

Chem 355 Lab Manual

Fall, 2024

**Minnesota State University Moorhead
Department of Chemistry**

**Dr. Craig P. Jasperse
Phone: 477-2230
Hagen 407J**

**Email: jasperse@mnstate.edu
Website: www.mnstate.edu/jasperse**

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CHEMISTRY 355 SYLLABUS FALL 2024

Dr. Craig P. Jasperse
Office: Hagen 407J Research Lab: Langseth324
Telephone: 477-2230
e-mail: jasperse@mnstate.edu

web: <http://www.mnstate.edu/jasperse/>
Office Hours: M 1-3; T 9-11:30;
W 9-10:30; 1-3; F 9-10:30, 1-3, available most
non-Thursday afternoons as well

Required Text and Materials:

Classroom: Langseth307 (lab)

- 1) Safety Goggles
- 2) Lab Manual (print from website, see <http://www.mnstate.edu/jasperse/Chem355/Chem355.html>)

Lab Schedule: Langseth307	Thursday 9:00-11:50	Thursday 1:30-4:20
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Grading Policy: Attendance:

1. Laboratory attendance is important! In the event of an absence, you will receive zero points for that experiment. Attending a different session for a given week may be possible upon arrangement.
2. **Individual Lab Scores:** Most experiment will require completion of a lab report, perhaps answers to some questions, and often identification of unknowns. Some of the grade will be based on quality of results, for example successful identification of an unknown, or high yield, or high product purity. Unless notified otherwise lab reports should be completed by the following lab period.
3. **Write Your Own Lab Report.** While some experiments may be done with a partner, you should keep your own observations and write your report individually, unless told otherwise.
4. Instructor's **evaluation of your laboratory technique and understanding:** This will make up 20% of the total grade.

Tentatively letter grades will be assigned as follows:

A/A- (≥90%)	B-/B/B+ (≥80%)	C-/C/C+ (≥70%)	D-/D/D+ (≥60%)
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The instructor reserves the right to lower the requirement for a letter grade, but will not raise it.

Keys-Cards and Door Access: The doors will be locked all the time. You will always need your key-card (your MSUM ID card) in order to get in. The card will work **M-F, 7:30am-9:00pm, in rooms 305 and 307 (main lab and NMR room).**

Safety Notes: Noncompliance may result in dismissal from lab and a zero for the week!

1. Wear safety goggles in the organic laboratory.
2. Dispose of chemical wastes in appropriate containers.
3. The impact of the chemicals used in some of these experiments on unborn babies is not fully known. If you are pregnant or become so, I advise you to drop organic chemistry laboratory.

Course Description

CHEM 355 Organic Chemistry Laboratory I (1 credit)

Techniques for the purification, synthesis, and characterization of organic compounds and the study of organic reactions. **Prerequisite:** Chem 210L

Student Learning Outcomes/Course Objectives

Students should master the laboratory techniques required for the purification, characterization, identification, and synthesis of various organic compounds. The ability to identify unknowns, including via use of spectroscopy, is an important outcome goal.

Academic Honesty

For a full description of the MSUM Academic Honesty Policy, please see the Student Handbook. (<http://www.mnstate.edu/sthandbook/POLICY/index.htm>)

ACCESSIBILITY: Minnesota State University Moorhead is committed to providing equitable access to learning opportunities for all students and strives to make courses inclusive and accessible in accordance with sections 504 and 508 of the 1973 Rehabilitation Act and the Americans with Disabilities Act. The University will make reasonable accommodations for students with documented disabilities. Accessibility Resources (AR) is the campus office that collaborates with students in need of special accommodations and assists in arranging reasonable accommodations. If you have, or think you may have, a disability (e.g. mental health, attentional, learning, chronic health, sensory or physical):

- Please contact AR at (218) 477-2167 or accessibility@mnstate.edu to schedule an appointment.
- If you are already registered with AR and have a current Accommodation Letter, please schedule an appointment to discuss implementation of your accommodations.
- Additional information is available on the AR website: <http://www.mnstate.edu/accessibility>

Melting Range

Background Information The melting range of a pure solid organic is the temperature range at which the solid is in equilibrium with its liquid. As heat is added to a solid, the solid eventually changes to a liquid. This occurs as molecules acquire enough energy to overcome the intermolecular forces previously binding them together in an orderly crystalline lattice. Melting does not occur instantaneously, because molecules must absorb the energy and then physically break the binding forces. Typically the outside of a crystal will melt faster than the inside, because it takes time for heat to penetrate. (Imagine an ice cube melting from the outside in, and not doing so instantly...)

The melting range of a compound is one of the characteristic properties of a pure solid. The melting range is defined as the span of temperature from the point at which the crystals first begin to liquefy to the point at which the entire sample is liquid. Most pure organics melt over a narrow temperature range of 1-2°C, if heated slowly enough. Impure samples will normally have melting ranges that are both larger (>1°C) and begin lower.

Taking the melting range of a sample is useful for two reasons:

1. Identification of an unknown sample (compare it's observed melting range with that of known compounds)
2. Assessment of sample purity for a known substance. By comparing observed range for an actual sample to the known range for a pure sample, you can tell whether your actual sample is pure or contaminated (the range is depressed and broadened)

The presence of impurity has two effects on a substance's melting range:

1. Melting range depression (lower end of the range drops)
2. Melting range broadening (the range simply increases. Often the low end drops a lot, the high end less so or sometimes not much at all.) A melting range of 5° or more indicates that a compound is impure.

Why? The reason for this depression/broadening is that contaminants disrupt the consistency and organization of the crystal lattice at the molecular level. Contaminants don't "fit" correctly into what would be the normal pure lattice. **How does this manifest itself?**

1. The disruption weakens the lattice, so that the lattice can be broken down more easily; the weakened structure melts more easily at reduced temperature (depression).
2. Disruption of the lattice makes it non-uniform. At the molecular level, the molecules closest to the impurities melt fastest. Further away from the impurities, the crystal lattice is relatively undisturbed and therefore melts at or nearer the normal temperature.

Miscellaneous notes on melting range depression/broadening:

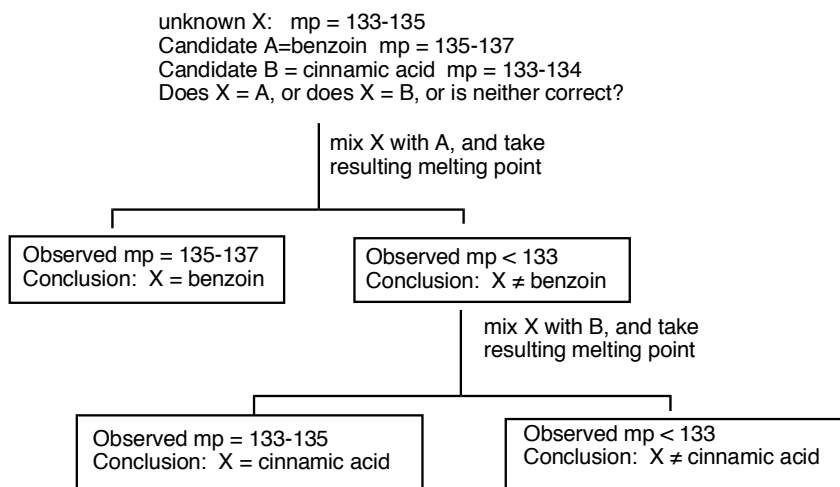
1. Only "soluble" impurities, which are incorporated into the crystal structure at the molecular level, cause depression and broadening. An insoluble piece of metal or wood ionic salt crystal has negligible effect, because only a few organic molecules will be in contact and will be affected.
2. At the chemical level, it is impossible to "raise" the melting point of an already pure substance. It's melting point can be depressed by contamination, but not raised. Practical: If the melting point for an unknown sample is observed to be in between that of two candidates whose pure mp's are known, the unknown can't actually be equal to the lower-melting candidate. (Short of the rapid-heating effect, see later.) Most likely the unknown sample is an impure version of the higher melting candidate. For example: suppose an unknown sample X melts at 148-152°, and is thought to be either candidate A (known

range is 141-142°) or B (known range is 161-162°). Sample X cannot be candidate A, but it can be an impure and thus depressed version of candidate B.

- Often contaminated solids are purified by recrystallization. If the resulting melting range is unchanged, the original sample probably was pure to begin with. But if the resulting melting point gets higher, the original sample was obviously impure.
- When crystals are isolated by filtration from a solvent, it is important to allow complete drying/evaporation of the solvent in order to get a good melting range. Residual solvent functions as a contaminant and will depress/broaden the melting range for a crystal.
- When two chemicals are mixed, the resulting melting point is **not** the average of the two mp's. It is always depressed from the melting point of the major component in the mixture. This is true even if the impurity is higher melting (when pure) than the major component. For example, if a chemical that normally melts at 130° is contaminated by a small amount of material that when pure melts at 200°, the resulting mixture will not melt between 130° and 200°. Rather, the melting point of the major component will be depressed, and the observed melting range will begin lower than 130°.
- Even when two chemicals with exactly the same melting point when pure are mixed, the resulting melting point is depressed.

Mixed Melting Points

That mixtures have depressed melting points, even when both components have comparable melting points when each is pure, provides a useful laboratory technique. Consider the following situation and flow chart. If an unknown candidate X melts at a temperature close to that of two potential candidates A and B, you can identify it by taking X+A mixed melting point, and X+B mixed melting point. If X is equal to either candidate, one of these mixed melting points will not be depressed. If the mixture with X+A is not depressed, X = A. if the mixture with X+B is not depressed, X = B. If both mixtures are depressed, then X ≠ A or B.



The Rate of Heating, and Some Practical Tips

It takes time for a crystal to absorb heat and to melt, from the outside in. Just as when you place an ice-cube into a liquid that is $>0^\circ$, it doesn't melt instantly. To get maximal accuracy in taking a melting range, heating should proceed at only $1^\circ/\text{minute}$! This is the standard heating rate when publishing melting ranges in scientific journals. This is also inconveniently slow, especially if you don't know where your sample is likely to melt (as when examining an unknown).

- Q: What happens if I heat too fast? A: Your melting range will be too broad, but this time you will see inflation on the high end! If a sample should melt at $130\text{-}131^\circ$, but you are heating fast, it will still probably begin to melt at about 130° , but the full sample won't have time to absorb heat and finish melting by 131° . Instead, the heating device may have warmed well above 131° before the interior liquefies, so the observed range may appear to be $130\text{-}136^\circ$. Both the magnitude of the range and the high end of the range may be misleading.
- For doing routine samples, it is appropriate to be warming at 5 degrees per minute around the temperature at which melting occurs. This broadens the range somewhat, but not badly. And it keeps the melting point experiment from taking forever.
- Practical tip 1: If the approximate temperature at which your sample should melt is known, the sample can be quickly heated to within $10\text{-}15^\circ$ of its melting point. Then the heating rate can be slowed to $2\text{-}4^\circ$ per minute until the sample melts. For example, if you know your material should melt around 180° , but you are just trying to check the purity, you can heat rapidly until you are up to 165° or so, and only when you are getting close turn the heating rate down.
- Practical tip 2: If you have no clue where your sample will melt, it's common to heat rapidly to get a ballpark estimate of where melting will occur. 60° ? 140° ? 240° ? If it turns out to be 240° and you heated only cautiously from the beginning, it will take a loooooong time to get to the measurement. By heating rapidly, you can get an "orientation melting point" quickly, and then repeat with more care for a more precise reading. Often you don't even need to prepare a fresh sample, because after cooling the melted sample often recrystallizes.
- Practical tip 3: Course versus finely ground. Heat transfer problems are minimized if the sample is ground finely. If the particles are too coarse, they do not pack as well, causing air pockets that slow heat transfer. Because the thermometer keeps heating while the sample is melting rather slowly, the high end of your range will be inflated.
- Practical tip 4: Loading too much sample makes it harder for the interior to get heated and melted. Because the thermometer keeps heating while the sample is melting rather slowly, the high end of your range will be inflated.
- Practical tip 5: Sometimes it's hard to recognize the initiation of a melt. When some liquid first appears, against a backdrop of solid, it's not always easy to recognize, especially for an inexperienced user. This may someti

"Sagging"

Sometimes slight changes, such as shrinking and sagging, occur in the crystalline structure of the sample before melting occurs. The temperature at the bottom end of the melting range corresponds to the first appearance of liquid within the sample mixture; if the crystals are changing their appearance, but you don't yet see any actual liquid, you should not record this as the lower end of the melting range yet.

The Experiment: (Work alone or with One Partner)**Overview, if working with a partner: You will run three samples.**

1. One will be either pure urea (mp = 132-133) or pure cinnamic acid (mp = 133-134). Whichever you run should be the opposite of what your partner runs. Record your range, and share your observed results with your partner
2. The second will be mixture of the two, either 4:1 cinnamic acid:urea or 1:4 cinnamic acid:urea. Whichever mixture you run should be the opposite of the mixture that your partner runs. Record your range, and share your observed results with your partner.
3. The third will be an unknown. Record your range and identify which of the unknown candidates is really yours. (You and partner must run different unknowns. You do not need to share this result with your partner.)

Unknown Candidates

Acetanilide 112-115
Benzoic Acid 118-123
Cinnamic acid 131-134
Salicylic acid 155-160
Sulfanilamide 163-166
Succinic acid 184-185

Learning goals:

- Learn how to run a melting point device and measure melting range
- By comparing results for the two mixtures, see how not all mixtures depress/broaden to the same extent.
- Identify your unknown from the list shown below.

If working alone: You will run five samples.

1. Run both pure urea (mp = 132-133) and pure cinnamic acid (mp = 133-134).
2. Run both the 4:1 cinnamic acid:urea and the 1:4 cinnamic acid:urea mixtures.
3. Run one unknown. (You and partner must run different unknowns.)

Lab Report Requirements

No introduction or procedure write-up is required.

Fill in the data section on the report hand in (next page in manual), and answer the questions.

Melting Point Lab Report. Chem 355

Name:

Partner's Name (if you shared data with a partner:

Experimental Datamelting range

- My Known: (U or C or both)
- My mixture: (4:1 C:U or 4:1 U:C or both)
- Partner's mixture (4:1 C:U or 4:1 U:C)
- My Unknown: (1, 2, 3, or 4...)
- Which compound is your unknown? (from the list on previous page)
- Any doubts, discussion, or logic on your identification of unknown. (Not necessary, but if you have a tricky one or one that for whatever reason you get wrong, if your discussion shows some reasonable analysis or logic, it may help you get partial credit! ☺)

Discussion questions:

1. Compare the ranges observed with the two mixtures.
 - a. Did they depress and broaden about the same, or different?
 - b. What does that say about the degree of depression and broadening that occurs when mixtures are used? Do all impurities depress to the same degree, or by some predictable formula? Or do you think it's more of a case-by-case deal?
2. Strictly speaking, why is it incorrect to speak of a melting "point"?
3. How will your melting range be perturbed if you haven't completely dried your sample? (For example, after you've filtered crystals away from a solvent, and/or have washed the crystals with solvent...) (Be specific, for example, "low end depressed" or "high end inflated")

4. What's the advantage of a finely powdered sample over a coarser sample? How will your melting range be perturbed with coarse sample? (Be specific, for example, "low end depressed" or "high end inflated")

5. What's the advantage of putting in a relatively small amount of sample as opposed to putting in lots and lots of sample? How will your melting range be perturbed with huge sample? (Be specific, for example, "low end depressed" or "high end inflated")

6. Why is it desirable to heat the sample relatively slowly? How will your melting range be perturbed by heating too fast? (Be specific: "low end depressed" or "high end inflated")

7. You have a sample that you are sure is Jaspersium, which has a list melting range of 145-146.
 - Suppose you run your sample and observe a melting range of 145-151. Is your sample impure, or did you heat too fast?

 - Suppose you run your sample and observe a melting range of 139-145. Is your sample impure, or did you heat too fast?

8. You have isolated an unknown compound that shows an observed melting range of 90-94. Which is it more likely to be, candidate X (list mp 97-98) or candidate Y (list mp 80-83). Why might your sample not have the same melting range as either of the known compounds, given that it must be one of them?

9. Three test tubes labeled A, B, and C contain substances with approximately the same melting points. How could you prove the test tubes contained three different chemical compounds?

Background:

Impurities often contaminate organic compounds, whether they have been synthesized in the laboratory or isolated from natural sources. Recrystallization is the most important method for removing impurities from solid organic compounds. It is suitable for both small scale (<0.5 g) and large scale (>100g) work. **The basic recrystallization plan is to dissolve an impure solid in a hot solvent, then cool the solution so that the desired molecules recrystallize while the impurities remain in solution.** Subsequent filtration separates the solid crystal from the liquid solvent.

The dependence of solubility on temperature is key. Solubility of sample in solvent will always be higher at high temperature, but will decrease at low temperature. A solvent that can fully dissolve a solid while hot may thus become saturated as the temperature is reduced, resulting in crystal formation. Soluble impurities stay in solution because they are not concentrated enough to saturate the solution. However, even when the solvent is cold, at least some (if not all) of the desired compound will remain dissolved and will be lost during filtration.

The choice of solvent for a recrystallization is crucial. For a successful recrystallization **the dissolving power of the solvent must be “mediocre”, neither too good nor too bad.** Why?

- If the solvent is too good, then even when the solvent is cold the sample will remain dissolved and you won't be able to harvest any crystals.
- If the solvent is too bad, then even when the solvent is hot it still won't be able to dissolve the sample, and the impurities won't be freed from the original sample.
- An effective solvent must be mediocre, good enough to dissolve the sample at high temperature (so that the impurities are freed), but weak enough so that at least some of your sample crystallizes out after cooling (so that you get at least some yield harvested.)

Necessary sources of mass loss: The yield for a recrystallization can never be 100%. Why not? Because while the chilled solvent is saturated and should release some crystals, at least some of your desired material will remain dissolved in the cold solvent and will be lost when the crystals and solvent are separated. **The primary necessary source of mass loss is to the solvent.** Obviously additional mass will be lost to physical handling, and some of the lost mass is simply the impurities that you wanted to lose. (But normally the mass of impurities is only a few percent or less.)

Unnecessary sources of mass loss: While losing mass to the solvent is inevitable, unnecessary losses to solvent are common and should be avoided. Some unnecessary losses to solvent result from the following:

- Using too much solvent. The more solvent that you use, the more sample will remain in the solvent even after cooling.
- Inadequate warming. If you don't warm your solvent to boiling temperature, you will not benefit from its maximum dissolving ability, and will need to use extra solvent to make up for it. The unnecessary extra solvent will retain additional sample even after cooling.
- Inadequate cooling. If you don't cool below room temperature, for example, more sample will remain dissolved than if you cool to 0°C.
- Excessive washing by solvent. Not only surface impurities but also some crystal will be lost when you wash your crystals. (There is usually some sort of happy medium required, because some rinsing is usually required).
- Choosing a poor solvent in the first place. If your solvent is too good, even after cooling it will still retain much or all of the sample.

Ideal: Use a Minimum of Hot Solvent so that you are at the Saturated/Dissolved Borderline at the Boiling Point. In order to maximize your purity, you'd like to use enough solvent to dissolve the crystals and keep the impurities in solution even after cooling. In order to maximize your yield, you'd like to minimize the amount of solvent used so that as little as possible sample remains in solution after cooling. The best way to accomplish both goals is to use enough solvent so that it can dissolve everything while hot, but to use no more than the minimum required so as to maximize yield after cooling. The minimum required is when your solution is just barely at the saturation point while boiling hot. Use just enough solvent so that the material is just barely soluble, or is just a little cloudy to show that it's just barely saturated.

Four Ways To Achieve Just-Barely-Saturated/Just-Barely-Dissolved Borderline. In all cases, heat to just barely gently boiling.

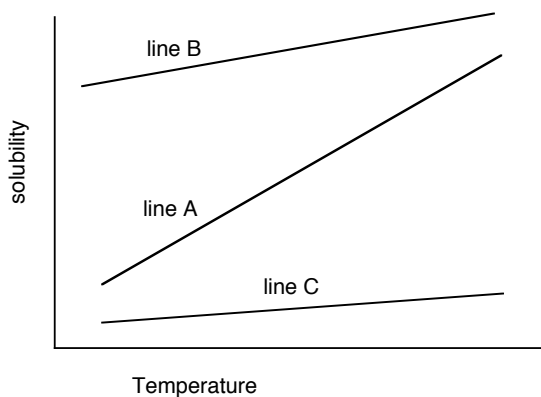
- Add more hot solvent (if solubility is too low)
- Add some superior solvent (if solubility is too low)
- Boil solvent away (if solubility is too high)
- Add ‘bad solvent’ (if solubility is too high) that will reduce the solubility

Mixed Solvents Often it’s difficult to find a single solvent that is appropriately “mediocre”. Frequently it’s easier to work with a solvent mixture. If the dissolving power of your initial solvent is too strong, you can add some bad solvent to reduce the dissolving power. As a solvent with poor dissolving properties is added, the overall dissolving power of the solvent gets worse and worse. Eventually, the saturation point should be reached. This is often the most convenient way to do recrystallizations.

Alternatively, if the dissolving power of your initial solvent ends up being not high enough, you can add a superior solvent to get the solid fully dissolved.

- A very common “mixed solvent” combination involves an alcohol as the “good solvent” and water as the “bad solvent”. This is effective because many organics are hydrophobic. By adding water, you can rapidly reduce their solubility.
- When mixed solvents are used, it is essential that both are co-soluble with each other. Trying to add water as the “bad solvent” to a hydrocarbon solvent like hexane or toluene fails, because the water simply forms a separate layer and doesn’t actually do anything.

Choosing a Solvent As discussed previously, you don’t want too good a solvent (line B) or too bad a solvent (line C). And you’d like a solvent with as sharp as possible a dependence of solubility on temperature (line A), so that it’s pretty soluble hot but not very soluble cold. Trial and error experimentation is often required for finding a suitable solvent. Like-dissolves-like considerations can sometimes provide helpful guidance as to which solvents might be too good, or which might be hopelessly bad. For somewhat polar molecules containing oxygen or nitrogen atoms, alcohol/water or alcohol/pentanone mixed solvents are frequently a fine choice.



The boiling point of the solvent is also worth considering. A relatively high boiling point is good because it allows a large temperature differential between boiling hot solvent and the chilled solvent. Diethyl ether, for example, boils at only 35°C, so the solubility of a sample isn’t likely to drop as much upon cooling from 35°C to 0°C as if water is used, where the hot/cold difference could be 100°C. On the other hand, you don’t want to use a solvent whose boiling point is so high that the sample will simply melt when the solvent is heated to boiling. It’s also easier to dry the crystals if the solvent isn’t too high boiling,

so that it evaporates easily and won’t depress the melting range.

Summary of the four criteria for selecting a recrystallizing solvent:

1. compound being purified must be insoluble in the solvent at room temperature
2. compound must be soluble in the boiling solvent
3. solvent’s boiling point must be lower than the compound’s melting point
4. an abundant quantity of crystals must be recoverable from the cool solvent

Crystallization Summary

1. **Choosing the Solvent.** “Like dissolves like.” Some common solvents are water, methanol, ethanol, ligroin, and toluene. When you use a solvent pair, dissolve the solute in the better solvent and add the poorer solvent to the hot solution until saturation occurs. Some common solvent pairs are ethanol-water, diethyl ether-ligroin, toluene-ligroin, and t-butyl methyl ether-hexane.
2. **Dissolving the solute.** To the crushed or ground solute in an Erlenmeyer flask, add solvent, add a boiling stick, and heat the mixture to boiling. Add more solvent as necessary to obtain a hot, saturated solution. (Do not use a beaker, because the large mouth allows solvent evaporation to be too fast and uncontrolled.)
3. **Filtering suspended solids (if necessary).** If it is necessary to remove suspended solids, dilute the hot solution slightly to prevent crystallization from occurring during filtration. Filter the hot solution. Add solvent if crystallization begins in the funnel. Concentrate the filtrate to obtain a saturated solution.
4. **Crystallizing the solute.** Let the hot saturated solution cool spontaneously to room temperature. Do not disturb the solution. Slow cooling gives the best crystals. Cooling while clamped in the air, or while standing on a watch glass that is resting on your round-bottomed flask holder is a good way to do it. Put a watch glass or inverted beaker over the top of your flask so that solvent doesn't evaporate away while still hot. Then cool it in ice. If crystallization does not occur, scratch the insides of the container, add seed crystals, or for many solvents add ice chip(s).
5. **Collecting and washing the crystals.** Collect the crystals using a Hirsch funnel (<0.2 grams) or a Buchner funnel (>0.2 g), a filter flask, and aspirator suction. Place a filter paper on the surface, wet the filter paper with solvent, and apply suction to make sure the paper seals. Break the vacuum, add crystals and liquid, and apply vacuum. After solvent disappears, break vacuum, add cold wash solvent, apply vacuum, and repeat until crystals are clean and filtrate comes through clear. The wash solvent is normally either a small amount of an ice-cold portion of the main recrystallization solvent, or else a somewhat “worse” solvent (although it shouldn't normally be a totally “bad” solvent). For example, if 80% ethanol/water is used for a recrystallization, it would be common to wash with 60% ethanol/water to avoid dissolving much crystal.
6. **Drying the product.** Aspirate the sample for as long as is convenient. Press the product on the filter to remove solvent. Then remove it from the filter, squeeze it between sheets of filter paper to remove more solvent, and spread it on a watch glass to dry
7. **Analyzing the product.** Take a melting point of the final product. But since incomplete drying will contaminate the crystal and depress the melting point, it is normally best to wait for 15 hours or more before doing so.

PART 1: Macroscale Recrystallization of Phthalic Acid from Water

Weight out about 1 g of phthalic acid. (Record exact mass). Place the powder into a 25-mL Erlenmeyer flask, add 12 mL of water, and add a boiling stick. (The stick facilitates even boiling and prevents “bumping” explosions). Heat on a hot plate until the water begins to boil gently. (Avoid a hard boil. If much of your solvent boils away, the sample will either not dissolve in the first place or will not be able to remain dissolved). Once the solution has reached the boiling point and the sample has dissolved, remove it from the hot plate and move it onto a watch glass suspended on a round-bottomed flask holder (cork ring or rubber ring). (A convenient way to transfer a hot flask is to get a wet paper towel to hold it with, and transfer it by hand.) Remove the boiling stick and cover the top of the flask with an inverted 50-mL beaker. (This is to prevent further hot solvent from evaporating away.) The reason you don’t want to put your flask on the bench top is that heat transfer will be too fast and it will cool too quickly, resulting in inferior and less pure crystals. Allow the flask to cool until it is no longer hot to the touch. (10 minutes.) Then place it in an ice bath so that it gets as cold as possible and the smallest necessary amount of desired product stays in solution. (5 minutes).

Collect the crystals using a Buchner funnel. (See picture below, and instructions on page 17 of

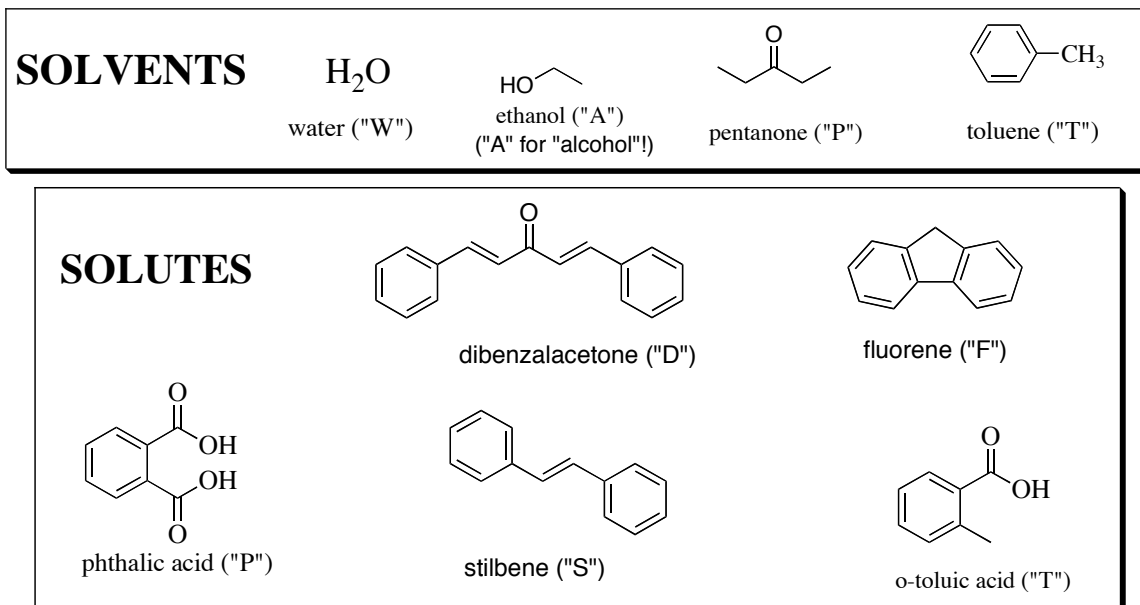


this handout). Make sure you have a filter flask (with an arm on the side for attaching the tubing), that you have a rubber adapter between the flask and the Buchner funnel, and that you put filter paper onto the funnel. With the Buchner funnel on top plus the tube, the flask will be top-heavy and will very easily tip over. To avoid this, you should clamp it to keep it secure (see picture). Attach the tubing to the vacuum, and turn the vacuum on full blast to get maximum suction, and to hold the filter paper tight. Pour your crystals and solvent onto the paper. Use a micro-spatula with a bent-hook and perhaps additional cold water to try to get all of your crystals into the Buchner funnel. Rinse the crystals with a ~5mL of ice-cold water. (Pour this into your original flask first to help rinse out some residual crystals there, before pouring

it through your Buchner funnel.) Break the vacuum before you add the rinse solvent; this allows all of the crystals in the Buchner funnel to be exposed to the rinse solvent. Let the solution stand for at least 20 seconds, then reapply the vacuum and pull the solvent through again. Maintain vacuum for at least ten minutes, and preferably longer if you are doing something else. It should run for at least ten minutes if you want to get final mass and melting point today; if it hasn’t been dried accurately residual solvent will inflate the mass reading but depress the melting range.

After allowing time to dry, weigh the crystals, record your final mass and calculate your % yield, and take a melting range for the final product. The melting point can be taken today, or sometime during the week. (The range should fall somewhere in the 190-220 area. So set the melting apparatus high enough, maybe at 6 or so, so that it doesn’t take forever to warm up. If a previous user has been on the melting machine, so long as the temperature has cooled below 160° it should be cool enough for the next student to get on and get started.)

PART II: Recrystallization Experiment 3.1.



Overview: For each of 5 solutes, you will screen its solubility in each of the 4 different solvents shown above: water, ethanol, 3-pentanone, and toluene. (5 x 4 = 20 tests/test tubes!) The big idea is that for each of the solutes, you should be able to decide which of the solvents would be suitable for carrying out a recrystallization. Repeat tests as needed.

Procedure: Add about 70 mL of hot tap water to a 150-mL beaker, and heat it on a hot plate (set around 6, maybe, to start?) to a gentle boil (just barely boiling). It will take a little while for the water to heat up, so start this before you'll actually need the hot water bath.

For each solute you will test the four solvents. It works best to try all four solvents for a given solute before beginning with the next solute.

For each solute: weight out about 0.16 g of the solute, and divide it into four roughly equal piles. Place these into four test tubes (about 40mg per tube). The easiest way to do this is to weigh it first, divide it on weighing paper, push the portions onto separate pieces of weighing paper, and then pour those portions into your test tubes. (Note: If the solid is "chunky", try to crush it before putting it into the test tubes to facilitate solubility.)

Then add 1 mL of each of the four solvents. (Be sure to label your test tubes adequately!) Stir with a wooden stick for 20-60 seconds. Record the results ("s" = soluble, "i" = insoluble, "ss" = slightly soluble.) For those that don't dissolve at room temperature, place the test tube into the hot water bath (2 minutes) and record the results again. If it still doesn't dissolve, add another 1mL of solvent to the hot solution, continue heating for another two minutes, and repeat your observation. (Sometimes more solvent will enable something to dissolve that wouldn't dissolve in a lesser amount of solvent.) (Note: There is no point in heating a test tube with something that dissolved already at low temp; things never "undissolve" at higher temperature!) Record all your observations.

- **Summary:** This is the standard process for finding which solvents are suitable for recrystallizing a particular solid.
- **What constitutes a suitable solvent?** If your results are "s" (soluble) even at room temperature, the solvent is unsuitable because it's too good. You'll never be able to harvest any crystals. If your results are "i" (insoluble) even at high temperature, the solvent is unsuitable because it's too bad. You'll never be able to free the impurities. The ideal solvent should be "i" (or perhaps "ss") at room temperature but then "s" at high temperature, so that you can both free the impurities (at high temperature) but also recover crystals (at low temperature).

RECRYSTALLIZATION REPORT

Name:

Report requirements (Part 1):

1. Report your initial mass, your mass recovery, and your % yield.
2. Report your dry melting range.
3. Explain very briefly why dissolving and then reforming crystals can improve their purity.
4. Explain very briefly why recrystallization can never result in 100% mass recovery (even if you used perfectly pure material).
5. Explain very briefly why mass recovery is greater if you cool to 0°C rather than merely room temperature.
6. Explain very briefly why mass recovery is reduced if you use an excess amount of boiling solvent.
7. Explain very briefly why washing product crystals with excessive amounts of solvent, especially warm solvent, can result in reduced mass recovery.
8. Given:
 - The solubility of **X** at 100°C in water is 18.0 g/100 mL water.
 - The solubility of **X** at 0°C in water is 3.6 g/100 mL water.How many mL of boiling water would be required to dissolve 25g of **X**? If that solution was then cooled down to 0°C, how many grams of **X** could then crystallize out? What would be the maximum yield recovery for **X**?
9. An ideal recrystallization solvent is able to fully dissolve a solute only when hot, but not when cold.
 - Why is a solvent that can dissolve the solute even when it is cold useless for recrystallizations?
 - Why is a solvent that can't dissolve the solute even when hot useless for recrystallizations?

Report requirements (Part 2):

Fill out the table below. Convenient standard abbreviations are “i” = insoluble and “s” = soluble. (Sometimes “ss” = slightly soluble may also be useful, if it’s clear something is dissolving somewhat, but not completely.) (Don’t worry about distinguishing “insoluble” from “slightly soluble”.)

Beside the names for the five solutes, write down which (if any) of the solvents would be appropriate for recrystallization. (It’s possible that none of the solvents screened will look good for a particular substrate, and it’s also possible that several will.)

Recrystallization Solute/Solvent Sheet Chem 355

Solute	WATER ("W")			PROPANOL ("A")			3-PENTANONE ("P")			TOLUENE ("T")		
	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent
"D" Dibenzalacetone												
"F" Fluorene												
"P" (Pthallic Acid)												
"S" Silbene												
"T" o-Toluic Acid												

Standard abbreviations: "I" = insoluble, "ss" = slightly soluble, "s" = soluble

Which solvents (if any) would be appropriate for the recrystallization of the following substrates? There may be more than one. Make sure that your answers are consistent with the observations in the table above.

"D"
Dibenzalacetone

"F"
Fluorene

"P"
(Pthallic Acid)

"S"
Silbene

"T"
o-Toluic Acid

MOLECULAR STRUCTURE

For each of the following molecules, make the models and then draw the models, using the hash/wedge/straight-line convention. Use tetravalent atoms. Make double bonds by using two of the soft, flexible white bonds to make “banana double bonds”.

- **For molecules involving lone-pairs, draw them with the lone pairs shown.** Use a hash, wedge, or straight-line to show where in 3-D space the lone pair is, and then put a “double-dot” on the end to illustrate that it’s a lone-pair rather than an atom.
- **Draw in all hydrogens.** Use a hash, wedge, or straight-line to show where in 3-D space the hydrogen is, and draw an H at the end. (In regular “skeleton structures” H’s may be omitted, but for this exercise you need to draw them in to practice and to help understand where they actually sit.)
- **You do not need to write “C” on carbons.** As in regular “skeleton structures”, the understanding is that any vertex (or end of stick) is a C unless indicated otherwise. But anything that isn’t a carbon (whether H, N, O, Br, or lone-pair) you need to specify.

Guidelines for Drawing Models:

A. 3-D Perspective

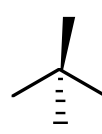
1. Keep as many atoms as possible in a single plane (plane of the paper) by zig-zagging.
Connections within the paper are drawn with straight lines.
2. Use wedges to indicate atoms that are in front of the plane.
3. Use hashes to indicate atoms behind the plane.

B. For any tetrahedral atom, only 2 attachments can be in the plane, 1 must be in front, and 1 behind.

- if the two in the plane are “down”, the hash/wedge should be up
- if the two in plane are “up”, the hash/wedge should be down.
- the hash/wedge should never point in same direction as the in-plane lines, or else the atom doesn’t look tetrahedral
- for polyatomic molecules, it is strongly preferable to NOT have either of the in-plane atoms pointing straight up. Straight-up in-plane atoms do not lend themselves to extended 3-D structures.



Good! Look tetrahedral



Bad! These don't look tetrahedral!

1. ALKANE. butane, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$

- take the chain and wiggle around all the single bonds.
- The most stable actual shape is the one with the carbons zig-zagged and co-planar.
- Notice the symmetry possible.

2. ALKANE. Pentane, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$

3. HALOALKANE. 2-bromobutane, $\text{CH}_3\text{CHBrCH}_2\text{CH}_3$

-notice that if the 4 carbons are co-planar zig-zagged, the attached Br can't be in the same plane.

-Compare with a partner two structure in which the Br is in front(wedged) in one versus behind (hashed) in the other. Are they the same molecule, or isomers? (Q2 on "same-or-different" page)

-ignore the lone pairs on the Br (in this case)

4. ALKENE. Draw both: a) trans-2-butene, $\text{CH}_3\text{CH}=\text{CHCH}_3$
and b) cis-2-butene

(trans means the two CH_3 groups are on the opposite sides of the double bond; cis means they are on same side)

-notice that not only the 2 double-bonded

C's but also the four atoms directly

attached are all co-planar.

5. ALKYNE. 2-butyne, CH_3CCCH_3

-draw Lewis structure first

6. WATER. H_2O

-DRAW at least 2 different orientations, and specify the lone-pairs.

-Draw pictures in which both the oxygen and both the hydrogens are in the plane of the paper.

-For building the model, visualize a lone-pair by using a stick without an atom at the end.

-draw in the lone pairs for this and all following pictures. (For this assignment; not normally required for class!)

7. ALCOHOL. Ethanol, $\text{CH}_3\text{CH}_2\text{OH}$

8. ETHER. Diethyl ether, $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3$

9. FORMALDEHYDE. CH_2O .

-for 9-16, make sure you draw the Lewis structure before you build models and draw the 3-D picture. If you don't know the connectivity, you have no chance!

10. ALDEHYDE. $\text{CH}_3\text{CH}_2\text{CHO}$.

11. KETONE. $\text{CH}_3\text{CH}_2\text{C}(\text{O})\text{CH}_2\text{CH}_3$.

12. ACID. $\text{CH}_3\text{CH}_2\text{CO}_2\text{H}$.

13. ESTER. $\text{CH}_3\text{CH}_2\text{CO}_2\text{CH}_3$.

14. AMMONIA. NH_3

15. AMINE. $(\text{CH}_3\text{CH}_2)_2\text{NH}$

16. AMIDE CH_3CONH_2 .

17. CYCLIC COMPOUNDS

A. Cyclopropane (CH₂)₃

-notice how hard this is, how the bonds “bend”, etc.. Real cyclopropane experiences real “ring strain” based on the impossibility of achieving 109° bond angles.

18. Things that can't be completely drawn “3-D”. 2-methylbutane, CH₃CH₂CH(CH₃)₂

-notice that not all 5 of the carbons can be coplanar. Structures like this can't be illustrated completely or easily. What you should do is simply draw “CH₃” as being out-of-plane, but don't try to illustrate the “3-D-ness” of that carbon. Ask instructor for confirmation.

19. CYCLIC COMPOUNDS

B. Cyclohexane (CH₂)₆

-Don't bother to draw! Too tough! But do build the model.

1) notice that the 6 carbons do not easily remain coplanar. By puckering, ideal 109° bond angles can be achieved.

2) In the best model, 3 H's point straight down, 3 H's point straight up, and 6 H's essentially extend almost horizontally. The “horizontal” H's are called “equatorial” and the “vertical” H's are called “axial”.

3) Try to put colored balls into the “axial” positions. Then try to manipulate the model so that the “axial” atoms become “equatorial”, and the “equatorial” atoms become “axial”.

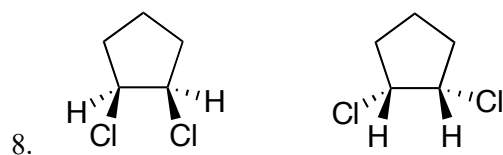
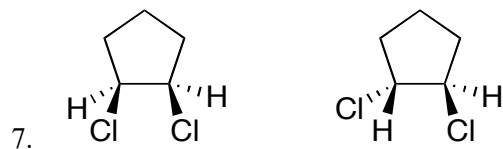
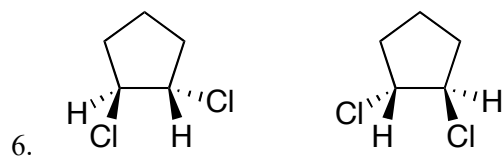
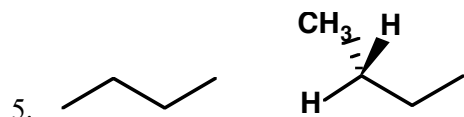
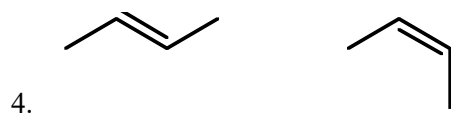
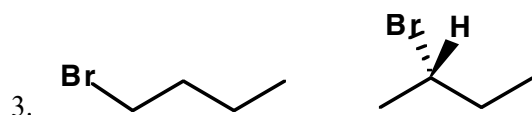
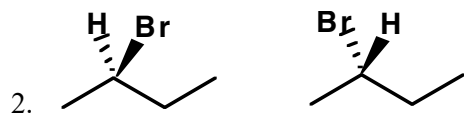
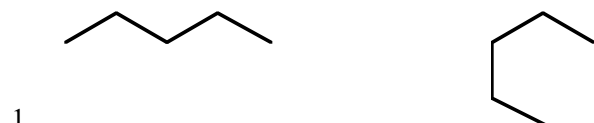
-ask instructor to come over and give you cyclohexane spiel

SAME OR DIFFERENT?

Rules:

1. Structures which can be interchanged or made equivalent by rotations around single bonds are considered to be the same.
2. “Isomers” are things with the same formula that can't be made superimposable by simple rotations around single bonds.
(not required, but for class will eventually need to be able to distinguish “structural isomers” from “stereoisomers”)

Classify the following pairs as “same” or “isomers”



Chem 355 Jasperse

RECRYSTALLIZATION-Week 2

1. Mixed Solvent Recrystallization of Acetanilide
2. Mixed Solvent Recrystallization of Dibenzylacetone
3. Recrystallization of an Unknown

Background

Review: Recrystallization is an important technique for purifying organic solids. The contaminated solid is dissolved in a minimum of hot solvent, then cooled. The amount of solvent that is used should be just enough so that the solvent is just barely saturated or almost saturated when it is boiling hot. Upon cooling the solubility decreases, and crystal formation can occur. The new crystals are purer than the original because impurities are left in the solvent. Slow, gradual cooling is best for formation of pure crystals. Filtration then provides purified material. Some mass loss always occurs, because the solvent holds not only the impurities but also some of the desired material as well. Additional unnecessary mass loss can occur if you use too much solvent, don't heat your solution to boiling in the process of dissolving your sample, if you don't cool adequately, or if you wash your product crystals excessively. An appropriate solvent needs to have mediocre dissolving power: strong enough to dissolve the sample when boiling hot, but not able to dissolve too much of the sample when cold.

General Mixed Solvent Procedure, Concept: Often it's difficult to find a single solvent with appropriate dissolving power. Further, it's often difficult to decide exactly how much of the solvent is ideal. Frequently the use of mixed solvents is a practical and convenient solution.

In the usual mixed solvent recrystallization procedure, dissolve your sample in a sufficient quantity of your "better" solvent by heating it up to the boiling point. A 4 mL/1 g ratio is the default starting guess. Add more solvent if necessary, or boil some off if you judge it's obviously way more than needed. Then add "bad" solvent (usually hot water), until either you reach a visible "saturation" point (the "lucky" situation, where you can see crystals or slight cloudiness beginning to form) or until you have a 1:1 solvent ratio. Let cool so as to grow more crystals and harvest by filtration.

An alternative and often preferred strategy is if you intentionally or unintentionally start with a solvent that does not have enough dissolving power to dissolve the solid, even when hot. You can then add as much hot "better solvent" as needed to barely dissolve the sample (while boiling hot.)

When mixed solvents are used, it is essential that they be co-soluble. Otherwise the bad solvent will simply create a second layer, but the sample can remain soluble in the original layer.

Ethanol/water combinations are commonly used because ethanol has good dissolving ability for many organics, but is also infinitely co-soluble with water. Addition of water can rapidly and dramatically reduce the solubility of many organics and thus induce crystallization. While organic mixtures are also frequently useful, the difference in character between two organics is rarely as dramatic as the difference between water and an organic solvent.

Difficult Crystallizations: Sometimes crystallization is slow or difficult. Crystallization must start on some nucleation center. (Crystals grow when molecules "fit" onto some preexisting surface.) Sometimes this will happen spontaneously, but sometimes it is difficult. The formation of "supersaturated" solutions, in which the solvent holds more sample than it could if equilibrium existed, are routine. Some common techniques for initiating crystallization include:

- Seeding the saturated solution with some of the desired sample that is already in solid form.
- Scratching the insides of your flask with a rough glass rod. (By scratching the surface of your glass, you can get a rough edge which may coincidentally serve as a crystallization surface.)
- Using old, scratched up flasks!
- Leaving a boiling stick, preferably broken off so it has rough shards sticking out at the end.
- Adding an ice chip. (The surface is often rather rough, and can serve as a nucleation site. In addition, because the surface is pure water, the solvent composition near the ice chip is not representative of the bulk solvent distribution. Being water-rich, solubility may be especially poor resulting in crystal initiation. The ice chip serves to provide a local area of extremely "bad solvent".)
- Wait a long time!
- Find a better solvent.

Crystallization Summary

1. **Choosing the Solvent.** “Like dissolves like.” Some common solvents are water, methanol, ethanol, ligroin, and toluene. When you use a solvent pair, dissolve the solute in the better solvent and add the poorer solvent to the hot solution until saturation occurs. Some common solvent pairs are ethanol-water, diethyl ether-ligroin, toluene-ligroin, and t-butyl methyl ether-hexane.
2. **Dissolving the solute.** To the crushed or ground solute in an Erlenmeyer flask, add solvent, add a boiling stick, and heat the mixture to boiling. Add more solvent as necessary to obtain a hot, saturated solution. (Do not use a beaker, because the large mouth allows solvent evaporation to be too fast and uncontrolled.)
3. **Filtering suspended solids (if necessary).** If it is necessary to remove suspended solids, dilute the hot solution slightly to prevent crystallization from occurring during filtration. Filter the hot solution. Add solvent if crystallization begins in the funnel. Rinse thoroughly. Concentrate the filtrate to obtain a saturated solution.
4. **Crystallizing the solute.** Let the hot saturated solution cool spontaneously to room temperature. Do not disturb the solution. Slow cooling gives the best crystals. Cooling while clamped in the air, or while standing on a watch glass that is resting on your round-bottomed flask holder is a good way to do it. Put a watch glass or inverted beaker over the top of your flask so that solvent doesn't evaporate away while still hot. Then cool it in ice. If crystallization does not occur, scratch the insides of the container, add seed crystals, or for many solvents add ice chip(s).
5. **Collecting and washing the crystals.** Collect the crystals using a Hirsch funnel (<0.2 grams) or a Buchner funnel (>0.2 g), a filter flask, and aspirator suction. Place a filter paper on the surface, wet the filter paper with solvent, and apply suction to make sure the paper seals. Break the vacuum, add crystals and liquid, and apply vacuum. After solvent disappears, break vacuum, add cold wash solvent, apply vacuum, and repeat until crystals are clean and filtrate comes through clear. The wash solvent is normally either a small amount of an ice-cold portion of the main recrystallization solvent, or else a somewhat “worse” solvent (although it shouldn't normally be a totally “bad” solvent). For example, if 80% ethanol/water is used for a recrystallization, it would be common to wash with 60% ethanol/water to avoid dissolving much crystal.
6. **Drying the product.** Aspirate the sample for as long as is convenient. Press the product on the filter to remove solvent. Then remove it from the filter, squeeze it between sheets of filter paper to remove more solvent, and spread it on a watch glass to dry
7. **Analyzing the product.** Take a melting point of the final product. But since incomplete drying will contaminate the crystal and depress the melting point, it is sometimes best to wait for 15 hours or more before doing so.

Part I: Mixed Solvent Recrystallization of Acetanilide (partner permitted). (Supersaturation).

Purpose: Do mixed solvent recrystallization involving “super-saturation”, where no visible saturation appears; practice tricks for inducing difficult crystallization.

Detailed Procedure: Add about 50-mL of hot water to each of two 150-mL beaker, and warm these on each of your two hot plates. Warm to ~70-85° but less than boiling. Use a thermometer to monitor, supported by metal ring clamped above bath. Typically set your hot-plate power to 4 to achieve a good temperature. (You may perhaps need to adjust slightly.)

Weigh about 2 g (write down exactly) of acetanilide, and place it in a 25-mL Erlenmeyer flask. Add a boiling stick. Add 4 mL of ethanol and heat this to boiling by placing the flask into the hot water bath. Once it has dissolved, add three pipet squirts of hot water (instructor will demonstrate). You can transfer hot water directly from your hot water bath by pipet. In this example of “super-saturation” (review prelab intro), visible crystals/cloud-point will not appear. After the 3 pipets of water (~50% water), don’t add anymore. (In general, if you’ve added 50% water and still haven’t seen visible saturation, assume you have super-saturation as in this example.)

Let the solution cool slowly to room temp, and further cool on ice. If crystallization does not ensue, try standard crystallization tricks (scratch, add broken boiling stick, add ice crystals, seed, see instructor...). Once crystals have formed and are cold, filter using your Buchner funnel and the aspirator. Wash using some ice-cold 50-50 ethanol-water. Vacuum for as long as is convenient, so the sample is as dry as possible. Weigh the product. You can take your melting point same day or later during the week. Acetanilide mp: 112-115

Part II: Mixed Solvent Recrystallization of Dibenzalacetone (partner permitted). (Saturation)

Purpose: Observe how dramatically a “bad solvent” (water) can induce visible saturation/crystallization, when “super-saturation” does not occur.

Procedure: Weigh about 1 g (write down exactly) of dibenzalacetone and place it in a 25-mL Erlenmeyer flask. Add 4 mL of ethanol and heat to boiling by placing it in a hot water bath, as in Part I. Once you have the solution dissolved, add water slowly, dropwise, until the solution reaches a “cloud point”. (Try to count your drops). At this cloud point, your solution is visibly saturated!

Let the solution cool slowly to room temp, and further cool on ice for at least 5 minutes. Once crystals have formed and are cold, filter using your Buchner funnel and the aspirator. Wash using some ice-cold ethanol, and aspirate thoroughly under vacuum. Get your yield. You can take your melting point same day or later during the week. Pure dibenzalacetone mp: 108-111

Part III: Recrystallization and Identification of an Unknown. (work solo)

Purpose: To identify a suitable recrystallization solvent (or solvent combination) for an unknown; to do a recrystallization without instructions; and to identify an unknown.

Choose one of the unknowns (make sure you write down your letter in your lab report!) **Screen various solvents** (as we did last week) to determine which might be suitable for recrystallizing your particular unknown. Weigh out about 0.16 g of the solute, and divide it into four roughly equal piles. Place these into four test tubes. Add 1 mL of each of the four solvents. Check the solubility at room temperature and at hot temperature. Solvents available: water, ethanol, pentanone, toluene.

After identifying a reasonable solvent, or one that could be used as the “good” solvent in a solvent pair (normally in combination with water or pentanone), **proceed to actually recrystallize about 1 g** (write down exactly) **of your unknown**. Start with 4mL of your primary solvent per the one gram of solute. Choose ethanol if possible as your solvent, because it “solvent pairs” so beautifully. Water can be subsequently added if you want to diminish dissolving power; pentanone can be added to improve dissolving power. (Do not exceed 3 pipets water.) However, using ethanol or mixed solvents won’t always be appropriate, it depends on your unknown. **Rinse with whatever solvent or solvent blend that you recrystallized with.**

Get your final yield, and take your melting point same day or later during the week. If you have been successful, your melting point should be sufficiently accurate so that you can identify your unknown from the list of candidates on following page.

Note: The solvent/solid ratio in the solvent screening is 1 mL/0.04 g, which is 25mL/1g. Normally you start with a 4mL/1g ratio as your first guess for the bulk recrystallization. As a result of this difference in solvent/solid ratio, some solvents that look to have satisfactory dissolving power in the solvent screening tests don’t come close to fully dissolving the sample when you try the actual bulk recrystallization. In such cases, rather than adding enough solvent to reach the 25mL/g ratio, the easier and higher-yielding solution is normally to add some “better solvent” to get the crystals to dissolve. (All of this done with hot solvents, of course.)

Review: Two Ways To Achieve Just-Barely-Saturated/Just-Barely-Dissolved Borderline.

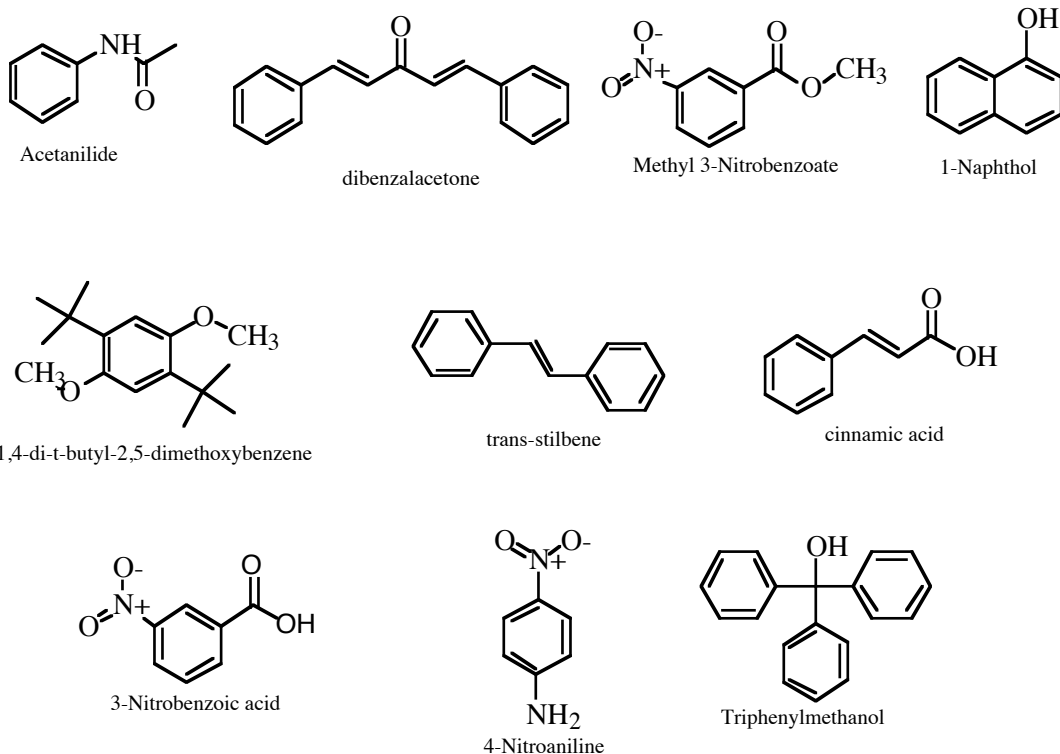
In all cases, heat to boiling, and only adjust by adding "hot" solvent, whether that be superior solvent or "bad" solvent.

- Add some hot superior solvent (if solubility is too low. Preferred route)
- Add some hot 'bad solvent' (if solubility is too high)
- Other possibility is to simply add more of the same solvent, if your solubility is too low; or to boil some of your solvent away, if the solubility is too high. But usually the first two options are faster and more convenient.

SOLVENTS	H_2O	$\text{HO}-\text{CH}_2-\text{CH}_3$	$\text{CH}_3-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_3$	$\text{C}_6\text{H}_5-\text{CH}_3$
	water ("W")	ethanol ("E")	pentanone ("P")	toluene ("T")

Recrystallization Unknown Candidates:

methyl 3-nitrobenzoate	78-80	cinnamic acid	133-134
1-naphthol	95-96	3-nitrobenzoic acid	140-142
1,4-di-t-butyl-2,5-dimethoxybenzene	104-105	4-nitroaniline	148-150
trans-Stilbene	121-122	triphenylmethanol	160-165

Recrystallization Unknown Candidates

Name: _____

Recrystallization #2 Lab Report (may work with partner)

Part 1: Acetanilide

Initial Mass: _____ Final Mass: _____ % Yield: _____ Melting Range: _____

To the best of your knowledge, how much water did you add?

If you needed any “tricks” to induce crystallization, what did you try and what worked?

Any problems, difficulties, excuses, or interesting observations?

Part 2: Dibenzalacetone (may work with partner)

Initial Mass: _____ Final Mass: _____ % Yield: _____ Melting Range: _____

To the best of your knowledge, how much water did you add?

Any problems, difficulties, excuses, or interesting observations?

Part 3: Unknown (work solo)

Initial Mass: _____ Final Mass: _____ % Yield: _____ Melting Range: _____

Which unknown letter did you use? _____

What was the chemical identity of your unknown? _____
(See list of candidates on previous page)

Solvent Screening:

Water			Ethanol			Pentanone			Toluene		
RT	Hot	Extra Solvent	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent

What solvent or solvent mixture did you choose?

Approximately how much of each solvent did you use?

Any problems, difficulties, excuses, or interesting observations?

LIQUID/LIQUID SEPARATION: EXTRACTION OF ACIDS OR BASES FROM NEUTRAL ORGANICS. Introduction.

Background Extraction is one of humankind's oldest chemical operations. The preparation of a cup of coffee or tea involves the extraction of flavor and odor components from dried vegetable matter with hot water. Many other substances, flavors and spices and perfumes and medicines, have been extracted from plants for centuries (quinine, morphine, menthol...). Many undesirable drugs are also isolated by extraction (cocaine from coca leaves). Extraction, like recrystallization, is based on solubility factors.

The most common and simple separation in organic chemistry involves the separation of neutral organics from ionic compounds, whether the ionic compound is an inorganic salt (NaCl) or is an ionized version of the organic. The two most commonly ionized organic families are carboxylic acids, which are ionized by deprotonation to their carboxylate RCO_2^- form, or basic amines, which are ionized by protonation to their ammonium RNH_3^+ form.

Neutrals and ionics are easily separated because ionics are preferably soluble in water rather than in organic solvents, whereas neutral organics are preferably soluble in organic solvents rather than in water. The following three separations are thus common:

1. A neutral/ionic mixture is shaken with ether and water.
 - The neutral goes into the ether layer.
 - The ionic goes into the water layer.
2. A neutral/carboxylic acid mixture is shaken with ether and NaOH/water. (Part 1)
 - The neutral goes into the ether layer.
 - The carboxylic acid is deprotonated by NaOH to its carboxylate form (RCO_2^-), which goes into the water layer.
3. A neutral/amine mixture is shaken with ether and HCl/water. (Part 2)
 - The neutral goes into the ether layer.
 - The basic amine is protonated by HCl to its ammonium form (RNH_3^+), which goes into the water layer.

Once a chemical is separated from its original mixture, it must still be isolated from solvent.

1. Isolating a neutral from ether solvent:
 - **Dry** The ether will contain not only the neutral solute, but also some water. The water is absorbed by a chemical drying agent (usually sodium sulfate or magnesium sulfate or calcium chloride).
 - **Filter (and rinse)** The drying agent is then usually removed by filtration. (Rinse!)
 - **Concentrate** The solvent is then removed by simple distillation, leaving the desired neutral as the residue. The simple distillation is usually done via a "rotary evaporator".
2. Isolating a neutral carboxylic acid from the NaOH/water layer:
 - **Acidify/Neutralize** HCl is added to acidify the water. In the process the carboxylate anion RCO_2^- is protonated and reverts to its neutral form RCO_2H .
 - **Filter or Extract** Because the acid is now neutral, its solubility in water will be low. If it crystallizes, you can filter it. If it comes out of the water as an oil, you can extract it in ether!
3. Isolating a neutral amine from the HCl/water layer:
 - **Basify/Neutralize** NaOH is added to basify the water. In the process the ammonium cation RNH_3^+ is deprotonated and converted back to its neutral form RNH_2 .
 - **Filter or Extract** Because the amine is now neutral, its solubility in water will be low. If it crystallizes, you can filter it. If it comes out of the water as an oil, you can extract it in ether!

Partition Coefficients and Multiple Extractions

In the presence of two solvents (ether and water in our case), each specific chemical has a characteristic “partition coefficient”, with the following formula:

$$\text{Partition coefficient} = \frac{\text{solubility in ether}}{\text{solubility in water}}$$

The partition coefficient basically tells you what fraction of the material will partition into each solvent layer. If the value is 4:1, that means 80% will partition into the ether layer, and 20% will partition into the water layer.

- Ideally, the distribution will be either zero (all stays in water) or infinity (totally in ether).
- This is not often the case. Frequently some of the neutral organic material will be lost to the water layer, and sometimes some of the ionic material will go into the ether layer. In either case, either the yield and/or the purity will not be 100%.

To improve extraction efficiency, **often two (or more) extractions may be appropriate.**

- **Example 1: Suppose you are trying to get all of your organic material into the organic phase,** but the partition coefficient for your desired neutral organic is only 4:1. If you do one separation, you should have 80% of the material in the ether extract, and 20% of the material in the water phase. By extracting the water again with more ether, you should get 80% of the remaining 20% that was in the water, i.e. you should get another 16% out into the ether, and now only 4% of the neutral should remain in the water. A third ether extraction of the water should take out 80% of the remaining 4%, thus leaving less than 1% of your material left in the water layer. Combine all the ether extracts, dry/concentrate, and you should get 99% yield.
- **Example 2: Suppose you are trying to use aqueous base to extract a carboxylic acid from a neutral organic,** but only 90% of the acid goes into the NaOH/water and 10% stays in the ether. If you do only one separation, your neutral organic will still be contaminated by the residual 10% of acid. But if you do a second extraction with NaOH/water, 90% of that 10% will be extracted as well, and now only 1% of the acid will remain in the ether layer to contaminate your neutral.

The process of extracting from a particular phase, to either make sure you get all the target organic out (example 1) or to make sure you remove all of an undesired contaminant (example 2) is often referred to as “**washing**”. In example 2, the carboxylic acid was “washed out” of the ether layer by a couple of NaOH/water “washes”.

To determine how many “extractions” are required to achieve a target minimum of non-extracted material, use y^x , where “y” is the fraction that survives a particular extraction, and “x” is the number of extractions. (In example 1, $y^x = 0.20^3 = 0.008 = 0.8\%$.)

Choice of Organic Solvent

1. **Low Boiling Point** Since you normally have to distill off your solvent at the end, a low-boiling solvent that can be simply distilled away quickly and rapidly is very desirable.
2. **Good Dissolving Ability for Organics** Obviously you’d like your organic solvent to have much better dissolving ability for organics than does water. Sometimes the nature of the solute dictates which solvents are acceptable.
3. **Low Miscibility with Water** You’d like relatively water to dissolve into the organic phase, and vice versa.
4. **Higher or Lower Density Than Water, Depending on Extraction Purpose** Typically when multiple extractions/washes are used, it is desirable to have the “extraction solvent” be denser than the solvent that is “being washed”.
 - **If you are going to “wash” the organic solvent several times with water** (example 2), it is technically convenient if the organic layer floats on the water layer. **This is true for ether.**
 - **If you are going to “wash” the water layer several times** to make sure you get all your organic material into the organic phase, it is more convenient to use a solvent that is more dense than water, so that the water will float on the organic solvent and you can pour the organic solvent out the bottom. This is not true for ether, so it isn’t that convenient for multiple washes/extractions from water. **Dichloromethane, which is more dense than water, is frequently used** instead for doing multiple washes/extraction from a water layer.
5. **Safe, Cheap, Unreactive...**

LIQUID/LIQUID SEPARATION: EXTRACTION OF ACIDS OR BASES FROM NEUTRAL ORGANICS. PROCEDURES.

Carboxylic acid unknown options (Part 1): benzoic acid (mp 123) or 2-chlorobenzoic acid (mp 141)
Amine unknown options (Part 2): 4-chloroaniline (mp 68-71) or ethyl 4-aminobenzoate (mp 90)
Neutral options (same choices for both Part 1 and Part 2): 1,4-dimethoxybenzene (mp 57), naphthalene (mp 82), dibenzalacetone (mp 110-111), or benzoin (137). Note: You may have the same neutral in both parts.

For flow chart, use “N” for neutral, “RCO₂H” for protonated carboxylic acid, “RCO₂⁻” for ionic carboxylate salt, “RNH₂” for neutral amine, and “RNH₃⁺” for ionic ammonium salt.

Part 1: Separation of a Neutral from a Carboxylic Acid.

Setup:

1. Attach your small metal ring to one of the vertical rods on your rack
2. Get your separatory funnel and a glass stopper out of your organic kit. Rest the separatory funnel into the ring.
3. Make sure the stopcock is closed (and screwed tight)!

Procedure:

Phase 1: Separating the two Chemicals into Two Liquid Phases. Extracting the Acid.

1. Weight out about 2 g (record exact weight) of a 50/50 mixture (by weight) of N/RCO₂H. (In other words, the mixture consists of 1 gram of neutral and one gram of acid). Pour the solid mix into your separatory funnel.
2. Add 20 mL of diethyl ether (“ether”). If the mixture doesn’t quite fully dissolve, don’t worry about it, just carry on.
3. Add ~10grams of ice (needn’t be precise, just something to absorb the exotherm when the base is added).
4. Add 10 mL of 3M NaOH to the separatory funnel, stop it, shake vigorously, vent, and allow the layers to separate. (Purpose: to convert the neutral acid into carboxylate anion, which should then go into the aqueous layer rather than staying in the ether layer).
5. Label a 125-mL Erlenmeyer flask as “Flask 1” with your Sharpie pen.
6. Get a couple of pieces of pH paper or litmus paper.
7. Drain off the aqueous layer into Flask 1. (Be sure you have removed the stopper from your separatory funnel first.) (Note: it is better to have a little water stay in the ether layer than to have some of the ether layer go into the aqueous.)
8. Add an additional 5 mL of 3M NaOH to the separatory funnel, shake the mixture as before, let it settle, and again drain the aqueous layer into Flask 1.
9. Dip a boiling stick into your Flask 1 solution, and touch it onto a stick of pH paper to confirm that it is basic.
10. Save Flask 1, the contents of which you will process a little later.

Phase 2: Isolating the Neutral Organic from the Ether Phase.

11. Carefully drain the ether layer into a 125-mL Erlenmeyer flask (labeled “Flask 2”).
12. Rinse the separatory funnel with an additional 5-mL of ether, and add that rinse to Flask 2.
13. Add sodium sulfate to Flask 2 and swirl. The amount required depends on how much water is in the mixture. Typically one full scoopula of sodium sulfate should suffice, but frequently additional drying agent is required. If the solution is dry, the liquid should look very clear and not cloudy, and at least some of the granules should not clump together. If all of the moisture has been absorbed, there should be at least some fine granular “non-clumpy” sodium sulfate granules left, and the solution should be clear. (Purpose: the sodium sulfate is intended to absorb any water that is in the ether solution.). If possible, it’s helpful to have instructor take a look to confirm all is well.
14. Pre-weigh a 50-mL round-bottomed flask, and then clamp it onto a vertical rod.

15. Take your long stem funnel and push a little glass wool into the neck. A little bit will suffice.
16. Pour the ether solution from Flask 2 through the glass-wool plugged funnel into the round-bottomed flask. The wool should be sufficient to filter off the solid sodium sulfate, and only allow the solution to get into the flask.
17. Rinse Flask 2 and the sodium sulfate pad with 10 mL of ether, and pour the rinse through the funnel into the round-bottomed flask.
 - At this point, there should be only ether and neutral in the flask. The acid should have been removed by the NaOH; the water should have been removed by the sodium sulfate; and the sodium sulfate should have been removed by the filtration.
18. Concentrate the ether solution in the round-bottomed flask by rotary evaporation. Be sure the aspirator power is on; that the top air valve is closed; and that you have an adapter for a good glass seal. Make sure that the spinner is also turned on. Get help the first time you use this!
 - Note: This is a standard simple distillation to remove the volatile ether while leaving the higher boiling, less volatile organic material behind. The vacuum further lowers the boiling point for the ether so that it comes off very quickly.
19. While working on other tasks anyway, let the flask stand to dry for an additional 15 minutes or more. Once the sample has concentrated to dryness, weight the flask and calculate your mass yield.
 - Note: If the mass exceeds 1.0 gram, it's probably not dry; consult instructor.
20. Take a melting point.
 - You have now completed isolation of sample from Flask 2.
 - Note: the melting points are likely to be somewhat depressed, because the products will have some impurities. The products could be further purified by recrystallization, but time does not permit!

Phase 3: Isolating the Neutral Carboxylic Acid from the Aqueous Phase.

21. Acidify the contents of Flask 1 by adding concentrated hydrochloric acid (probably labeled as 6.5M HCl) pipet-by-pipet, while testing with pH or litmus paper until the solution is decidedly acidic (pH<4). There is little harm in adding extra acid. (Be sure you use concentrated probably 6.5M hydrochloric acid, rather than dilute 1.5M HCl. Otherwise it will take too long to neutralize the water, and your yield will go down because of so much solvent.)
22. Cool flask 1 in ice, for ≥ 2 minutes, then filter (Buchner funnel), rinsing with a little cold water. Let the product dry thoroughly, weigh it, and test its melting point.
 - Note: If the mass exceeds 1.0 gram, it's probably not dry; consult instructor.
 - Note: the melting points are likely to be somewhat depressed, because the products will have some impurities. The products could be further purified by recrystallization, but time does not permit!

Part 2: Separation of a Neutral from a Basic Amine.

(See previous page for list of unknown candidates.)

The procedure should be largely analogous to that used for extracting an acid, with one huge difference: now you want to extract a basic amine instead of an acid. (When you extracted the acid, you used dilute basic water; to extract the basic amine instead, should you again use dilute basic water, or will you want to use dilute acidic water instead?)

Create a flow chart analogous to that used for the acid, and show it to instructor before going ahead. Keys to consider: since an amine is basic rather than acidic, should you use HCl or NaOH to ionize it and make it water soluble in the first separation? And once you have ionized it, will you use HCl or NaOH to neutralize it and make it water insoluble? In other words, what changes in your flow chart and procedure result from the fact that you are extracting an amine rather than an acid?

Once you have established and checked your separation/purification plan, proceed to isolate the second neutral and the amine. Record their masses, and record their melting points.

Note: This time, when using acid use dilute (probably 1.5M) aqueous HCl; and when using base, use relatively concentrated (probably 10.0M) aqueous NaOH.

Extraction/Acid-Base/Separatory Funnel Lab Report Name:

1. Yields, Melting Ranges, and Identification: (see two pages earlier for candidates)

Part 1: Starting Mass:

Neutral: Isolated yield (in grams) melting range: Identity:

Carboxylic Acid: Isolated yield (in grams) melting range: Identity:

Part 2: Starting Mass:

Neutral: Isolated yield (in grams) melting range: Identity:

Amine: isolated yield (in grams) melting range: Identity:

- Complete the flow chart for Part 1 (opposite side). Use "N" for the neutral organic unknown, "RCO₂H" for the acid in its neutral form, and "RCO₂⁻" for the carboxylate anion form.
- Include an analogous flow chart for Part 2 (opposite side), with any adjustments required due to starting with a basic amine rather than an acid. Use "N" for the neutral organic unknown, "RNH₂" for neutral amine, and "RNH₃⁺" for ionic ammonium salt.
- Why is it necessary to remove the stopper from a separatory funnel when draining the liquid through the stopcock?
- The pK_as of chemicals HX and HY are 5 and 7 respectively. The pK_a of carbonic acid H₂CO₃ is 6. If you made up an ether solution of chemicals HX and HY in a separatory funnel, and then added an aqueous solution of sodium bicarbonate NaHCO₃ to that separatory funnel, would both HX and HY stay in the ether layer? Or would either or both of them transfer into the aqueous layer? If one goes into the water layer, will it be in its neutral HX/HY form, or in its deprotonated anionic form?

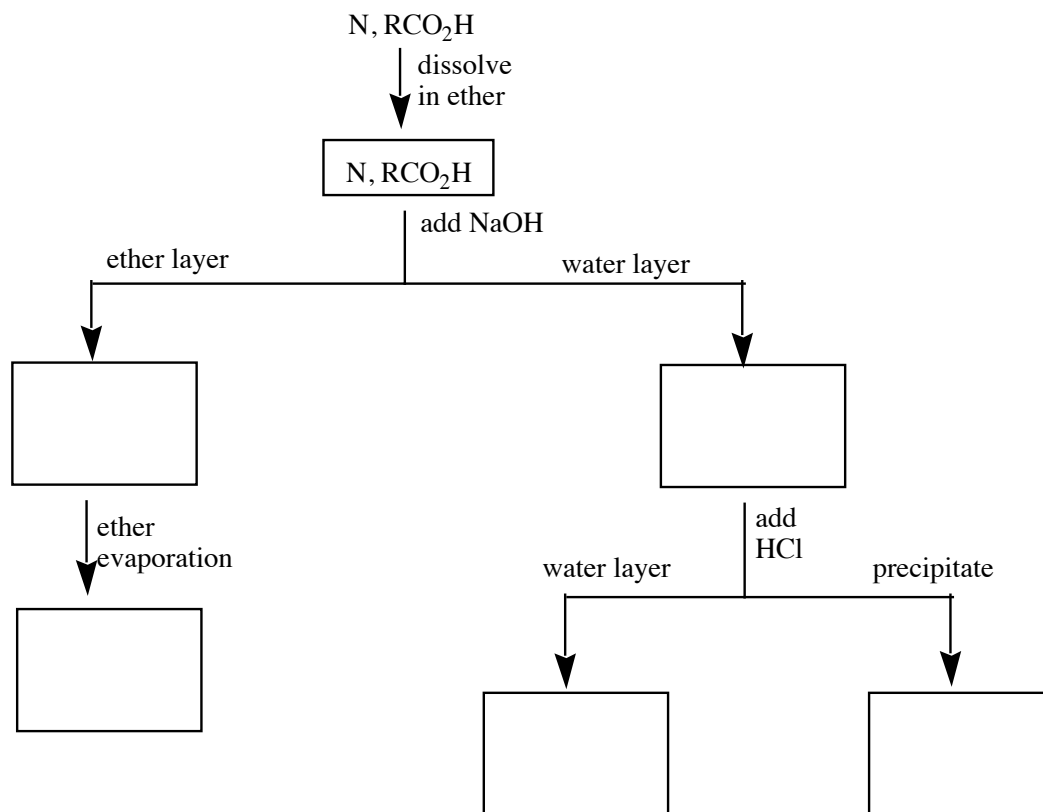
HX: ether layer or water layer?

Will it be in its HX or X⁻ form?

HY: ether layer or water layer?

Will it be in its HY or Y⁻ form?

- Suppose you have an organic sample **X** that is somewhat soluble in water, even though it is somewhat more soluble in dichloromethane or ether solvents. But if you do a single extraction, you get only 60% of your material to transfer from the water to the organic layer.
 - How many "washes" would it take to extract over 90% of your organic material extracted from the water layer?
 - In this case, would it be better to extract with dichloromethane or with ether?
- Suppose you have an organic sample **X** that is contaminated with an impurity. When you wash with an aqueous phase, **X** stays exclusively in the organic phase, and most (about 80%) but not all of the impurity washes out into the water phase. How many aqueous extracts should you do so that less than 1% of your impurity remains in the organic layer? Will it be more convenient to use ether or dichloromethane as your organic solvent?

Flow Chart for the Separation of Neutral from Carboxylic Acid

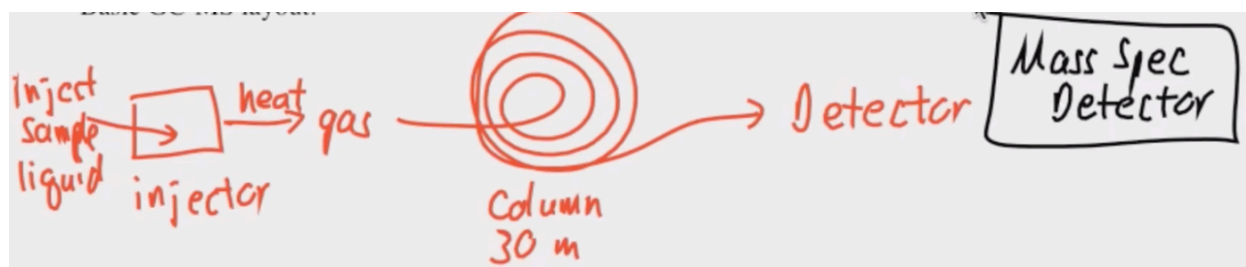
Create Your Own Flow Chart for the Separation of a Neutral from a Basic Amine

Chem 355 Jasperse Gas Chromatography-Mass Spectroscopy

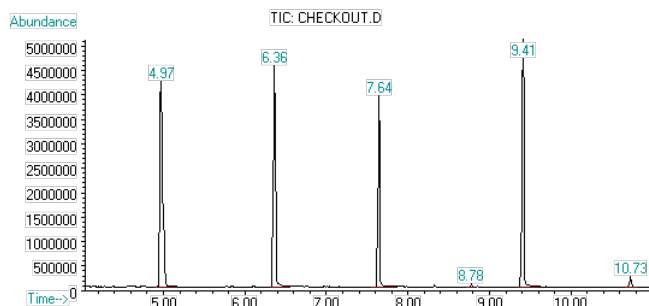
BACKGROUND Every type of chromatography depends on the distribution of a substance between two phases, a **mobile phase** and a **stationary phase**. Recall that in the liquid/solid chromatography the mobile phase was liquid flowing over a stationary solid phase.

In **gas chromatography**, the mobile phase is a stream of gas that flows through a narrow tube, which is coated on the inside with a non-mobile liquid film. A solution is syringed into a high-temperature injector where it is vaporized then carried through the column in a high-pressure gas (the mobile phase). For this lab, the injector will be 300°C; **the column will be 30m long with an internal diameter of 0.25mm**; the **film** will be **moderately polar** (with hydrogen bonding) with a 0.25µm thickness; and we will use 40 psi of helium gas as the mobile phase.

Basic GC-MS layout: (to be described and sketched in during the pre-lab video...)



Typical Look for a Gas Chromatogram:



The solutions injected will be mixtures of three substrates diluted in ethyl acetate solvent. Each of the three solutes will have distinct “retention times”. **GC retention times depends on several factors:**

1. **Sample polarity.** **More polar** samples stick to the polar film better, and **move slower**.
2. **Sample size:** **Larger molecules** are more likely to condense into the liquid phase and **move slower**. Smaller molecules vaporize more easily and remain in the mobile phase.
3. **Boiling point:** **Lower-boiling samples** boil more easily, and in the gas phase get carried through the column **faster**. Samples with higher boiling points spend are harder to get and to keep in the mobile vapor phase, so they move slower. Both the sample polarity and the sample size really relate to the boiling point.

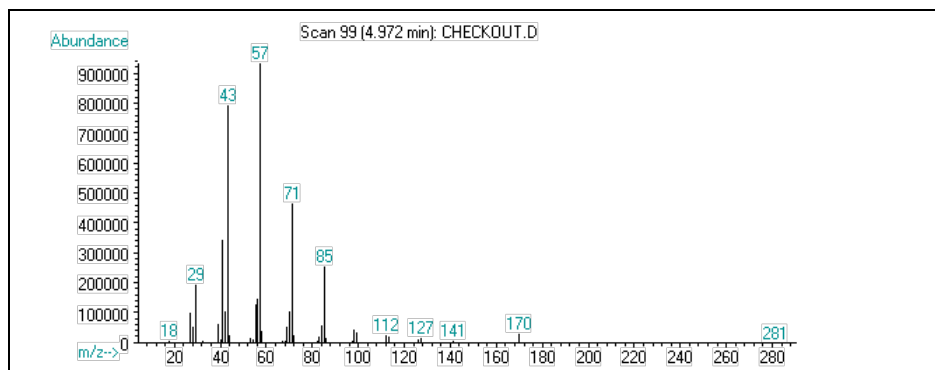
GC has **extraordinary separating power**. With a 30-meter column, there is a lot of opportunity to achieve separation! The retention times are very precise and characteristic, and the ability to separate is much greater than with most other forms of chromatography.

GC is **very sensitive**. Very dilute samples can be injected and trace amounts can be detected (as little as 10^{-9} g).

DETECTION can involve either **mass spectrometry** (“MS” = “mass spec”) or **flame ionization detection** (“FID”). Our instrument will use both methods, but the primary focus will be on the mass spec detection.

Flame ionization detection involves passing the sample through a flame (both hydrogen gas and compressed air must be supplied.) The flame ionizes the molecules and the ions are detected. The process is highly sensitive for carbon-containing molecules. FID is nice in that it is relatively inexpensive, and any organic chemical will be detected.

Mass spectrometry is more helpful in that it provides the molecular weight and valuable **information about the molecular structure**. MS knocks an electron out of a molecule. The result is both a cation (it lost an electron, so it becomes charged) and a radical (it lost one electron, so now there is an unpaired electron left somewhere.) The energy of the process and the instability of the radical cation usually result in fragmentation into multiple pieces. A typical mass spectrum is shown below.



Mass spectrometry is invaluable for sample identification. **No two molecules give exactly the same mass spectrum**. Thus the MS provides an unambiguous identification; the mass spectrum is like a molecular fingerprint. The sensitivity and identifying power of GC-MS make it a primary tool in forensic science and in Olympic drug testing. Our mass spectrometer is what's called a "**low resolution**" mass spec; it can determine molecular weights to the nearest tenth of a gram. More expensive "**high resolution**" mass spectrometers can give molecular masses to the nearest 0.0001 gram, and are even more powerful for identification purposes.

Mass spectrum interpretation is both simple and hard, depending. The hard part is that molecules are often ionized with so much energy that they fragment into many pieces and in sometimes unpredictable ways. (The process has been compared to shooting a bullet through a vase and looking at the pieces afterwards.) Analysis of some fragmentation patterns is discussed later.

NIST Library

Matching. Many molecules have been analyzed by mass spectrometry before, and their spectra have been filed with the National Institute of Standards and Technology (NIST). The 2008 NIST library includes over 220,000 mass spectra. When the NIST library is available, the computer can check for spectra that might match.

Molecular Ion, Molecular Weight and Molecular Formula: While ionization often leads to fragmentation, usually some of the parent molecular ion will appear. (Not always.) The molecular ion (M^+) provides the molecular weight for the molecule. With high resolution mass spec, the molecular ion gives not only the molecular weight but also the exact molecular formula.

Molecular Ion recognition and Isotope lines. The molecular ion should be the highest line in the spectrum, because the fragments are smaller. However, while most carbons are C^{12} , 1.1% of carbons are C^{13} isotopes. Thus a molecule with 10 carbons will have not only an M^+ line but also an $M+1$ line that is about 11% as tall as the main M^+ line. While this is often too small to register, it is often visible and should not be mis-identified as giving the molecular weight. Several finesse notes:

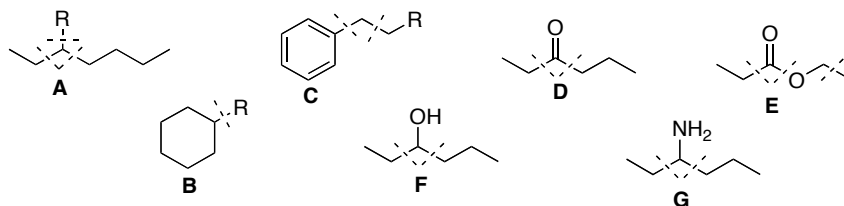
- For molecules that have **C, H, and O only**, the molecular ion M^+ will always have an **even number**. An odd number either implies that either some other element is included, or that you are looking at $M+1$ ion rather than M^+ , or that it isn't really the molecular ion at all but is actually a fragment.
- Normally the M^+ and $M+1$ ions will be the lines furthest to the right in a mass spectrum. But sometimes there is some "bleed" from the column film. In our case, **if you see lines at 207, 191, or 177, ignore these**. They are background bleed signals and not your molecular ion.

Even-versus-Odd Numbered Fragments: Even-numbered fragments are the result of multiple processes. For this week's lab, don't analyze or try to figure out any even-numbered fragments (other than the molecular ion line).

- For molecules that have **C, H, and O only**, the unbroken molecule will always have an even molecular weight.
- But whenever a break happens, both resulting fragments ("primary fragments") will have odd-numbers.
- Primary fragments sometimes undergo secondary reactions, resulting in new pieces ("secondary fragments") that may be even-numbered.
- **For today's lab, don't think about or try to analyze any even-numbered secondary fragments**
- **Focus only on odd-numbered fragments that might be understandable primary fragments.**

General mass spectrometry fragmentation guidelines:

1. For today, look for odd-numbered “primary fragments” only; other than the molecular ion don’t spend any time on even-numbered secondary fragments.
2. **It is common to fragment either at a functionalized carbon or at the adjacent C-C bond.**
3. **Cyclic molecules with side chains tend to fragment at the connection point.**
4. More substituted bonds fragment more easily.
 - cations and radicals are stabilized by substitution. Thus fragmentation at substituted bonds leads to stabilized cation and radicals fragments.
5. **Size** increases fragmentation, all else being equal.
6. Double bonds and especially **aromatic rings** reduce fragmentation.
 - This is due to charge delocalization
 - Aromatic molecules tend to have relatively strong molecular ion signals.
7. Cyclic molecules with no side chains tend to have strong molecular ion signals. But when they do fragment, it can be difficult to recognize the pieces.
8. Oxygenated primary fragments will often subsequently add one or even two extra hydrogens, leaving secondary-fragment lines one or two mass unit heavier than the primary fragment.

**Some General Fragmentation Notes for Famous Families:**

1. **Acyclic alkanes:** break wherever but especially at branches. (See A). Usually show M⁺.
Cyclic alkanes with branches: tend to break at the branch point. (B).
2. **Acyclic alkenes:** typically break at the allylic site. Usually show M⁺.
3. **Substituted Aromatics:** tend to break at the ring or at the benzylic site. (C). Usually show strong M⁺.
4. **Ketones:** typically break at the carbonyl bond (see D), and sometimes also one bond further. Usually show strong M⁺.
5. **Acyclic esters:** sometimes break at the carbonyl bond (see E), but have other break points. Sometimes don’t show any molecular ion or only a weak molecular ion.
6. **Alcohol and amines:** often break rapidly at the functional carbon (see F and G). Often show no molecular ion.
7. **Cyclic components can sometimes make things crazy! Subdivision within the ring requires two breaks, so often show strong M⁺.**
8. **Oxygenated fragments often add one or even two H’s after the initial break.**

Basic GC-MS Operation Compressed Draft 4 For Chem 355 Organic Unknowns Lab

Note: The following assumes the gc/ms program has been opened and warmed up; that an appropriate “method” and “sequence” have been selected; and that Jasperse will turn things off.

Sequenced Data Acquisition: Using the Autosampler to Sequence Runs Automatically

Note: this assumes that Jasperse has already prepared a “sequence”, but you are trying to add your sample to the lineup.

- **If you’re first in line, get Jasperse to come and help. Or hit “OK” and “Run Sequence”.**

1. Add your sample to the back of the line in the autosampler.

- Do NOT leave any open holes (unless the sample belonging in that hole is being sampled and is in the injector tray.)
- Filling a “sample-is-in-the-injector-tray” hole will cause a system freeze. When the machine tries to put the injection sample back, it will have no place to go.

2. Open “edit sequence” by clicking the “edit” icon on the yellow panel high on the computer screen.

- This will open a spreadsheet that you can edit.
- Add your names in the “sample” box that goes with your vial number.
- **Click OK.** Note: if you don’t click “OK”, the machine will freeze at the end of the current run. NEVER leave the spreadsheet page open unless somebody behind you is going to close it.

Data Processing/Analysis: Getting and Printing the GC Graph, % Report, and/or Mass Spec.

- Note: data analysis can be done while acquisition is ongoing.
- Note: Data files are in a Data Folder, usually open on the left. Or, you can click “Data Analysis from the yellow panel on top of the GC software field.

3. Open a data file: double click with the left mouse button to.

- Data file will have the names “Vial-1” or “Vial-2”, so **remember which vial was yours.**
- Your data files should be within an Organic Lab folder.

4. Printing GC Graph, % report, and retention times: Click Method>Run Method

- Repeat as many times as needed to provide prints for each student in your group.

5. Printing Mass Specs: Click the 5th Hammer button.

- Click the 5th hammer button as many times as needed to provide prints for each student in group.
- Note: You don’t need to wait for a print to finish before clicking the hammer again. If you’ve got 5 partners, just click the hammer five times and the prints will come out one by one....

The Experiment

Time overview:

1. Instructor will give each student printout data for Sample A
2. Each student or pair-of-students will prepare one sample.
3. We will all go over to the GC-MS and instructor will show the instrument, how it works, how to run it, how to use the software, how to print extra copies of the GC data and the mass spec data, etc..
4. Students will bring along their sample printout for Sample A, and their Basic GC-Operation instruction sheet. (Previous page.)
5. We will all return to lab, and discuss how to analyze and report on Sample A.
6. As the unknown samples complete, you will then be able to get data and printouts for your unknown samples, and come back to lab to analyze and process them.

Sample A Data Analysis: The instructor will give each student a copy of the GC-MS data for Sample A.

- Everybody will be responsible for analyzing it.
- Bring this with you to the GC-demo with the instructor, so that you have a reference sample data and printout to look at when the instructor is discussing aspects of a printout.

Unknown Sample

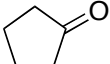
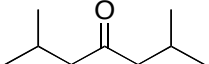
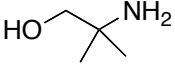
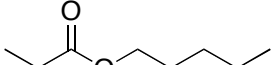
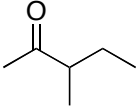
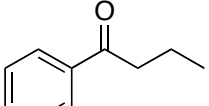
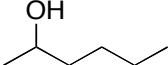
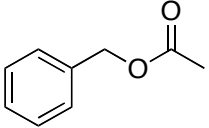
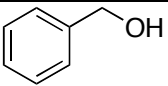
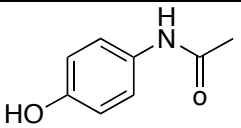
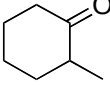
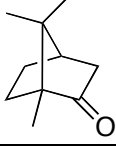
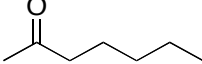
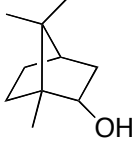
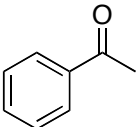
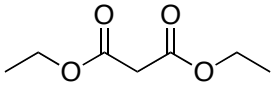
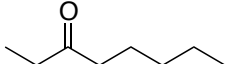
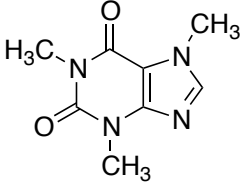
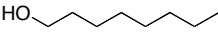
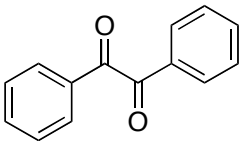
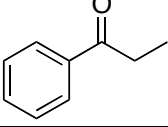
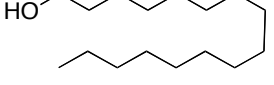
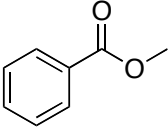
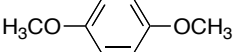
1. You may work with a partner (prepare one sample between the two of you); or you may work individually (prepare and analyze your own sample.)
2. Sample preparation: Using the pipets attached to each unknown sample, fill a GC-MS sample vial to ≥ 0.5 mL. Filling it deeper won't do any harm.
 - Note: Samples A-G are already highly dilute.
 - Ethyl acetate is the solvent.
3. Sample submission: Using the Basic GC-Operation instruction sheet as a guide, place your vial into the autosampler, and enter needed submission information on the computer.
4. **Record your autosampler number spot; finding your data later will depend on knowing your number!**
 - The data is filed by Vial number, not by student names....
 - So when you go back to get your data, you need to know whether you're Vial-14 or Vial-12 or whatever!!!!)
5. After the GC-MS queue has run your sample, you will need to find and open the data file, and print needed data. (Each partner will need to have a copy of the GC data AND the MS data.)

Notes: the unknown components are all taken from the table shown on the following page.

Tips:

1. Interpretation is best done by:
 - Finding the molecular ion. If you can figure the molecular weight, in most cases that's as good as identifying your candidate.
2. Ignore any peaks at 207, 191, and 177. These are released from the column and are not produced from your molecule.
3. Once you know what your molecules are, look at the mass spectra for each one and try to find one or two fracture points leading to major recognizable peaks.
4. Look for odd-numbered fragments that correlate to breaks next to a functional group, and that would have mass of ≥ 45 .

GC-MS Candidates, with Molecular Weights and Structures

Compound	MW	Structure	Compound	MW	Structure
Cyclopentanone	84		2,6-Dimethyl heptanone	142	
2-amino-2-methyl-1-propanol	89		n-Pentyl propionate	144	
3-Methyl-2-pentanone	100		Butyrophenone	148	
2-Hexanol	102		Benzyl acetate	150	
Benzyl Alcohol	108		Acetaminophen	151	
2-Methyl Cyclohexanone	112		Camphor	152	
2-Heptanone	114		Isoborneol	154	
Acetophenone	120		Diethyl malonate	160	
3-Octanone	128		Caffeine	194	
Octyl Alcohol	130		Benzil	210	
Propiophenone	134		Hexadecanol	242	
Methyl Benzoate	136				
Dimethoxybenzene	138				

See hand-in sheets on following pages.

GC-MS Lab Report

Name:

Part 1: Group SAMPLE A

1. Record the retention times, the molecular weights, and the structure for the three components. (See the list on the earlier page).

	Retention Time	Molecular Weight	Unknown Structure
--	----------------	------------------	-------------------

First Peak

Second Peak

Third Peak

2. Redraw the three unknown structures, and write in the molecular weight under each one.
- Look at your mass spec for each unknown and the lines that actually appear in the mass spectra, and for each unknown **draw out two** "fragments" that match up with actual fragmentation peaks that are actually visible in the mass spec. (Given the original structure of the unknown, the mass of the fragment, and typical fragmentation patterns.)
 - Draw the fragment number beneath each figure.
 - Note: each fragment must be a cation, and must have a molecular weight that matches a line that you actually see in the mass spectrum.
 - Note: Look for odd-numbered fragments, since even-numbered fragments are not primary fragments.

Unknown Structure	One Fragmentation Peak and What it Might Be:	Second Fragmentation Peak and What it Might Be:
Unknown 1	1.	2.
Unknown 2	1.	2.
Unknown 3	1.	2.

Part 2: Individual/Partner GC-MS

3. Which sample did you and your partner run? _____
4. Attach a printout of BOTH the chromatogram and a printout of each of the three mass spectra.
5. Record the retention times, the molecular weight, and draw the structure for the three unknowns. (See the list on the earlier page).

	Retention Time	Molecular Weight	Unknown Structure
--	----------------	------------------	-------------------

First Peak

Second Peak

Third Peak

6. Redraw the three unknown structures, and write in the molecular weight under each one.
- For each unknown **draw out two** “fragments” that match up with actual fragmentation peaks that are actually visible in the mass spec.
 - Draw the fragment number beneath each figure.
 - Reminder: each fragment must be a cation; must have a molecular weight that matches a line that you actually see in the mass spectrum; and you should look for odd-numbered fragment.

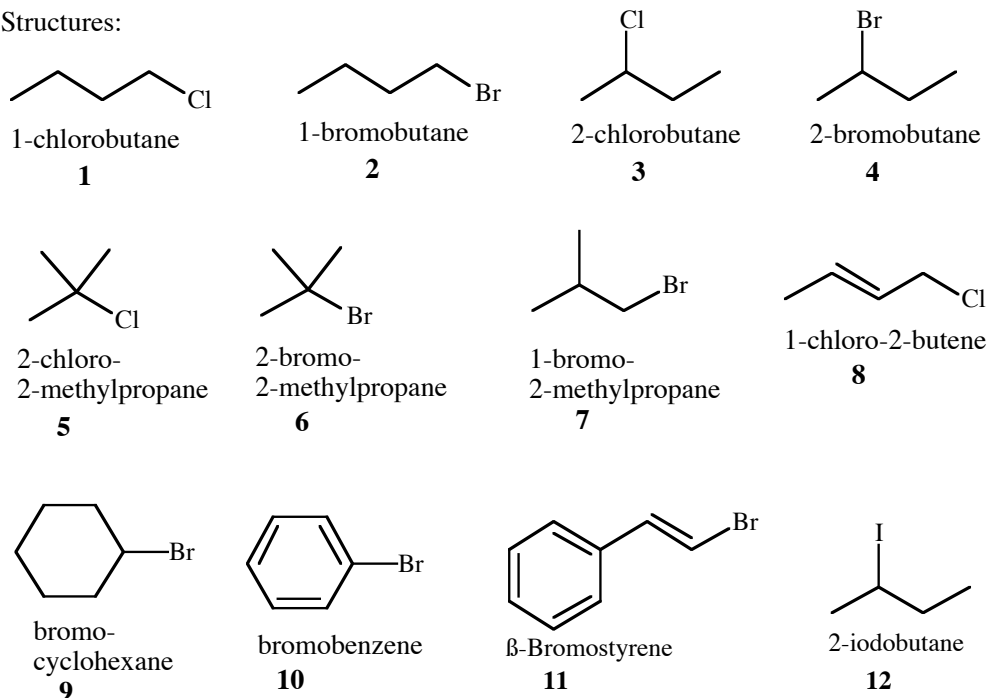
Unknown Structure	One Fragmentation Peak and What it Might Be:	Second Fragmentation Peak and What it Might Be:
Unknown 1	1.	2.

Unknown 2	1.	2.
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Unknown 3	1.	2.
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Chem 355-Jasperse**STRUCTURAL EFFECTS ON SUBSTITUTION REACTIONS**

Structures:



General Procedure: In each test, add 5 drops of haloalkane to a test-tube, then add 1 mL of solution (NaI/acetone for the S_N2 reactions, AgNO₃/ethanol for the S_N1 reactions), and mix by stirring vigorously with a boiling stick, and watch for the formation of precipitate. (For NaI reactions, sometimes an initial false precipitate forms and persists, that clears away if you mix it up well at the start.) For the NaI experiments, if neither of them react within 3 minutes, then place the tubes in a 50° water bath (use 50-mL beaker); allow to stand until at least one of them gives precipitate. Do not allow the bath temperature to exceed 60° or the acetone may evaporate away and you'll get false results.

What is happening, and what are the precipitates? In the NaI experiments, substitution by iodide generates either insoluble NaCl or NaBr. In the second set of experiments insoluble AgCl or AgBr are reaction products as the halide is substituted by an ethoxy group. Thus, in both types of reaction the formation of precipitate gives a qualitative and visible measurement of relative reaction speed.

For the S_N2 reaction (Part 1), you'll need samples 1, 2, 3, 4, 7, 8, 10, 11. For the S_N1 reaction (Part 2), you'll use all samples except for 7 and 11.

Notes

1. Crotyl chloride **8** is a lachrymator (makes you cry). Do not spill it, keep it the hood as much as possible, and when you rinse it out do so in the hood!
2. You are using so many test tubes that you will need to wash them between sets of experiments. Make sure that they are washed very carefully, with water and then acetone, before reusing. If there is residual haloalkane in a tube, it can really mess up your results and give you false positives. If there is water in your test tubes, it will dissolve NaCl/NaBr salts and give you false negative data.
3. In part 1, the NaI/acetone should be added last. Otherwise you get false precipitate when relatively non-polar haloalkane can cause some of the NaI to precipitate. NaI precipitate should dissolve upon mixing/shaking.
4. In NaI reactions, often yellow color will develop. This means nothing. Iodide is air-oxidized to yellow iodine, but this has no pertinence to the experiment.
5. Silver nitrate spills give brown spots! Avoid spilling. A spot on your fingernail will last till your nail grows out! (And on your clothes, forever?).

Some Arrow-Pushing Guidelines

1. Arrows follow electron movement.
2. Some rules for the appearance of arrows
 - The arrow must begin from the electron source. There are two sources:
 - a. An atom (which must have a lone pair to give)
 - b. A bond pair (an old bond that breaks)
 - An arrow must always point directly to an atom, because when electrons move, they always go to some new atom.
3. Ignore any Spectator Atoms. Any metal atom is always a “spectator”
 - When you have a metal spectator atom, realize that the non-metal next to it must have negative charge
4. Draw all H's on any Atom Whose Bonding Changes
5. Draw all lone-pairs on any Atom whose bonding changes
6. **KEY ON BOND CHANGES**. Any two-electron bond that changes (either made or broken) must have an arrow to illustrate:
 - where it came from (new bond made) or
 - an arrow showing where it goes to (old bond broken)
7. **Watch for Formal Charges and Changes in Formal Charge**
 - If an atom's charge gets more positive => it's donating/losing an electron pair => arrow must emanate from that atom or one of its associated bonds. There are two “more positive” transactions:
 - When an anion becomes neutral. In this case, an arrow will emanate from the atom. The atom has donated a lone pair which becomes a bond pair.
 - When a neutral atom becomes cationic. In this case, the atom will be losing a bond pair, so the arrow should emanate from the bond rather than from the atom.
 - If an atom's charge gets more negative => it's accepting an electron pair => an arrow must point to that atom. Ordinarily the arrow will have started from a bond and will point to the atom.
8. **When bonds change, but Formal Charge Doesn't Change, A “Substitution” is Involved**
 - Often an atom gives up an old bond and replaces it with a new bond. This is “substitution”.
 - In this case, there will be an incoming arrow pointing directly at the atom (to illustrate formation of the new bond), and an outgoing arrow emanating from the old bond that breaks

Chem 355-Jasperse

Name:

STRUCTURAL EFFECTS ON SUBSTITUTION REACTIONSPart 1: The S_N2 Reaction (NaI/acetone)

Report your observations, based on how fast precipitate formation is observed. Do you get instant precipitation? Does it take minutes for much precipitate to build up? Do you need to heat in order to get much precipitate? After comparing, rank the relative reactivity of the competing substrates.

1. Leaving Group: Br vs Cl

Run 1 vs 2

Run 3 vs 4

2. Primary/Secondary/(Tertiary): (With tertiary, results in this reactions are confusing due to competing side reactions, so we aren't actually racing.)

Run 2 vs 4

Run 1 vs 3

3. Double bonds part 1: Alkyl vs. Allylic

Run 1 vs 8

4. Compare 2 vs 8. This is an apples/oranges comparison; which is more important, the leaving group or the allylic double bond effect?

Run 2 vs 8

5. Double bonds part 2: Alkyl vs. Alkenyl ("vinyl") or Aryl. (Stir with boiling sticks for 10 and 11. Look for just one winner, neither of two losers should react at all).

Run 2 vs 11 vs 10

6. Steric effects: Both 2 and 7 are both primary. Are they equal, and if not why not?

Run 2 vs 7

7. Temperature. Did heating samples sometimes lead to reactions that didn't go at room temperature?

Part 2: The S_N1 Reaction (AgNO₃/ethanol)

1. Leaving Group: I vs. Br vs Cl (Record 1st/2nd/3rd places)

Run 12 vs 3 vs 4

2. Primary/Secondary/Tertiary: (Record 1st/2nd/3rd places)

Run 1 vs 3 vs 5

Run 2 vs 4 vs 6

3. Double bonds part 1: Alkyl vs. Allylic:

Run 1 vs 8

4. Double bonds part 2: Alkyl vs. Alkenyl ("vinyl")/Aryl.

Run 9 vs 10

Name:

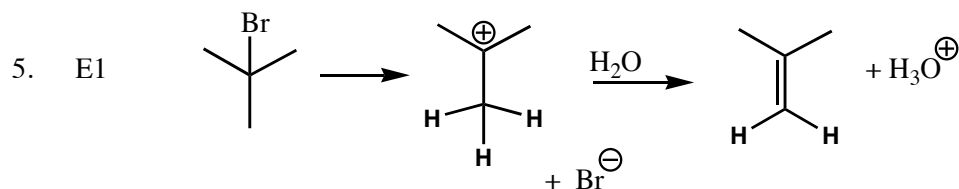
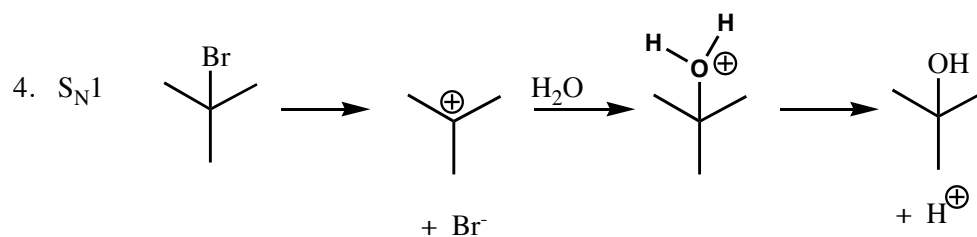
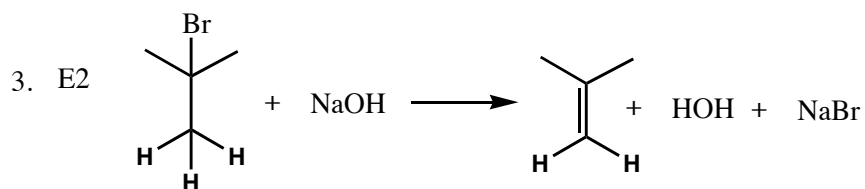
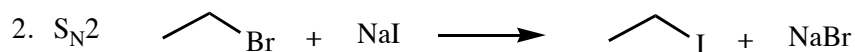
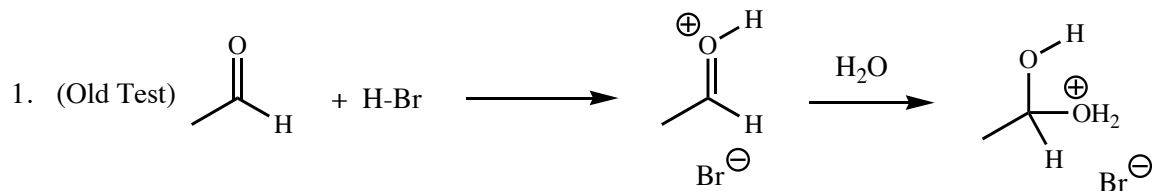
STRUCTURAL EFFECTS ON SUBSTITUTION REACTIONS

1. When considering the leaving groups I, Br or Cl, what was the relative reactivity in S_N1 reactions? In S_N2 reactions (didn't actually use the iodide there)?
2. When considering primary versus secondary versus tertiary haloalkanes, what was the relative reactivity toward S_N1 reactions? Toward S_N2 reactions (we didn't actually run a tertiary there)?
3. What was the effect of the "allylic" double bond in **8** on S_N1 reactivity? On S_N2 reactivity?
4. What was the effect of the halide being directly attached to an aryl/alkenyl carbon (**10** and **11**) on the S_N2 reactivity? S_N1 reactivity?
5. Both **2** and **7** are primary bromides. Can you explain the difference in their S_N2 reactivity, if there was any?
6. What would be the specific mathematical effect on the reaction rate if you carried out the sodium iodide-in-acetone reactions on the alkyl halides using an iodide solution half as concentrated? ("Slower" or "faster" is not specific enough.)

Name:

Arrow-Pushing Practice:

- Draw arrows for each of the steps in the following reactions.
- Include all formal charges, where present.
- Include all lone-pairs on atoms that react.
- Draw in all hydrogens on atoms that react. (It is not useful to draw in all H's on atoms that don't react.)
- Remember that arrows track the movement of electrons, so an arrow should go from the source of electrons and point directly to the atom that accepts them.



BACKGROUND Chromatography is a powerful technique for the separation and purification of both solids and liquids on relatively small scale (ideally <10g). Chromatographic techniques are also invaluable as analytical techniques for analyzing tiny quantities of material (as little as 10^{-9} g). This is one of the four major purification techniques. Advantages for chromatography are its power and generality (not limited to liquids or solids or the need for ionizability). A disadvantage is the limitation in scalability (has problems with hundreds of grams of material).

1. Recrystallization
2. Distillation
3. Liquid/Liquid Separation (Separatory Funnel Separation)
4. Chromatography

Every type of chromatography depends on the distribution of a substance between two phases, a **mobile phase** and a **stationary phase**. (In a river, the running water would be called the mobile phase and the riverbed the stationary phase...) In today's case, the mobile phase will be an organic solvent, the stationary phase a polar surface. A particular chemical will partition between being bound to the surface, where it doesn't move, and being dissolved in the solvent, such that it flows along. Thus different chemicals move at different speeds, depending on adsorption/solubility equilibrium. The more tightly the sample binds to the surface, the less it will move. Anything that impacts the sample's partition between binding to the stationary phase versus dissolving in the mobile phase will impact the sample's mobility.

Practical Summary: A sample "stuck" to a surface is "washed along" with a solvent. "Less sticky" things move faster!

Different types of chromatography use different binding principles for "sticking" to the stationary phase, and are useful in different contexts of science.

- Organic Chemistry (today): A polar surface binds polar organics
- Biochemistry
 - Size exclusion: surface pores can fit small molecules, exclude larger molecules
 - Charge: cationic surfaces bind anionic chemicals, anionic surfaces bind cationic chemicals
- Gas/Liquid Chromatography (Organic and Analytical Chemistry): the "stationary phase" is actually a nonvolatile liquid coating on the walls of a tube; the mobile phase is gas passing through the tube. Volatile chemicals are more likely to evaporate from the liquid phase and fly along in the gas phase. Less volatile chemicals are better retained in the liquid phase and thus move more slowly. Polarity can also be used to attract materials to the stationary phases.

ANALYTICAL TLC (THIN LAYER CHROMATOGRAPHY)

TLC chromatography uses glass or plastic plates coated with a thin layer of adsorbent as the stationary phase. Silica gel ($\text{SiO}_2 \cdot x\text{H}_2\text{O}$) and alumina ($\text{Al}_2\text{O}_3 \cdot x\text{H}_2\text{O}$) are the most common solid adsorbents. Both are polar, hydrogen-bonding adsorbents, with lots of polar, hydrogen-bonding "sticky sites". Samples are applied to the surface, and then the organic "eluent" (solvent) is applied and runs up the plate. (The flow of the eluent results from capillary action.)

The mobility of a particular chemical depends on its partition between the mobile phase (the eluent) and the stationary phase (silica gel). The more tightly the sample binds to the silica (the "stickier" it is), the less it will move. The less well it binds, the more it will dissolve in the solvent and flow up the plate.

1. **Sample Polarity and Sample Movement:** A typical ranking of sample polarity in terms of functional groups, all else being equal, is in the order shown. In practice, **a more polar sample will bind to the stationary phase better, and will not move as much.** A more nonpolar, less sticky sample will move faster and farther

- **Polarity Pattern:**
Carboxylic acids > alcohols > amines > ketones/aldehydes > esters > ethers > halocarbons > arenes > alkanes
- **Adding additional nonpolar hydrocarbon to a given molecule moves it in the non-polar direction (tiebreaker).** For example, C_4H_9OH will be more polar than $C_7H_{15}OH$.
- **Key: More polar sample → moves less. Less polar sample → moves farther.**

2. **Eluent Polarity and Sample Movement:** Eluents have the same order of polarity. But **while a sample's movement decreases with increasing sample polarity, a sample's movement increases with increasing eluent polarity.** A good-binding polar eluent competes for the sticky sites on the silica, and either "displaces" the substrate from the surface or else prevents the sample from binding to the sticky sites on the surface. The result is that the sample will have its adsorption/solubility partition moved away from the adsorbed side toward the dissolved side. The practical result is that increasing eluent polarity means that the substrate will move to a greater degree.

- **Eluent factor: The more polar the eluent, the faster and farther samples will move**

3. **Response Factors:** Movement is quantified by " R_f " (**R**esponse_{factor}) values: relative to where the sample begins, this is the distance the sample travels divided by the distance that the eluent travels. For a given surface, substrate, and eluent, the R_f is characteristic and is useful for identification. For a series of substrates, their relative R_f 's reflect their relative polarities.
4. **Sample Visualization:** Visualizing samples is crucial, since most organics are colorless. UV (ultraviolet light) or a chemical colorizing dip will be used. (UV is ideal, but is only applicable to molecules with extensive systems of sp^2 atoms that are able to absorb UV light.)

Summary: For silica gel surfaces, which are polar, the following relationships are true:

1. When two samples are run under identical conditions, **the more polar sample will move less and have the lower R_f ; the less polar sample will move more and have the higher R_f .**
2. When the same sample is run under two different solvent conditions, **any sample will have a higher R_f with the more polar eluent, and a lower R_f with the less polar eluent.**

COLUMN CHROMATOGRAPHY

While TLC is useful as an analytical tool, chromatography can also be used as a purification technique. But to separate larger than analytical quantities of chemical, a larger amount of solid surface material must also be used, and larger volumes of solvents must also be used.

The general idea is that if sufficient quantities of solvent are used, solutes will eventually "wash off" of the surface. The differential mobilities of different compounds allow them to come off at different speeds. Individual collection of the different fractions, followed by reconcentration, enables isolation of pure compounds from initial mixtures.

Eluent Polarity Ramping: In practice solvent polarity "ramping" is commonly used. In this technique, a relatively nonpolar solvent is used first, which is only able to selectively wash off mobile, nonpolar substrates, while leaving polar substrates behind ("stuck" to the solid surface). Then a more polar solvent is applied which is able to wash off the more polar substrate. In today's lab we will do a very abrupt increase in solvent polarity to make things go faster. But often this is done gradually.

Pressure is frequently used to push solvent through more quickly and speed up the process. We will use modest pressure in today's experiment.

In today's experiment, the samples will be colored, so it will be relatively easy to see them separating and moving. Most ordinary organics are colorless. When colorless organics, a series of different solvent fractions are collected in test tubes or flasks. Then the same visualization techniques that are used for TLC are applied to determine which fractions actually have chemicals

AUTOMATED "FLASH" COLUMN CHROMATOGRAPHY

While manual column chromatography is still widely used, many research labs now use automated chromatography. Automated "flash" chromatography involves special high-grade silica cartridges; the ability to program solvent mixtures in order to ramp up the eluent polarity; and a built-in ultraviolet detector.

The standard process is to dissolve the sample in some organic solvent; add some silica; and concentrate the mixture such that the sample is finely dispersed over the surface of the silica and blend can be easily poured. (This will have already been done for you in advance of today's lab.) Solvent is then delivered through the mixture and through a silica cartridge, after which fractions are collected in a series of test tubes. The contents of a tube can be analyzed by GC-MS (introduced later this semester) or NMR (also introduced later this semester). Test tubes containing a particular component can be combined and concentrated to provide the purified chemical.

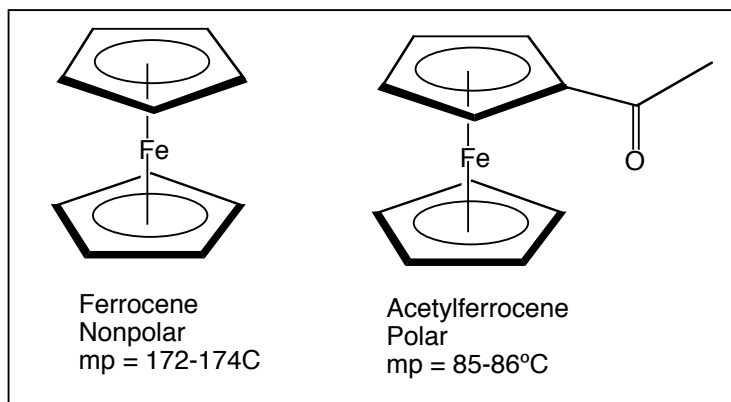
The Experiments

Part I: AUTOMATED “FLASH” COLUMN CHROMATOGRAPHY

1. Jasperse will demo this procedure. We'll either try to all squeeze in around the combi-flash machine and see how things work. Or else will split that up into two groups, half the lab early in the lab period, and then the rest will need to pause what they're doing and come over later to see how it works.
 2. Once actually started, a run will take about 15 minutes: two minutes to equilibrate and rinse out some of the tubes and columns, then ten minutes of actual collection in test tubes, then some rinsing.
 3. **Analyze and identify one of the unknown components by GC-MS.**
 - After a run is completed, the two or three different components of the unknown mixture will be located in different test tubes.
 - Each set of partners will be responsible to analyze and identify one of the unknowns.
 4. **Vial Preparation for GC-MS Analysis.**
 - Use a pipet to transfer ≥ 0.5 mL of solution from a test tube containing your sample into a GC-MS vial.
 - The samples are already plenty dilute from the solvent, so no further dilution is required.
 - Submit the vial to the GC-MS sequence, using the procedures you used in earlier week.
 - Be sure to remember which spot in the tray you are using!
 5. Unknown Candidates with Molecular weights are shown on the lab report hand-in page.
 - You should be able to identify your unknown directly from matching your sample's molecular weight with the sample with that molecular weight on the table.
 - So, super easy!
-

Part II: COLUMN CHROMATOGRAPHY**Separation of nonpolar Ferrocene(mp 172-174°C) from polar Acetylferrocene (mp 85-86°C).****Overview**

In this experiment, a small-scale chromatographic separation of non-polar ferrocene (mp 172-174°) and relatively polar acetylferrocene (mp 85-86°) will be attempted. These structurally interesting iron-containing molecules have been chosen for the experiment specifically because they are colored (unlike most organics). So their visible color will enable you to see the separation and chemical movement as it happens. The solid surface will be silica; the nonpolar solvent will be “petroleum ether” (a misnomer, it is a mixture of low-boiling alkane isomers); and the polar solvent will be 50/50 diethyl ether/petroleum ether. The column will be packed with silica gel. Then a 50/50 mixture of ferrocene and acetylferrocene will be poured on top. Nonpolar petroleum ether will wash off the nonpolar ferrocene while leaving the polar acetylferrocene behind. More polar 50/50 diethyl ether/petroleum ether will then be used to wash off the acetylferrocene. Both wash solutions will then be concentrated to give the purified samples.



More polar 50/50 diethyl ether/petroleum ether will then be used to wash off the acetylferrocene. Both wash solutions will then be concentrated to give the purified samples.

Preparing the sample:

1. Weigh out approximately 0.1g of 50/50 pre-mixed ferrocene/acetylferrocene material onto some weighing boat. (Record the exact weight of the mixture).

Preparing the column:

2. Plug the end of a 4-mL “monster” pipette (the “column”) with glass wool. A long-nosed regular pipette serves as a good ramrod. (The “monster” pipets are on the middle table, and grab a big blue pressure bulb.)
 - a. Note: This is a special pipet, with thicker glass and a larger diameter than you normally use. Make sure you get the correct pipet.
3. Weight out ~1g of silica and add this to the pipet. (Doesn’t need to be weighed carefully). (Use weighing boat to try to funnel it in). Your column should be approximately half full.
4. Securely clamp the column, and tap it to try to level the surface of the silica.
5. Take your dry sample (see above) and pour it (carefully!) onto the column, again using the weighing boat. Again tap the surface to try to level the material.

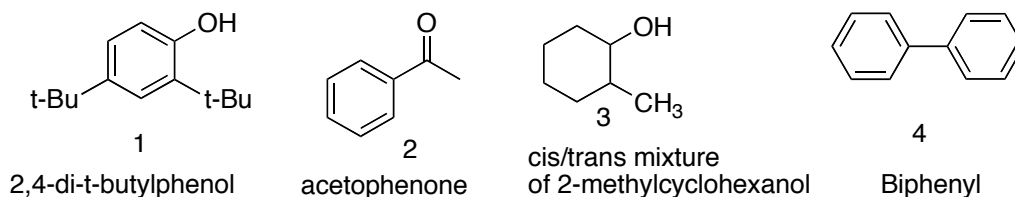
Applying the sample to the column:**Eluting the Nonpolar Substrate:**

6. Clamp down a 150-mL ground-glass jointed Erlenmeyer
7. Get 15 mL of petroleum ether and use it to wash the mobile, nonpolar substrate off from your column into the Erlenmeyer. Hopefully by the end the bottom portion of your column should be essentially white and there should be no yellow color coming off anymore.
8. Note: If you release the pressure on your big blue pipet bulb, while it is still held tightly onto your pipet, it will probably suck up all of the silica! Not a good plan. So after you have apply pressure to the big blue pipet bulb, be sure to take it off of the pipet before relaxing your grip and releasing the pressure. Otherwise, you’ll have to start over.

9. Concentrate the solution by first adding a vacuum adaptor, and attach the vacuum hose. Gradually turn your vacuum open (turn counterclockwise to open) until it is wide open. Let it vacuum for around 10 minutes.
10. Take a melting point for your ferrocene. (You may need to use a bent microspatula to scrape off enough solid material to do the melting point.)

Eluting the Polar Substrate:

11. Clamp down another 150-mL ground-glass jointed Erlenmeyer with a small stir bar in the bottom.
12. Now use 10-15 ml of 50/50 diethyl ether/petroleum ether solvent to wash the more polar acetylferrocene off of the column and into your second Erlenmeyer. You should be able to see the colored band as it moves through the column. There will be some residual gray or brown color that will not wash off; these are impurities that we don't want anyway.
13. Concentrate the solution by under vacuum for 10 minutes.
14. Take a melting point for your acetylferrocene. (You may need to use a bent microspatula to scrape off enough solid material to do the melting point. It won't be much.)

Part III: TLC (Thin Layer Chromatography)4 Substrates, Unknown CandidatesGoals

- Use TLC mobility to observe the TLC behavior and rank the "TLC polarity" of the 4 reference substrates, from least polar to most polar. (Some may be essentially tied).
- Determine how each substrate can be visualized. Which are UV active, and which appear only when using a visualizing "dip"?
- Observe the dependence of TLC mobility on solvent polarity.
- Calculate R_f values
- Identify two unknowns by TLC.
- Learn general analytical TLC techniques.

Procedure

Work with a partner on this experiment. Each of you will need at least 4 TLC plates (two for each eluent). Each of you will identify two unknowns. Do not do the same unknowns as your partner.

Preparing the Plates:

1. Prepare the two plates for your first eluent: Use a pencil to mark 4 spots.
 - Give at least a 1 cm margin from the bottom. **Otherwise the sample may subsequently submerge, get dissolved away, and not get drawn up the plate.**
 - Avoid placing spots within 0.8 cm of the sides.
 - Use a pencil to mark placement of your original spots.
2. On plate 1, write **1, X** (the letter for your first unknown), **Y** (the letter for your second unknown) and **2**.
3. On plate 2, write **3, X** (the letter for your first unknown), **Y** (the letter for your second unknown) and **4**. (Both unknowns should be on each plate).
4. Then use the capillary tubes to apply your chemical solutions onto your TLC plates.
 - Spots should be neither too heavy nor too light (strong enough to be able to visualize, but **light enough to avoid overlap and chemical "tailing"**).
 - Before running your plates, check your second plate by UV. Biphenyl (**4**) should be easily visible. If not, your spot sizes may be too small. [Note: some spots are not very UV active, and may not appear. The point here is that if you don't even see #4, which is strongly visible, something is wrong. But don't worry if some of your spots show little or nothing by UV.]

To run the TLC's:

1. Place 3 full pipets of eluting solvent into a 50-mL beaker, and put a watch-glass on top to prevent solvent evaporation.
 - The eluent choices are 2% ethyl acetate/hexane, 10% ethyl acetate/hexane, and 20% ethyl acetate/hexane.
 - One partner should run both the 2% and 10% solutions. The other partner should run both the 10% and 20% solutions. (I want both of you to run 10% just to see how much scatter there is or isn't between two different scientists.)
 - You don't want to put in so much eluent that your spot will get submerged, in which case it will get dissolved away and not get drawn up the plate.
 - Ethyl acetate is an ester. The more ethyl acetate is present in the mixture, the more polar the eluent should be.
2. Carefully put your two TLC plate(s) into the beaker, and put the watch-glass back on top. The eluent will creep up the plate.
 - You can easily put both plates 1 and 2 in at the same time.
 - Avoid putting plates in crooked, or touching the walls.
 - You'd like the solvent line on the bottom to be level.
 - Note: the spots must not be submerged in solvent, or they will simply dissolve and not be drawn up the plate.
3. After the eluent has risen a significant distance, (it should **not** be allowed to get all the way to the top), remove the plate(s) and immediately mark with pencil the top distance that the eluent went.
 - If the solvent reaches the top, your sample can keep creeping up the plate and you will get falsely high R_f 's.
 - Note: It's important to keep the cover on your beaker. Otherwise evaporation competes with elution and you will get falsely high R_f 's.

Eluent choice: You will test two different solvent mixtures, as will your partner. One of you should run both the 2% and 10% ethyl acetate/hexane solvents; the other should run both the 10% and 20% ethyl acetate/hexane solvents. Since each of you will test two solvents, and for each solvent you will need 2 plates, that means each of you will be running 4 plates total.

Visualizing the spots:

1. Look at your plates under UV light, and circle with pencil the spots that you can see.
 - Spots may seem weaker than before; during the process the sample gets "stretched" out, so the signal intensity essentially gets diluted.
 - Not all samples will give UV spots.
2. After marking the UV active spots, take your plate to the "p-Anisaldehyde Dip" station. (Caution: 5% sulfuric acid!)
 - Dip your plate into the solution, using forceps
 - Try to let the excess liquid drain off
 - Then dry the plate with a heat gun.
3. Circle the new spots that appear, and record their color. (Some spots may differ in color, and the colors may have diagnostic value).

Calculate the R_f Values for All Your Spots: This will be the ratio of the distance traveled by your spot relative to the distance traveled by the solvent. You can qualitatively do this just by eye-ball analysis to get values to nearest tenth. (Ex. 0.1 vs 0.2 0.3 vs 0.4, etc.)

- Do not measure relative to the bottom of the plate. Measure relative to where the samples were applied. That's the starting line, because when the eluent climbs that far is when the race between eluent and sample to climb the plate begins.

Name: _____

Chromatography Lab Report

Part 1: Combiflash ChromatographyCombiflash band (1st big signal or the 2nd?...): _____

Identification of unknown (see Table): _____

Table 1: "Combiflash" Candidates:

<u>mw (g/mol)</u>	<u>Name</u>		<u>mw (g/mol)</u>	<u>Name</u>
106	Ethylbenzene		154	Biphenyl
108	Benzyl Alcohol		180	Stilbene
119	Benzotriazole		181	Methyl 3-nitrobenzoate
120	Acetophenone		184	Diphenylmethanol
134	Propriophenone		210	Benzil
135	Acetanilide		234	Dibenzylacetone
138	4-nitroaniline		244	Triphenylmethane
148	Butyrophenone		260	triphenylmethanol

Part 2: Column Chromatography Melting Ranges:

Nonpolar Ferrocene melting range: _____ Polar Acetylferrocene melting range: _____

Part 3: TLC1. Fill out the R_f data in the chart below for the two columns that you ran yourself (either first two, or last two).

- An eyeball estimate of R_f is satisfactory; one sig. fig. is probably appropriate (0.2, 0.3...)
- Remember that the R_f value for a spot will be fall somewhere from $0.0 \leq R_f \leq 1.0$, and is the ratio of the distance traveled by the spot (middle of the spot) relative to the distance traveled by the solvent, relative to where the spot began.
- Put a star above each of the two columns that you did yourself.
- Copy R_f data from partner and fill in those two columns.
- Note: You and your partner's R_f's may differ, but the relative ordering should be analogous.

2% Ethyl 10% Ethyl 10% Ethyl 20% Ethyl
Acetate/Hexane Acetate/Hexane Acetate/Hexane Acetate/Hexane

SubstrateR_fR_fR_fR_f

2,4-di-t-Butylphenol 1

Acetophenone 2

2-Methylcyclohexanol 3
(cis/trans, may give two spots)

Biphenyl 4

First Unknown

Second Unknown

2. Rank the observed polarity of the 4 samples **1-4**. In case of a close race, your eyes will be best for seeing which is a little faster. You may need to look at the results using more than just one eluent strength in order to be sure. Some might be too close together to tell with certain eluent strengths.

Most Polar: _____ > _____ > _____ > _____ Least Polar

3. Identify your two TLC Unknowns:

First Unknown: Letter _____ Identity _____

Second Unknown: Letter _____ Identity _____

4. Did increasing the polarity of your eluent increase or decrease your Rf's?
5. Given that the solid surface is polar, explain why polar **samples** have lower Rf values than less polar ones.
6. Explain why increasing **eluent** polarity increases the Rf value for a given sample?
7. In what order, from top to bottom, would you expect to see the spots for naphthalene (C₁₀H₈), butyric acid (CH₃CH₂CH₂CO₂H), and phenyl acetate (CH₃CO₂C₆H₅)? (May want to revisit the **Sample Polarity and Sample Movement** section of prelab to help with this.)

Top

Middle

Bottom

8. In what order, from top to bottom, would you expect to see the spots for the following: (May want to revisit the **Sample Polarity and Sample Movement** section of prelab to help with this.)
- acetic acid=CH₃CO₂H Top
 - butanal=CH₃CH₂CH₂CHO; 2nd
 - 2-octanone=CH₃COCH₂CH₂CH₂CH₂CH₂CH₃ 3rd
 - decane=C₁₀H₂₂; 4th
 - 1-butanol=CH₃CH₂CH₂CH₂OH Bottom
9. If an eluent of too low polarity is used for the development of a TLC plate, will the sample spots be somewhere in the middle, way at the bottom, or way at the top of the plate?
10. If an eluent of too high polarity is used for the development of a TLC plate, will the sample spots be somewhere in the middle, way at the bottom, or way at the top of the plate?

Basic GC-MS Operation Compressed Draft 3 For Chem 355 Organic Unknowns Lab

Note: The following assumes that the hydrogen and compressed air gases have been turned on; that the machine has been warmed up; that the gc/ms program has been opened; that an appropriate “method” and “sequence” have been selected; and that Jasperse will shut things down.

Sequenced Data Acquisition: Using the Autosampler to Sequence Runs Automatically

Note: this assumes that Jasperse has already prepared and started a “sequence” (“Grignard..” for example, but you are trying to add your sample to the lineup. If you’re first in line, get Jasperse to come and help.

1. **Add your sample to the back of the line in the autosampler.**
 - Do NOT leave any open holes (unless the sample belonging in that hole is being sampled.)
 - Filling a “sample-is-in-the-injector-tray” hole will cause a system freeze.
2. **Open “edit sequence” by clicking the “edit” icon on the yellow panel** low on the computer screen.
 - This will open a spreadsheet that you can edit.
 - Add your names in the “name” box that goes with your vial number.
 - **Click OK.** Note: if you don’t click “OK”, the machine will freeze at the end of the current run. NEVER leave the spreadsheet page open unless somebody behind you is going to close it.

Data Processing/Analysis: Getting and Printing the GC Graph, % Report, and/or Mass Spec.

- Note: data analysis can be done while acquisition is ongoing.
 - Note: this assumes that the “**gems data analysis**” software and appropriate analysis method are opened. In the data analysis page, check on the top blue line to see if it says “Enhanced data analysis-ADEFAULT-RTE.M...”, or “Grignards”, or something that fits the experiment for the week. If not, check with Jasperse or open it. (ex, Method > Load Method > Yes > ADefault-RTE.M > OK.)
3. **Open a data file** using the left mouse button to double click.
 - Your data file should be within the folder Organic Lab within the Data folder.
 - Data file will have the names “Vial-1” or “Vial-2”, so **remember which vial was yours.**
 4. **Printing GC Graph, % report, and retention times: Click Method>Run Method**
 - Repeat as many times as needed to provide prints for each student in your group.
 5. **Printing Mass Specs: Click the 2nd Hammer icon.**
 - Click the 2nd hammer icon as many times as needed to provide prints for each student in group.
 - Note: You don’t need to wait for a print to finish before clicking the hammer again. If you’ve got 5 partners, just click the hammer five times and the prints will come out one by one....

Background Distillation is a widely used technique for purifying liquids. The basic distillation process involves heating a liquid such that liquid molecules vaporize. The vapors produced are subsequently passed through a water-cooled condenser. Upon cooling, the vapor returns to its liquid phase. The liquid can then be collected.

The ability to separate mixtures of liquids depends on differences in volatility (the ability to vaporize). For separation to occur, the vapor that is condensed and collected must be more pure than the original liquid mix. Distillation can be used to remove a volatile solvent from a nonvolatile product; to separate a volatile product from nonvolatile impurities; or to separate two or more volatile products that have sufficiently different boiling points.

Vaporization and Boiling When a liquid is placed in a closed container, some of the molecules evaporate into any unoccupied space in the container. **Evaporation**, which occurs at temperatures below the boiling point of a compound, involves the transition from liquid to vapor of *only* those molecules at the liquid surface. Evaporation continues until an equilibrium is reached between molecules entering and leaving the liquid and vapor states. The pressure exerted by these gaseous molecules on the walls of the container is the **equilibrium vapor pressure**. The magnitude of this vapor pressure depends on the physical characteristics of the compound and increases as temperature increases. In an open container, equilibrium is never established, the vapor can simply leave, and the liquid eventually disappears. But whether in an open or closed situation, evaporation occurs only from the surface of the liquid.

If a liquid is heated to its boiling point, quite a different phenomenon occurs. The **boiling point is the temperature at which the vapor pressure of a liquid is equal to the external pressure** applied to the surface of the liquid. This external pressure is commonly atmospheric pressure. At the boiling point, bubbles of vapor are produced throughout the liquid, not just at the surface, and the vapor pressure inside the bubbles is sufficiently high to allow them to grow in size. The escape of these bubbles results in the characteristic chaotic motion of the liquid identified as **boiling**.

When a pure liquid boils, liquid is converted to vapor rapidly. Even if the heating rate increases, the temperature of the boiling liquid doesn't change, only the rate of vaporization. The energy supplied by heating is used by the liquid-vapor phase change.

Mixtures When a mixture of liquids is heated, the vapor pressure above the mixture equals the sum of the vapor pressures of the individual compounds. When their combined vapor pressures equal the external pressure, then boiling ensues just as for a pure liquid. However, the vapor above a mixture always has a different composition than the liquid mixture itself. The vapor above a liquid is always enriched in the more volatile component.

The table on the right shows the difference in composition between liquid and vapor for mixtures of cyclohexane (bp 80°C) and toluene (bp 110°C). Notice that a 50/50 liquid mix is 80/20 in the vapor, and a 75/25 liquid mixture provides vapor that is 90% cyclohexane. In all cases, the vapor is significantly enriched in the lower boiling cyclohexane.

The temperature column in the middle gives the boiling points for the liquid mixtures. Notice that the top is pure cyclohexane, and the bottom pure toluene. But for any mixture of the two, the boiling point is somewhere in between that of pure cyclohexane and pure toluene.

That the vapor is enriched in the more volatile component is the key to separating mixtures. In a distillation, liquid is vaporized, then the vapor is condensed. If the vapor above a mixture is pure, then a single vaporization/condensation provides pure product. This is often true, one component of the mixture is nonvolatile, or is very much less volatile than the other. For a single **simple distillation** to provide good separation, two liquids in a mixture should differ in boiling points by at least 100°C. But if you vaporize 50/50 cyclohexane/toluene and then condense the vapor, the condensate will still not be fully pure; it will be only 80% cyclohexane. Simple distillation would enrich cyclohexane, but would not provide pure cyclohexane.

Cyclohexane/ Toluene Liquid	Temp °C	Cyclohexane/ Toluene Vapor
100/0	80°	100/0
85/15	82°	95/5
75/25	84°	90/10
65/35	86°	88/12
58/42	88°	84/16
50/50	90°	80/20
44/56	92°	70/30
38/62	94°	64/36
32/68	96°	52/48
25/75	98°	46/54
21/79	100°	41/59
18/82	102°	37/63
12/88	104°	30/70
7/93	106°	20/80
3/97	108°	12/88
0/100	110°	0/100

Fractional Distillation But consider what might happen if you did a series of vaporization-concentration cycles on a cyclohexane/toluene mixture. If you start with a 50/50 liquid mix, the vapor will be 80/20. If you condense some of that 80/20 vapor, the vapor above an 80/20 liquid mix would in turn be over 90% pure. If you condense that vapor, you will have 93/7 liquid. But the vapor above that liquid will in turn be >98/2 pure in cyclohexane. If you then condense that vapor, the resulting condensate will be quite pure in cyclohexane. Thus by doing four distillations, you could have relatively pure cyclohexane.

This kind of sequence of multiple distillations is involved in a process called “**fractional distillation**”. A fractional distillation apparatus includes a column placed in between the boiling pot and the condenser. The fractionating column is filled with packing material with high surface area (typically glass beads or metal wire.) The vapors generated in the pot rise up the fractionating column and encounter cooler surfaces, upon which they condense. The condensed liquid is then reheated by rising hot vapors and reevaporize. This process of condensation and reevaporation may occur again and again as the vapors rise up the column. These composition changes are reflected by a *decrease* in boiling temperature as the mixture moves up the fractionating column. If the condensation-reevaporation is repeated a sufficient number of times, the vapors of the more volatile compound reach the top of the column in a pure form. As these vapors move into the condenser, the compound condenses and is collected as a purified liquid. SLOW DISTILLATION IS KEY!

Purification of the high-boiling component: As the more volatile component is being selectively removed, the residual liquid is increasingly enriched in the less volatile component. Thus, a separation of the two compounds is achieved.

However, as the more volatile compound is removed, and the composition of the residual liquid becomes enriched in the less volatile compound, the boiling temperature of the residual liquid also creeps up. If a cyclohexane/toluene mixture is originally 50/50, then the liquid boils at 91°C. But as the cyclohexane is removed, the boiling temperature of the liquid gets higher and higher. (And it gets harder to purify the lower-boiling fraction.) After a while, all of the low-boiling material is removed. At this point, the only material that can climb all the way up the fractionating column is the low boiling component, and you can distill it over as well. By changing collectors, you can thus isolate both the more volatile and less volatile components in reasonable purity. SLOW DISTILLATION IS KEY!

Technical Aspects for Fractional Distillation: SLOW DISTILLATION IS KEY!

- The fractionating column must be positioned vertically so that condensed liquid can percolate down through the rising hot vapors. This percolation promotes equilibration/heat exchange between the liquid and vapor phases, a condition that allows the column to operate at maximum efficiency and provide an optimum separation.
- A crucial factor is the distillation rate. In order to get the maximum number of vaporization/condensation cycles and maximum purification, fractional distillation must be conducted slowly. A one mL per minute rate (or slower) is recommended for best results in a fractional distillation; simple can go faster. Slow, gradual distillation essentially allows the best equilibration and heat transfer. If you heat too fast, vapors may not condense as quickly as desired, and may waste some of the column.
- Packing material is also crucial. High surface area packing material provides surface on which condensation can occur. The more easily vapor can condense, the more distillation cycles you get.

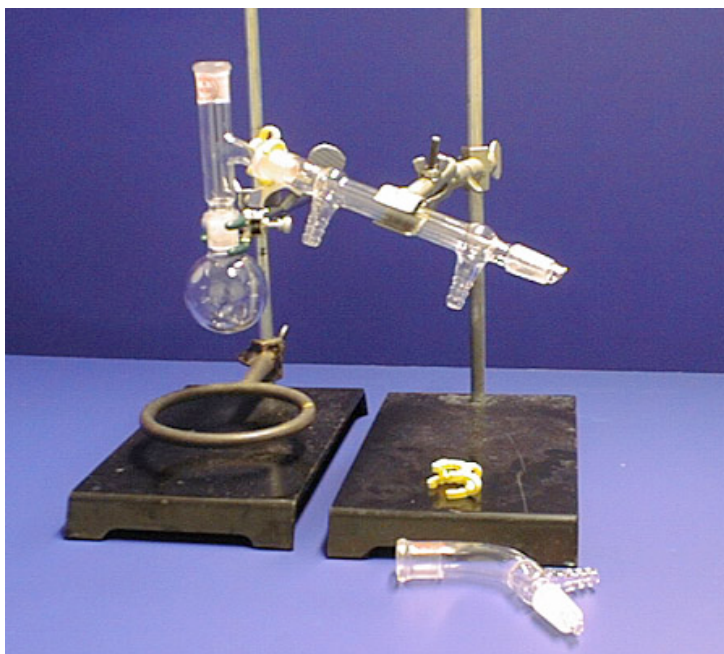
Miscellaneous SLOW DISTILLATION IS KEY!

- At reduced pressure, liquids boil at lower temperatures. (The external pressure is less, so it's easier to build up enough vapor pressure to escape.) High-boiling liquids are often distilled under vacuum.
- Simple distillation is useful when there are large differences in boiling point (>100°C.) Often organic solvents will be much more volatile than the target samples, so simple distillation is useful for rapid removal of the solvent. Simple distillation is faster than fractional. But fractional is much more powerful for more difficult separations.
- The temperature of the vapor is a direct reflection of it's composition.
- When the temperature of the vapor is changing, it's because the composition of the vapor is changing.
- The vapor temperature and composition of the vapor is almost constantly changing because the composition of the residual liquid is continuously getting depleted in the more volatile component.
- In a distillation curve, there will always be middle portion reflecting mixtures. For a typical purification, three separate collections would be made: the initial relatively horizontal portion (reflecting relatively pure volatile component); a middle portion which would be thrown away (reflecting mixtures not worth saving); and a subsequent relatively high-boiling horizontal portion (reflecting relatively pure less volatile component.)

Part I: Simple Distillation of Cyclohexane/Toluene

Setup:

1. Securely clamp a 100-mL round-bottomed flask to one of the vertical rods way at the left extreme of your hood. (Find flask in your kit).
 - The neck of the flask has a “lip”.
 - If you have a 3-fingered clamp, try to have all three fingers of the clamp completely below this fat lip, so that the “lip” has no chance of slipping through.
2. Add a 3-way connector (#10 in your kit map).
3. To the almost horizontal branch of the connector, attach a condensing tube (#12 in your kit map).
 - Use a blue Keck clip to hold the joints snug between the connector and the condensing tube.
 - Note: you do not need a Keck clip to connect the bottom flask to the 3-way connector; gravity will naturally hold the connector into the flask.
 - a. But, gravity will NOT naturally connect the condensing tube onto the connector!
 - b. In general, Keck clips are ONLY used when an attachment is angling downward and gravity might otherwise cause it to fall.
 - You don't need the metal clamp on the condenser that's shown in the picture. Skip it.
4. Set your hot plate on a jack, and place the jack and hotplate underneath your round-bottomed flask.
5. Plug the hot plate into one of the top two outlets.
 - Don't use either of the bottom two outlets.
6. Get out a 100-mL graduated cylinder, and place a liquid funnel into the top.
7. Raise the entire array high enough so that the 100-mL graduated cylinder fits underneath the end of the condensing tube to collect the distillate. Again, make sure your 100-mL flask, on which the rest of the array rests, is very securely clamped! It should be able to hold everything up even without the support of the hotplate.
8. Note: The picture shown isn't perfect. You don't need the ring underneath; your Keck clips will be blue, not yellow; and you don't need the extra clamp to secure the condensing tube.
9. Use rubber tubing to connect the a water tap (lowest green outlet at back of hood) to the lower end of condenser); a second hose should run from the higher of your condense and feed into drain in your hood.
 - **MAKE SURE THE SECOND HOSE IS FEEDING INTO THE DRAIN, AND IS NOT HOOKED UP TO THE VACUUM OR TO ANOTHER TAP OF ANY KIND. HAVE INSTRUCTOR DOUBLE-CHECK!**
10. Add 60 mL of 50/50 cyclohexane/toluene and 2-3 boiling chips to your flask. You can just drop in the chips, but you may wish to use your long-stemmed funnel to pour in the liquid.
11. To the open tube on top, add a thermometer. (There will probably be a setup display on a table.)
12. Adjust the position of the thermometer so that the alcohol liquid is just below the branch point of your array.
13. Try to have a lab instructor check your setup to make sure everything is good!



Doing the Distillation SLOW HEATING IS NOT CRUCIAL FOR SIMPLE DISTILLATION

1. Turn the condenser water on, but do so only very gently. All you need is enough flow to keep the water circulating and keep the condenser cold. You do not need to turn it on full blast like when you use the aspirator. Again, make sure this is draining into a sink!
2. Turn your hotplate setting to 10 to warm up the solution to the boiling point as fast as possible. Since this is a simple distillation anyway, you may as well distill it over pretty quickly.
3. Record your thermometer temperatures (which reflect the composition of the vapor that is actually distilling over at any point in time) at 2 mL intervals.
4. Continue the distillation until you have collected at least 50 mL of liquid..
5. Turn off the heater and lower the heating mantel away from the flask to allow cooling. Allow the flask to cool for a few minutes.

Part II: Fractional Distillation of Cyclohexane/Toluene**Setup**

6. Pour the liquid that you collected in Part I back into the round-bottomed flask.
7. Your setup for the fractional distillation will be very similar to what you did previously, except for the following changes:
 - You will insert a steel-wool packed distilling column (#13 in your kit map) in between your flask and your three-way connecting tube. (You do not need to clean out your condensing tube, you can use the exact same “top half” glassware from your previous setup, even if it is slightly contaminated by a little distillate. The only difference is that the steel-wool column is now added in.)
 - Because of the height of the fractionating column, you can probably rest your heating mantle on the bench top, or close to it, and still have enough height to fit your graduated cylinder to collect drops

Doing the Distillation. SLOW AND STEADY IS CRUCIAL

8. Proceed as above, with the following adjustments:
 - a. Set your hotplate power to ~7.5. (This may not be perfect for everybody, but is a good first guess.)
 - b. An ideal drop rate is one drop per second, and ≤ 1 mL per minute. If you are collecting more than 1 mL per minute, you're going too fast. It's especially important that the solution climb through the packing relatively slowly at the beginning.
 - c. This time record temperatures at 1-mL increments, beginning at 1-mL.
 - d. As the cyclohexane distills away, the composition in the residue will be continuously changing, and getting harder to boil. As a result, you may need to raise the setting on your hotplate to sustain a reasonable distillation rate, particularly as you approach 30 mL of collected liquid..
 - e. Continue the distillation until you have collected at least 40mL of product and the temperature has stabilized. (Discuss with instructor.)

Name:

Distillation Lab Report

1. Plot your **temperature (y-axis)** versus **mL collected (x-axis)**. **Plot both distillations on the same graph.** Since little of the action takes place near room temperature, **have the low end of your y-axis be 80°C, with a high end of your y-axis 112°C.** You may prepare your graph on computer with Excel, but I will also accept hand-drawn graphs or other graph procedures. (Graphing difficulty isn't the goal!). Either staple your graph to this sheet or else generate your graph on the other side of this sheet for handing in your lab report.
2. Why is the vertical change in the fractional distillation so much sharper than in the simple distillation? (In other words, why does it jump from say 85°C to 105°C over such a smaller number of mL with fractional than with simple distillation? And why does it wait longer to creep up over, say, 90°C?)
3. Give a brief discussion of how simple and fractional distillation differ. What is the difference? Why? When and why would you choose fractional distillation? Would there be any circumstances in which you'd choose simple distillation?
4. For the simple distillation, compare your vapor temperatures at 2 mL, 16 mL, and 30 mL. Why is the temperature different at these different times? Does the temperature also change like that in the fractional distillation?
5. Why is better separation of two liquids achieved by slow rather than fast distillation? (Particularly in the case of fractional distillation?)
6. Explain why a lot of packing material with a lot of surface area is helpful for an effective fractionating column? In our case, you had steel wool in your column. What would be worse if you didn't have the steel wool present?
7. What effect does doing a distillation under reduced pressure have? For a particular sample, will the boiling point be unchanged, go up, or go down if you try to distill it under a reduced pressure/vacuum type situation?
8. If you wanted to collect material that was >90% pure cyclohexane from your fractional distillation, which section would you save? (For example, the first 5 mL? First 10?) How about 95% or 80%? (Looking at the chart on the first page of the prelab is relevant!)
 - a. >90% pure:
 - b. >95% pure?
 - c. >80% pure?

I. Introduction to Spectroscopy Spectroscopy involves gaining information from the absorption, emission, or reflection of light from a sample. There are many other examples of spectroscopy in our experience, but three familiar real-life examples include:

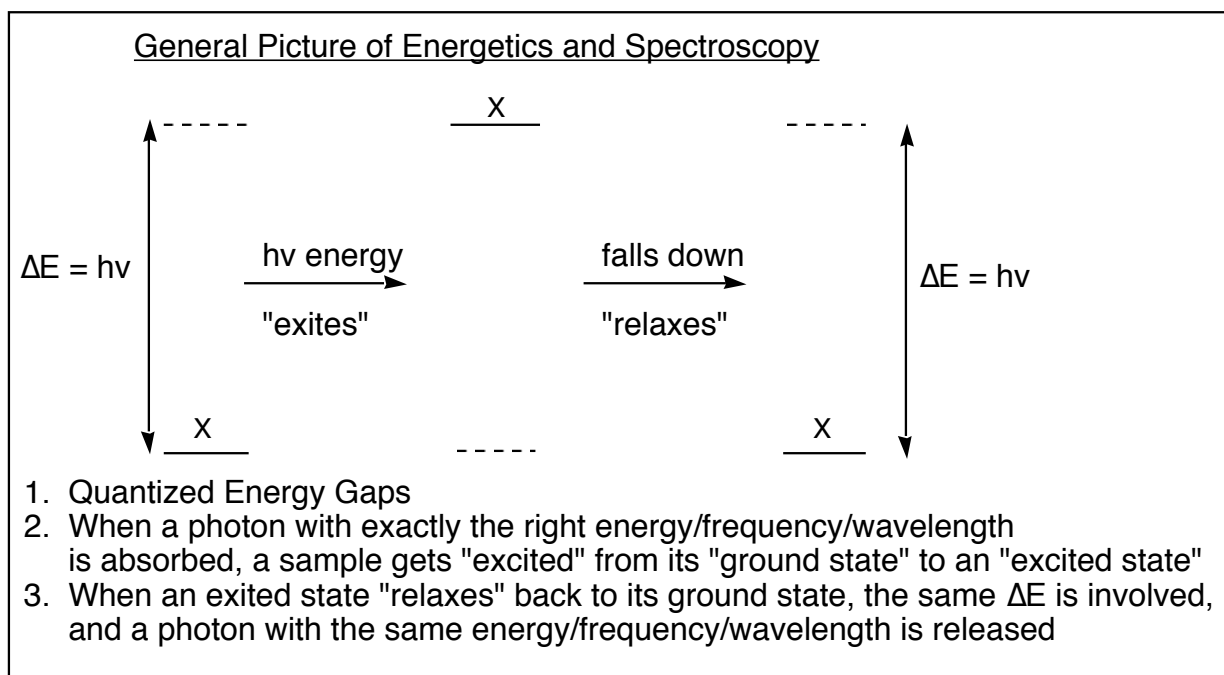
1. X-rays. Dense bone absorbs x-ray radiation.
2. Grocery store scanners. A monochromatic laser is either absorbed (black bar) or reflected (white bar). The simple black-or-white lines with their yes-or-no absorption-or-reflection response essentially produces a binary code, from which products and prices can be determined.
3. Stop lights. A lens is adjusted at timed intervals to enable emission of green, red, or yellow light.

In organic chemistry, the most important type of spectroscopy is "NMR" ("Nuclear Magnetic Resonance" spectroscopy). NMR spectroscopy is routinely used for chemical analysis, whether to identify the structure of an unknown, to assess the purity of a product, or to determine ratios of isomers. This week we will use carbon-13 NMR; later we will use hydrogen NMR. Both of these will be used later in the year, especially during second semester lab. During second semester lecture, we will revisit NMR and spend time and a test on interpretation of NMRs. Magnetic Resonance Imaging ("MRI") is an important hospital application of NMR. (The name was changed from NMR to MRI because some patients were afraid of the word "nuclear"!)

II. General Aspects of Spectroscopy Physics The fundamental principles of chemical spectroscopy are illustrated below. Spectroscopy involves having quantized energy levels. You are familiar with the concept of quantized energy levels for electrons (1s, 2s, 2p, 3s, 3d etc.) and electron spins (spin up or spin down), but other things are also quantized (vibrational energies, rotational energies...).

Given that there is an exact energy gap between two quantized energy states, a photon of precise energy must be absorbed in order to excite a molecule from the ground state. When an excited state relaxes back to the ground state, that same photon is released. By measuring the exact frequencies of photons that are either absorbed or emitted, we can measure ΔE . The quantity of photons can tell us about how much material is absorbing or emitting.

The chemist must then be able to interpret what the frequencies of the photons mean in terms of chemical structure.



III. NMR Physics

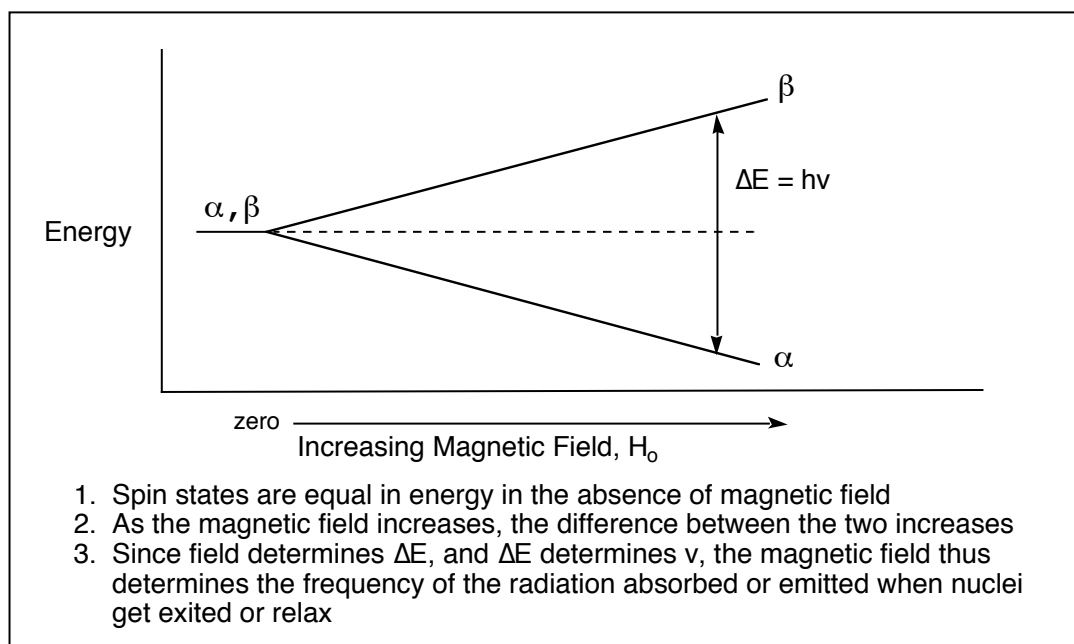
Certain nuclei (not all) have quantized “nuclear spins”. Being charged objects that spin, a result is that they are magnetic. (A circular flow of charge or electricity always produces a magnetic field, according to the “right hand rule” of electromagnetism.) Nuclei that have quantized spin states are referred to as “NMR active”. Just as electrons have quantized spin states (spin up or spin down), NMR-active nuclei also have quantized spin states, spin up or spin down.

Some NMR-active nuclei: H-1, C-13, N-15, F-19, P-31, Si-29, Se-79, Sn-119

Some NMR-inactive nuclei: C-12, N-14, O-16

The list of NMR inactive nuclei is somewhat unfortunate for organic chemistry! We are largely interested in the chemistry of carbon and the 2nd row elements, but unfortunately the dominant isotopes for carbon, nitrogen, and oxygen are all NMR inactive! Fortunately at least carbon-13 is active. Although only 1% of carbons are C-13, that’s still enough to give us useful information. Hydrogen is also NMR active, and can give us a lot of information (later...).

In the presence of an applied magnetic field, nuclear magnets can align with (spin down, \downarrow) or against (spin up, \uparrow) the field. The energy gap between these spin states is quantized, and depends on the strength of the magnetic field. (As with a bar magnet, the stronger the field, the greater the preference for the magnet to line up correctly...). To “excite” a nucleus from the more stable \downarrow state to the less stable \uparrow state, radiation with the correct photon frequency is required. When an excited nucleus relaxes back to the \downarrow state, a photon with that same frequency is emitted. Since magnetic field strength determines ΔE , and ΔE determines ν , the magnetic field thus determines the frequency of the radiation absorbed or emitted.



When an external magnetic field is applied, will all nuclei have the same ΔE and the same photon frequency? No!

1. Different nuclei (H-1 versus C-13) have very different ΔE . Thus an MRI can easily identify whether a particular nuclei is or is not present.
2. In different chemical environments, the same nucleus will have different ΔE .

The second point is the key to ¹³C NMR. Although the external magnetic field (applied by the spectrometer) may be the same, different carbons in a molecule experience or “feel” difference magnetic fields. This is due to the magnetic fields produced by local electrons and by other nuclei (because moving electrons function as “electron magnets” and moving nuclei function as “nuclear magnets”). The magnetic influence of local electrons and nuclei can reinforce or partially counteract the external field, so that every different carbon “feels” a different H_{actual} . (H = magnetic field)

$$H_{\text{actual}} = H_{\text{applied}} + H_{\text{electrons}} + H_{\text{nuclei}} \quad H_{\text{actual}} \propto \Delta E \propto \nu$$

IV. The Actual Experiment

The actual steps in the experiment include:

1. Prepare the sample. For C-13, put 0.2 mL of sample into your NMR tube. Add 0.8mL of CDCl₃. (Less is appropriate for H-NMR.)
2. Insert the sample into the magnetic field. (We'll use robotics for this.)
3. "Lock" the magnetic field. (So it doesn't drift.)
4. "Shim" the applied magnetic field. (Make it as consistent as possible in the observation window, from top to bottom, front to back, left to right.)
5. Blast the sample with radiation to excite the nuclei. Rather than dialing through the different frequencies, a broad range of frequencies is applied so that all the carbon nuclei can get excited at the same time. After briefly blasting, the radiation is turned off.
6. Detect/listen to the signals (actually in the radio frequency!) as the excited nuclei relax and release photons. (Many different signals with different frequencies are released simultaneously, each with it's own wavelength...)
7. Repeat the irradiate-then-detect sequence repeatedly to build up the weak signal.
8. "Fourier Transform" (mathematical operation) to deconvolute the complex signal pattern resulting from the many overlapping frequencies. The Fourier Transform enables the computer to identify all the individual photon frequencies that summed up to give the total signal. An imperfect analogy would be to have every possible radio station broadcasting at the same time; then the Fourier Transform would essentially be able to identify and pick out each station one at a time and make sense of it.

Note: Many of these operations are best done by a computer. (The Fourier Transform especially!) Each of these steps also involves a number of software commands. So that you can acquire data and focus on chemical interpretation of the data, rather than being totally distracted by learning a lot of software commands, many steps have been automated and programmed for you.

V. Interpreting C-13 NMR

While the physics of what happens is interesting, for the most part you the chemist will be engaged in interpreting the data that comes out at the end. This is true for the use of many instruments in science and health care. You need to learn some basic operational skills so that you can use the instrument safely and accurately. But being able to interpret the data is really what you need to be able to do at the end.

We will run three types of C-13 NMR's this week. The first, called "decoupled" C-13 NMR, will show a unique line for each type of carbon present. The second, called "DEPT" (Distortionless Enhancement by Polarization Transfer) will differentiate CH₂ carbons ("evens") from CH and CH₃ carbons ("odds"), and will not include carbons that don't carry any hydrogens. The third, called "coupled" C-13 NMR, will "split" the decouple carbon lines into doubles (for CH), triplets (for CH₂), or quartets (for CH₃). The three

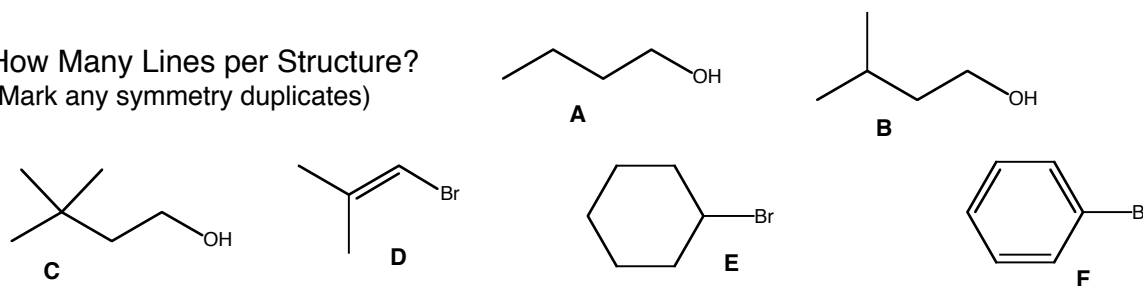
Decoupled C-13 NMR**Summary of Decoupled C-13 NMR Interpretation:**

1. **Count how many lines** you have. **This will tell you how many types of carbons** you have. (Symmetry equivalent carbons can at times cause the number of lines to be less than the number of carbons in your structure.)
2. **Check diagnostic frequency windows** ("chemical shift windows") of the lines **to provide yes-or-no answers regarding the presence or absence of key functional groups** in your molecule.

1. Number of Lines and Number of Symmetry-Unique Carbons

- a. Each "unique" carbon gives a separate line.
 - This is due to having different electronic environments, and because spinning electrons create magnetic fields that counteract or reinforce the applied field.
- b. Symmetry duplicates give the same line.
 - If due to molecular symmetry two carbons have exactly the same chemical environment, naturally they will absorb and emit exactly the same photon frequency, and give exactly the same line in the spectrum.

How Many Lines per Structure?
(Mark any symmetry duplicates)



2. **“Chemical Shifts” of the Lines** (This reflects the energies or photon frequencies/wavelengths associated with the lines.)

220-160	C=O carbonyl carbons, sp^2 hybridized
160-100	C alkene or aromatic carbons, sp^2 hybridized
100-50	C-O oxygen-bearing carbons, single bonds only, sp^3 hybridized
50-0	C alkyl carbons, no oxygens attached, sp^3 hybridized

- Notice that sp^2 hybridized carbons come above 100, sp^3 hybridized come below
- Notice that oxygenated carbons come higher than non-oxygenated analogs. An sp^3 -hybridized carbon with an oxygen comes higher than without, just as an sp^2 -hybridized carbon comes higher with oxygen than without
- How do I process and use what I see from my Chemical Shifts?**
 - Check each of the four zones. Each one gives you a yes or no answer about the presence of absence of the featured group.**
 - Check 220-160. Do I have any carbonyl carbons or not? Easy yes or no question.
 - Check 160-100. Do I have any alkene/aromatic carbons? Yes or no! If I do, then how many? If I have two, I probably have an alkene! If I have four to six, I probably have a benzene!
 - Check 100-50. Do I have an oxygenated sp^3 carbon? Yes or no! Alcohols and esters will normally have one carbon in the 100-50 zone. Ethers will have two.
 - Check 50-0. I'll almost always have some lines there! But how many should tell me how many types of non-oxygenated sp^3 carbons I have.

Using Chemical Shifts to Identify Functional Groups in Simple Molecules:

- An alcohol should show one carbon in the 50-100 zone.
- A ketone should show one carbon in the 160-220 zone.
- An ester should show one carbon in each of the 50-100 and the 160-220 zones.
- An aromatic should show at least four different carbons in the 100-160 zone.

3. **Signal Height/Size** Two tips:
- Carbons without attached H's are short. This is common for carbonyls and for substituted carbons in a benzene ring.
 - Symmetry duplication amplifies signal height. (If you have two copies of a carbon, the line will probably be taller than normal!)
4. **Subtracting the Solvent Lines: Don't Count the 3-Line Triplet at 77** Our samples are routinely diluted with $CDCl_3$, which has a carbon and thus gives a signal. Usually lots more solvent gets used than solute, so potentially the solvent lines could dominate. Fortunately deuterated carbons give a different look: $CDCl_3$ will give a 3-line “triplet” signal at 77. Ignore this signal! Don't count it as three more unique carbons in your molecule! Don't conclude that you have three oxygenated sp^3 carbons!

5. **How do I know what's a real line, from a carbon in my compound from an impurity that I should ignore?** No simple way! With experience or some advanced experiments you can often tell, but there is no automatic way to know. For today, **if in doubt ask the instructor!** The instructor will confirm which lines you should or shouldn't consider in doing your analysis

Practical Use of Decoupled C13 NMR:

- How many lines/carbons do I have?
- How many are carbonyls (160-220), how many are aromatic (100-160), how many are oxygenated (50-100), and how many are non-oxygenated (0-50)?
- Do the chemical shifts suggest ketone, ester, aromatic, or alcohol?

DEPT NMR: Distinguishing C and CH₂ carbons from CH and CH₃ carbons.

The DEPT experiment is done in conjunction with a decoupled C-13 NMR. While more elaborate and even more informative versions of DEPT are available, at the cost of extra time, this week we will use a basic version (called DEPT 135).

Use the following DEPT clues:

- **CH₂ carbon lines will usually point down**
- CH and CH₃ carbon lines will usually point up
- Carbons with no directly attached hydrogens will not appear.

Practical: Look at your decoupled C13 spectrum beside your DEPT spectrum.

- Which carbons are “quaternary” carbons? (the ones with no hydrogens vanish from your DEPT spectrum.
 - These are usually carbonyls or substituted aromatic carbons.
- Which carbons are CH₂ carbons?
 - Are any of these oxygenated? (in the 50-100 zone)?
- How many CH/CH₃ carbons do you have, and in which zones?

Coupled C-13 NMR

Whereas “decoupled” C-13 NMR spectra show nice sharp singlet lines for each type of carbon, “coupled” C-13 spectra show the following:

- CH₃: four lines (“quartet”)
- CH₂: three lines (“triplet”)
- CH: two lines (“doublet”)
- C (no hydrogens): one line (“singlet”)

The information is complementary to DEPT information in that both help to differentiate among different carbons.

Coupled C-13 is not used real often in the real world for at least two reasons:

- Signal to noise: The signal to noise is a lot worse than in decoupled C-13 or DEPT NMR, and the cost of improving the signal-to-noise is taking more time.
- Overlap: With coupled C-13 NMR, there are a lot more lines, and overlapping of lines becomes normal and confusing for non- simple molecules.

Practical: Use the coupled carbon can **differentiate CH₃ from CH carbons**

C13-NMR Interpretation

- Count how many lines** you have. **This will tell you how many types of carbons** you have. (Symmetry equivalent carbons can at times cause the number of lines to be less than the number of carbons in your structure.)
 - Each “unique” carbon gives a separate line.
 - Symmetry duplicates give the same line.
 - If there are more carbons in your formula than there are lines in your spectrum, it means you have symmetry.
- Check diagnostic frequency windows** (“chemical shift windows”) of the lines **to provide yes-or-no answers regarding the presence or absence of key functional groups** in your molecule.

220-160 C=O carbonyl carbons, sp² hybridized

160-100 C alkene or aromatic carbons, sp² hybridized

100-50 C-O oxygen-bearing carbons, single bonds only, sp³ hybridized

50-0 C alkyl carbons, no oxygens attached, sp³ hybridized

- Use DEPT and/or Couple C13 NMR to Differentiate C, CH, CH2, and CH3 carbons.**

<u>Type of C</u>	<u>Name</u>	<u>DEPT-135</u>	<u>Coupled C13</u>
CH ₃	Methyl	Up	Quartert (q)
CH ₂	Methylene	Down	Triplet (t)
CH	Methane	Up	Doublet (d)
C (no attached hydrogens)	Quaternary	Absent	Singlet (s)

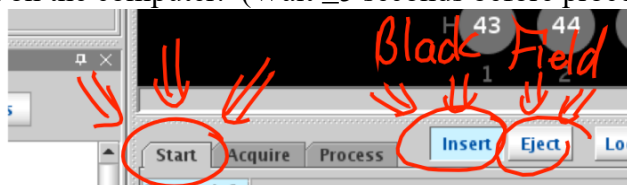
- Aromatics, Symmetry, and C-13 Signals.** Most aromatics have symmetry, and both the number of aromatic lines and the splitting of the aromatic lines can be indicative of the substitution pattern on a benzene. Mono- and para-disubstituted benzenes have symmetry.

4 lines	s, d, d, d	Monosubstituted benzene. (Has symmetry)
4 lines	s, s, d, d	Para-disubstituted benzene. (Has symmetry)
6 lines	s, s, d, d, d, d	Ortho- or meta-disubstituted benzene. (Has no symmetry)

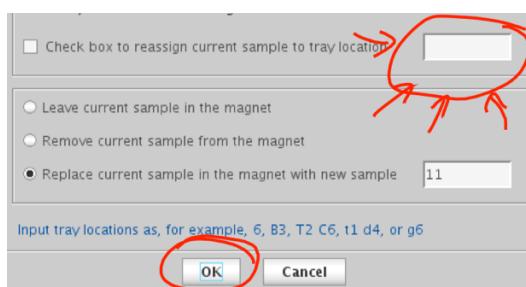
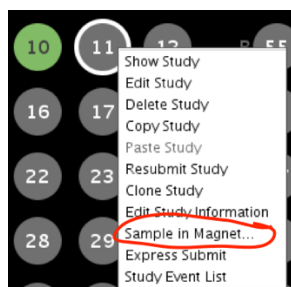
- Signal Height/Size**
 - Carbons without any attached H’s are short. This is common for carbonyls (aldehydes are the only carbonyl carbons that have hydrogens attached) and for substituted carbons in a benzene ring.
 - Symmetry duplication multiplies signal height (if you have two copies of a carbon, the line will probably be taller than normal!)

User's Guide to NMR, 2024 Without Autosampler: Draft 2/1/2024. Help: Dr. Jasperse, Hagen 407J, 477-2230

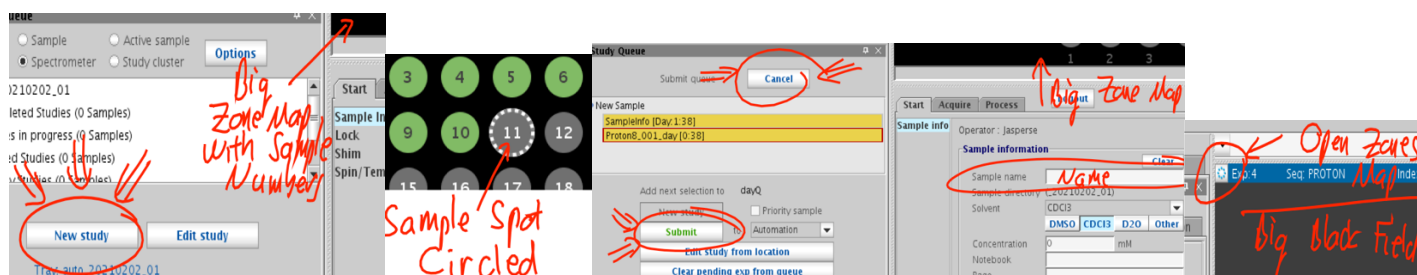
1. **Prepare sample** in lab; **add sample to sample-holder**; adjust sample depth using **golden depth finder**
2. **Eject/Insert** (Sample Exchange):
 - a. Hit "**eject**" button (below black field) to eject existing sample. (If not visible, click "start" button to make it so)
 - b. **Manually lift out sample-in-sample-holder** combination from the probe (place it in a box)
 - c. **Place your sample-in-sample-holder** into the probe
 - d. Hit "**insert**" button on the computer. (Wait ≥ 5 seconds before proceeding with step 3a).



3. **Spot Assignment:** (Each sample needs to be assigned a sample spot number)
 - a. **Right-click** on the lowest-numbered gray spot number in the zones map. (A pulldown will appear)
 - b. Select "**Sample in Magnet**" (3rd line from the bottom of the pulldown);
 - c. **Enter your spot number** into the upper field. (Remember your spot number)
 - d. Hit **OK**.



4. **NMR-Experiment Submission:**
 - a. Click "**New Study**" button in lower left. (A yellow experiment file-name will appear).
 - b. The default experiment is "Proton-8"; for something different select from panel on upper left.
 - c. **Left-mouse single-click on your sample spot**. (A white circle will appear around the sample spot)
 - d. Enter student name(s) into **Sample Name** field, which is underneath the black field
 - e. Submit: click the **green "Submit"** button on the lower left side. (your sample spot should turn color)
 - f. Hit "**Cancel**" to leave submit-sample mode.
 - a. Don't forget to do this. If you do, it will cause problems for both you and the ensuing user.
 - b. The yellow experiment file-name will disappear; unfortunately the zones map will too.
 - g. Re-open "zones" map: **Click on little circle icon** (⚙️) to the upper left of the big gray/black panel, and the zones map with all the sample spot numbers should re-open.
 - a. Note: An experiment should take about 7 minutes.
 - b. There should be an automatic one-page printout upon completion.



5. **Printing an extra copy** of spectrum (in case you have a partner)
- Must be in zones-map display. If not, click on little circle icon (⚙️) upper left of the spectra-display panel.
 - a. **Right click on sample number**, and a pulldown will appear
 - b. Click “Show Study”
 - c. **Double click on green “PROTON_01”** file that will appear in the lower left-hand area. (below your name)
 - c. Your spectrum should now appear in the display field, where the zones-map appeared before
 - d. Click “Process” button underneath the spectrum display field. (“Start” was highlighted previously)
 - e. Click blue-text-on-white-background “Print” button on lower right to print another copy.



6. Horizontal Expansions

- a. Steps 5a-d above describe how to get your spectrum loaded into the display field.
- b. With spectrum displayed on screen, use a panel of display icons on the far upper right
- c. Click on the **magnifying glass icon (6th icon down, 🔍)**
- d. Move your cursor to the left end of the zone you want to expand, then **hold down left mouse button and slide it** to the other end of the zone you want to expand, then release the button.
- a. To return to the full display, you can either click on the 3rd icon (⏏️) or the 5th icon (🔍).
- e. Click blue-text-on-white-background “Print” button on lower right to print a copy. (Twice for 2 copies)



7. Exiting so that NMR is Ready for the Next user

- a. Click “Start” button underneath the spectrum display field. (“Process” was highlighted previously)
- b. Re-open “zones” map: **Click on little circle icon (⚙️)** to the upper left of the big gray/black panel, and the zones map with all the sample spot numbers should re-open.



General:

1. Each pair of students (or individual if working alone), should prepare and run one unknown samples.
2. Each will also be given printouts for a second sample.
3. You will interpret and identify both samples, the one you ran yourself and the one you were given.
 - You can solve the “given” spectrum while you’re waiting your turn on the NMR.
4. You will also complete the “Prediction Page” (probably two pages after this page.)
 - You can work on the “prediction” page while waiting your turn on the NMR.
 - So, time-wise, you should be able to use your time well whether you are first or last in line for using the NMR. ☺

Prepare the sample

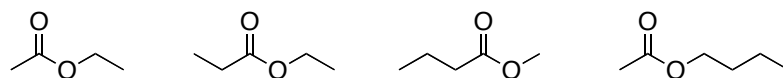
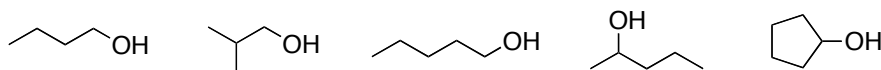
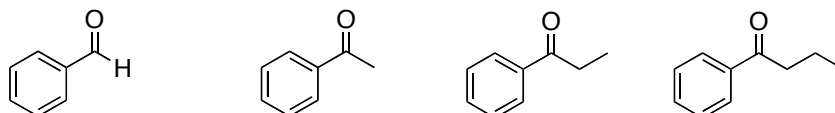
1. Put 0.2 mL of sample into an NMR tube.
 - The exact loading volume is not critical.
2. Then add 0.8 mL of CDCl₃ solvent. Again, the exact volume is not critical.
3. Put a cap on the sample.

Load and Run the Samples, and Print the Results: See the NMR Usage Instructions.

- For this week, you will run the sequence of experiment called C-DEPT
- You will need to click/select that at stage 4b of the usage guide.

Printing note:

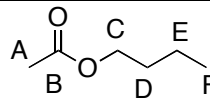
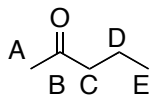
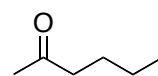
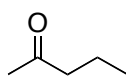
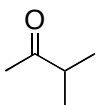
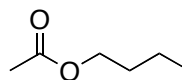
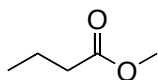
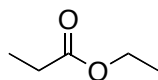
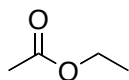
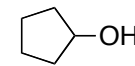
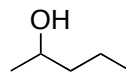
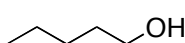
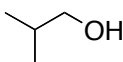
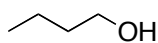
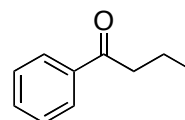
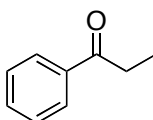
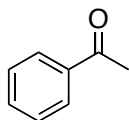
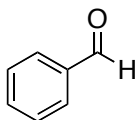
- The instrument can auto-print the three spectra, but you will also want to print copies for your partner.
- A copy machine could be used to do this, or
- The prints could be done from the NMR, see the NMR Usage Instructions

Unknown CandidatesSimple KetonesEstersAlcoholsAromatic Carbonyls

C-13 NMR Lab Handin**Name**

For each of the two unknowns that you will analyze, hand in the following:

- For each of the 15 unknown candidates shown on the next page, (“Prediction Page”), predict how many carbons you’d get for each box. Hand in this page.
- Attach the six NMR’s that you should have printed. These should be:
 - The decoupled C13 NMR for your sample that you ran with your partner.
 - The DEPT spectrum for your sample that you ran with your partner.
 - The coupled C13 NMR for your sample that you ran with your partner.
 - The decoupled C13 NMR for the sample that was given to you.
 - The DEPT spectrum for the sample that was given to you.
 - The coupled C13 NMR for the sample that was given to you.
- Directly on each the two decoupled NMR’s, write down which unknown it was. (“Unknown A”, “Unknown B”....).
- Then draw the chemical structure for each of the two unknown, again directly on the decoupled NMRs.
- Write a letter by each of the carbons in your structures (see examples below)
- Next to each carbon line in the decoupled NMR, assign the letter of the carbon that best fits.
 - Note: in some cases there will be ambiguity. So for example, you might have two lines in the same zone and write “C or D” by each of them, for example.

Example of drawing molecules and then Lettering each of the Carbons**Unknown Candidates**Simple KetonesEstersAlcoholsAromatic Carbonyls

Introduction to 1H-NMR Spectroscopy Hydrogen NMR interpretation is more complex than ^{13}C -NMR, but provides extra information that is unavailable from carbon NMR. In interpreting carbon NMR, we focused on how many unique carbon lines were present, and where they were located (chemical shifts). In hydrogen NMR, but two additional factors, “integration” and “splitting”, are useful.

The four facets of 1H NMR spectroscopy:

1. Number of signal sets => the number of symmetry-unique hydrogens
2. Chemical shifts => chemical environment/hybridization/functional groups
3. Integration => how many hydrogen atoms cause a signal.
 - 3H => CH_3 group (or 2H and 1H groups superimposed)
 - 2H => CH_2 group (or two nonequivalent 1H groups superimposed)
 - 1H => CH or OH group
4. Splitting => information about how many H's are connected to adjacent carbons
 - N lines => N-1 “neighbor” H's (when working from spectrum to structure)
 - N neighbors => N+1 lines (when you know what a structure is, and you're trying to predict what it's spectrum should look like)

Summary of Steps in 1H NMR Interpretation: (Not all will be needed to get Answers Today)

1. **Count how many signal sets** you have. **This will tell you how many types of hydrogen-bearing carbons** you have.
 - Hydrogens attached to symmetry-equivalent carbons will give equivalent signals
2. **Check diagnostic “chemical shift” windows** of the lines **to provide yes-or-no answers regarding the presence or absence of key functional groups** in your molecule.
3. Check the integration of each signal set.
 - 3H => CH_3 group 2H => CH_2 group 1H => CH or OH group
4. Check the splitting of each signal set.
 - For a signal set with N lines => N-1 hydrogens will be attached to carbons directly connected to the carbon of the signal set

I. Number of Signal Sets

1. Nonequivalent H's have different chemical environments and give different signals
2. Symmetry-equivalent H's have the same chemical environment and give the same signal
 - The number of signal sets tells you how many different types of hydrogens are present
3. On an **achiral** molecule (alkenes excepted), hydrogens on a given carbon will be equivalent.
 - all three H's on a CH_3 group
 - both H's on a CH_2 group
4. The number of signal sets may sometimes differ from the number of carbons:
 - a. Symmetry equivalent carbons and hydrogens
 - b. Hydrogen-free Carbons: No attached H, no H signal! (Carbonyl carbons rarely have H's...)
 - c. OH Groups: OH as well as CH's give hydrogen signals
 - d. CH_2 H's are NONEQUIVALENT in “Cis/Trans” Situations:
 - In **Alkenes**, or when there is a **chiral center** in the molecule.
5. Strategy Keys:
 - a. If possible, determine how many signal sets you have in a spectrum. (Useful when working from spectrum to structure).
 - b. For a particular structure, determine how many signal sets you should have. (Useful when matching unknown candidate structures with actual spectra, as in today's lab.)
 - c. **End-Check: Check that the number of signal sets in your spectrum matches with the structure you believe you actually have! If not, structure needs correction!**
 - d. **Beware of overlaps!**

II. “Chemical Shifts” of the Signal Sets

7's (6.5-8.4)	<u>Aromatic</u> sp ² hybridized C-H's
3's (3.3-4.5)	<u>Oxygenated</u> sp ³ hybridized C-H's (halogenated and nitrogenated alkyl C-H's will also come in this window, although no candidates for today's lab). Oxygenated sp ³ -carbons are routinely present for the following functional groups that contain oxygen single bonds: <ul style="list-style-type: none"> • <u>alcohols</u>, • <u>ethers</u>, or • <u>esters</u>
2's (1.8-3.1)	<u>Allylic</u> sp ³ hybridized C-H's (sp ³ hybridized C-H's that has a double bond attached to the sp ³ hybridized C). Allylic signals routinely appear when one of the following double-bonded functional groups is present: <ul style="list-style-type: none"> • <u>carbonyls</u>, (ketones, esters, aldehydes, acids, amides) • <u>alkenes</u>, or • <u>aromatics</u>
1's (0.7-1.9)	sp ³ hybridized C-H's, with <u>no attached Functional Groups</u> <ul style="list-style-type: none"> • <u>Note:</u> Many molecules with non-functional alkyl portions will give a lot of signal in this area.
0-5 (anywhere!) (normally 1.5-3.5 range)	<u>Alcohol</u> O-H hydrogens

How do I process and use what I see from my Chemical Shifts?

- 1. Check each of the zones. Each one gives you a yes or no answer about the presence of absence of the featured group.**
 - Do I have something in the 7's? (Other than a solvent singlet...)? If yes => aromatic
 - Do I have something in the 3's? If yes => alcohol, ether, or ester
 - Do I have something in the 2's? If yes => ketone, aromatic, or ester
 - Do I have something in the 1's? If yes => some nonfunctional alkyl carbons (or OH)
- 2. Use the three functional-group chemical shift zones to determine which functional-group family you've got. (See page with the unknown candidates).**
 - Combined with knowing how many unique carbons exist for each unknown, functional-group ID combined with #-of-unique-carbons gets you a long way to matching your unknown to one of the candidates. Probably only one or two candidates will fit.
- 3. End-Check: Check that the functional groups indicated by your chemical shift information match with the structure you believe you actually have! If not, structure needs correction!**

Miscellaneous Chemical Shifts Notes

1. Approximate 1's, 2's, 3's, and 7's and spillover: The regions are somewhat approximate, and have some spillover. But it's still useful to basically talk about the "1's", "2's", "3's", etc. to discuss the major windows. Even though something might actually come at 4.2, it's still useful to refer to that as appearing in the "3's" group and make conclusions accordingly. I'll still refer to something as coming in the "1's" group even if it comes at 0.8.
2. Hybridization: sp^2 hybridized C-H's come above 5, sp^3 hybridized C-H's come below
3. Oxygenated C-H's come higher than non-oxygenated analogs.
4. OH's are wildcards because they can come anywhere, and can cause confusion.

III. Integration Unlike in carbon NMR, the sizes of H-NMR signal sets are very useful and informative.

1. The signal area ("integral") is proportional to the number of hydrogens causing the signal.
 $CH_3 \Rightarrow 3H$ $CH_2 \Rightarrow 2H$ $CH \text{ or } OH \Rightarrow 1H$
2. The key is not the signal height, but rather the signal **area**.
 - The signal **area** is measured by "integration lines". Differentiate integration marks, and what they mean, from signal lines themselves.
3. Relative areas correlate ratios of H's. **Convert to simple whole-number ratios** (and round off freely).

1:1 \Rightarrow CH ₂ to CH ₂ , or CH ₃ to CH ₃	1.5:1 \Rightarrow 3H:2H (CH ₃ to CH ₂)
2:1 \Rightarrow 2H:1H (CH ₂ to OH)	5:2 \Rightarrow 5H:2H (C ₆ H ₅ to CH ₂ , common with aromatics)
3:1 \Rightarrow 3H:1H (CH ₃ to OH)	6:1 \Rightarrow Common with isopropyls, CH(CH ₃) ₂
4. Clean sets involving equivalent H's give clean, symmetric signal sets:
 - a. 1H \Rightarrow CH or OH
 - b. 2H \Rightarrow CH₂
 - c. 3H \Rightarrow CH₃
 - d. 6H \Rightarrow 2 equivalent CH₃ groups
5. Unsymmetrical messy sets involving overlapping signal sets. (these will routinely not look nice and symmetric...)
 - a. 3H \Rightarrow OH overlapping a CH₂
 - b. 4H \Rightarrow two overlapping but not exactly equivalent CH₂ groups; or a CH₃ overlapping an OH or CH
 - c. 5H \Rightarrow common in the 7's, for 5 overlapping arene H's; also common in the 1's, when a CH₃ and CH₂ overlap

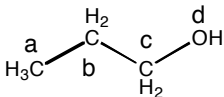
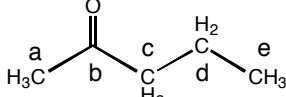
How do I process and use what I see from my Integrations?

1. Distinguish "Clean" Signal Sets from Overlapping Signal Sets
 - o Clean ones look symmetric, overlapping sets do not
2. **For the Clean sets, the integration tells you what kind of group you have**
 - a. 1H \Rightarrow CH or OH (methine or hydroxyl group)
 - b. 2H \Rightarrow CH₂ (methylene group)
 - or 2 symmetry-equivalent arene H's, if the 2H is in the 7's
 - c. 3H \Rightarrow CH₃ (methyl group)
 - d. 6H \Rightarrow 2 equivalent CH₃ groups
3. **End-Check: Check that the "groups" your integration shows match with the structure you believe you actually have! If not, your structure needs to be corrected!**

IV. Splitting Hydrogen signals are routinely split into multiple lines. The number of lines in a signal set tell us nothing about “the signal” C-H’s themselves that cause the signal (whether it’s a CH₃ or CH₂ group, or whether it’s allylic or oxygenated...). But the splitting tells us something else that is really useful: what kind of CH groups are attached to the group of interest! It provides great information about “neighbor groups” and helps explain how the components of an organic molecule are sequenced.

Rules of “Splitting”

- **N-1 Rule:** **N lines =>N-1 neighbor H’s** (H’s directly attached to carbons attached to the signal C-H group causing the signal)
 - The N-1 Rule is useful when working from spectrum to actual structure
 - **N+1 Rule:** **N neighbor H’s =>N+1 lines**
 - The N+1 Rule is useful when working from structure to actual spectrum
1. OH hydrogens don’t participate in splitting ~75% of the time. About 25% of time they do.
 2. C-H hydrogens participate in splitting (always)
 3. For today’s labs and for simple molecules, the N-1/N+1 rules are good. The rules actually work only if the neighbor H’s are equivalent. The rule can break down when some of the neighbor H’s differ significantly from each other
 4. Splitting from H’s further distant than neighbor carbons sometimes occurs, but usually the amount of splitting is too small to worry about
 5. Physics Origin: hydrogens are quantized little magnets. Neighbor hydrogen magnets can align so as to either reinforce (spin up) or counteract (spin down) the external magnetic field

N+1 Rule (Given structure, how many lines a spectrum should give)					
					
Neighbors	2	3+2	2	0	Neighbors
Lines	3	6	3	1	Lines
(Notice: OH doesn't split...)					
N-1 Rule (Given spectrum, how many neighbors a structure should have)					
	Lines	1 (s)inglet		Lines	2 (d)oublet
	Neighbors	0		Neighbors	1
	Lines	3 (t)riplet		Lines	4 (q)uartet
	Neighbors	2		Neighbors	3
etc.					

6. Splitting nicknames:
 - 1 line =>singlet (s) 2 lines =>doublet (d) 3 lines =>triplet (t)
 - 4 lines =>quartet (q) 5 lines =>pentet (p) >5 lines =>multiplet (m)

How do I process and use what I see from my Splitting?

1. Use **integration** for a given signal to determine if your signal set is a CH₃, CH₂, or CH group
2. Then use the number of lines in the signal set and the N-1 Rule to see how many hydrogens must be present on neighboring carbons that are attached to your signal set
3. **End-Check:** **Check that the structure you believe you actually have would give the splitting you are actually seeing in your spectrum. If not, your structure needs to be corrected!**

V. Standard Summary Report and/or Prediction Formats There is a standard summary report format for H-NMR's which addresses chemical shift, integration, splitting, and the source hydrogens.

Ex: $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{C}(\text{O})\text{CH}_3$ (I'll number the carbons from left to right...)

Summary Report Format

Shift	Int	#lines(split)	Source
3.79	2H	3 (t)	(CH2-2)
3.48	3H	1 (s)	(CH3-1)
2.34	2H	3 (t)	(CH2-4)
2.16	3H	1 (s)	(CH2-6)
1.55	2H	5 (p)	(CH2-3)

Prediction Format

Source	Shift	Int	#lines(split)
(CH3-1)	3's	3H	1 (s)
(CH2-2)	3's	2H	3 (t)
(CH2-3)	1's	2H	5 (p)
(CH2-4)	2's	2H	3 (t)
(CH2-6)	2's	3H	1 (s)

VI. Miscellaneous

- Subtracting the Solvent Lines: Don't Count the Singlet at 7.26** CDCl_3 is routinely used as solvent, but is contaminated by trace CHCl_3 which gives a signal at 7.26.
- Subtracting the Reference Line: Don't Count the Line at 0** A reference chemical $[(\text{CH}_3)_4\text{Si}]$ is included to define where "zero" is.
- Subtracting the Water Line:** Often a little moisture will be in the solution. This will often appear somewhere around 1.6, but it wanders depending on hydrogen-bonding factors.
- Subtracting the Acetone Line?** Acetone shows a singlet at around 2.15. If acetone has been used to rinse but hasn't dried yet, this will appear. But it normally integrates incorrectly.
- How do I know what's a real signal versus a signal arising from an impurity that I should ignore?** For today, if in doubt ask the instructor! The instructor will confirm which lines you should or shouldn't consider in doing your analysis. However, one useful recognition tip is that if something integrates badly, it's likely a contaminant. Integrals are supposed to be nice whole-number ratios (1:1, 2:1, 3:2, etc.)
- Beware of Overlapping.** Overlapping is most routine in the benzene area (7's), and also in the alkyl area (1's), but happens elsewhere as well. OH signals often overlap other signals. For this week, if in doubt ask.

Summary of ¹H-NMR Interpretation

I. Number of Signal Sets

II. “Chemical Shifts” of the Signal Sets

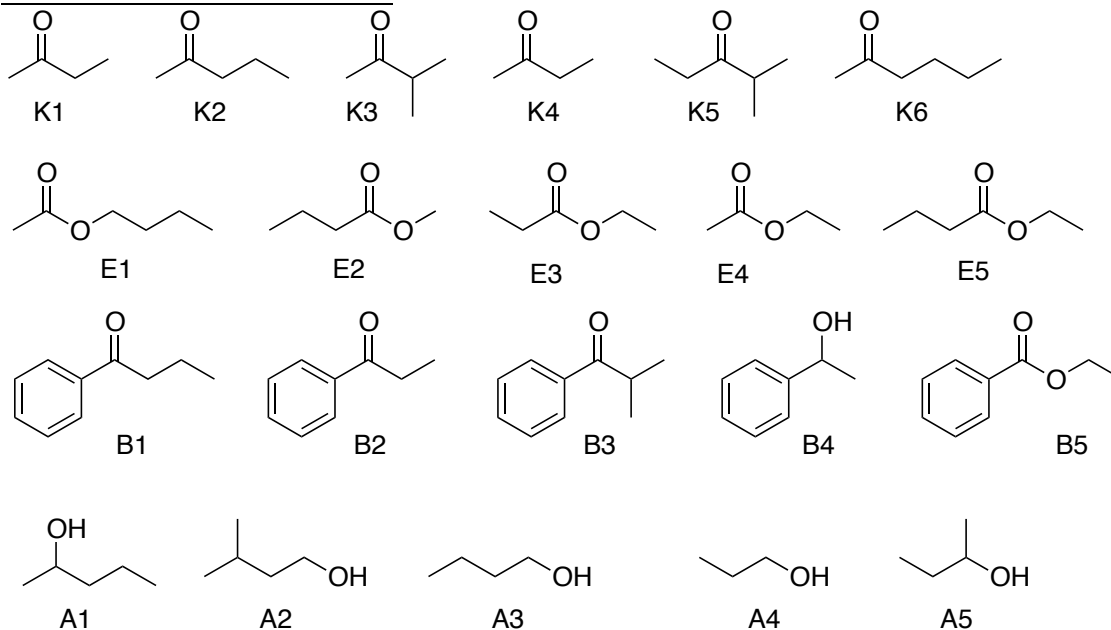
7's (6.5-8.4)	<u>Aromatic</u> sp ² hybridized C-H's
3's (2.8-4.5)	<u>Oxygenated</u> sp ³ hybridized C-H's. Oxygenated sp ³ -carbons are routinely present for the following functional groups that contain oxygen single bonds: <ul style="list-style-type: none"> • <u>alcohols</u>, • <u>ethers</u>, or • <u>esters</u>
2's (1.8-3.1)	<u>Allylic</u> sp ³ hybridized C-H's (sp ³ hybridized C-H's that has a double bond attached to the sp ³ hybridized C). Allylic signals routinely appear when one of the following double-bonded functional groups is present: <ul style="list-style-type: none"> • <u>carbonyls</u>, (ketones, esters, aldehydes, acids, amides) • <u>alkenes</u>, or • <u>aromatics</u>
1's (0.7-2.0)	sp ³ hybridized C-H's, with <u>no attached Functional Groups</u> <ul style="list-style-type: none"> • <u>Note:</u> Many molecules with non-functional alkyl portions will give a lot of signal in this area.
0-5 (anywhere!) (normally 1.5-3.5 range)	<u>Alcohol</u> O-H hydrogens

III. Integration These must be simple whole-number ratios (2:1, 3:1, 3:2, etc..)

IV. Splitting

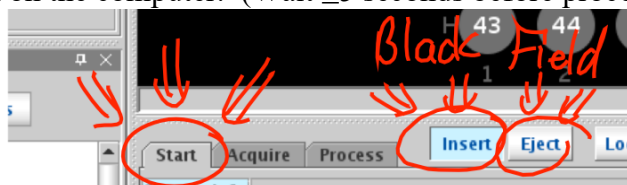
- **N-1 Rule:** N lines =>N-1 neighbor H's (H's directly attached to carbons attached to the C-H group causing the signal)
 - The N-1 Rule is useful when working from spectrum to actual structure
- **N+1 Rule:** N neighbor H's =>N+1 lines
 - The N+1 Rule is useful when working from structure to actual spectrum

Note: OH hydrogens don't participate in splitting (normally)

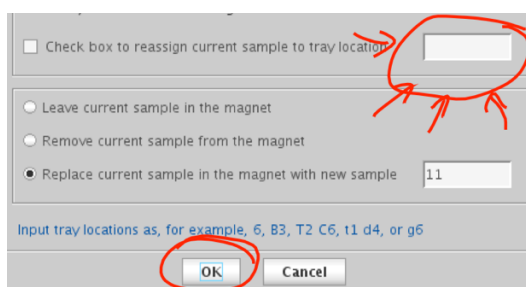
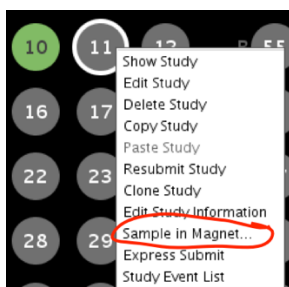
Hydrogen NMR, The Experiment. What you need to do, an Overview.**H-NMR Unknown Candidates****Lab and Lab Report Requirements**

- Prepare and run one sample.** (This can be shared with a partner.)
 - Using a syringe, add 0.1 mL of unknown sample. Add this first.
 - Add 0.8 mL of CDCl₃ solvent.
 - Cap and shake to ensure mixing.
 - The experiment run will be "Proton8". This should auto-load in the procedure manual,
- Get at least one full print.
 - Horizontal expansions are not required but are usually very helpful to be able to see and interpret the splitting
- Identify and interpret at least two NMR spectra.**
 - You will be given the other NMR.
 - You could be solving the "given" NMR during time while you might be waiting for your turn to run your own sample.
 - Summarize your actual data, your structure identification, and your data interpretation on the **Data Report and Interpretation Page**
- Predict what some other structures would give. There is a handin form ("**Prediction Page: Hydrogen NMR Lab Handin**")
 - You could be completing the prediction page during time while you might be waiting for your turn to run your own sample.

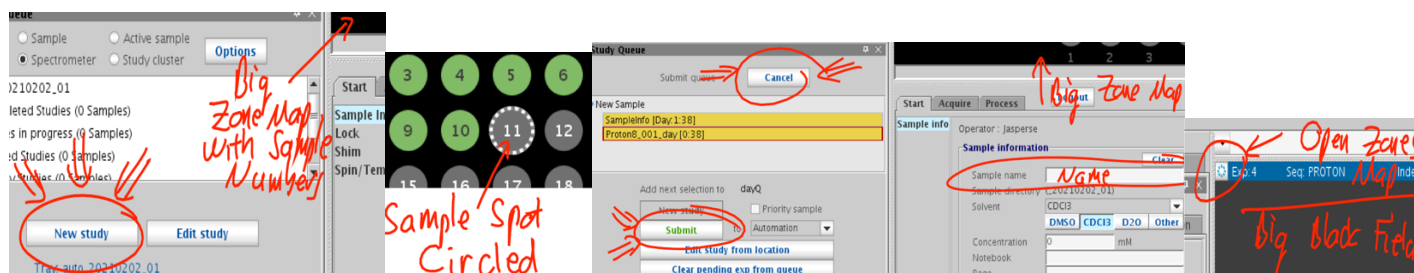
1. **Prepare sample** in lab; **add sample to sample-holder**; adjust sample depth using **golden depth finder**
2. **Eject/Insert** (Sample Exchange):
 - a. Hit **"eject"** button (below black field) to eject existing sample. (If not visible, click "start" button to make it so)
 - b. **Manually lift out sample-in-sample-holder** combination from the probe (place it in a box)
 - c. **Place your sample-in-sample-holder** into the probe
 - d. Hit **"insert"** button on the computer. (Wait ≥ 5 seconds before proceeding with step 3a).



3. **Spot Assignment:** (Each sample needs to be assigned a sample spot number)
 - a. **Right-click** on the lowest-numbered gray spot number in the zones map. (A pulldown will appear)
 - b. Select **"Sample in Magnet"** (3rd line from the bottom of the pulldown);
 - c. **Enter your spot number** into the upper field. (Remember your spot number)
 - d. Hit **OK**.



4. **NMR-Experiment Submission:**
 - a. Click **"New Study"** button in lower left. (A yellow experiment file-name will appear).
 - b. The default experiment is **"Proton-8"**; for something different select from panel on upper left.
 - c. **Left-mouse single-click** on your sample spot. (A white circle will appear around the sample spot)
 - d. Enter student name(s) into **Sample Name field**, which is underneath the black field
 - e. Submit: click the **green "Submit" button** on the lower left side. (your sample spot should turn color)
 - f. Hit **"Cancel"** to leave submit-sample mode.
 - Don't forget to do this. If you do, it will cause problems for both you and the ensuing user.
 - The yellow experiment file-name will disappear; unfortunately the zones map will too.
 - g. Re-open "zones" map: **Click on little circle icon** (⚙️) to the upper left of the big gray/black panel, and the zones map with all the sample spot numbers should re-open.
 - Note: An experiment should take about 7 minutes.
 - There should be an automatic one-page printout upon completion.

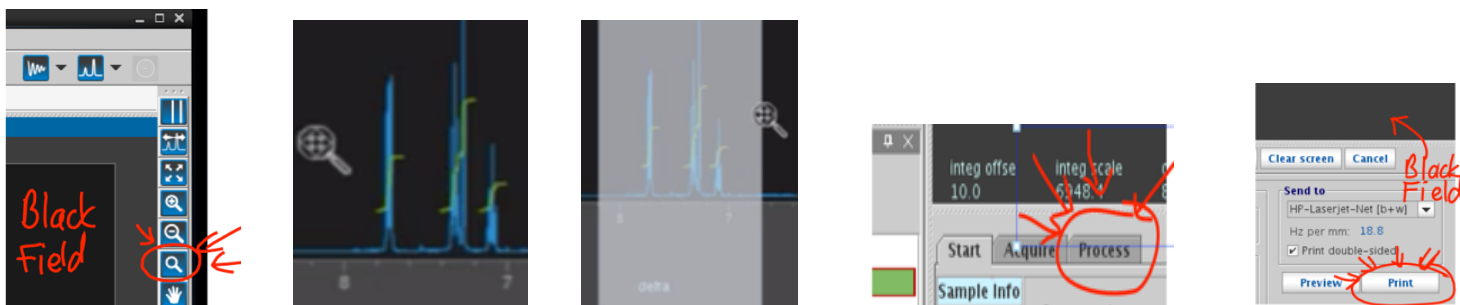


5. **Printing an extra copy** of spectrum (in case you have a partner)
- Must be in zones-map display. If not, click on little circle icon (⚙) upper left of the spectra-display panel.
 - a. **Right click on sample number**, and a pulldown will appear
 - b. Click “Show Study”
 - c. **Double click on green “PROTON_01”** file that will appear in the lower left-hand area. (below your name)
 - Your spectrum should now appear in the display field, where the zones-map appeared before
 - d. Click “Process” button underneath the spectrum display field. (“Start” was highlighted previously)
 - e. Click blue-text-on-white-background “Print” button on lower right to print another copy.



6. Horizontal Expansions

- a. Steps 5a-d above describe how to get your spectrum loaded into the display field.
- b. With spectrum displayed on screen, **use a panel of display icons on the far upper right**
- c. Click on the **magnifying glass icon** (6th icon down, 🔍)
- d. Move your cursor to the left end of the zone you want to expand, then **hold down left mouse button** and **slide it** to the other end of the zone you want to expand, then release the button.
 - To return to the full display, you can either click on the 3rd icon (⏪) or the 5th icon (🔍).
- e. Click blue-text-on-white-background “Print” button on lower right to print a copy. (Twice for 2 copies)



7. Exiting so that NMR is Ready for the Next user

- a. Click “Start” button underneath the spectrum display field. (“Process” was highlighted previously)
- b. Re-open “zones” map: **Click on little circle icon** (⚙) to the upper left of the big gray/black panel, and the zones map with all the sample spot numbers should re-open.



Prediction Page: Hydrogen NMR Lab Handin _____ **Name** _____

A. For each of the following chemicals, completely fill out the “Prediction Format” tables to predict what you would expect.

Standard Prediction Format: Ex: CH3OCH2CH2CH2C(O)CH3 (Carbons numbered left to right...)

Source	Shift	Int	#lines(split)
(CH3-1)	3's	3H	1 (s)
(CH2-2)	3's	2H	3 (t)
(CH2-3)	1's	2H	5 (p)
(CH2-4)	2's	2H	3 (t)
(CH2-6)	2's	3H	1 (s)

Notes:

- Write numbers or letters next to each carbon in each structure to be used for identification purposes
- For the number of lines, you can include a number, you are not required to use the s, d, t, q descriptors
- For the chemical shifts for OH hydrogens, just write in “???”
- For OH hydrogens, assume they are 1line singlets and that they do not split CH hydrogens
- For the chemical shifts for others, enter either “1's”, “2's”, “3's”, or “7's”
- Aromatic hydrogens tend to overlap. For aromatic hydrogens, just combine them all. For example, write “aryl” for source; “7's” for chemical shift; “5H” for integration, and leave # lines empty.

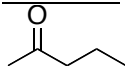
Structure



Predicted NMR

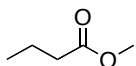
Source	Shift	Integ.	# lines

Structure

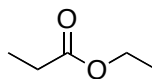


Predicted NMR

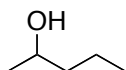
Source	Shift	Integ.	# lines



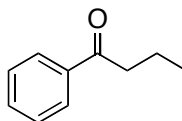
Source	Shift	Integ.	# lines



Source	Shift	Integ.	# lines



Source	Shift	Integ.	# lines



Source	Shift	Integ.	# lines

Data Report and Interpretation Page.

B. Draw the structures and use the Standard Summary Report format to interpret the features of the two unknowns, the NMR that you ran and the other NMR that you interpreted.

Example **Standard Summary Report:** $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{C(O)CH}_3$ (Numbered from left to right...)

Shift	Int	#lines(split)	Source
3.79	2H	3 (t)	(CH2-2)
3.48	3H	1 (s)	(CH3-1)
2.34	2H	3 (t)	(CH2-4)
2.16	3H	1 (s)	(CH2-6)
1.55	2H	5 (p)	(CH2-3)

1. Which unknown did you run yourself? (H1, H2, ...) _____
2. Draw its structure and make up numbers or letters next to each carbon.

Structure

Actual NMR

Chemical Shift (to the nearest 0.1 ppm)	Integ.	# lines	Source

3. If you know, which was the other NMR that you analyzed? (H1, H2, ...) _____
 - Note: you don't need to know or report this if you don't actually know, which is well possible...
4. Draw the chemical structure and make up numbers or letters next to each carbon.

Structure

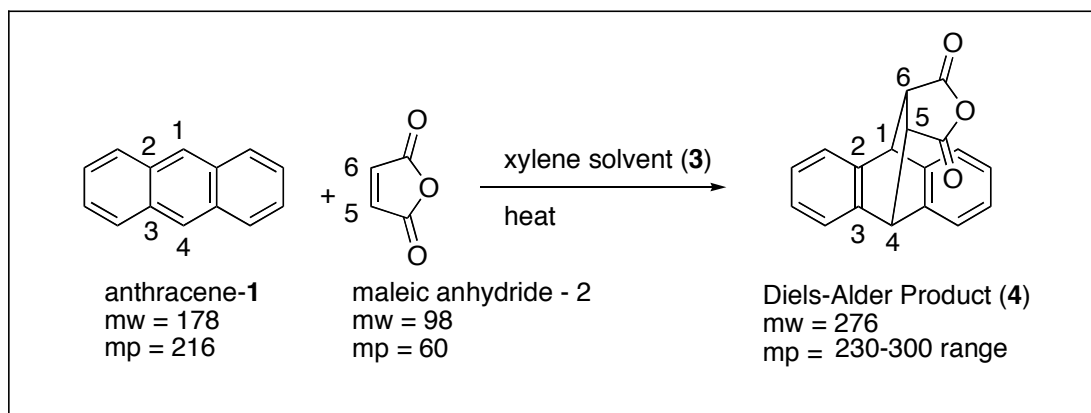
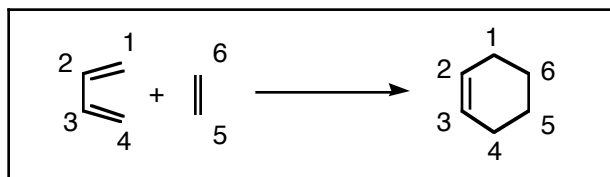
Predicted NMR

Chemical Shift (to the nearest 0.1 ppm)	Integ.	# lines	Source

C. Attach your NMR printouts. At minimum, include the unexpanded NMR printouts for both of the two samples. If you printed out horizontal expansions or printouts with manual integrations, you can include those too.

Diels-Alder Reaction

General Diels-Alder Reaction: A conjugated “diene” reacts with a “dienophile” to produce a cyclohexene ring. The “dienophile” is activated by electron-withdrawing substituents (carbonyls). The diene must be in a “cisoid” conformation in order to react. Attachments to the reactants remain attached as spectator atoms.



Overview of Actual Reaction: Anthracene (1) will serve as a student-friendly low-smell Diels-Alder diene, with the labeled carbons functioning as the reactive diene. Maleic anhydride (2) will function as the dienophile. Xylene (dimethylbenzene) is used as a high-boiling solvent so that the reaction will work fast enough to complete conveniently. In terms of activation, notice that maleic anhydride is a highly reactive dienophile, due to the presence of two electron-withdrawing carbonyl substituents. Anthracene, however, is an unusually unreactive diene. This is due to both steric effects, but more importantly because the “diene” is really part of an aromatic ring system and is thus stabilized. This stabilization in the reactant reduces the reactivity (stability/reactivity principle). The “cyclohexene” ring produced in every Diels-Alder reaction is hard to visualize, but consists of the six labeled atoms in the product.

Reaction Setup: Use a dry a 25-mL round-bottomed flask with a small stir bar. Clamp the flask very securely above a hot-plate/stir-plate near a sink. Weigh out 0.80g of anthracene and 0.40g of maleic anhydride (both are solids) and add them to the flask. Add 10mL of xylene via syringe. (The xylene will be in the liquids-dispensing hood. Return the xylene syringe after injecting, so that other students can use it!) Attach a reflux condenser to your flask, and tubing so that water can flow through the condenser. (The array needs to be set up near a sink so that the tubes will reach. The water should enter the bottom connector; the hose from the top connector should flow into the sink.)

Reaction Conditions: Turn the magnetic stirrer on, then warm the solution to “reflux” (until it boils steadily) by setting your hot plate to setting 8 (for the heater). Note: the boiling point for the xylene solvent is 138°; the actual temperature is actually somewhat hotter than that, because the dissolved solutes elevate the boiling point to some degree. Reflux the solution for 30 minutes. (Write up your report while you wait! Be sure to include observational details, including colors and color changes and

solubilities and solubility changes.) Allow the solution to cool for 10 minutes, then place it in an ice bath for 10 minutes to complete the crystallization of the product.

Isolation of the Product: Collect the crystals by vacuum filtration using a Buchner funnel. Try to crush any chunks. Make up a mixture of 4 mL ethyl acetate and 4 mL of hexane in a grad cylinder. Disconnect the aspirator, add half of the ethyl acetate/hexane mixture, and reconnect the aspirator. Repeat this sequence again with the other half. Vacuum dry for at least 8-10 minutes before weighing the product for a yield calculation and taking the melting point.

Caution: Xylene and ethyl acetate are both strong smelling chemicals. Be very careful to rinse them out only in the hood. And be very careful to keep them covered to reduce fumes.

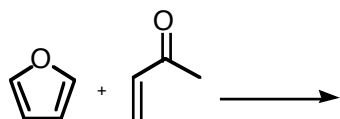
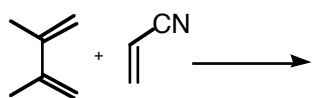
Lab Report: Should follow the standard synthesis layout. (See website and/or handout)

- Note: the “Standard Synthesis Layout” used a different reaction as an example.
- Adapt your report to the actual reaction you’re doing today. This obviously will involve showing the reactants and products involved in the actual reaction!
- Draw the chemical equation
- Write down each chemical used and the quantity.
- For the diene and the dienophile, determine the numbers of moles used. (One or both of these will be the limiting reactant, and thus their moles factor into yield calculations). Neither the original solvent nor any wash solvents need any mole calculations. (These are not limiting, so they have no yield impact).
- Identify the limiting reactant, and calculate the theoretical yield.
- Write up the procedure followed, including descriptive information (times, temperatures, color changes). This should be in past tense: what you actually did, and what you saw.
- Report the observed melting point
- Report the observed mass yield.
- Calculate the actual percent yield.

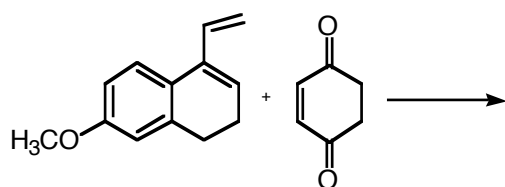
Name:

Questions:

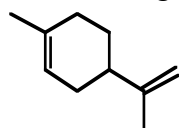
1. Maleic Anhydride is an exceptionally reactive dienophile. Why?
2. Anthracene is an unusually unreactive diene. Explain why? (Two factors, actually...)
3. Draw the products of the following Diels-Alder reactions.



4. Draw the product of the following Diels-Alder reaction. Note: One can imagine the left reactant potentially providing more than one “diene” group. You may wish to consider why one diene group might be more reactive than any others (or conversely why other diene groups might be less reactive ...).



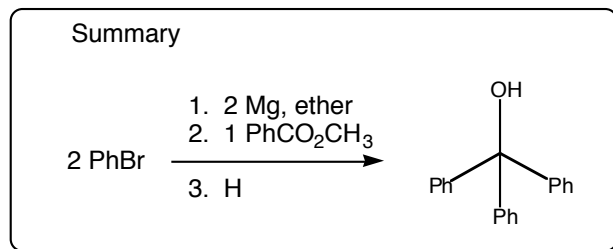
5. What starting materials would be used to prepare the following compound by the Diels-Alder reaction?



Standard Synthesis Laboratory Report Format: The following layout is standard for a “synthesis reaction” report. Provide the parts and information in the sequence specified.

1. Title = Reaction Summary

For an organic reaction, there is no point in having a Worded Title: The chemical reaction is the best title summary of what you did!



2. Listing of all Chemicals Used

- This should include all chemicals used, including solvents.
- For each chemical, you should include the actual quantity used and measured. For example, with the methyl benzoate you measured a volume by syringe, rather than by weighing on a balance. So you should list the volume you actually used rather than just the weight.
- For reactants that might possibly be limiting reactants and might possibly factor into calculation of the theoretical yield, you must include more than just the quantity of chemical used. You should also include a conversion from what you measured into the number of moles used.
- In some cases, there may be considerable roundoff (you needn't keep precise record of the quantity of solvent that was used, for example, or of sodium sulfate drying agent...)
- If a person was later to repeat your experiment, they should be able to look at this list and know all the chemicals they'd need to have on hand and in what quantities, in order to complete the experiment.

3. Calculation of Theoretical Yield

- Specify which chemical is the limiting reactant
- Given moles of limiting reactant, calculate theoretical moles of product
- Given moles of product, calculate theoretical grams of product.
- Note: Why do this so early in report?
 - First, because it fits in near your mole calculations above.
 - Second, if calculated in advance. as with most research, you know which chemical is limiting and thus must be measured most carefully, but you also know which are in excess and thus need not be measured with equal precision.
 - Third, it's nice to know approximately how much material is expected, so you can recognize whether your actual results are reasonable or problematic.

4. Writeup of Actual Procedure.

- For this particular experiment, the “procedure” section will be by far the biggest portion of your report.
- This should be a concise but detailed description of things, including:
 - What you actually did (even if not recommended or not from recipe)
 - All observations should be included. These include all observed changes, such as:
 - Changes in **color**
 - Changes in **solubility** (formation of precipitate or cloudiness...)
 - Changes in **temperature** (like, reaction became hot...)
 - Formation of **bubbles**
 - Time and temperature details:
 - Whenever you heat something or cool something, the procedure should specify
 - Specify times. Whether you boiled for 5 minutes or 5 hours matters!
- Writing details: As a record of what actually happened, the report must be written in **past tense**, not **command tense**. (Rather than “Add this”, should read “I added this”, or “I dropped that...”)
- Use of personal pronouns is accepted in this class. You may use “I” or “we” to simplify writing.

5. Product Analysis

- Any NMR, mp, bp, TLC information. For this report, mp and TLC information must be included.
- Final yield and percent yield information.

6. Discussion/Summary. Need not be long, but any conclusions or excuses would go here...

7. Answers to any assigned Questions

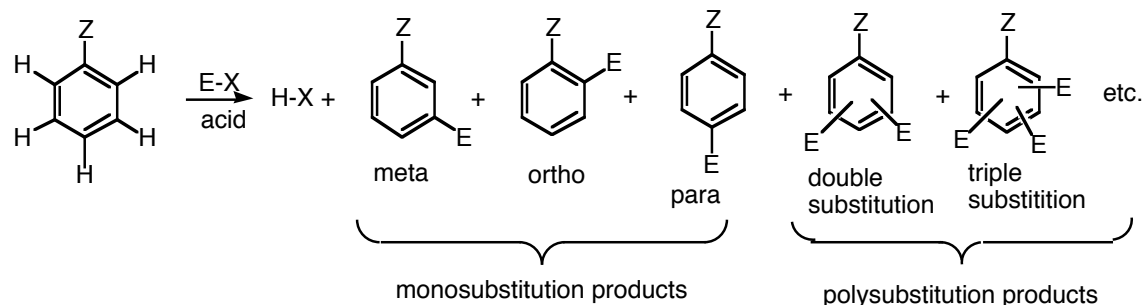
NITRATION OF METHYL BENZOATE

General Issues with Electrophilic Aromatic Substitution Reactions:

Aromatic substitution reactions involve the substitution of one (or more) aromatic hydrogens with electrophiles. Two major synthetic issues are always involved.

1. Monosubstitution versus Polysubstitution

- Because there is more than one benzene hydrogen available, can the reaction be disciplined so that monosubstitution occurs rather than polysubstitution?
- Selective **monosubstitution** is possible only if the monosubstitution product is **less** reactive than the original reactant. If the reactivity of the monosubstitution product equals or exceeds that of the original reactant, the monosubstitution product(s) will proceed on to polysubstitution products.
- There are two reasons why a monosubstitution product might be less reactive:
 - **Electronic reasons.** If the “E group” that added is electron withdrawing, it will make the product aromatic ring less electron rich and subsequently less reactive toward subsequent electrophilic addition.
 - **Steric reasons.** Replacement of a small H with a larger “E group” will make the monosubstitution product more crowded, which may interfere with subsequent addition of additional electrophiles.

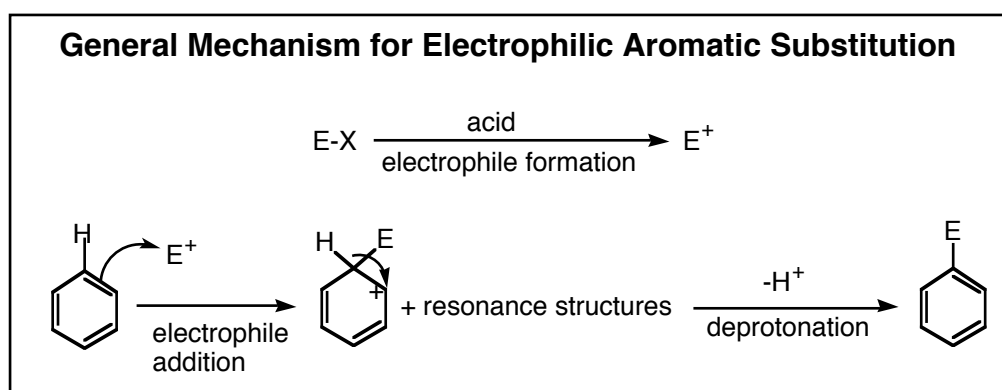
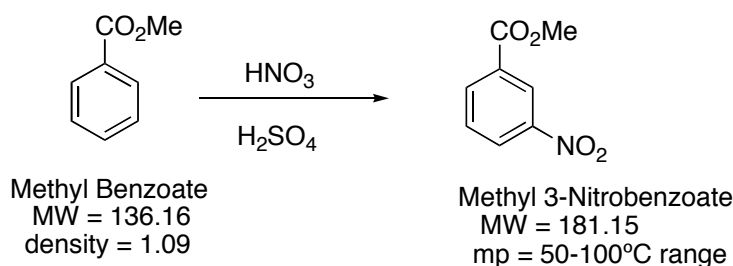


2. Position of Substitution: Ortho, Meta, or Para To a Pre-existing Substituent?

- Even if a reaction can be disciplined such that monosubstitution occurs to the exclusion of double or triple substitution, what happens when substitution occurs on a benzene that already has a substituent attached ($Z \neq H$)? Will ortho, meta, and para hydrogens be substituted with equal ease, so that a statistical mixture of ortho-, meta-, and para-disubstituted products form? Or will substitution be selective? Somewhat selective substitution is ordinarily possible based on two reasons:
 - **Electronic reasons.** Rate-determining addition of E^+ occurs with differing speeds because of the electronic impact of Z on the delocalized cationic charge. If Z is an electron donor, it will stabilize positive charge and facilitate ortho and para addition relative to meta addition. If Z is an electron withdrawer, it will destabilize positive charge and deactivate ortho and para addition relative to meta addition.
 - **Steric reasons.** Depending on the size of both Z and E, they will interact to varying degrees in the pathway leading to the ortho product. Thus the **ortho** product is normally destabilized for steric reasons relative to either the meta or the para products. Steric factors only impact when an electrophile adds ortho to a non-hydrogen. If an electrophile adds in between two non-hydrogens, steric problems are really awful.

General Mechanism for an Electrophilic Aromatic Substitution:

The general mechanism for all electrophilic aromatic substitutions is summarized below. First, a reactive electrophile E^+ must be generated by interaction of a reactant with acid (either a Lewis acid or a normal Bronsted acid). The mechanism for the E^+ formation depends on the electrophile. Once an active electrophile is available, it adds to an aromatic ring to give a cationic intermediate. The allylic nature of the cation means that it always has at least three meaningful resonance structures, and sometimes more. The positive charge is always distributed to the carbons that are ortho and para relative to the carbon to which the electrophile has added. Notice that the carbon to which addition occurs is temporarily tetrahedral, and that the ring temporarily loses its aromaticity when addition occurs. Once the cation has formed, subsequent deprotonation occurs (from the carbon onto which the electrophile has added), and aromaticity is restored. The two steps, electrophilic addition followed by loss of the proton, constitute a “substitution”; the electrophile takes the place of the hydrogen on the ring.

**Today's Actual Reaction:****Reaction Procedure:**

1. From a buret, add 6 mL of concentrated sulfuric acid directly to a 50-mL Erlenmeyer flask containing a stir bar. (If you don't have a very clean Erlenmeyer, do not wash now! The water will do more harm than any residue that may be present.)
2. Set an ice bath on a stir plate and cool the solution in an ice bath. Turn the stirrer on.
3. Measure out 2.00 mL of methyl benzoate via syringe from the reagent bottle, and inject it directly from the syringe into the cooled, stirring sulfuric acid solution.
4. From a buret, measure about 1.4 mL of concentrated nitric acid into your 10mL graduated cylinder. The accuracy does not need to be high. Then add the nitric acid dropwise, by long-stemmed pipet, over 3-4 minutes, to the methyl benzoate/sulfuric acid solution, which should still be kept cold in the ice bath and being continuously stirred. After completion stir for 5 more min.
5. Remove the cold bath and let the mixture stand at room temperature for 20 minutes, with continuous stirring.

Isolation of the Crude Product:

1. Transfer the solution (carefully) onto a pile of ice (about 20 g) in a small beaker (150 mL) by using a pipet. (The product will likely crystallize.)
2. Add another 10 mL of ice-cold water to the original Erlenmeyer, and clean your pipet that you used for the transfer by drawing up water and shooting it back out three times. Swirl the water around in the Erlenmeyer so that as much as possible of the original solution has a chance to go into the water.
3. Add another 20 mL of cold water. Pour the aqueous solution from the Erlenmeyer into the beaker, and swirl thoroughly.
4. Rinse the original Erlenmeyer with another portion of cold water.
5. By now the product should have crystallized. Isolate the crude crystals by suction filtration, using your medium-sized Buckner funnel. (Try to get the ice to melt first!) (Wet the filter with water.)
6. Wash once with about 20 mL of ice-cold water.
7. Do a second wash with about 10 mL of a methanol/water mixture (about 8/2 methanol/water ratio).
8. Measure the mass of the crude product.
9. Prepare a sample for GC/MS analysis. Do this by adding a spatula tip (0.010 g?) to a GC/MS vial, and add one pipet of methanol. Submit to the GC/MS queue.
10. Save a few of the crude crystals to get a crude melting point. (Only enough for a melting point!)

Recrystallization of the Crude Product:

1. The main batch of crystals should be purified by recrystallization. (Prior to recrystallization, up to 20-30% may be ortho-, para-, or polynitrated material plus possible starting material).
2. Pour some hot tap water into a 150-mL beaker, and warm on a hot plate. (Setting 4 is probably good). (Note: if you pour hot water in in the first place, it doesn't take as long to heat up as if you start with cold water! Brilliant, huh?) You will subsequently warm a 25-mL Erlenmeyer in this water bath, so you probably don't need it to be more than 40-50 mL full. You will subsequently want to be mildly boiling methanol (bp = 64°C) in the water bath, so you'd like it to get hotter than 64° but you don't want it way hotter, in other words you don't want a hard boil.
3. Transfer the crystals from the filter paper into a 25-mL Erlenmeyer. Use a spatula to scrape.
4. Add 6 mL of methanol to the Erlenmeyer. (Use some of this to rinse off the filter paper and the spatula, if some crystals are sticking.)
5. Add a boiling stick, and then place the Erlenmeyer with the product/methanol mixture into the warm water bath to heat it to a gentle boil.
6. Depending on how much product you made and on how wet it may have been, the 6-mL of methanol may be more than plenty or may be too little. If your yield is either really good, or if your raw crystals are very wet with water, it may require more methanol. So once your solution has warmed to a boil, if the crystals don't dissolve within two minutes then add more methanol as needed until the crystals do dissolve. (But just barely. Remember that for a recrystallization, in order to get optimal yield you don't want to use an unnecessary excess of hot solvent....)
7. Once you think you have optimized your solvent conditions for the recrystallization, remove the flask from the heat bath and let the solution cool slowly on a watch glass with a beaker over the top to prevent further solvent evaporation.
8. After cooling to room temperature, cool it on ice, and suction filter to get the purified product.
9. Be sure to rinse your crystals; what would be an appropriate wash solvent or combination to use?
10. Prepare a sample for GC/MS analysis. Do this by adding a spatula tip (0.010 g?) to a GC/MS vial, and add one pipet of methanol. Submit to the GC/MS queue.

11. Let the crystals dry, then get the mass yield and take a melting point. When you take your melting point of the recrystallized material, also take a melting point of the crude material in order to compare so you can see whether recrystallizing actually helped.
12. Typical yields should be 50-75%. The melting point should fall somewhere in the 50-100° range, so don't heat too fast. (Power setting of 4 would probably be good.)
13. Summary of Required Data:
 - Mp, mass yield, GC/MS data, and % yield for both crude and purified material.
 - No NMR or TLC required.

Caution: Safety Note: Both conc. sulfuric acid and conc. nitric acid are very potent and will dissolve you, your clothes, your papers, or anything else they touch! Avoid pouring; try to use burets/pipets exclusively, or as much as possible. Rinse your glassware and pipets thoroughly with water after usage.

Cleanup: If an aqueous acid waste bottle is out, put your original solution (following filtration) into that. If not, dilute the original solution with water, neutralize with sodium carbonate (expect it to fizz!), and pour down the drain.

Pour the methanol from the recrystallization into the organic waste container.

Questions:

1. Draw the mechanism for the reaction.
2. If you didn't already do so in your answer to question 1, draw out the three resonance structures for the carbocationic intermediate after NO₂ addition (prior to proton loss).
3. The para product is not formed to a significant extent. Draw the carbocationic intermediate that would be involved in the formation of the para product (had it actually formed), and its resonance structures. Explain why para product formation is much slower than meta-product formation. (Hint: is the CO₂Me substituent an electron donor or withdrawer? A cation stabilizer or destabilizer?) Circle the most problematic resonance of the three resonance structures.
4. In the experiment, an excess of nitric acid was used. Given that the nitro group is an electron-withdrawing group, explain why your reaction stopped with mostly only single nitration but didn't go on further to give lots of double nitration?

Lab Report:

- Standard synthesis lab report format. Make sure to follow that to get full credit!
- Make sure you remember to answer the above questions, and staple those answers to the back of your report.
- This lab report will need much more discussion/analysis than the previous report. In particular, you need to present/discuss/analyze the differences between the crude material (pre-recrystallization) and the purified material (following recrystallization). A four-column table, with the second column for the "Crude" and the third column for the "Purified" would be good. A first column should include the retention times for the three different structural isomers, and in the fourth column you should indicate which GC peaks were the ortho, meta, and para products.) The mass/yield changed; the melting range changed; and the GC purity changed dramatically. Why did they change? Should they have changed? Where did the "lost mass" go, and was it appropriate or was it a failure on your part that the mass decreased as it did? Present the data in an organized way, and discuss at least a little bit.

Basic GC-MS Operation Compressed Draft 3 For Chem 355 Organic Unknowns Lab

Note: The following assumes that the hydrogen and compressed air gases have been turned on; that the machine has been warmed up; that the gc/ms program has been opened; that an appropriate “method” and “sequence” have been selected; and that Jasperse will shut things down.

Sequenced Data Acquisition: Using the Autosampler to Sequence Runs Automatically

Note: this assumes that Jasperse has already prepared and started a “sequence” (“Grignard..” for example, but you are trying to add your sample to the lineup. If you’re first in line, get Jasperse to come and help.

1. **Add your sample to the back of the line in the autosampler.**
 - Do NOT leave any open holes (unless the sample belonging in that hole is being sampled.)
 - Filling a “sample-is-in-the-injector-tray” hole will cause a system freeze.
2. **Open “edit sequence” by clicking the “edit” icon on the yellow panel** low on the computer screen.
 - This will open a spreadsheet that you can edit.
 - Add your names in the “name” box that goes with your vial number.
 - **Click OK.** Note: if you don’t click “OK”, the machine will freeze at the end of the current run. NEVER leave the spreadsheet page open unless somebody behind you is going to close it.

Data Processing/Analysis: Getting and Printing the GC Graph, % Report, and/or Mass Spec.

- Note: data analysis can be done while acquisition is ongoing.
 - Note: this assumes that the “**gems data analysis**” software and appropriate analysis method are opened. In the data analysis page, check on the top blue line to see if it says “Enhanced data analysis-ADEFAULT-RTE.M...”, or “Grignards”, or something that fits the experiment for the week. If not, check with Jasperse or open it. (ex, Method > Load Method > Yes > ADefault-RTE.M > OK.)
3. **Open a data file** using the left mouse button to double click.
 - Your data file should be within the folder Organic Lab within the Data folder.
 - Data file will have the names “Vial-1” or “Vial-2”, so **remember which vial was yours.**
 4. **Printing GC Graph, % report, and retention times: Click Method>Run Method**
 - Repeat as many times as needed to provide prints for each student in your group.
 5. **Printing Mass Specs: Click the 2nd Hammer icon.**
 - Click the 2nd hammer icon as many times as needed to provide prints for each student in group.
 - Note: You don’t need to wait for a print to finish before clicking the hammer again. If you’ve got 5 partners, just click the hammer five times and the prints will come out one by one....

Library Matching: With a data file open (as described in #3 above):

6. **Right mouse double-click on a peak in the top window** to get its individual mass spectrum to appear in the lower window.
7. **Right mouse double-click on the mass spectrum to get a library search results**
 - Note: the library searches aren’t perfect and don’t always find the very best structure match.

•

Summary of ¹H-NMR Interpretation

I. Number of Signal Sets

II. "Chemical Shifts" of the Signal Sets

9's (9.0-10.0)	<u>Aldehyde</u> sp ² hybridized C-H's
7's (6.5-8.4)	<u>Aromatic</u> sp ² hybridized C-H's
5's (4.8-6.8)	<u>Alkene</u> sp ² hybridized C-H's
3's (2.8-4.5)	<u>Oxygenated</u> or <u>Halogenated</u> sp ³ hybridized C-H's (halogenated and nitrogenated alkyl C-H's will also come in this window, although no candidates for today's lab). Oxygenated sp ³ -carbons are routinely present for the following functional groups that contain oxygen single bonds: b. <u>alcohols</u> , c. <u>ethers</u> , or d. <u>esters</u>
2's (1.8-2.8)	<u>Allylic</u> sp ³ hybridized C-H's (sp ³ hybridized C-H's that has a double bond attached to the sp ³ hybridized C). Allylic signals routinely appear when one of the following double-bonded functional groups is present: e. <u>carbonyls</u> , (ketones, esters, aldehydes, acids, amides) f. <u>alkenes</u> , or g. <u>aromatics</u>
1's (0.7-2.0)	sp ³ hybridized C-H's, with <u>no attached Functional Groups</u> h. <u>Note:</u> Many molecules with non-functional alkyl portions will give a lot of signal in this area.
0-12 (anywhere!)	<u>Alcohol/Acid</u> O-H hydrogens (N-H hydrogens likewise) i. <u>alcohols</u> , j. <u>carboxylic acids</u>

1. Check each of the zones. Each one gives you a yes or no answer about the presence of absence of the featured group.
2. End-Check: Check that the functional groups indicated by your chemical shift information match with the structure you believe you actually have! If not, structure needs correction!
3. The regions are somewhat approximate, and have some spillover.
4. For multi-functional complex molecules, there are more complex ways for a C-H to come in some of the above window. For example, an sp³-hybridized C-H with two attached oxygens can come in the 5's, or an sp³-hybridized C-H that is doubly allylic can come in the 3's. In other words, the impact of functional groups is roughly additive.

III. Integration These **must be simple whole-number ratios** (2:1, 3:1, 3:2, etc..)

IV. Splitting

- **N-1 Rule:** **N lines =>N-1 neighbor H's** (H's directly attached to carbons attached to the C-H group causing the signal)
 - The N-1 Rule is useful when working from spectrum to actual structure
- **N+1 Rule:** **N neighbor H's =>N+1 lines**
 - The N+1 Rule is useful when working from structure to actual spectrum

Note: OH hydrogens don't participate in splitting (normally)

Summary of C13-NMR Interpretation

- Count how many lines** you have. **This will tell you how many types of carbons** you have. (Symmetry equivalent carbons can at times cause the number of lines to be less than the number of carbons in your structure.)
 - Each “unique” carbon gives a separate line.
 - Symmetry duplicates give the same line.
 - If there are more carbons in your formula than there are lines in your spectrum, it means you have symmetry.
- Check diagnostic frequency windows** (“chemical shift windows”) of the lines **to provide yes-or-no answers regarding the presence or absence of key functional groups** in your molecule.

220-160	C=O carbonyl carbons, sp^2 hybridized
160-100	C alkene or aromatic carbons, sp^2 hybridized
100-50	C-O oxygen-bearing carbons, single bonds only, sp^3 hybridized
50-0	C alkyl carbons, no oxygens attached, sp^3 hybridized

- Use DEPT and/or Coupled C13 NMR to Differentiate C, CH, CH₂, and CH₃ carbons.**

<u>Type of C</u>	<u>Name</u>	<u>DEPT-135</u>	<u>Coupled C13</u>
CH ₃	Methyl	Up	Quartern (q)
CH ₂	Methylene	Down	Triplet (t)
CH	Methane	Up	Doublet (d)
C (no attached hydrogens)	Quaternary	Absent	Singlet (s)

- Aromatics, Symmetry, and C-13 Signals.** Most aromatics have symmetry, and both the number of aromatic lines and the splitting of the aromatic lines can be indicative of the substitution pattern on a benzene. Mono- and para-disubstituted benzenes have symmetry.

4 lines	s, d, d, d	Monosubstituted benzene. (Has symmetry)
4 lines	s, s, d, d	Para-disubstituted benzene. (Has symmetry)
6 lines	s, s, d, d, d, d	Ortho- or meta-disubstituted benzene. (Has no symmetry)

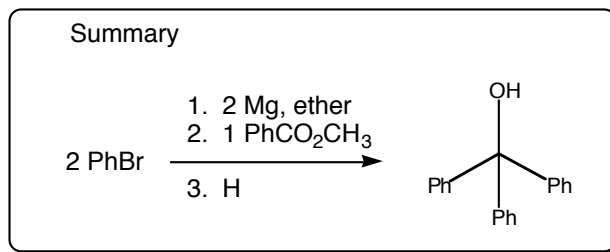
- Signal Height/Size**

- Carbons without any attached H's are short. This is common for carbonyls (aldehydes are the only carbonyl carbons that have hydrogens attached) and for substituted carbons in a benzene ring.
- Symmetry duplication multiplies signal height (if you have two copies of a carbon, the line will probably be taller than normal!)

Standard Synthesis Laboratory Report Format: The following layout is standard for a “synthesis reaction” report. Provide the parts and information in the sequence specified.

1. Title = Reaction Summary

For an organic reaction, there is no point in having a Worded Title: The chemical reaction is the best title summary of what you did!



2. Listing of all Chemicals Used

- This should include all chemicals used, including solvents.
- For each chemical, you should include the actual quantity used and measured. For example, with the methyl benzoate you measured a volume by syringe, rather than by weighing on a balance. So you should list the volume you actually used rather than just the weight.
- For reactants that might possibly be limiting reactants and might possibly factor into calculation of the theoretical yield, you must include more than just the quantity of chemical used. You should also include a conversion from what you measured into the number of moles used.
- In some cases, there may be considerable roundoff (you needn't keep precise record of the quantity of solvent that was used, for example, or of sodium sulfate drying agent...)
- If a person was later to repeat your experiment, they should be able to look at this list and know all the chemicals they'd need to have on hand and in what quantities, in order to complete the experiment.

3. Calculation of Theoretical Yield

- Specify which chemical is the limiting reactant
- Given moles of limiting reactant, calculate theoretical moles of product
- Given moles of product, calculate theoretical grams of product.
- Note: Why do this so early in report?
 - First, because it fits in near your mole calculations above.
 - Second, if calculated in advance. as with most research, you know which chemical is limiting and thus must be measured most carefully, but you also know which are in excess and thus need not be measured with equal precision.
 - Third, it's nice to know approximately how much material is expected, so you can recognize whether your actual results are reasonable or problematic.

4. Writeup of Actual Procedure.

- For this particular experiment, the “procedure” section will be by far the biggest portion of your report.
- This should be a concise but detailed description of things, including:
 - What you actually did (even if not recommended or not from recipe)
 - All observations should be included. These include all observed changes, such as:
 - Changes in **color**
 - Changes in **solubility** (formation of precipitate or cloudiness...)
 - Changes in **temperature** (like, reaction became hot...)
 - Formation of **bubbles**
 - Time and temperature details:
 - Whenever you heat something or cool something, the procedure should specify
 - Specify times. Whether you boiled for 5 minutes or 5 hours matters!
- Writing details: As a record of what actually happened, the report must be written in **past tense**, not **command tense**. (Rather than “Add this”, should read “I added this”, or “I dropped that...”)
- Use of personal pronouns is accepted in this class. You may use “I” or “we” to simplify writing.

5. Product Analysis

- Any NMR, mp, bp, TLC information. For this report, mp and TLC information must be included.
- Final yield and percent yield information.

6. Discussion/Summary. Need not be long, but any conclusions or excuses would go here...

7. Answers to any assigned Questions

