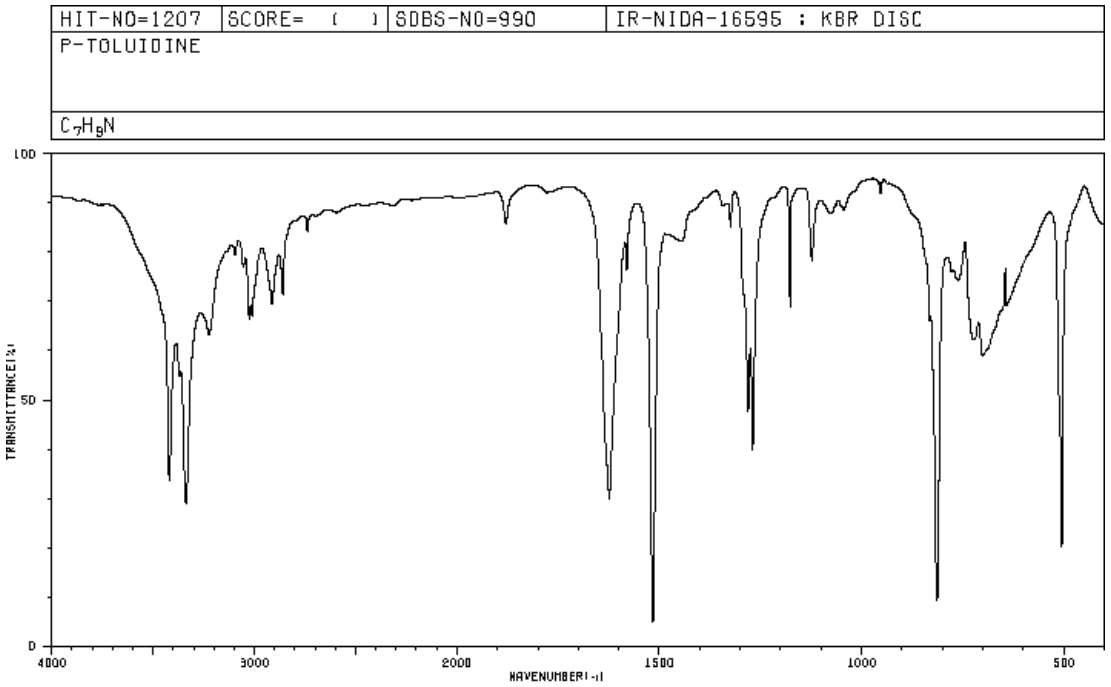
Infrared Spectrum of *p*-nitrotoluene



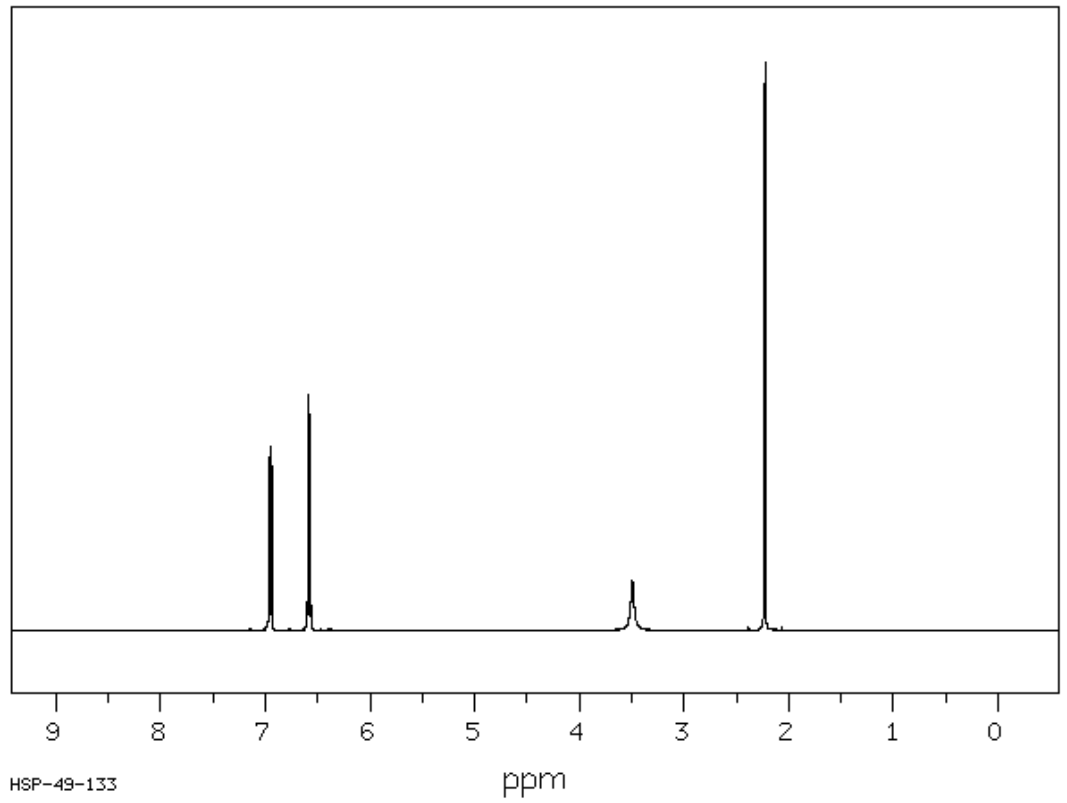
^{1}H-NMR Spectrum of *p*-nitrotoluene (90 MHz in $CDCl_3$)



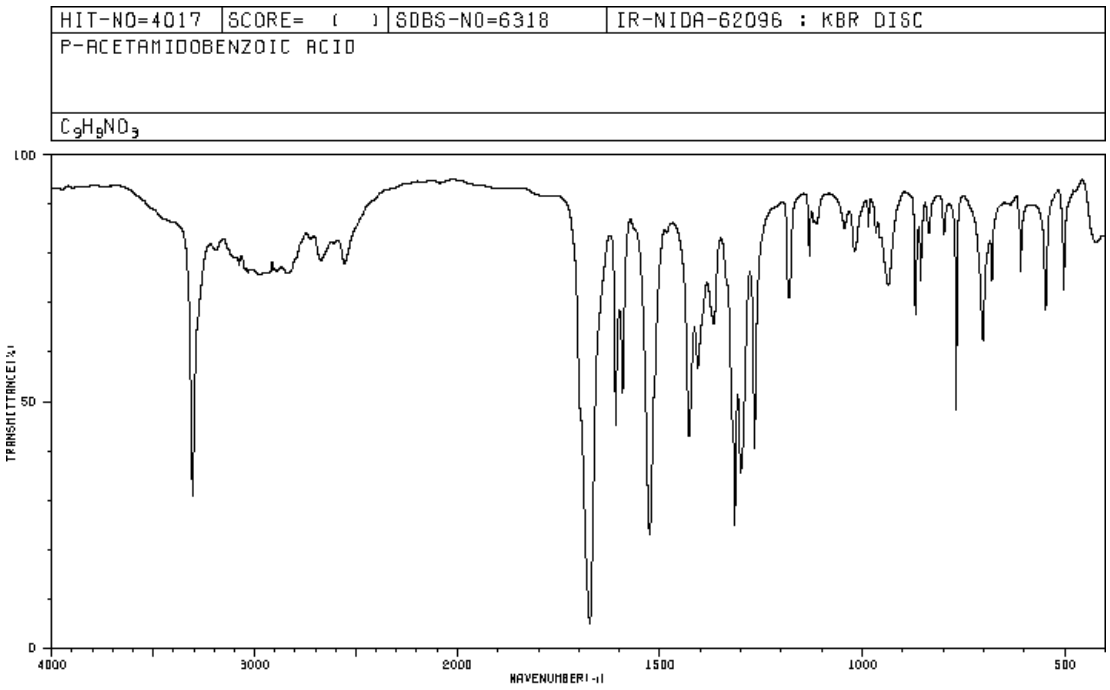
Infrared Spectrum of *p*-methylaniline (*p*-toluidine)



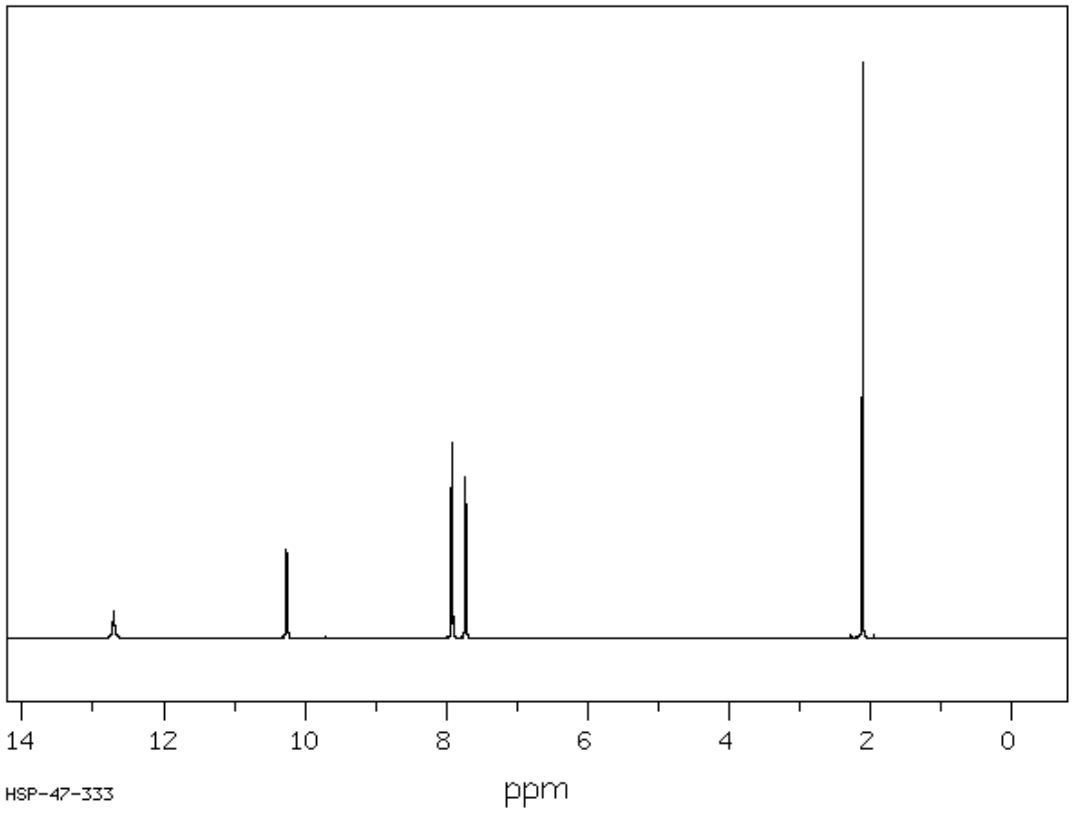
^{1}H-NMR Spectrum of *p*-methylaniline (400 MHz in $CDCl_3$)



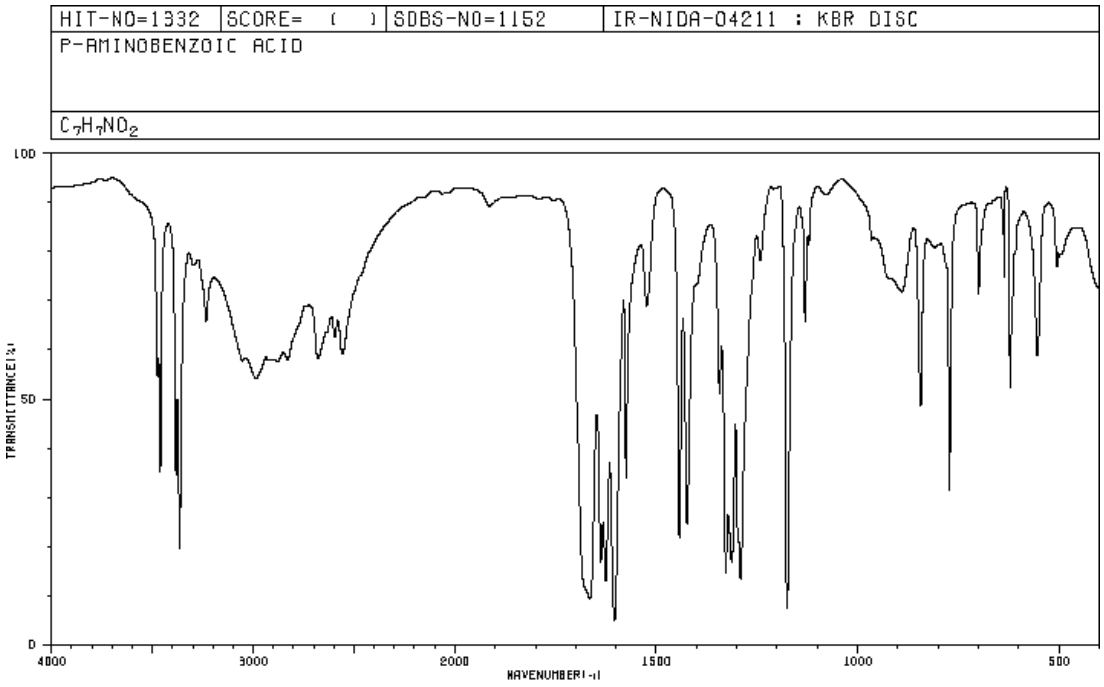
Infrared Spectrum of *p*-acetamidobenzoic acid



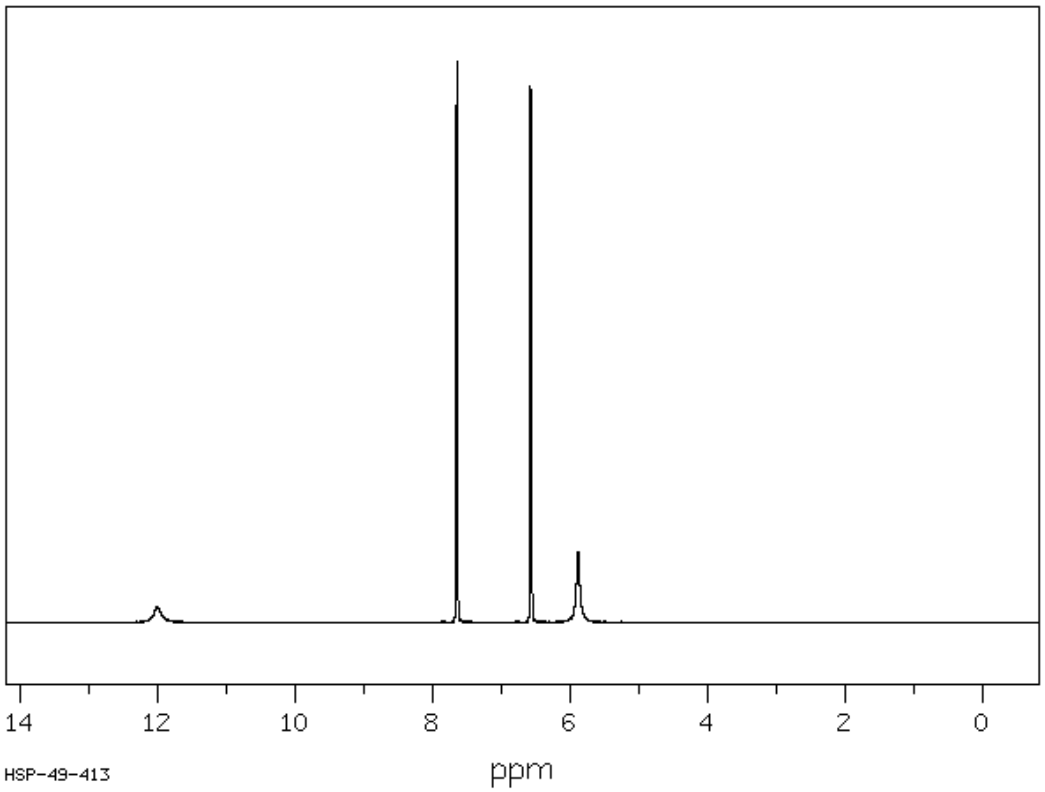
^{1}H-NMR Spectrum of *p*-acetamidobenzoic acid (400 MHz in DMSO-d_6)



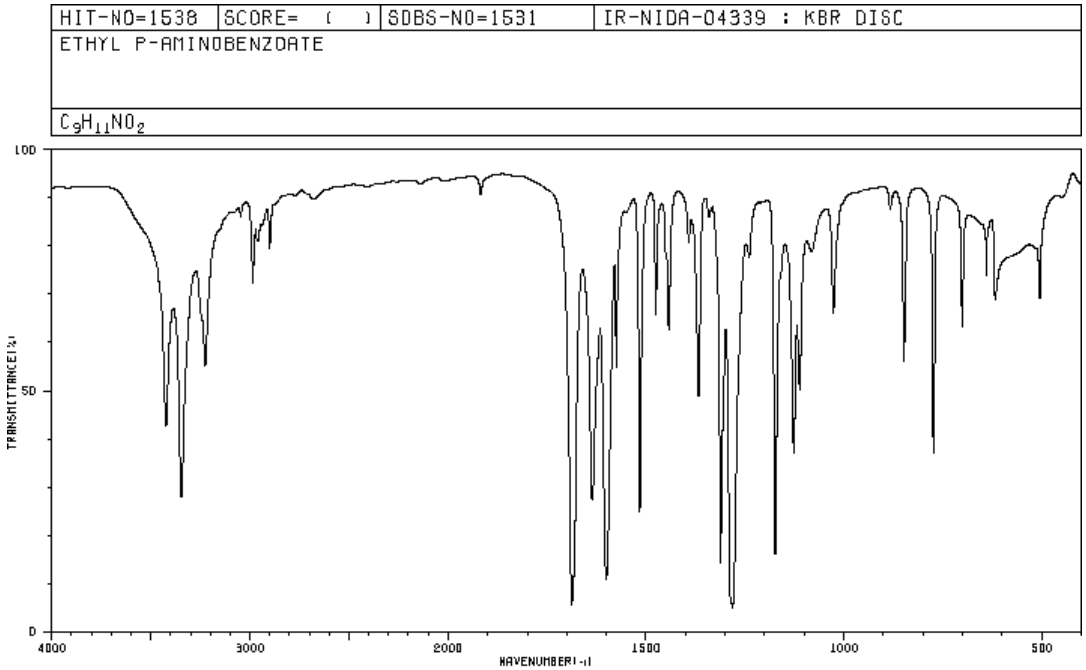
Infrared Spectrum of *p*-aminobenzoic acid



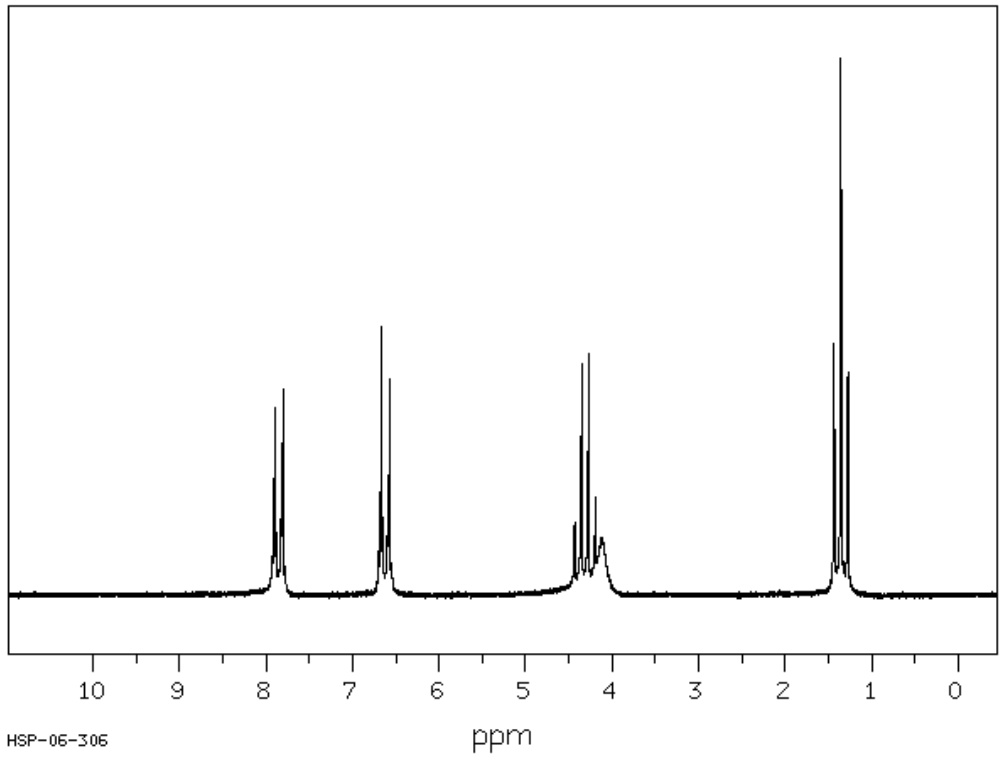
^{1}H-NMR Spectrum of *p*-aminobenzoic acid (400 MHz in DMSO-d_6)



Infrared Spectrum of Ethyl *p*-aminobenzoate (benzocaine)



^{1}H-NMR Spectrum of Ethyl *p*-aminobenzoate (90 MHz in $CDCl_3$)



Questions

Answers to be submitted with your report.

1. In Step 6 Part A, what is the purpose of adding sodium hydroxide to the reaction mixture?

2. In the discussion pertaining to the hydrolysis of 4-acetamidobenzoic acid, it was argued that the presence of the electron-withdrawing carboxyl group in the para position could result in the occurrence of some nucleophilic displacement if the hydrolysis was carried out under acidic conditions and an elevated temperature. What would the product of such a nucleophilic displacement reaction?

3. Write the balanced equation for the oxidation of 4'-methylacetanilide to 4-acetamidobenzoic acid as carried out in Part C of the synthesis.

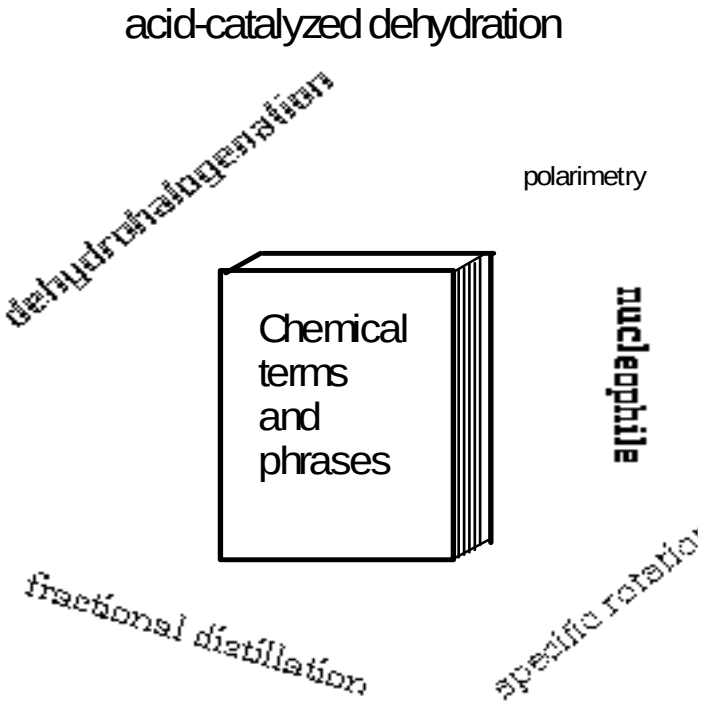
4. Write the mechanism for the reaction of 4-methylaniline with acetic anhydride. What was the purpose of adding sodium acetate to the reaction mixture when you performed this acetylation in Part B of the synthesis?

ATHABASCA UNIVERSITY

CHEM360

ORGANIC CHEMISTRY II

Glossary 2009-2012



Chem 360 Glossary of Terms and Phrases

absolute configuration that the R enantiomer is dextrorotary and that S enantiomer is levororotary. J.M. Bijvoet in 1949-1951 proved conventions are correct using X-ray spectroscopic methods on tartaric acid salts.

absorb to take up a substance in bulk.

absorbance is the common logarithm of the reciprocal of the transmittance of a pure solvent or Absorbance =2-log(%Transmittance)

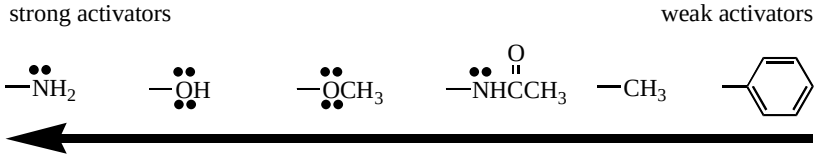
acetanilide (mp. 114-116° C) is an odourless compound in the form of white, shining crystalline leaflets or a white crystalline powder. It is soluble in hot water, alcohol, ether, chloroform, acetone,glycerol and benzene. Used as a rubber accelerator, in the manufacture of dyestuffs and intermediates, as a precursor in pencillin manufacture and as a painkiller.

acetone (aka 2-propanone, CH_3COCH_3), is a clear, colorless, volatile, extremely flammable liquid, miscible with water, used as a solvent and reagent.

achiral molecule (a-ky´-rul, Gr. a*cheir*= 'away from' handed), a type of molecule that is superimposable on its mirror image. It is not optically active and does not exist as a pair of enantiomers.

activated charcoal a water insoluble carbon powder added during hot gravity filtrations to adsorb (i.e., remove) high molar mass (coloured) impurities from the product. (see also recrystallization). If your product is coloured, do not use!

activating group is a substituent on an aromatic ring which increases the reactivity of the aromatic ring towards electrophilic substitution relative to benzene.



alcohol(s) (R-OH, IUPAC ending = ol, functional group name = hydroxyl) are organic derivatives of water. They have higher water solubilities (one hydroxyl group can solubilize 3-4 'C'-atoms) and boiling points than hydrocarbons of similar molecular weight (see Table 6.2) due to intermolecular hydrogen bonding. The alcohols can be primary, secondary, or tertiary depending on the number of carbon atoms attached to carbon bonded to the hydroxyl. Compounds that contain more than one hydroxyl group are call polyhydric alcohols (2OH=glycols or diols, 3OH=triols).

Physical Properties of Some Alcohols:

Name	Formula	Mol. Wt.	Mp (°C)	Bp (°C)	Sp. gravity
methyl alcohol (methanol)	CH_3OH	32.04	-97	64.7	0.792
ethyl alcohol (ethanol)	CH_3CH_2OH	46.07	-114	78.3	0.789
n-propyl alcohol (1-propanol)	$CH_3CH_2CH_2OH$	60.11	-126	97.2	0.804
isopropyl alcohol (2-propanol)	$CH_3CHOHCH_3$	60.11	-88	82.3	0.786
ethylene glycol	$HOCH_2CH_2OH$	62.07	-12	198	1.11
n-butyl alcohol (1-butanol)	$CH_3(CH_2)_3OH$	74.12	-90	117.7	0.810
isobutyl alcohol	$(CH_3)_2CHCH_2OH$	74.12	-108	107.9	0.802
sec-butyl alcohol (2-butanol)	$CH_3CH_2CHOHCH_3$	74.12		99.5	0.808
t-butyl alcohol	$(CH_3)_3COH$	74.12	25	82.5	0.789
n-pentyl alcohol (1-pentanol)	$CH_3(CH_2)_4OH$	88.15	-79	137.3	0.814
phenol	C_6H_5OH	94.11	43	181.7	1.058
n-hexyl alcohol (1-hexanol)	$CH_3(CH_2)_5OH$	102.2	-52	155.8	0.820
cyclohexanol	$C_6H_{11}OH$	100.2	25.1	161.1	0.962
n-heptyl alcohol (1-heptanol)	$CH_3(CH_2)_6OH$	116.2	-34	176	0.822
n-octyl alcohol (1-octanol)	$CH_3(CH_2)_7OH$	130.2	-16.7	194.4	0.820
n-nonyl alcohol (1-nonanol)	$CH_3(CH_2)_8OH$	144.3	-5.5	213.5	0.827
n-decyl alcohol (1-decanol)	$CH_3(CH_2)_9OH$	158.3	7	229	0.830
1-undecanol	$CH_3(CH_2)_{10}OH$	172.3	19	243	0.830

lauryl alcohol (1-dodecanol)	n-$C_{12}H_{25}OH$	186.3	24	259	0.831

Boiling Point (Bp) of Other Hydrocarbons:

Name	Formula	Mol.Wt.	Bp (°C)
ethane	CH_3CH_3	30.07	-89
ethanal	CH_3CHO	44.05	20.8
propane	C_3H_8	44.11	-42
propanal	CH_3CH_2CHO	58.08	48.8
butane	C_4H_{10}	58.12	0
pentane	C_5H_{12}	72.15	36
diethyl ether	$CH_3CH_2OCH_2CH_3$	74.12	34.5
pentanal	$CH_3(CH_2)_3CHO$	86.14	103
hexane	C_6H_{14}	86.18	69

In syntheses, alcohols are versatile and can be converted into many aliphatic compounds. Reactions of alcohols can be divided into 2 types: C-O bond attacks (e.g., dehydration of alcohols to alkenes, alcohols to alkyl halides), and O-H bond attacks (e.g., alcohols to ethers, alcohols to tosylates, alcohols to carboxylic acids).

Preparation of alcohols can occur by many means. e.g., (1) hydration or hydroboration of alkenes (2) reduction of carbonyl groups and acid derivatives, (3) Grignard addition.

aliphatic hydrocarbons (Gr. *aleiphar* = fat), one of two major broad categories of organic compounds (aliphatic or aromatic), originally meant that the compound's chemical behaviour was 'fat-like', it now means a compound reacts like and alkane, alkene, alkyne or one of their cyclic counterparts.

alkanes (straight chain = C_nH_{2n+2}, cycloalkanes = C_nH_{2n}, IUPAC ending = ane, no functional group name, only C-C single bond, aka parrafin =Lat. *parum affinis* = slight affinity, or aliphatic =Gr. *aleiphas* = fat) are hydrocarbons in which all of the carbon atoms are sp^3 hybridized and all the carbon-carbon bonds are single bonds resulting from the overlap of two tetrahedral carbon sp^3 orbitals (1.54 ± 0.01 angstroms, 85 ± 3 kcal/mol). The C-H bonds are also all nearly constant (1.09 ± 0.01 angstroms, 95 ± 3 kcal/mol).

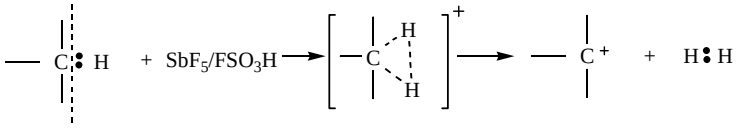
Some physical constants of n-alkanes (=homologous series) are:

Name	Formula (C_nH_{2n+2})	Mol. Wt.	Mp (°C)	Bp (°C)	(d^{20}_4) density	n_D^{20}
methane	CH_4	16.04	-183	-161.5		
ethane	CH_3CH_3	30.07	-172	-88.6		
propane	$CH_3CH_2CH_3$	44.11	-188	-42.1		
n-butane	$CH_3CH_2CH_2CH_3$	58.12	-135	-0.5		
n-pentane	$CH_3(CH_2)_3CH_3$	72.15	-130	36.1	0.626	1.3575
n-hexane	$CH_3(CH_2)_4CH_3$	86.18	-95	68.7	0.659	1.3749

Alkanes, although fairly unreactive, can undergo a few reactions:

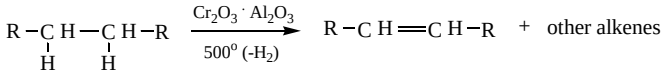
1. Polar reactions of Alkanes

i. Heterolytic cleavage

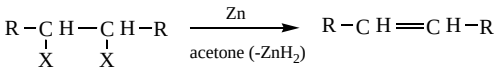


heterolytic cleavage of sigma bond | superacid | pentacoordinate carbon compound | carbocation

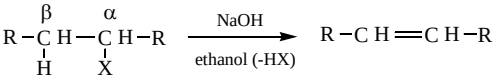
ii. Dehydrogenation (elimination reaction via catalyst)



iii. Dehalogenation (elimination reaction of vicinal (vic) dihalide)

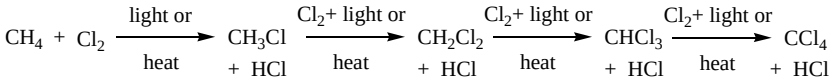


iv. Dehydrohalogenation (β−elimination reaction of alkyl halides)

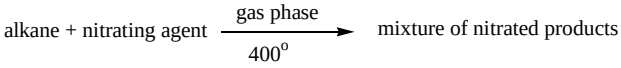


2. Radical reactions of Alkanes

i. Halogenation (via chain reaction)



ii. Nitration (via chain raction)



alkene(s) (C_nH_{2n}, IUPAC ending = ene, functional group name = C-C double bond, $R_2C{=}CR_2$, *aka* olefin =Lat.=*oleum*, oil + *facere*, to make) are hydrocarbons that contain one or more carbon-carbon double bonds. They are also referred to as unsaturated compounds. The carbon-carbon double bond is due to sp^2 hybridization, it is composed of a sigma bond and a pi bond (1.33 ± 0.01 angstroms, 152 ± 3 kcal/mol). Alkenes have planar geometry, restricted bond rotation (i.e., cis-trans isomers) and the geometry of the alkene can be described by the E,Z system using the Cahn-Ingold-Prelog sequence rules for nomenclature. Some physical constants of alkenes are:

Name	Formula (C_nH_{2n})	Mol. Wt.	Mp (°C)	Bp (°C)	d^{20}_4 density	n_D^{20} RI
ethylene	CH_2CH_2	20.05	-169	-103.7		1.363
propene	CH_2CHCH_3	42.08	-185.2	-47.4	0.5193	1.3567
1-butene	$CH_2CHCH_2CH_3$	56.12	-185.3	-6.3	0.5951	1.3962
1-pentene	$CH_2CH(CH_2)_2CH_3$	70.14	-138	30.0	0.6405	1.3715
1-hexene	$CH_2CH(CH_2)_3CH_3$	84.16	-139.8	63.3	0.6731	1.3837
cyclohexene	C_6H_{10}	82.15	-103.5	83.0	0.8102	1.4465

Unlike alkanes, alkenes are very reactive and can be converted into many aliphatic compounds. Reactions of alkenes are predominated by their electron-rich double bond and their reactions with electrophiles: e.g., addition of HX where the orientation of electrophilic addition is generally governed by Markovnikov's rule and Hammond's postulate. Reactions with other electrophiles (X_2, HOX, BH_3) may give rise to anti-stereochemistries and non-Markovnikov syn additions.

Preparation of alkenes is predominated by elimination reactions. e.g., (1) dehydration of alcohols (2) dehydrohalogenations (3) dehydrogenation (4) Hofmann elimination, (5) Cope elimination, (6) acetate pyrolysis, (7) tosylate elimination, and (8) Wittig reaction.

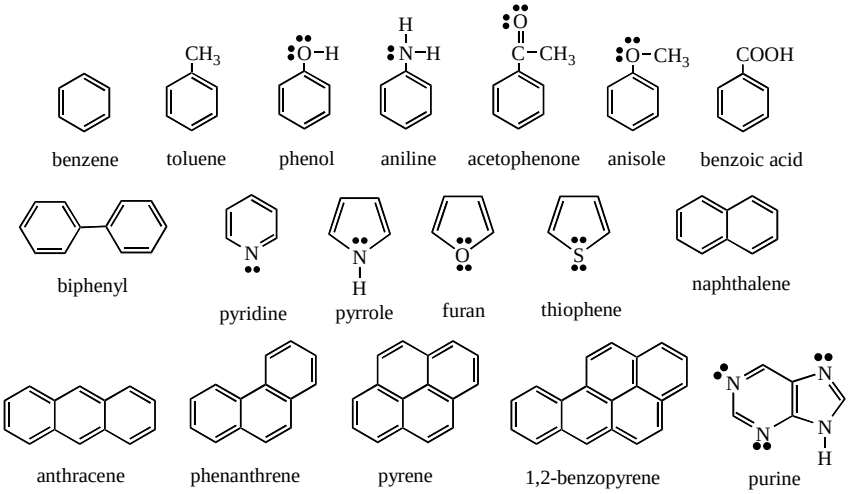
alkynes (C_nH_{2n-2}, IUPAC ending = yne, functional group name = C-C triple bond, aka acetylenes, are hydrocarbons that contain one or more carbon-carbon triple bond. They are also referred to as unsaturated compounds. The carbon-carbon triple bond is due to the overlap of two *sp* hybridized carbon atoms; it is composed of one strong sigma bond and two weaker pi bonds (1.20 angstroms, 196 kcal/mol). Simple alkynes have linear geometry, and therefore cannot exhibit cis-trans isomerism. Boiling points, melting points and sp.gravities of simple alkynes are normally slightly higher than the corresponding alkanes and alkenes due to their rod like structure. Some physical constants of alkynes are:

Name	Formula (C_nH_{2n})	Mol. Wt.	Mp (°C)	Bp (°C)	d^{20}_4 density	n_D RI
acetylene(ethyne)	CHCH	26.04	-81.8	-83.6	0.6208	1.0005
propyne	CH_3CCH	40.07	-101.5	-23.2	0.7062	1.3863
1-butyne	$CH_3CH2CCH$	54.09	-125.7	8.1	0.691	1.3962
1-pentyne	$CH_3(CH_2)_2CCH$	68.13	-90	39.3	0.695	1.3852
1-hexyne	$CH_2(CH_2)_3CCH$	82.15	-132	71	0.7155	1.3989

As a general rule, alkynes react with electrophilic reagents similar to alkenes although at a slower rate.

anti addition(s) a term used to describe the stereochemistry of an addition reaction, it refers to the addition of substituents to opposite faces of a double bond resulting in trans products.

aromatic compound(s) (C_nH_{2n-6}, contain an aromatic ring, base names: benzene, phenol, toluene, aniline, acetophenone, anisole, biphenyl) are a class of organic compounds that have a low carbon-hydrogen ratio and tend to be fragrant in nature. Aromatic compounds may also be heterocyclic (e.g., pyridine, pyrrole, furan, and thiophene) or polycyclic (e.g., naphthalene, anthracene, phenanthrene, pyrene and benzopyrene) or polyheterocyclic (e.g., purine).



aromatic orientation substituents on an aromatic ring can affect the orientation of the reaction depending on whether or not the substituent is an ortho, meta, or para directing group.

aromatic reactivity substituents on an aromatic ring can affect the reactivity of the ring relative to benzene depending on whether or not the substituent is an activating or deactivating group.

asymmetric carbon refers to a 'C' atom bonded to four different groups. Note: the presence of a asymmetric 'C' in a molecule only suggests the possibility that a molecule will be chiral. see also 'chiral center'.

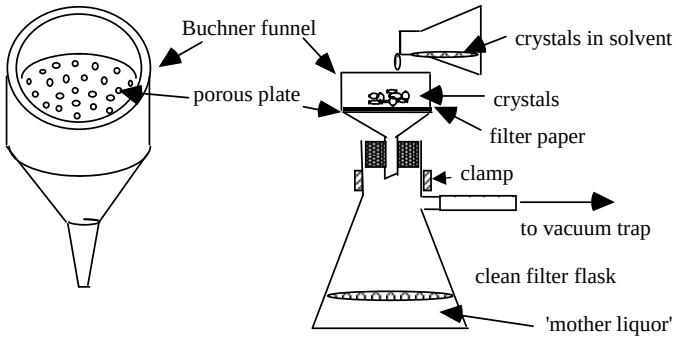
azeotrope is a mixture with a constant boiling point. e.g., 96% ethanol:4% water mixture boils to dryness at a constant temperature. Further definition includes a minimum boiling azeotrope (it boils off first, then the other components) and maximum boiling azeotrope (other components come off first, the azeotrope boils off last).

boiling point an important physical property of organic compounds, the boiling point of a compound is the temperature at which the liquid and gaseous phases of the compound are in equilibrium.

It is also the temperature at which the vapour pressure of a liquid becomes equal to the external pressure. Note: 'boiling range' is more correct as a small temperature difference occurs between the time a compound starts to vapourize and when vapourization is completed.

boiling stones or boiling chips are small granules of inert material (often silica) which are added to solutions/solvents to prevent bumping during boiling of the liquid. The stone provides extra points of nucleation where vaporization can take place (see also 'bumping of liquids').

Büchner funnel a funnel primarily used for separating crystals of product from the ice cold liquid solvent above them. Used in conjunction with vacuum filtration. (see also vacuum filtration and recrystallization).



bumping of liquids refers to a dangerous, massive, instantaneous vaporization of heated liquids caused by localized hot spots in the reaction vessel and resulting in splashes of hot liquid being thrown from the reaction vessel. Bumping can be alleviated by using boiling stones.

Cahn-Ingold-Prelog sequence rules a method of specifying the configuration of chiral carbon atoms (R or S configuration). The rules are as follows:

1. Rank the atoms directly attached to the chiral center in order of decreasing atomic number. The group with highest atomic number is ranked first, the group with lowest atomic number is ranked fourth.
2. If a decision about priority cannot be reached by applying rule 1., work outwards to the first point of difference.
3. Multiple bonded atoms are considered as if they were an equivalent number of singly bonded atoms. i.e., -CHO substituent = $-CH(OC)_2$.

The method requires that you mentally orient the molecule so that the group with lowest priority is pointing directly back, away form you.

carbocation a tri-valent carbon intermediate which has only six electrons in its outer shell and carries a formal positive charge. It is an electrophile that can accept an electron pair from a nucleophile. It is sp^2 hybridized and planar. see also electrophilic additions, Markovnikov's Rule, Hammond postulate, S_N1 reactions.

chiral molecule (ky´-ral, Gr. *cheir*=hand), a type of molecule that has a nonsuperimposable mirror image.

chiral centers one of the causes of chirality, refers to a 'C' atom bonded to four different groups. Note: the presence of a chiral center in a molecule only suggests the possibility that a molecule will be chiral. see also 'asymmetric carbon'.

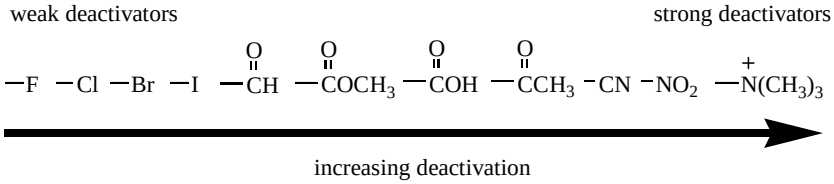
column holdup is the volume of retained liquid on the internal surfaces of the distillation system.

concentration a term which refers to the amount of solute dissolved in a given amount of solvent or solution. e.g., see molarity, molality, normality, parts per million, weight percentage.

condensation turning a vapour into a liquid by cooling a compound below its boiling point.

condenser is a jacketed glass column of jointware used in distillations. Cold water can be circulated through the condenser and causes condensation of vapour.

deactivating group is a substituent on an aromatic ring which decreases the reactivity of the aromatic ring towards electrophilic substitution relative to benzene.



dehydration, acid-catalyzed a type of E_1 elimination-polar reaction, the mechanism consists of a series of equilibria and involves the attack of an electrophile on a alcohol oxygen, loss of water to form a carbocation intermediate, and finally the elimination of a proton next to a cationic carbon atom. The reaction follows Hammond postulate and, like base-induced dehydrations, Zaitsev's rule normally).

reactivity order = tertiary R_3COH > secondary R_2CHOH > primary RCH_2OH

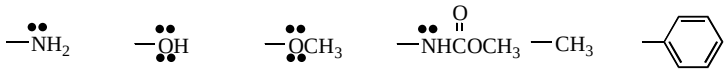
It is a commonly preferred method for the conversion of an alcohol to an alkene.

dextrorotary (Lat. *dextrorsum*=towards the right), a term to describe optically active molecules that rotate polarized light to the right (+).

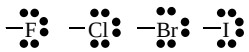
diastereomers are stereoisomers that are not enantiomers. i.e., not mirror images of each other.

directing substituents substituents on an aromatic ring can be three types: (1) ortho- and para-directing activators, (2) ortho- and para-directing deactivators and (3) meta-directing deactivators.

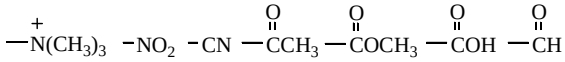
***ortho*- and *para*-directing activators** (resonance effect greater than inductive effect)



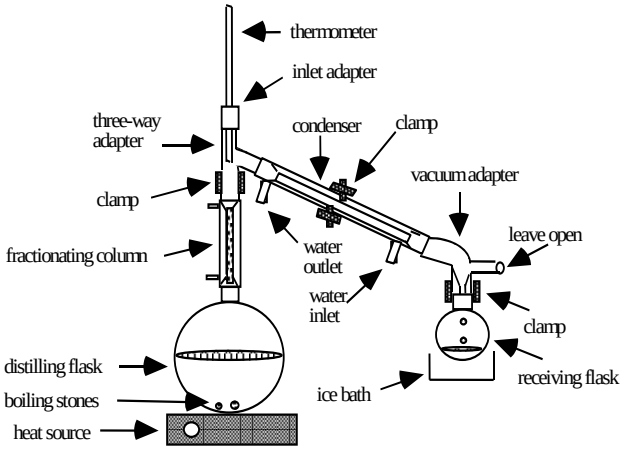
***ortho*- and *para*-directing deactivators** (inductive effect greater than resonance effect)



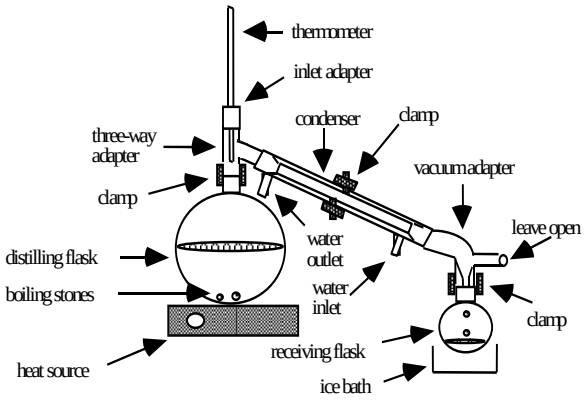
***meta*-directing deactivators**



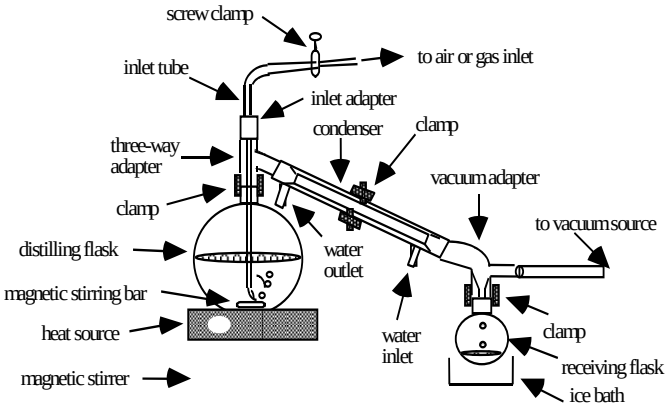
distillation, fractional a method for the separation of volatile compounds from a mixture of two or more miscible liquids with boiling points that differ by less than 25^{o} C. Employs the use of a fractionating column and occurs at atmospheric pressure.



distillation, simple a simple and effective method for the purification of a volatile liquid product from impurities with at least 25^{o} C difference in boiling point and non-volatile impurities. The crude liquid product is heated to a boil in a still pot (flask) and the vapours rise and are condensed into a receiver flask. Usually only refers to distillations below 150^{o} C and at 1 atmosphere of pressure.



distillation, vacuum usually only refers to distillations of liquid with a boiling point above 150^{o} C at 1 atmosphere of pressure. It is a method for the purification of a volatile heat-labile liquid product from its miscible impurities with at least 25^{o} C difference in boiling point and non-volatile impurities. The crude liquid product is heated to a boil in a still pot (flask) and the vapours rise and are condensed into a receiver flask.



drying agent used to dry wet solvents (solvents saturated with water). Some examples and their characteristics are:

	Drying Agent	Capacity/Efficiency:	Drying Compatibility:
1.	calcium chloride,	large/low	not good for alcohols, amines, phenols
2.	potassium carbonate	fair/fair	not good for acidic materials
3.	disodium sulfate	large/ slow and low	good with organic solvents
3.	magnesium sulfate	large/good and rapid	good with organic solvents
4.	calcium sulfate	large/good	good with organic solvents
5.	potassium hydroxide	large/v.g. and rapid	good for amines
6.	sodium metal	small/v.g and v.fast	good only for relatively dry solvents not good with acidic protons, halocarbons (violent rxns).
7.	phosphorous pentoxide	small/v.g and v.fast	good only for relatively dry solvents not good with alcohols, ketones, amines or acids
8.	metal hydrides (CaH_2)	small/v.g and v.fast	good only for relatively dry solvents

not good for cmpds. with acidic H, C-hetro-atom, double bonds, or chlorocarbons (violent reactions)

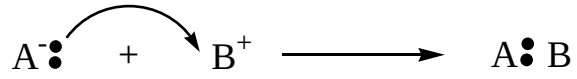
-small amounts of the drying agent are added to the material to be dried and the liquid then allowed to stand in a closed vessel. The drying agent is removed by gravity filtration or decantation.

E_1 reaction (E_1 = elimination, unimolecular) is one of four main polar reaction mechanisms in organic chemistry. More specifically, elimination reactions of alkyl halides. It is analogous to the S_N1 reaction. All E_1 eliminations occur by spontaneous dissociation of a halide and loss of a proton from the carbocation intermediate (rate limiting step). Occurs under solvolysis conditions in the absence of added base and shows first-order kinetics. Strongly affected by solvent, leaving group, and substrate structure. Shows no geometric requirement in the substrate.

E_2 reaction (E_2 = elimination, bimolecular) is one of four main polar reaction mechanisms in organic chemistry. More specifically, elimination reactions of alkyl halides. It is analogous to the S_N2 reaction. In E_2 eliminations, the base removes a proton at the same time as the leaving group dissociates and the reaction shows second-order kinetics. Strongly affected by solvent, type of nucleophile/base, leaving group, and substrate structure. Anti-periplanar geometry of substrate is preferred.

electrophile (electrons+.Gr. *phile*= attracted to) is an 'electron-loving' reagent with electron-poor sites that form a bond by accepting a pair of electrons from an electron-rich reagent. The term is specifically used when bonds to carbon are involved. Correlated to Lewis acids but refers to relative rates of organic polar reactions whereas Lewis acids are referring to relative equilibrium constants.

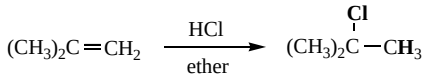
Examples of electrophiles are: alkyl halides, X^+, H^+, HX, Hg^{+2}, $AlCl_3$, BF_3.



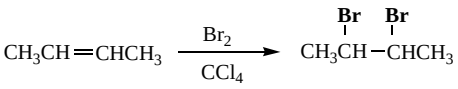
Nucleophile (electron-rich) Electrophile (electron-poor)

electrophilic additions a type of polar reaction. All proceed by an attack on an electrophile by an electron-rich double bond. Some examples are:

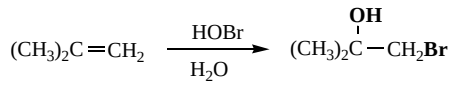
1. Addition of HX (X= Cl, Br, or I)



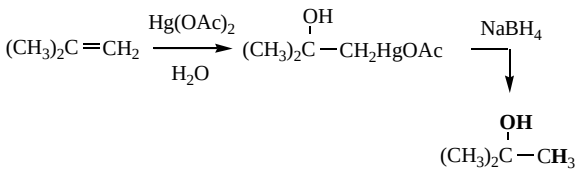
2. Addition of X_2 (X= Cl, or Br)



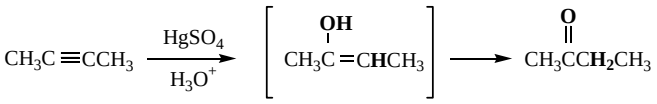
3. Halohydrin formation: Addition of HOX(X= Cl, Br or I)



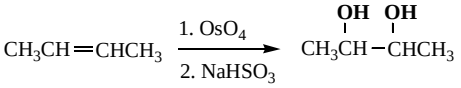
4. Hydration by oxymercuration: Addition of -Hg-OH



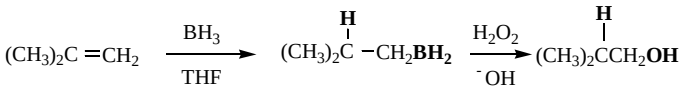
5. Alkyne hydration:



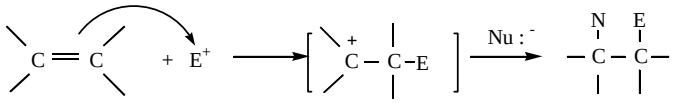
6. Hydroxylation by Osmium Tetroxide:



7. Hydroboration:



Rxn Mech.



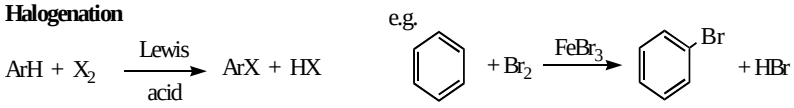
cation intermediate

where E^+ = electrophile (H^+, X^+, or Hg^{2+}) and $Nu:^-$ = nucleophile ($HO:^-$ or $X:^-$)

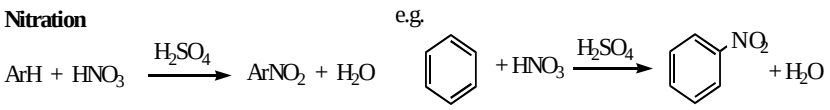
electrophilic aromatic substitution

perhaps the single most important type of reaction of aromatic compounds. They all proceed via a common two step mechanism. It involves the attack of an electrophile by an aromatic ring (pi electrons of the aromatic ring) and the formation of a carbocation intermediate. The loss of a proton is the second step. Overall the electrophile substitutes for one of the hydrogens. Because of its resonance forms, benzene will undergo electrophilic substitution reactions rather than addition reactions typically shown by alkenes. There are six primary types of electrophilic substitution reactions that are of importance:

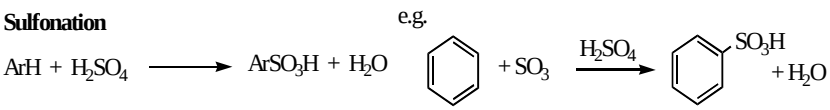
1. Halogenation



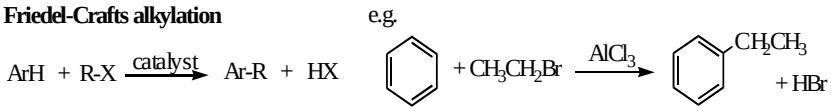
2. Nitration



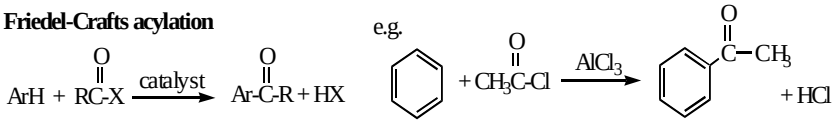
3. Sulfonation



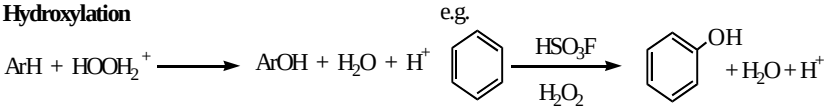
4. Friedel-Crafts alkylation



5. Friedel-Crafts acylation

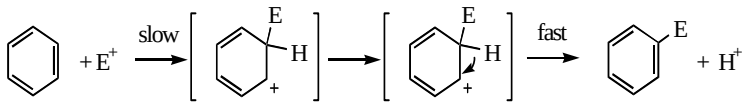


6. Hydroxylation



Phenol (67% Yield)

General mechanism for electrophilic aromatic substitution:



-a bimolecular reaction showing second order kinetics (Rxn Rate = k[ArH][E^+]). The rate limiting step is the formation of the carbocation intermediate.

emergent stem error emergent stem error occurs when a thermometer is not immersed to its recommended depth (see engraved line on stem, 76 mm from the bottom of the bulb). Corrected by the formula: emergent stem correction (to be added to t_1) = $0.00017 \times N(t_1-t_2)$ where N = length in degrees of exposed mercury column, t_1 = observed temperature, t_2 = temperature at middle of exposed column.

emulsion in chemistry, it refers to the appearance of a 'cloud of small droplets/particles' suspended in solution instead of two distinct layers in separatory funnels during extractions.

enantiomers (Gr. *enantio*=opposite) or optical isomers are stereoisomers that are nonsuperimposable mirror images of each other.

eutectic mixture (pron. yu-'tek-tik, Gr. *eutektos* = easily melted) is a mixture (i.e., an alloy or solution) having the lowest melting point possible. The melting point of an eutectic mixture has a sharp range which can be confused with that of a pure compound.

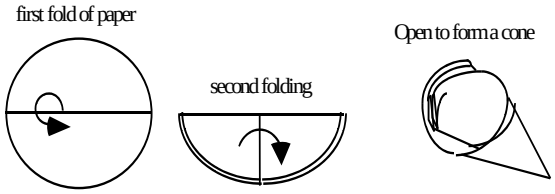
extraction a technique used in organic chemistry to separate components of an organic mixture. It refers to removing a component from a mixture of soluble components. It takes advantage of the difference in solubility of a substance in two immiscible liquids. The four classes of compounds commonly extracted are:

Compound Class	Examples:	Extract into:	Recover with:
1. Strong Acids	mineral, organic acids	sat.Na-bicarbonate	HCl (conc.)
2. Weak Acids	phenols, sustit.phenols	10% NaOH (aq)	HCl (conc.)
3. Organic Bases	aniline, triethylamine	10% HCl (aq)	NH_4OH, NaOH

4. Neutral Organic	amides, hydrocarbons	dichloromethane	same	

extraction, back- a technique used in organic chemistry to recover a component from a solvent in which it is partially soluble in. (see also extraction).

filter cone a way of quickly folding filter paper for use in gravity filtrations:



filter flask or 'suction flask' is an thick walled Erlenmeyer flask with a side arm on the neck which is used in conjunction with a Büchner funnel and water aspirator for collecting crystals of product . (see also vacuum filtration and recrystallization).

filter paper for clarifying solutions, collecting precipitates and crystals in gravity and vacuum filtrations. Common brand name Whatman™. Choice of 6 porosities from course to fine:

Whatman Grade#	Porosity	Flow rate	Surface	Particle Retention
Whatman 4	coarse	Fast 12s	smooth	20-25 μ
Whatman 1	medium	Med. 40s	smooth	11 μ
Whatman 2	med-Fine	Med. 55s	smooth	8 μ
Whatman 2V	medium	Med. 55s	sm.pleated	8 μ
Whatman 3	coarse	Slow 90s	sm.grained	6 μ
Whatman 5	fine	Slow 250s	sm.dense	2.5 μ

Remember to choose the right size of circle diameter for funnel.

Fischer projections named after Emil Fischer (1852-1919) as a standard method for depicting the 3-dimensional arrangement of atoms (i.e., configuration) in 2-dimensions (on paper). The tetrahedral carbon atom is represented by the intersection of two perpendicular crossed lines. Horizontal lines are bonds coming out of the page while vertical lines represent bonds going into the page.

Movements of the projections on paper allowed are:

(1) Rotate 180^{o} but not 90^{o} or 270^{o} and
(2) Hold any one group steady and rotate the other three clockwise or counterclockwise.

Assignment of R,S configurations to Fischer projections governed by the following rules:
(1) Assign priorities to the four substituents.
(2) Perform one of the allowed motions to place the lowest priority group at the top of the Fischer projection.
(3) Determine the direction of rotation in going from priority 1 to 2 to 3 to 4 and assign R or S configuration.

fore-run is the low-boiling point material collected from a distillation. The volume is measured and the fore-run is usually discarded.

fraction(s) what a fractional distillation separates components into.

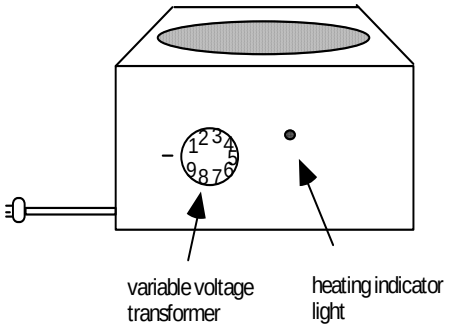
fractionating column very similar to the condenser except it is wider and it has projections at the end to help hold in the packing material (glass beads, glass helices, ceramic pieces, metal chips or twistings).

functional group(s) are structural features, composed of an atom or group of atoms with a characteristic chemical reactivity, which are part of a larger molecule that aid in the classification of organic compounds. Examples of functional groups are: C=C double bond, $R_2C=O$ carbonyl, -OH hydroxyl, C-X halide, C-OH alcohol, NO_2 nitro, $O=C-NH_2$ amide, NH_2 amine.

gas one of three common phases of matter (others are solids and liquids), it has no fixed shape or volume. Note: volumes of gases vary greatly with changes in temperature or pressure.

Hammond postulate proposed by George Simms Hammond (1921-) in 1955, an important explanation of the interplay between reactivity and stability of carbocations intermediates and the effect on the structure of the final product. "The more stable carbocation should form faster than the less stable one."

heating mantle a electrical heat source with an external or built in variable voltage transformer depending on the model.



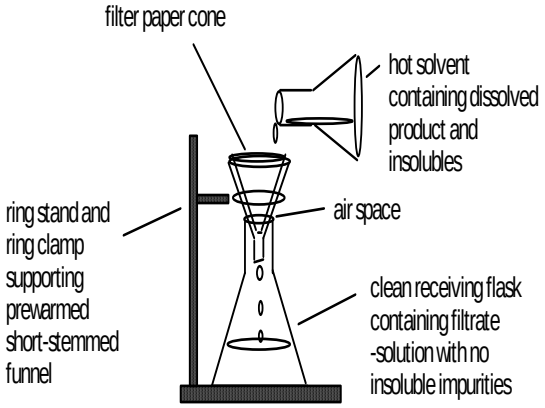
HETP or **h**eight **e**quivalent to 1 **t**heoretical **p**late is the length of fractionating column that equals one simple distillation.

homogeneous mixture or solutions that are a single phase in which a solution occurs and may be solid, liquid or gaseous. It has or any subsample of the mixture has the same set of intrinsic properties; each property of course dependent on the composition of the mixture.

homologous series a series of compounds that differ from one another by a constant unit (e.g.,, $-CH_2$ in alkanes).

homologs what members of a homologous series are called.(e.g.,, methane and ethane are homologs).

hot gravity filtration a method used during the purification and recrystallization of product to remove impurities less soluble than the product. Hot solvent containing dissolved product is poured through filter paper in a prewarmed (100-120° C) short-stemmed funnel and the filtered liquid is collected in a clean, dry receiving flask. Insolubles and boiling chips are retained on the filter. (see also recrystallization).



hydride shift a type of structural rearrangement that can occur during a reaction involving the formation of a carbocation.

hydrocarbon(s) are a family of organic compounds, containing only hydrogen and carbon, which can be subdivided into several groups based on the type of bond that exists between carbon atoms. Alkanes (contain all C-C single bonds), alkenes (contain one or more C-C double bonds), alkynes (contain one or more C-C triple bonds).

ice bath or more correctly, a 'water-ice' bath. Temperature 0-4° C. A flat bottomed vessel containing mostly water with some ice cubes which is used to cool solutions in flasks. i.e., during recrystallization.

immiscible pairs of liquids that do not mix in any proportions are said to be immiscible. E.g., water-hexane solvent system. The solubility of water in hexane is negligible. (i.e., water is immiscible in hexane).

inductive effect an electron-withdrawing effect important in the understanding of aromatic reactivity. Inductive effects are caused by the intrinsic electronegativity of atoms and to dipoles present in functional groups and involve donated or withdrawing electrons in sigma bonds or through space.

interface is the borderline between to immiscible liquids.

intrinsic properties are attributes which distinguish matter from all other types of matter. E.g.,, density, color, physical state, melting point, boiling point, refractive index, specific rotation, IR spectrum etc.

isomer a general term for compounds related to each other in one of two ways: as structural isomers or stereoisomers. Structural (constitutional) isomers have identical molecular formulas but differ in their atoms bonding sequence (e.g.,, butane and 2-methylpropane). Stereoisomers have identical molecular formulas and their atoms bonding sequence is the same. Stereoisomers differ in that their atoms are arranged differently in space. E.g., cis-trans isomers are a type of stereoisomer.

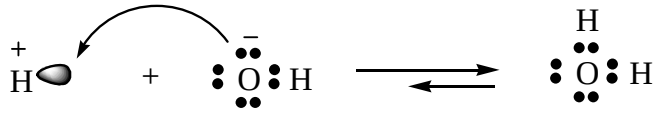
IUPAC system International Union of Pure and Applied Chemistry's system of nomenclature for organic molecules where each different compound has a different name. Has a set of rules which provides names for more than 2 million organic molecules plus millions more yet to be synthesized. E.g.,, For unbranched alkanes:
Rule 1. The base name of any group relates to the total number of carbon atoms in the group.

layer(s) refers to the formation of two phases when insoluble liquids are mixed together. i.e., The less dense top layer (light phase) floats on top the more dense lower layer (heavy phase).

leverorotary (Lat. *Laevus*=on the left hand), a term to describe optically active molecules that rotate polarized light to the left (-).

Lewis acid is a substance that accepts an electron pair.

Some Lewis acids are H_3O^+, BF_3, $AlCl_3$, $TiCl_4$, $ZnCl_2$, $FeCl_3$, and $SnCl_4$.



Hydronium ion (Lewis acid) electron accepting | Hydroxide ion (Lewis base) electron donating | Water

Lewis base is a substance that donates an electron pair (see also Lewis acid). Some examples of Lewis bases are hydroxides, amines, ethers, alcohols and ketones (O and N containing organic compounds). Not to be confused with nucleophiles. For instance, ethoxide ion ($CH_3CH_2O^-$) is a stronger base than ethylmercaptide ion ($CH_3CH_2S^-$) (K_a C_2H_5OH = ~10^{-18}, K_a C_2H_5SH = ~10^{-12}) however in many cases the ethylmercaptide ion is the stronger nucleophile.

liquid one of three common phases of matter (others are solid and gas), it has no fixed shape but does have a 'constant' volume. Note: volumes of liquids do not change greatly with changes in temperature or pressure.

Markovnikov's rule named after Vladimir Vassilyevich Markovnikov (1833?-1904), who published a paper in 1868 entitled "Materials on the Question of a Mutual Effect of Atoms in Chemical Compounds" in which he formulated an empirical rule for predicting the additions of hydrogen halides to asymmetrical alkenes. The modern rule was proposed in 1905 and states that 'in the ionic addition of an unsymmetrical reagent (e.g., HX) to an alkene, the positive portion (acid hydrogen) of the adding reagent bonds to the carbon with fewer alkyl substituents (or more hydrogen atoms) so as to produce a more stable carbocation. Then the negative portion (X group) always bonds to the carbocation (more alkyl substituted carbon or less hydrogenated carbon)'.

melting point an important physical property of organic compounds, the melting point of a compound is the temperature at which the solid and liquid phases of the compound are in equilibrium. Note: 'melting range' is more correct as a small temperature difference occurs between the time a compound starts to melt and when melting is completed.

meso compunds are compounds that are superimposable on their mirror images by virtue of a plane of symmetry, yet contain chiral centers, e.g., *cis* 1,2-dibromocyclopropane.

methyl shift a type of structural rearrangement that can occur during a reaction involving the formation of a carbocation.

minimum solvent the amount of solvent (usually hot) required to just dissolve the solute.

mixed melting point a method used to help find the identity of an unknown compound. Based on the premise that when an organic compound is impure, its melting point is lowered. i.e., mix genuine stock reagent with the unknown and if the melting point of the mixture is the same as the unknown, the identity of the unknown is that of the stock reagent. If it is different, then try again with another stock reagent!

mixed-solvent system used to recrystallize product when one cannot find a single solvent which completely dissolves your product. e.g., water:ethanol. Water:ethanol behaves like water at low temperatures, and it acts like ethanol at high temperatures.

miscible pairs of liquids that mix in all proportions are said to be miscible. e.g.,, water-acetone, water-methanol, water-ethanol, water-propanol solvent systems. the solubility of water in ethanol is ∞. All ratios of mixtures results in one dissolving completely in the other (i.e., water is completely miscible in acetone).

molality (abbr.=m) is the concentration of a solution expressed as moles of solute per kg of solvent. Note: the molality of a solution does not vary with temperature because masses do not change with temperature.

molarity (abbr.=M) is the concentration of a solution expressed as moles of solute per liter of solution. Note: the molarity of a solution changes with temperature because of expansion and contraction of the solution.

molar solution contains 1 mol or g mol wt. of the solute in 1 L of solution.

mole (abbr. = mol) the amount of substance of a system which contains as many elementary units (atoms, molecules, ions, electrons, other particles or groups of other particles) as there are atoms in 0.012 kg of carbon 12. i.e., Avogadro's number (6.0221367×10^{23}) of elementary units.

molecule is the smallest unit quantity of matter in a substance which can exist by itself and retains all the properties of the original substance.

molecular weight is the sum of the atomic weights of all the atoms in a molecule.

mole fraction (abbr.=X_A) is an expression of concentration of a component (A), defined as the number of moles of a component A divided by the total moles of all components.

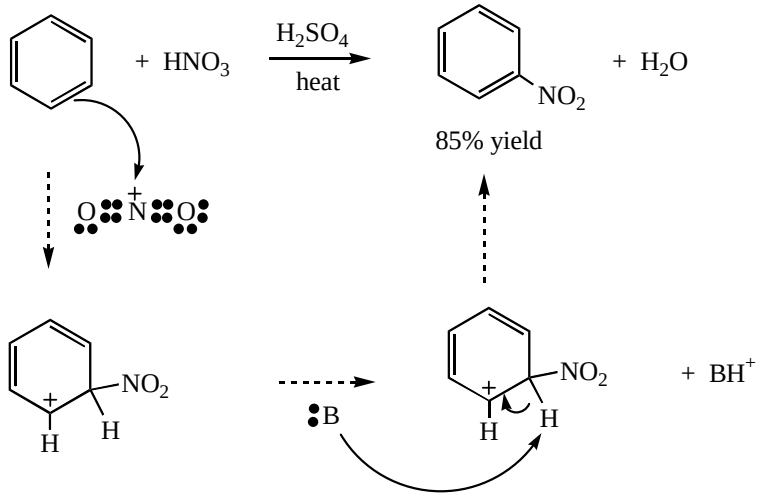
$$X_A = \frac{\text{moles component A}}{\text{total moles of all components}}$$

Note: The sum of all mole fractions for a given solution must = 1.

MSDS **M**aterial **S**afety **D**ata **S**heet is part of WHMIS (see below). These sheets give 'complete' details on the physical properties of the chemical, possible health effects that are produced upon exposure, preventative measures, etc.

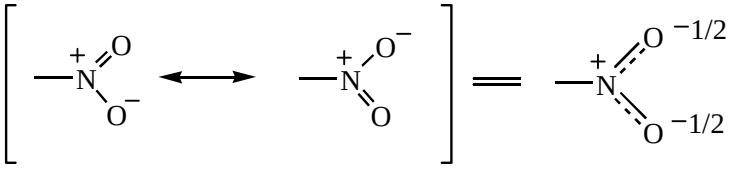
nitrating mixture a mixture of concentrated sulfuric and concentrated nitric acid which results in the formation of nitronium ions (NO_2^+), a strong electrophile which readily attacks aromatic systems.

nitration addition of a nitro group ($-NO_2$), into an organic system. Proceeds via an electrophilic substitution reaction mechanism analogous to halogenations.

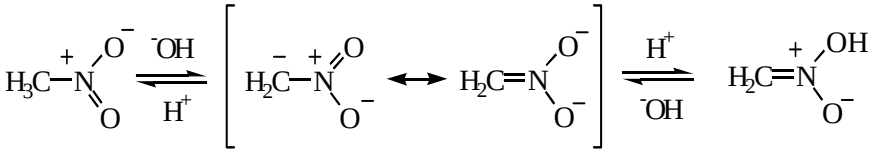


B: = H_2O, HSO_4^- or NO_3^-

nitro group a nitro group ($-NO_2$) is electronically similar to a carboxylate anion ($-CO_2^-$) and can have two equivalent resonance forms:



The nitro group is highly electronegative and nitro compounds are polar compounds of high boiling points but low water solubility. A nitro group is capable of stabilizing a negative charge on an adjacent atom; thus nitromethane is sufficiently acidic to dissolve in aqueous sodium hydroxide

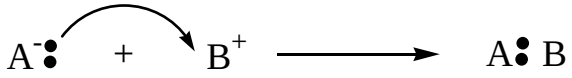


Nitromethane
pK_a 15

aci-Nitromethane

nucleophile (nucleus+.Gr. *phile*= attracted to) is an 'nucleus-loving' reagent with electron-rich sites that form a bond by donating a pair of electrons to an electron-poor reagent. The term is specifically used when bonds to carbon are involved. Correlated to Lewis bases but refers to relative rates of organic polar reactions whereas Lewis bases are referring to relative equilibrium constants.

Nucleophiles can be negatively charged (:$^-$Nu=**:**$^-$OH, **:**$^-$H, **:**X^-, NO_2^-, R3C:-), or neutral (**:**Nu-H= H_2O, ROH, **:**NH_3, R-NH_2). Note: If neutral, the nucleophile must be attached to a hydrogen atom which can be eliminated.



Nucleophile (electron-rich) Electrophile (electron-poor)

oiling out a phrase to describe the formation of an oil instead of crystals which can occur during recrystallization from a mixed-solvent system. It often happens when the boiling point of the recrystallization solvent is higher than the melting point of the compound

optical activity was discovered by Jean Baptiste Biot (1774-1862), a French physicist at Collège de France, in 1815. He observed that naturally occurring organic compounds (sugar, camphor) rotate the plane of polarization of an incident beam of polarized light.

optical isomers see enantiomers. Discovered by Louis Pasteur in 1848 while studying crystals of sodium ammonium tartrate salts.

parts per billion (abbr.=ppb) is an expression of concentration for very dilute solutions, similar to ppm, where the mass of solute in solution is divided by the total mass of solution all times 1 billion (e.g., 1μg/kg):

$$\text{ppb} = \frac{\text{mass of component in soln}}{\text{total mass of soln}} \times 10^9$$

parts per million (abbr.=ppm) is an expression of concentration for dilute solutions, similar to weight percentage, where the mass of solute in solution is divided by the total mass of solution all times 1 million (e.g., 1mg/kg):

$$\text{ppm} = \frac{\text{mass of component in soln}}{\text{total mass of soln}} \times 10^6$$

phase refers to portions of matter that are uniform in composition and in intrinsic properties.

plane-polarized light light obtained when passed through a polarizer. Polarized light consists of light waves oscillating in a single plane. Ordinary light is unpolarized since its electromagnetic waves oscillate in an infinite number of planes at right angles to the direction of light travel.

polarimeter an instrument used to measure the amount of optical rotation of optically active organic molecules.

polar reactions one of three fundamental types of organic chemical reactions (see also radical reactions, pericyclic reactions). Polar reactions can be classified into several general categories:

(1) Electrophilic addition reactions
(2) Elimination reactions
(3) Electrophilic aromatic substitution reactions
(4) Nucleophilic substitution reactions
(5) Nucleophilic aromatic substitution reactions

Polar reactions are between electron rich reagents and electron poor reagents. They are heterolytic processes and involve an even-numbered-electron species.

protecting group a group added to a sensitive or interfering functional group to protect it in a reaction with a reagent intended for a second functional group. Use of a protecting group involves three steps: (1) formation of an inert derivative, (2) performing the wanted reaction, and (3) removal of the protecting group.
e.g.,, protecting a sensitive amino group by reacting it with acetic anhydride (acetylation).
-protecting an alcohol with dihydropyran and converting the alcohol to a tetrahydropyranyl (THP) ether.
-protecting a carbonyl group by reacting it with ethylene glycol and conversion to an acetal.

pure compound a pure compound has a sharp melting point (1-2^{o} C). An impure compound has a broad depressed melting point.

racemic mixture (proun. ray-ceé-mic, Lat. *racemus*=cluster (of grapes)), or racemate is a 50:50 mixture of chiral enantiomers denoted by (±). Optical rotation is zero.

Raoult's Law defines the partial pressures of A and B vapors above a solution containing components A and B:

Raoult's law states that: $P_A = X_A P^o_A$ and $P_B = X_B P^o_B$

where P_A is the vapor pressure of the solution,
X_A is the mole fraction of the solvent, and
P^o_A is the vapour pressure of the pure solvent

-solutions that obey Raoult's law are called 'ideal solutions'.

R configuration (R abbr. for Lat. *rectus*=right) refers to the direction of travel (clockwise) around a chiral center in order of rank of substituents. (see also Cahn-Ingold-Prelog sequence rules).

recovery the final step of the extraction procedure, it is when the component is forced back out of solution by neutralization of the extraction medium.

recrystallization an important method of purification of organic compounds. It involves 5 steps: (1) dissolving the impure compound in minimum hot solvent, (2) performing hot gravity filtration after adding activated charcoal, (3) slowly cooling the filtrate, first to room temperature and then to 4^{o} C, (4) collecting the purified product

crystals by vacuum filtration and rinsing the crystals with a small volume of ice-cold solvent and finally (5) drying the purified product.

reflux ratio (R) R is the ratio of the volume of condensate formed at the top of the column and returned to the system to the volume removed as distillate.

$$R = \frac{\text{volume of condensate returned to the column}}{\text{volume of condensate removed as distillate}}$$

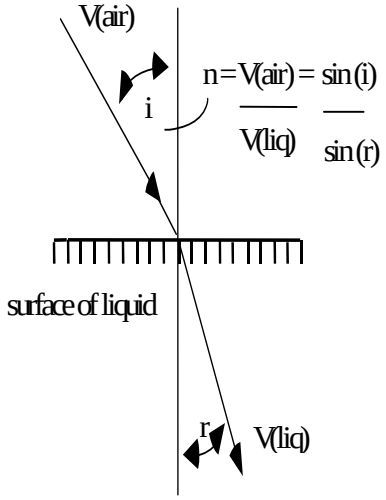
refractive index (abbr.= n_D^{20}) a specific physical property of liquids that therefore can be used in the identification of unknown compounds and to detect small quantities of impurities. It is based on the fact that light travels at a different velocity in liquid (V_{liq}) than in air (V_{air}).

The refractive index is inversely proportional to the temperature (it increases with decreasing temperature). This can be compensated for by using the following equation:

$n_D^{20} = n_D^X + (Temp_X - 20^o\ C) \times 0.00045^o\ C^{-1})$ where:

n_D^X = the measured refractive index at temperature x

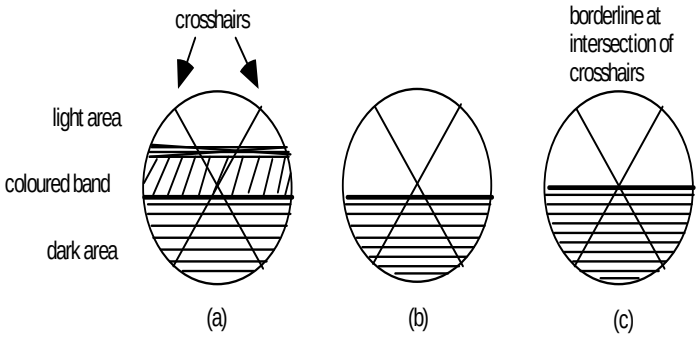
$Temp_X$ = the temp. of the sample at time of measurement



Light is refracted as it passes from air into a liquid.

refractometer a device used for the measurement of refractive index. It uses a sodium D line light source and can be temperature compensated to 20^o C. The machine must also be adjusted for chromatic aberration (by 'achromatizing the borderline'). Views through eyepiece of refractometer are seen below:

In (a) below, a coloured band appears between the light and dark areas. Reduce this coloured band to a minimum by rotating the compensator drum/dial just below the eyepiece. Now the eyepiece should look like (b). The final step before reading the refractive index is to adjust the borderline between the light and dark areas (using the side handwheel) so that it crosses the intersection of the two crosshairs as shown in (c).



regiospecific reactions (Lat. *rego* = to rule or govern) refers to reactions that from a standpoint of orientation tend to give predominately one addition product when or two or more possible isomeric products might have been formed.

resonance effect an electron effect important in the understanding of control of aromatic orientation. Resonance effects are caused by donating or withdrawing electrons and involve electrons in p-orbitals and aromatic ring pi electrons. Note: Some activators of aromatic rings (-OH, $-OCH_3$, $-NH_2$) show inductive effects due to their electronegativity but their resonance electron-donation effect is far greater and therefore they activate the aromatic ring.

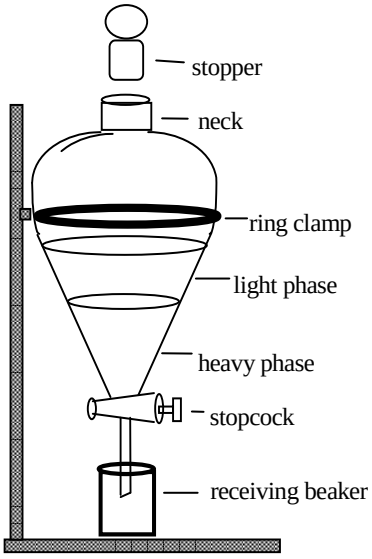
rotary evaporator an apparatus used for the evaporation of relatively large volumes of solvent. It uses a vacuum to keep the temperature low during the evaporation process.

salting out refers to the use of salt (note: sol. NaCl in ice cold water is 36g/100mL) to alter the ionic strength of water and thereby reduce the solubility of an organic compound which is partially soluble in water.

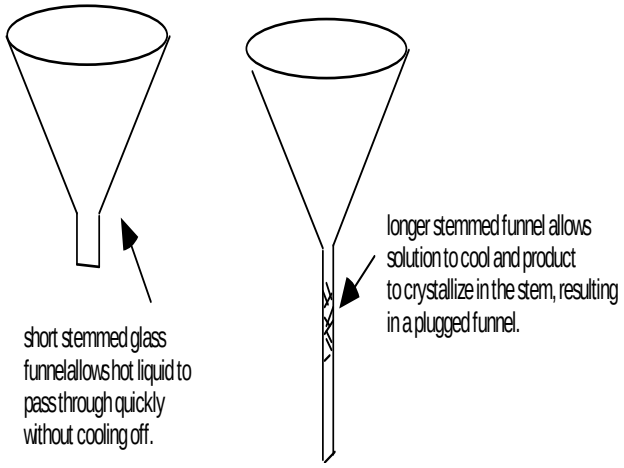
S configuration (S abbr. for Lat. *sinister*=left) refers to the direction of travel (counterclockwise) around a chiral center in order of rank of substituents. (see also Cahn-Ingold-Prelog sequence rules).

second crop a way of increasing the yield of purified product. It involves 5 steps: (1) saving the filtrate from the vacuum filtration and reducing the volume of solvent by boiling. Steps (2)-(5) are the same as for recrystallization. Note: the second crop is often not as pure as the first crop of crystals.

separatory funnel (a.k.a. 'sep funnel') used for extractions and separations of immiscible liquids. The bottom/heavy layer is let out the bottom by opening the stopcock and the top/light layer is poured out the top of the funnel.



short-stemmed funnel or 'stemless funnel' is a funnel primarily used for hot gravity filtrations. (see also hot gravity filtrations and recrystallization). The short-stem allows for the hot filtered product to pass quickly into the collection/receiving flask without crystallizing.



sigma (s) plane a kind of plane of symmetry used to study molecular conformations. It is a mirror plane that bisects a rigid object so that one-half of the object coincides with the reflection in the mirror of the other half. No molecule possessing a plane of symmetry can be chiral (i.e., no chiral molecule has a plane of symmetry). e.g.,, water has two (σ) planes, ammonia has three.

S_N1 reaction (S_N1 = substitution, nucleophilic, unimolecular) is one of four main polar reaction mechanisms in organic chemistry. More specifically, nucleophilic substitution reactions of alkyl halides. It is analogous to the E_1 reaction. S_N1 reactions occur via a carbocation intermediate (sp^2 hybridized, planar species; achiral) and result in varying degrees of racemic mixtures or rarely complete racemization (e.g., 80:20 or 50:50 mixture of enantiomers respectively). This is because the nucleophile may attack the carbocation 'equally' well from either side. The S_N1 reaction shows first order kinetics (Rate= k[RX]) with the rate-limiting step involving the formation of the carbocation intermediate. The S_N1 reaction is favoured by any factor that stabilizes the high-energy carbocation intermediate (Hammond postulate) and is not affected by the nature of the attacking nucleophile (solvolysis). The reaction is favoured by the leaving group that's the most stable ($Tosylate^- > I:^- > Br:^- > Cl:^- > H_2O:$), and the solvent used (fast in polar protic solvents, slow in non-polar solvents).

S_N2 reaction (S_N2 = substitution, nucleophilic, bimolecular) is one of four main polar reaction mechanisms in organic chemistry. More specifically, nucleophilic substitution reactions of alkyl halides. It is analogous to the E_2 reaction. In S_N2 reactions, there is a change (inversion) of configuration at the chiral center (nucleophile back-side attacks substrate from a position 180^o away from the leaving group), the reaction shows second order kinetics (Rate= k[RX][$Nu:^-$]) and takes place in a single step without intermediates. The S_N2 reaction is subject to alkyl steric effects, is affected by the nature of the attacking nucleophile, the leaving group (same as S_N1 reactions), and the solvent used (slow in protic, fast in polar aprotic solvents).

solid one of three common phases of matter (others are liquid and gas), it has fixed shape and volume. Note: volumes of solids change very little in with changes in

temperature or pressure.

solute in a solution, they are the components which are dissolved in the solvent.

solution is a homogeneous mixture of two or more substances.

solvation refers to the interaction of an ion with solvent molecules.

solvent in a solution, it is the component in greater abundance.

solvolysis in reactions, it refers to the solvent serving as both reaction medium and nucleophile. Has a strong effect on reaction rate. Important in many S_N1 reactions and the effect is explained by the Hammond postulate, and solvation and polarity (dielectric constants).

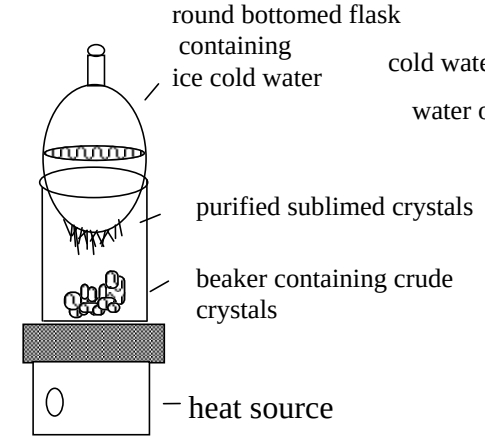
specific rotation $[\alpha]_D$ = standardized intrinsic physical property of optically active compounds. Defined as the observed rotation of light of 5896 angstroms wavelength (the yellow sodium D line) when passed through a sample path length of 1 decimeter (dm=10cm) with a sample concentration of 1 g/mL.

$$\text{Given: } [\alpha]_D^{20} \text{ for a solution} = \frac{(\alpha - \alpha_{blank})}{\text{STL (dm)} \times c}$$

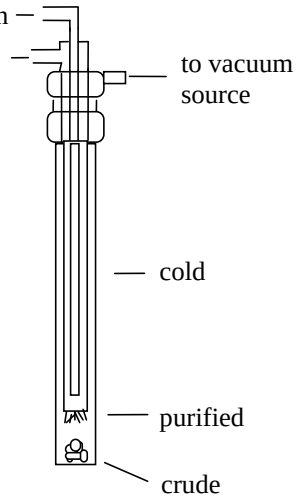
where α = observed rotation, α_{blank} = obs.rotation of solvent, STL=Sample Tube Length in dm, and c = conc. of sol'n (g/mL).

stereoisomers one of two types of isomer. They are compounds with identical chemical formula that have their atoms connected in the same order but differ in the spatial arrangement of those atoms.

sublimation (to sublime =the direct conversion of a solid to a vapour) is a procedure used for the purification of compounds that sublime. The impure solid is gently heated and the vapours of pure compound are collected on a cool surface.



crude sublimation apparatus



cold finger sublimator

suspension is a liquid mixture in which fine particles of a solid substance are dispersed or suspended.

sweating of solvent a result of escaping solvent previously trapped in the crystalline lattice.

symmetrical reagent in alkene addition reactions, it refers to a reagent that has identical parts to add to a double bond (e.g., H_2 or X_2).

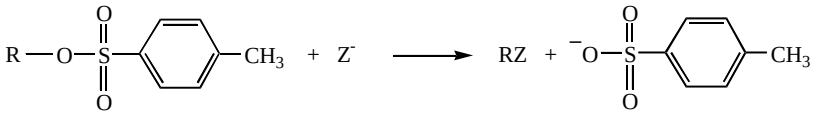
syn addition(s) a term used to describe the stereochemistry of an addition reaction, it refers to the addition of substituents to the same face of a double bond resulting in cis products.

theoretical plates an efficiency term used for fractionating columns where each theoretical plate is equivalent to one simple distillation.

thermometer calibration a procedure performed to correct for defects in accuracy in a thermometer used for melting point and boiling point determinations. Suggested standards are ice water (mp 0^o C), hydrocinnamic acid (mp 47-49^o C), acetanilide (mp 113-115^o C), adipic acid (mp 152-154^o C) and *p*-hydroxybenzoic acid (mp 215-217^o C).

throughput in reference to distillations, it is the maximum volume of distillate that can be obtained per unit of time while still maintaining equilibrium throughout the fractionating column

tosylate is an alkyl *p*-toluenesulfonate ester. It is a very good leaving group in nucleophilic substitution reactions.

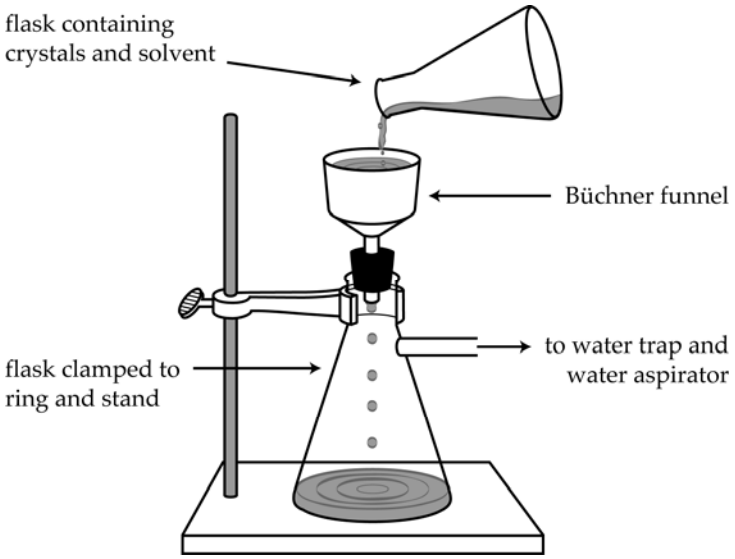


an alkyl tosylate Nucleophile tosylate leaving group

trituration a method for solidifying an 'oiled out' organic compound. It involves 4 steps: (1) removing a small sample of the oil with a Pasteur pipette and placing a few drops on a clean watch glass, (2) Add a few drops of solvent that the compound is known to be insoluble in, (3) using a glass rod beat (triturate) the solvent-oil mixture until it forms a crystalline solid and finally (4) use these crystals to seed the rest of the oil and cause the oil to crystallize.

unsymmetrical reagent in alkene addition reactions, it refers to a reagent that has non-identical parts to add to a double bond (e.g., H_2O, HOX or HX).

vacuum filtration or suction filtration, is a common method of collecting crystalline product. (see also recrystallization). It involves the use of a Büchner funnel, filter paper, filter flask and water aspirator (with water trap).

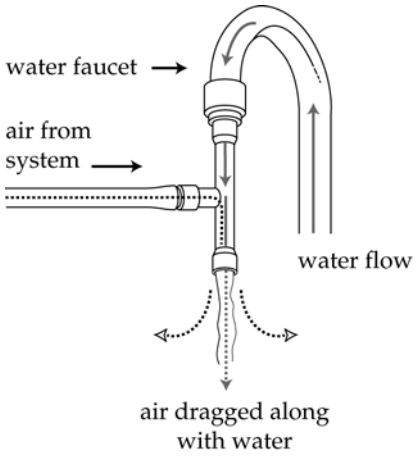


van der Waals forces intramolecular forces between non-polar molecules. They operate over very short distances and result from the induced polarization of the electron clouds in molecules. i.e., Temporary dipole moments in one molecule causes a temporary opposite dipole moment in another and a tiny attraction occurs between the two molecules. The cumulative effect of a very large number of these tiny attractive force interactions explains why molecules exist in a liquid state rather than a gaseous state. Note: These forces increase as molecule size increases.

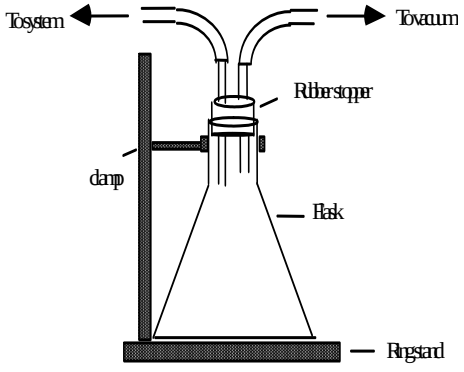
vaporization turning a liquid into a vapour by heating a compound to its boiling point.

washing a technique used in organic chemistry to purify a component which has been extracted from an organic mixture.

water aspirator a small device attached to a water faucet. It is used to create an inexpensive source of vacuum for use in vacuum filtrations.



Water Trap a safety apparatus used to prevent the back flow of water from a water aspirator into the filter flask during vacuum filtration.



Weight percentage abbr.=Wt.%, w/w, a quantitative expression of concentration, in parts per hundred, and is defined as the mass of the component in solution divided by the total mass of solution, all times 100%. Can also be expressed as w/v defined as the mass of the component in solution divided by the total

volume of solution, all times 100%.

$$\text{Wt\% (w/w)} = \frac{\text{mass of component in soln}}{\text{total mass of soln}} \times 100\%$$

WHMIS **W**orkplace **H**azardous **M**aterials **I**nformation **S**ystem (WHMIS) is a national system intended to provide laboratory personnel with uniform information on chemicals used in the workplace. Its three main features are: (1) chemical manufacturers supply a label outlining the products hazards and recommend emergency procedures, (2) the manufacturer provides a Material Safety Data Sheet (MSDS) for each hazardous product, and (3) Employers provide an appropriate education program for all workers who work with hazardous chemicals.

Zaitsev's rule (proun.= *Sayt zeff*), formulated by Alexander M. Zaitsev (1841-1910).Rule paraphrase = 'Base-induced elimination reactions generally give the more substituted alkene product'.

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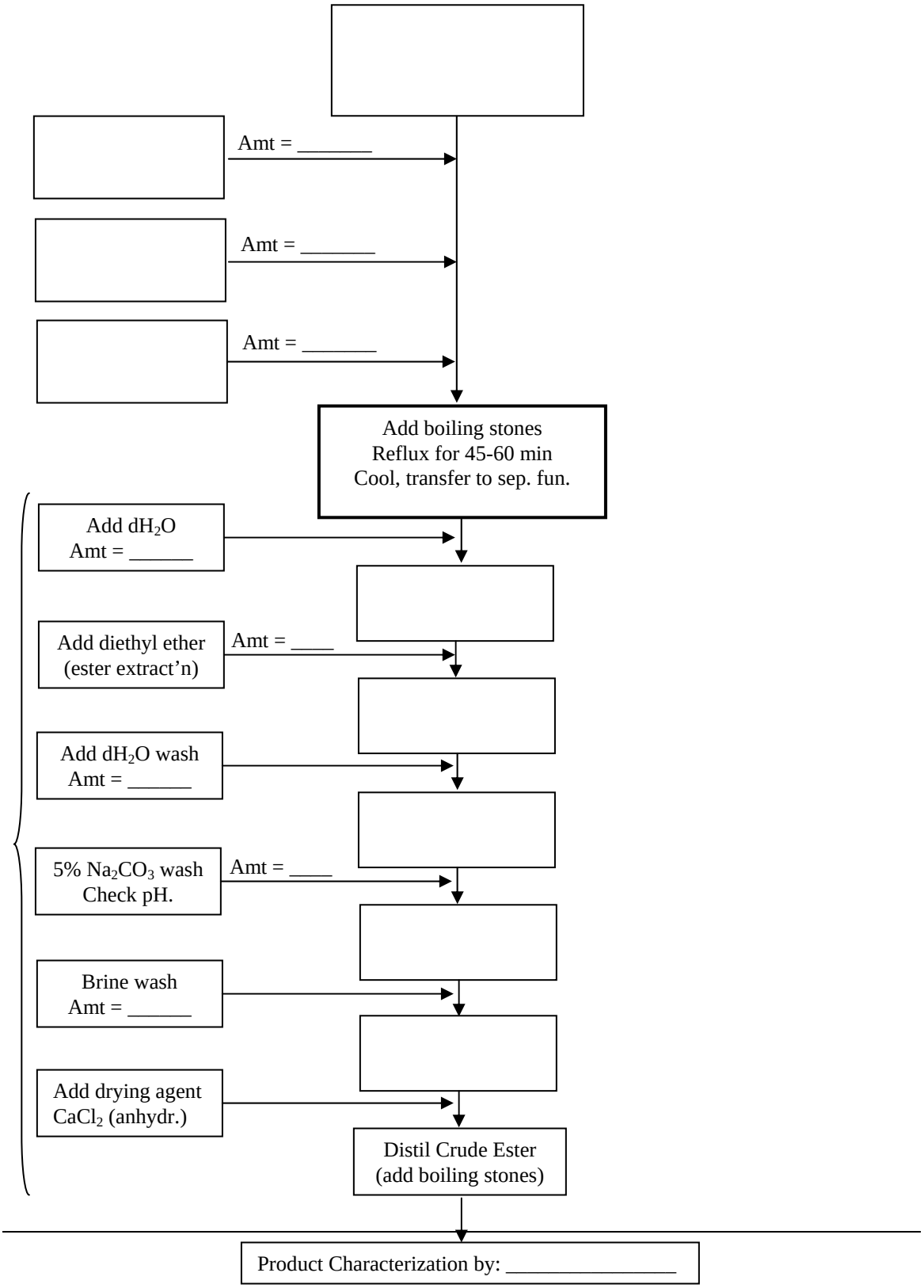
Origin of Common Names of Organic Compounds

Common Name	Root	Notes	Systematic Name
Acetic acid	L *acetum*, vinegar	Found in vinegar	ethanoic acid
Adipic acid	L *adeps*, fat	Formed when some unsaturated fats are oxidized	hexanedioic acid
Aniline	Sp *añil*, indigo, anil + -ine	First obtained by distillation of indigo; anil is the name for the indigo producing West Indian shrub *Indigofera suffrutincosa*	aminobenzene
Anisole	Gk *anison*, anise L *ole*, oil	From the aniseed of the Egyptian plant *Pimpinella anisum*	methoxybenzene
Arginine	L. *argentum*, silver	Forms a well defined silver salt	(S)-2-amino-5-guanidinopentanoic acid
Asparagine	Asparagus	First found in asparagus	(S)-2-amino-3-carbamoylpropanoic acid
Aspartic acid	-	Also related to asparagus	(S)-2-aminobutanedioic acid
Benzene			
Butyric acid	L *butyrum*, butter	Found in rancid butter	butanoic acid
Cumene		From cumin, a plant native to Egypt and Syria	isopropylbenzene
Cysteine	-	Reduction product of cystine	(S)-2-amino-3-mercaptopropanoic acid
Cystine	Gk *kystis*, bladder	First isolated from a bladder stone	bis(2-amino-2-carboxyethyl)disulfide
Formic acid	L *formica*, ant	Obtained from the destructive distillation of ants	methanoic acid
Furan	L furfur, bran	Short for "furfurane",	furan
Glutamic acid	*gluten* + amino	Obtained from hydrolysis of gluten	(S)-2-aminopentanedioic acid
Glutamine	-	Derived from glutamic acid	(S)-2-amino-3-carbamoylbutanoic acid
Glycine	Gk *glykys*, sweet	Tastes sweet	aminoethanoic acid
Histidine	Gk *histion*, tissue	Found in tissue?	
Hydroquinone			
Indole			
Isoleucine	-	Isomer of leucine	
Lactic acid	L lac, milk	First isolated from sour milk	2-hydroxypropanoic acid
Leucine	Gk *leukos*, white	Obtained in the form of white plates	
Lysine	Gk *lysis*, loosening	Discovered among the products from the hydrolysis of casein	
Methionine	Methyl + thio	Contains a S atom (Gk *theion* sulfur) with a methyl group attached	
Phenol			
Proline	pyrrolidine	Contains a pyrrolidine ring	2-pyrrolidinecarboxylic acid
Pyridine	Gk *pyro*, fire	Obtained by distillation of the oil derived from pyrolysis of bones	pyridine
Pyrrole	Gk pyrro, fiery red	First detected by the red color produced when its vapour came in contact with pine splinters moistened with conc. hydrochloric acid	pyrrole
Serine	L. *sericum*, silk	First isolated from silk	
Styrene	L *styrax*, storax	First obtained by distillation of liquid storax, a balsam from *Liquidambar styraciflua* and *Liquidambar orientalis*	ethenylbenzene
Tartaric acid			
Threonine		Has spatial configuration analogous to D-threose, a 4 carbon sugar	
Toluene		Obtained by distillation of tolu balsam, a fragrant, yellow-brown resin from the tolu tree, named after the seaport Santiago de Tolú, Columbia	methylbenzene
Tryptophan	Tryptic + Gk *phane* to appear (from)	Obtained from the pancreatic (tryptic) digestion of proteins	
Tyrosine	Gk *tyros*, cheese	Found in cheese	
Valine	valeric	Has carbon skeleton corresponding to isovaleric acid (3-methylbutanoic acid)	(S)-2-amino-3-methylbutanedioic acid
Xylene (*o*-, *m*-, *p*-)	Gk *xylon*, wood	First obtained from wood tar	1,x-dimethylbenzene

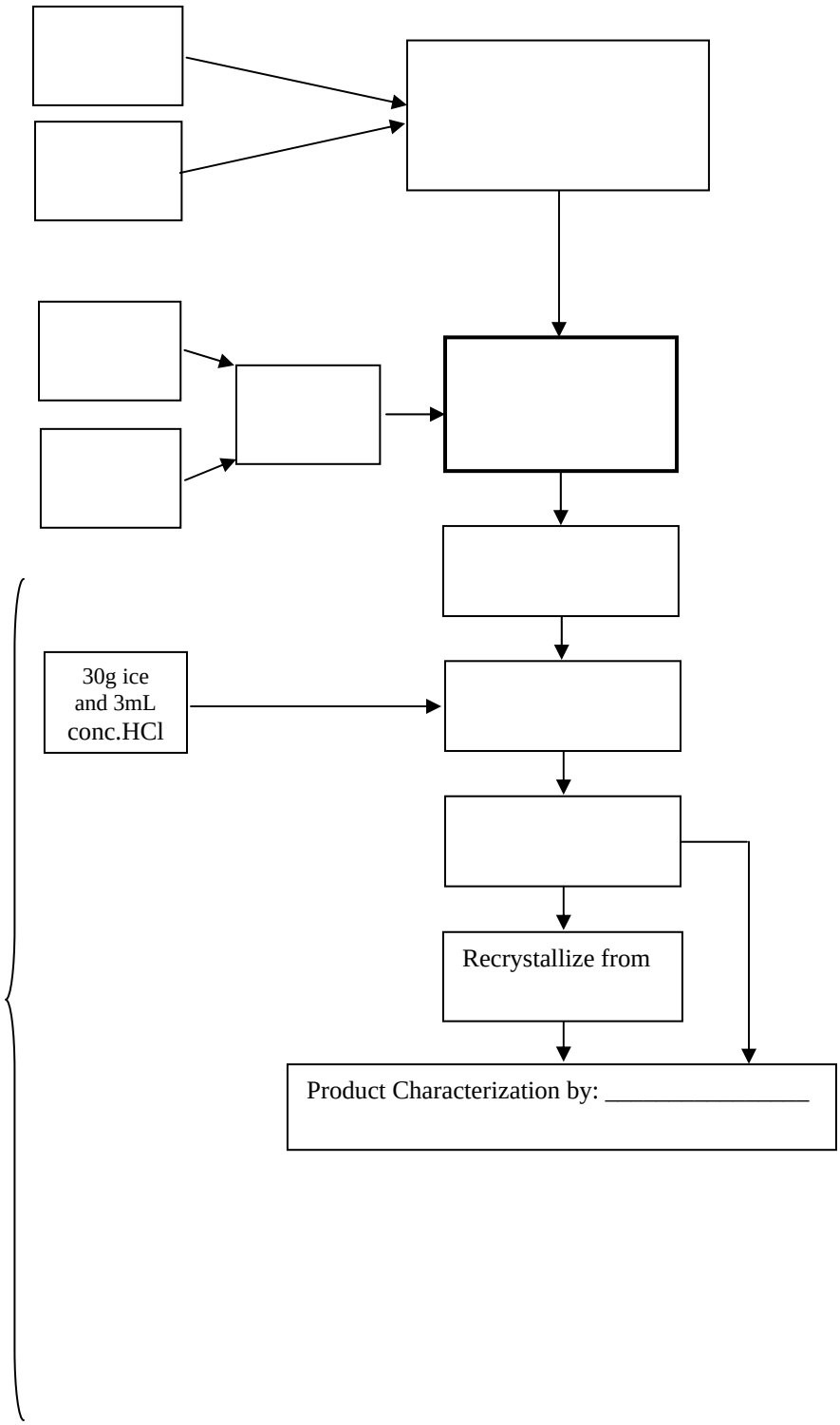
Reference: Leung, Sam H., 2000. Amino acids, aromatic compounds and carboxylic acids: How did they get their names? Journal of Chemical Education **77(1)**: 48-49.

SAMPLE EXPERIMENT 10 FLOW CHART



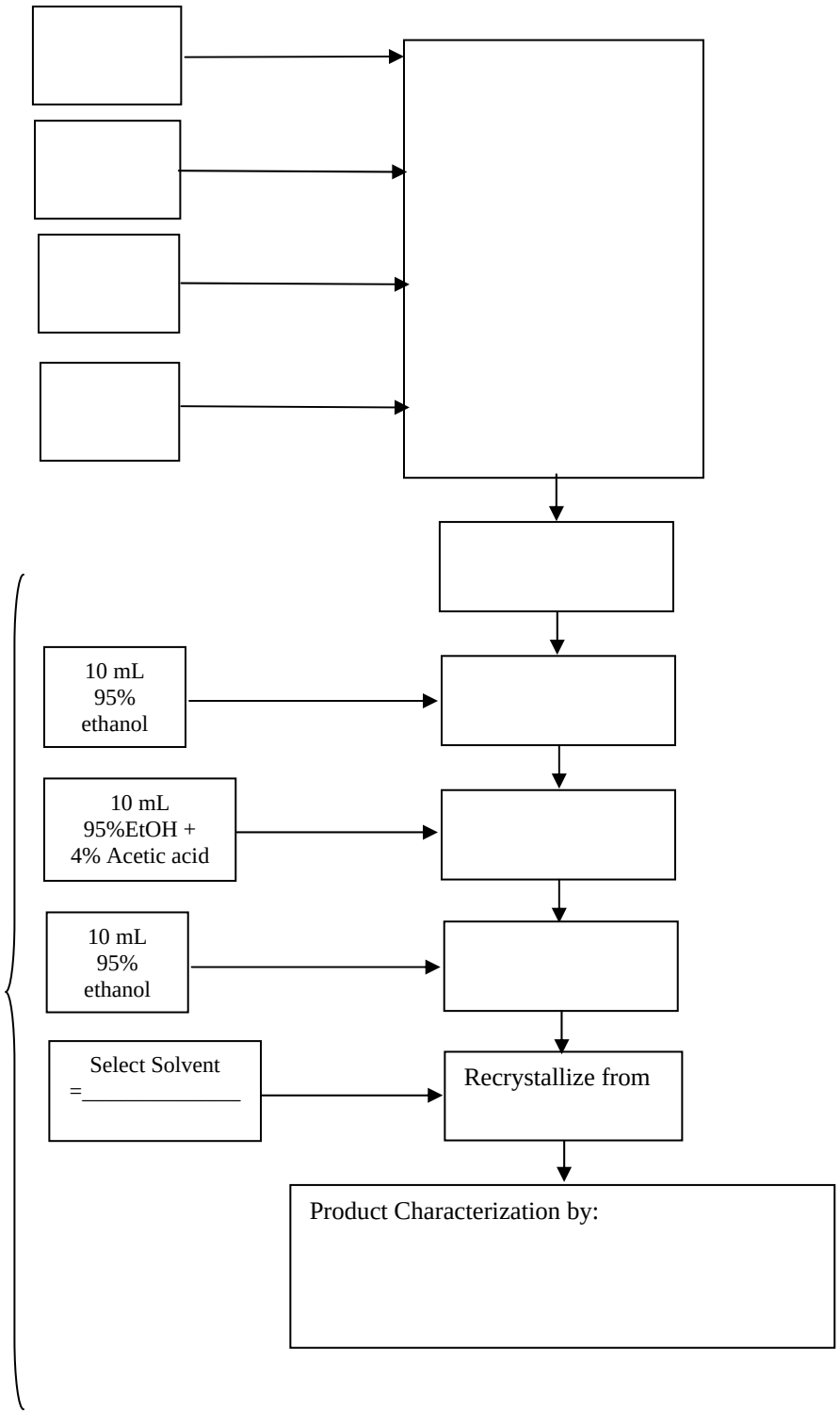
SAMPLE EXPERIMENT 12 FLOW CHART

REAGENT **PROCEDURE / STEP** **OBSERVATION**



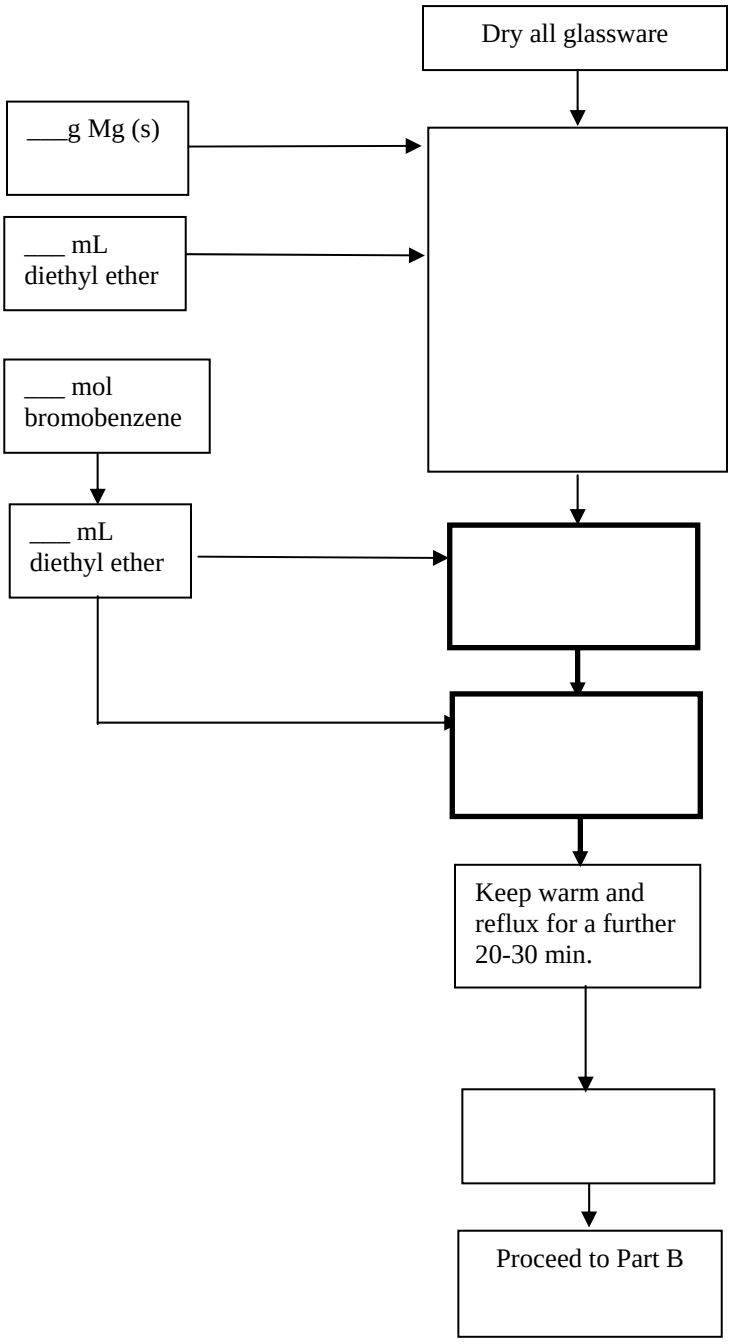
SAMPLE EXPERIMENT 13 FLOW CHART

REAGENT **PROCEDURE / STEP** **OBSERVATION**



SAMPLE EXPERIMENT 16 FLOW CHART Part A

REAGENT **PROCEDURE / STEP** **OBSERVATION**



Compound Name	Chemical Formula	Solid (S) or Liquid (L)	Formula Weight	MP or BP (°C)	Density (g/mL)	Refract. Index	Hazardous Properties*
acetanilide	$CH_3CONHC_6H_5$	S	135.17	113-115			Toxic, irritant
acetanilide,4-methyl	$CH_3CONHC_6H_4CH_3$	S	149.19	149-151			Irritant
acetanilide, *p*-nitro	$CH_3CONHC_6H_4NO_2$	S	180.16	216			Irritant
acetanilide, *o*-nitro	$CH_3CONHC_6H_4NO_2$	S	180.16	94	1.419		Irritant
acetanilide, *m*-nitro	$CH_3CONHC_6H_4NO_2$	S	180.16	154-156			Irritant
acetic acid, glacial (17.4 M)	CH_3CO_2H	L	60.05	118.1	1.049		Corrosive, hygroscopic
acetic acid, *p*-ethoxyphenyl	$C_2H_5OC_6H_4CH_2CO_2H$	S	180.2	87-90			Irritant
acetic anhydride	$(CH_3CO)_2O$	L	102.09	140	1.082	1.3900	Corrosive, lachrymator
acetone	CH_3COCH_3	L	58.08	56.5	0.7899	1.3590	Flammable, irritant
acetone, diethylamino	$(C_2H_5)_2NCH_2COCH_3$	L	129.2	64/16mm	0.832	1.4250	Irritant
acetophenone	$C_6H_5COCH_3$	L	120.15	202	1.030	1.5325	Irritant
activated carbon		S					(see charcoal)
allyl alcohol (2-propen-1-ol)	$CH_2=CHCH_2OH$	L	58.08	96-98	0.854	1.4120	Highly Toxic, flammable
ammonia (14.8 M)	NH_3	L	17.03		0.90		Corrosive, lachrymator
ammonium hydroxide (14.8 M)	NH_4OH	L	35.05		0.90		Corrosive, lachrymator
aniline	$C_6H_5NH_2$	L	93.13	184	1.022	1.5860	Highly toxic, irritant
aniline, 4-bromo	$BrC_6H_4NH_2$	S	172.03	62-64			Toxic, irritant
aniline, 4-chloro	$ClC_6H_4NH_2$	S	127.57	72.5			Highly toxic, irritant
aniline, *o*-ethyl	$CH_3CH_2C_6H_4NH_2$	L	121.18	210		1.5590	Toxic, irritant
aniline, 2-ethoxy	$CH_3CH_2OC_6H_4NH_2$	L	137.18	231-233	1.051	1.5550	Irritant, light sens.
aniline, 4-methyl	$CH_3C_6H_4NH_2$	L	107.16	196	0.989	1.5700	Toxic, irritant
aniline, 3-nitro	$NO_2C_6H_4NH_2$	S	138.13	114			Highly toxic, irritant
aspirin (see salicylic acid, acetate)	$CH_3CO_2C_6H_4CO_2H$	S	180.16	138-140			Irritant, toxic
benzaldehyde	C_6H_5CHO	L	106.12	179.5	1.044	1.5450	Hi.toxic, cancer susp.agent
benzaldehyde, 4-methyl	$CH_3C_6H_4CHO$	L	120.15	204-205	1.019	1.5454	Irritant (*p*-tolualdehyde)
benzaldehyde,4-methoxy	$CH_3OC_6H_4CHO$	L	136.15	248	1.119	1.5730	Irritant, (anisaldehyde)
benzaldehyde, 4-nitro	$NO_2C_6H_4CHO$	S	151.12	106			Irritant
benzene	C_6H_6	L	81.14	80.1	0.908	1.4990	Flamm., cancer susp.agent
benzene, bromo	C_6H_5Br	L	157.02	155-156	1.491	1.5590	Irritant
benzene, chloro	C_6H_5Cl	L	112.56	132	1.107	1.5240	Flammable, irritant
benzoate, ethyl	$C_6H_5CO_2C_2H_5$	L	150.18	212.6	1.051	1.5050	Irritant
benzoate, methyl	$C_6H_5CO_2CH_3$	L	136.15	198-199	1.094	1.5170	Irritant
benzocaine, 4-aminobenzoic acid, ethyl ester,	$H_2NC_6H_4CO_2C_2H_5$	S	165.19	88-92			Irritant
benzoic acid	$C_6H_5CO_2H$	S	122.12	122.4			Irritant
benzoic acid, 4-acetamido	$CH_3CONHC_6H_4CO_2H$	S	179.18	256.5			Irritant
benzoic acid, 4-amino	$H_2NC_6H_4CO_2H$	S	137.14	188-189	1.374		Irritant
benzoic acid, 3-chloro	$ClC_6H_4CO_2H$	S	156.57	158			Irritant
benzoic acid, 4-chloro	$ClC_6H_4CO_2H$	S	156.57	243			Irritant
benzoic acid, 3-hydroxy	$HOC_6H_4CO_2H$	S	138.12	210-203			Irritant
benzoic acid, 4-hydroxy	$HOC_6H_4CO_2H$	S	138.12	215-217			Irritant
benzoic acid, 2-methyl	$CH_3C_6H_4CO_2H$	S	136.15	103-105			See also *o*-toluic acid
benzoic acid, 4-methyl	$CH_3C_6H_4CO_2H$	S	136.15	180-182			See also *p*-toluic acid
benzoic acid, 4-nitro	$O_2NC_6H_4CO_2H$	S	167.12	239-241			Irritant
benzonitrile	C_6H_5CN	L	103.12	191	1.010	1.5280	Irritant
benzophenone	$(C_6H_5)_2CO$	S	182.22	49-51			Irritant
benzoyl chloride	C_6H_5COCl	L	140.57	198	1.211	1.5530	Corrosive, toxic
benzyl alcohol	$C_6H_5CH_2OH$	L	108.14	205	1.045	1.5400	Irritant, hygroscopic
benzyl amine	$C_6H_5CH_2NH_2$	L	107.16	184-185	0.981	1.5430	Corrosive, lachrymator
benzyl chloride	$C_6H_5CH_2Cl$	L	126.59	179	1.1002		Hi.toxic, cancer susp.agent
biphenyl	$C_6H_5C_6H_5$	S	154.21	69-71	0.992		Irritant
boric acid	H_3BO_3	S	61.83		1.435		Irritant, hygroscopic
Brady's Reagent	$(NO_2)_2C_6H_3NHNH_2$	L	See hydrazine, 2,4-dinitrophenyl				
bromine	Br_2	L	159.82	58.8	3.102		Highly toxic, oxidizer
butanal	$CH_3CH_2CH_2CHO$	L	72.11	75			Flammable, corrosive
1,3-butadiene, E,E-1,4-diphenyl	$C_6H_5C_4H_4C_6H_5$	S	206.29	153			Irritant
butane, 1-bromo	$CH_3CH_2CH_2CH_2Br$	L	137.03	101.3	1.276	1.4390	Flammable, irritant

Compound Name	Chemical Formula	Solid (S) or Liquid (L)	Formula Weight	MP or BP (°C)	Density (g/mL)	Refract. Index	Hazardous Properties*
butane, 2-bromo	$CH_3CH_2CHBrCH_3$	L	137.03	91.3	1.255	1.4369	Flammable, irritant
butane, 1-chloro	$CH_3CH_2CH_2CH_2Cl$	L	92.57	78.4	0.886	1.4024	Flammable liquid
butane, 2-chloro	$CH_3CH_2CHClCH_3$	L	92.57	68.2	0.873	1.3960	Flammable liquid
1-butanol	$CH_3CH_2CH_2CH_2OH$	L	74.12	117-118	0.810	1.3990	Flammable, irritant
1-butanol, 3-methyl	$(CH_3)_2CH(CH_2)_2OH$	L	88.15	130	0.8092	1.4053	Irritant
2-butanol	$CH_3CH_2CHOHCH_3$	L	74.12	99.5-100	0.807	1.3970	Flammable, irritant
2-butanone	$CH_3CH_2COCH_3$	L	72.11	80	0.805	1.3790	Flammable, irritant
2-butanone, 3-hydroxy-3-methyl	$(CH_3)_2C(OH)COCH_3$	L	102.13	140-141	0.971	1.4150	Irritant
1-butene, 3-chloro-	$CH_3CH(Cl)CH=CH_2$	L	90.55	62-65	0.900	1.4155	Flammable, lachrymator
3-buten-2-ol	$CH_2=CHCH(OH)CH_3$	L	72.11	96-97	0.832	1.4150	Flammable, irritant
n-butyl butyrate	$C_3H_7CO_2C_4H_9$	L	144.21	164-165	0.871	1.4060	Irritant
butyric acid	$CH_3(CH_2)_2CO_2H$	L	88.11	165.5	0.9577	1.3980	Corrosive, toxic
3-butyn-2-ol, 2-methyl	$CH{\equiv}CC(CH_3)_2OH$	L	84.12	104	0.868	1.4200	Flammable, toxic
calcium carbonate	$CaCO_3$	S	100.09		2.930		Irritant, hygroscopic
calcium chloride, anhydr.	$CaCl_2$	S	110.99		2.150		Irritant, hygroscopic
camphor (1R, +)	$C_{10}H_{16}O$	S	152.24	179-181	0.990	1.5462	Flamm., irritant
carbon dioxide, solid	CO_2	S	44.01	-78.5(subl.)			Frost bite burns
carbon tetrachloride	CCl_4	L	153.82	76	1.594		Susp. Cancer agent
charcoal (Norit)		S	Decolourizing agent, used in recrystallizations				Irritant
chloroform	$CHCl_3$	L	119.38	61.3	1.500		Highly toxic
cinnamaldehyde, *trans*	$C_6H_5CH=CHCHO$	L	132.16	246(decomp)	1.048	1.6220	Irritant
cinnamic acid, trans	$C_6H_5CH=CHCO_2H$	S	148.16	135-136			Irritant
crotonaldehyde	$CH_3CH=CHCHO$	L	70.09	102.4	0.846	1.4365	Highly toxic, flammab.
cyclohexane	C_6H_{12}	L	84.16	80.7	0.779	1.4260	Flammable, irritant
cyclohexane, bromo	$C_6H_{11}Br$	L	163.06	166.2	1.324	1.4950	Flammable, irritant
cyclohexane, methyl	$C_6H_{11}CH_3$	L	98.19	101	0.770	1.4220	Flammable, irritant
cyclohexene	C_6H_{10}	L	82.15	83	0.811	1.4460	Flammable, irritant
cyclohexanol	$C_6H_{11}OH$	L	100.16	161.1	0.963	1.4650	Irritant, hygroscopic
cyclohexanone	$C_6H_{10}(=O)$	L	98.15	155.6	0.947	1.4500	Corrosive, toxic
cyclohexanone, 4-methyl	$CH_3C_6H_9(=O)$	L	112.17	170	0.914	1.4460	Corrosive, toxic
cyclopentane	C_5H_{10}	L	70.14	49.5	0.751	1.4000	Flammable, irritant
cyclopentane, bromo	C_5H_9Br	L	149.04	137-138	1.390	1.4881	Flammable
cyclopentanone	$C_5H_8(=O)$	L	84.12	130.6	0.951	1.4370	Flammable, irritant
dichloromethane	CH_2Cl_2	L	84.93	40.1	1.325	1.4240	Toxic, irritant
diethyl ether (see ethyl ether)	$C_2H_5OC_2H_5$	L	74.12	34.6	0.708	1.3530	Flammable, toxic
1,4-dioxane	$C_4H_8O_2$	L	88.11	100-102	1.034	1.4220	Flamm., cancer susp.agent
diphenylmethanol	$(C_6H_5)_2CH(OH)$	S	184.24	65-67			Irritant
ethyl acetate	$CH_3CO_2C_2H_5$	L	88.11	76-77	0.902	1.3720	Flammable, irritant
ethyl alcohol, anhydrous	CH_3CH_2OH	L	46.07	78.5	0.785	1.3600	Flammable, poison
ethyl ether, absolute	$CH_3CH_2OCH_2CH_3$	L	74.12	34.6	0.708	1.3530	Flammable, irritant
fluorene	$C_{13}H_{10}$	S	166.22	114-116			Irritant
formaldehyde (sol'n)	$HCHO$	L	30.03	96	1.083	1.3765	suspect. Cancer agent
formamide, N,N-dimethyl	$HCON(CH_3)_2$	L	73.10	149-156	0.9487	1.4310	suspect. Cancer agent
furfuryl amine	$(C_4H_3O)CH_2NH_2$	L	97.12	145-146	1.099	1.4900	Irritant
gold	Au	S	196.97	1064	19.28		Expensive/valuable
***n*-hexane**	$CH_3(CH_2)_4CH_3$	L	86.18	69	0.659	1.3750	Flammable, irritant
hydrazine, 2,4-dinitrophenyl	$(NO_2)_2C_6H_3NHNH_2$	70% soln	198.14				Flammable, irritant
hexanes	C_6H_{14}	L	86.18	68-70	0.672	1.3790	Flammable, irritant
hydrochloric acid, conc. 12 M	HCl	L	36.46		1.20		Corrosive, highly toxic
iodine	I_2	S	253.81	133	4.930		Corrosive, highly toxic
isoamyl acetate (isopentyl acetate)	$CH_3CO_2C_5H_{11}$	L	130.19	142	0.8670	1.4000	Flammable, irritant
isoamyl alcohol	$(CH_3)_2CH(CH_2)_2OH$	L					(see 1-butanol, 3-methyl-)
isopentyl alcohol	$(CH_3)_2CH(CH_2)_2OH$	L					(see 1-butanol, 3-methyl-)
lichen		S					Allergin
ligroin (high bp petrol. Ether)	C_6-C_7 (light naphtha)	L		60-80	0.656	1.3760	Flammable, irritant
Lucas Reagent		Solution	of hydrochloric acid/zinc chloride (from zinc dust)				Toxic, irritant

Compound Name	Chemical Formula	Solid (S) or Liquid (L)	Formula Weight	MP or BP (°C)	Density (g/mL)	Refract. Index	Hazardous Properties*
magnesium (metal)	Mg	S	24.31	651	1.75		Flammable
magnesium oxide	MgO	S	40.31		3.58		Moist. Sens., irritant
magnesium sulfate, anhydrous	$MgSO_4$	S	120.37		2.660		Hygroscopic
magnesium sulfate, 7-hydrate	$MgSO_4.7H_2O$	S	246.48		1.670		(psom salt)
manganese dioxide	MnO_2	S	86.94	535 (dec.)	5.026		Oxidizer, irritant
methanol, anhyd.	CH_3OH	L	32.04	64.5	0.791	1.3290	High. Toxic, flammable
methanol, diphenyl	$(C_6H_5)_2CH(OH)$	S	184.24	69			Irritant
methanol, triphenyl	$(C_6H_5)_3C(OH)$	S	260.34	164.3			Irritant
methylene chloride	CH_2Cl_2	L	84.93	40.1	1.325	1.4230	See dichlormethane
mineral spirits (light kerosene)	C_{12}-C_{14}	L		179-210	0.752	1.4240	Flammable, irritant
naphthalene	$C_{10}H_8$	S	128.17	80.5			Flamm., susp.cancer agent
nitric acid (conc. 15.4 M)	HNO_3	L	63.01		1.400		Corrosive, oxidizer
2-octanone	$CH_3(CH_2)_5COCH_3$	L	128.22	173	0.819	1.4150	Irritant
pentane	C_5H_{12}	L	72.15	36.1	0.626	1.3580	Flammable, irritant
2-pentanol, 4-methyl	$C_6H_{14}O$	L	102.18	132	0.802	1.4110	Irritant
3-pentanol	$C_2H_5CH(OH)C_2H_5$	L	88.15	115/749mm	0.815	1.4100	Flammable, irritant
3-penten-2-one, 4-methyl	$(CH_3)_2C=CHCOCH_3$	L	98.15	129	0.858	1.4450	Flammable, lachrymator
1-pentene, 2-methyl	C_6H_{13}	L	84.16	62	0.682	1.3920	Flammable, irritant
1-pentene, 4-methyl	C_6H_{13}	L	84.16	53-54	0.665	1.3820	Flammable, irritant
2-pentene, 2-methyl	C_6H_{13}	L	84.16	67	0.690	1.400	Flammable, irritant
2-pentene, 3-methyl	C_6H_{13}	L	84.16	69	0.698	1.4040	Flammable, irritant
2-pentene, 4-methyl	C_6H_{13}	L	84.16	57-58	0.671	1.3880	Flammable, irritant
petroleum ether, (Skelly B)	Mixt. Of C_5-C_6	L		35-60	0.640		Flammable, toxic
petroleum ether, hi bp (ligroin)	Mixt. Of C_6-C_7	L		60-80	0.656	1.3760	Flammable, toxic
phenethyl alcohol	$C_6H_5CH_2CH_2OH$	L	122.17	221/750mm	1.023	1.5320	Toxic, irritant
phenol	C_6H_5OH	S	94.11	40-42	1.071		Highly toxic, corrosive
phenol, 2,4-dimethyl	$(CH_3)_2C_6H_3OH$	S	122.17	22-23	1.011	1.5380	Corrosive, toxic
phenol, 2,5-dimethyl	$(CH_3)_2C_6H_3OH$	S	122.17	75-77	0.971		Corrosive, toxic
phenylacetylene	$C_6H_5C\equiv CH$	L	102.14	142-144	0.930	1.5490	Flamm., cancer susp.agent
phenylmagnesium bromide	C_6H_5MgBr	L	181.33		1.134		Flammable, moist.sensit.
phosphoric acid (85%, 14.7 M)	H_3PO_4	L	98.00		1.685		Corrosive
potassium chromate	K_2CrO_4	S	194.20	968	2.732		Canc.susp.agent, oxidizer
potassium dichromate	$K_2Cr_2O_7$	S	294.19	398			Hi.toxic, canc.susp.agent
potassium hydroxide	KOH	S	56.11				Corrosive, toxic
potassium iodide	KI	S	166.01	681	3.130		Moist.sens., irritant
potassium permanganate	$KMnO_4$	S	158.04	d<240	2.703		Oxidizer, corrosive
propane, 2-chloro, 2-methyl	$(CH_3)_3CCl$	L	92.57	50	0.851	1.3848	Flammable
propane, 2-nitro	$(CH_3)_2CHNO_2$	L	89.09	120	0.992	1.3940	Canc.susp.agent, flamm.
propanoic acid (or propionic acid)	$CH_3CH_2CO_2H$	L	74.08	141	0.9930	1.3869	Corrosive, toxic
1-propanol	$CH_3CH_2CH_2OH$	L	60.11	97.4	0.8035	1.3850	Flammable, irritant
1-propanol, 2-methyl-	$(CH_3)_2CHCH_2OH$	L	74.12	108.1	0.8018	1.3955	Flammable, irritant
2-propanol, 2-methyl-	$(CH_3)_3COH$	L	74.12	82.3	0.7887		Flammable, irritant
propionate, ethyl	$C_2H_5CO_2C_2H_5$	L	102.13	99	0.891	1.3840	Flammable, irritant
propionic acid	$C_2H_5CO_2H$	L	74.08	141	0.993	1.3860	Corrosive, toxic
rosaniline hydrochloride	$C_{20}H_{14}(NH_2)_3Cl$	Solution	337.86	250 (dec)			Susp. cancer agent
salicylic acid	$HOC_6H_4CO_2H$	S	138.12	158-160			Toxic, irritant
salicylic acid, acetate ester	$CH_3CO_2C_6H_4CO_2H$	S	180.16	138-140			Irritant, toxic
Schiff's Reagent		Solution	of roseaniline hydrochloride & sulfur dioxide				Toxic
silane, tetramethyl	$Si(CH_3)_4$	L	88.23	26-28	0.648	1.3580	Flammable, hygroscopic
silica, sand	SiO_2	S	60.09	NA			abrasive
silver nitrate	$AgNO_3$	S	169.88	212	4.352		Highly toxic, oxidizer
sodium acetate	CH_3CO_2Na	S	82.03				hygroscopic
sodium acetate, trihydrate	$CH_3CO_2Na\ 3H_2O$	S	136.08	58	1.45		Hygroscopic
sodium bisulfite	$NaHSO_3$	S			1.480		Severe irritant
sodium borohydride	$NaBH_4$	S	37.38	400			Flam. solid, corrosive
sodium bicarbonate	$NaHCO_3$	S	84.01		2.159		Moist. sensitive
sodium carbonate	Na_2CO_3	S	105.99	851	2.532		Irritant, hygroscopic

Compound Name	Chemical Formula	Solid (S) or Liquid (L)	Formula Weight	MP or BP (°C)	Density (g/mL)	Refract. Index	Hazardous Properties*
sodium chloride	NaCl	S	58.44	801	2.165		Irritant, hygroscopic
sodium dichromate, dihydrate	$Na_2Cr_2O_7.2H_2O$	S	298.00		2.350		Hi.toxic, cancer susp.agent
sodium hydrogen carbonate	$NaHCO_3$	S	84.01		2.159		See sodium bicarbonate
sodium hydroxide	NaOH	S	40.00				Corrosive, toxic
sodium iodide	NaI	S	149.89	661	3.670		Moist.sens., irritant
sodium metabisulfite	$Na_2S_2O_5$	S	190.10		1.480		Moist.sens., toxic
sodium methoxide	$NaOCH_3$	S	54.02				Flam. solid, corrosive
sodium sulfate	Na_2SO_4	S	142.04	884	2.680		Irritant, hygroscopic
styrene	$C_6H_5CH=CH_2$	L	104.15	146	0.909		Flammable
styrene, β-bromo	$C_6H_5CH=CHBr$	L	183.05	112/20mm	1.427	1.6070	Irritant
sucrose	$C_{12}H_{22}O_{11}$	S	342.30	185-187	1.5805		Tooth Decay!
sulfur dioxide	SO_2	Gas	64.06	-10 bp			Nonflamm, corrosive
sulfuric acid (conc. 18 M)	H_2SO_4	L	98.08		1.840		Corrosive, oxidizer
sulfurous acid	H_2SO_3	L	82.08		1.030		Corrosive, toxic
L-tartaric acid	$HO_2CC_2H_2(OH)_2CO_2H$	S	150.09	171-174			Irritant
tetrahydrofuran	C_4H_8O	L	72.11	65-67	0.889	1.4070	Flammable, irritant
tetramethylsilane	$Si(CH_3)_4$	L	88.23	26-28	0.648	1.3580	Flammable, hygroscopic
tin	Sn	S	118.69		7.310		Flammable solid, moist.sens.
Tollen's Reagent		L	See ammonia + silver nitrate				
toluene	$C_6H_5CH_3$	L	92.14	110.6	0.867	1.4960	Flammable, toxic
toluene, 4-nitro	$NO_2C_6H_4CH_3$	S	137.14	52-54	1.392		Hi.toxic, irritant
o- or 2-toluic acid	$CH_3C_6H_4CO_2H$	S	136.15	103-105			Probable irritant
p- or 4-toluic acid	$CH_3C_6H_4CO_2H$	S	136.15	180-182			Probable irritant
triethylphosphite	$(C_2H_5O)_3P$	L	166.16	156	0.969	1.4130	Moist. sens., irritant
triphenylmethanol	$(C_6H_5)_3C(OH)$	S	260.34	164.3			Probable irritant
urea	NH_2CONH_2	S	60.06	135	1.335		Irritant
(-) usnic acid	$C_{18}H_{16}O_7$	S	344.32	198			Toxic
(+) usnic acid	$C_{18}H_{16}O_7$	S	344.32	201-203			Toxic
water	H_2O	L	18.02	100		1.33	Will burn skin when hot
water, ice	H_2O	S/L	18.02	0	1.00		Frostbite, hypothermia
xylenes	$CH_3C_6H_4CH_3$	L	106.17	137-144	0.860	1.4970	Flammable, irritant
zinc, dust	Zn	S	65.37	419.5			Flammable, moist.sens.
zinc chloride, anhydrous	$ZnCl_2$	S	136.28	283	2.91		Corrosive, toxic

*Be sure to consult the chemical's MSDS for more specific detail on hazardous properties.