Chem 355 Jasperse **Chromatography**

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 get ($SiO_2 \bullet xH_2O$) and alumina ($Al_2O_3 \bullet xH_2O$) 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$_{\underline{f}actor}$) 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. Work in teams with 3 sets of partners or individuals. That will allow up to six students to experience the "Combiflash" instrument at a time; that four rounds of students will be able to work through the "Combiflash" instrument in a given lab period. Each round may take 15-30 minutes.

2. Choose one of four mixtures ("A", "B", "C", or "D"). Each mixture will have three chemicals from the following list of candidates. The chemicals are imbedded on silica gel. The concentrations are 0.10g of each component per gram of powder.

3. Weigh out 2.0 g of your mixture. (Remember to record which mixture you are using.)

4. Pour the mixture into a "loading cartridge" (see box on Combiflash cart). Place a white filter on top, and loosely push the filter cap down using the white ramrod. Note: do **NOT** press it tight; leave air space at least the thickness of the white filter between the top of the powder and the filter. Now you can wait until you have an opportunity to actually run your chromatography.

5. When it's your turn to run your sample, get Jasperse to come over to demonstrate attachment of your cartridge, to initiate the run, and to give a little spiel about the instrumentation.

6. The run will take about 12 minutes: two minutes to equilibrate and rinse out some of the tubes and columns, then ten minutes of actual collection in test tubes.

7. Each set of partners should take the test tubes containing one of the three components.
   - Note: The last component may not look as tall or sharp as the first two; this is OK. It's normal for the last peak to be broadest, plus in today's mixtures the last sample may include some amine functionality which cause some dragging. Also, since the intensity of detected signal depends on UV absorbance, not all samples will give equally intense signals.

8. Pour the test tubes into a pre-weighed Erlenmeyer that has ample space (after you add the liquid, it shouldn't be more than half full…), add a boiling stick, and boil to dryness or almost dryness in a hot-water bath. (If dipped rapidly and directly into a fully boiling water bath, the solvent might rapidly boil over, so be careful…). If necessary, Jasperse may be able to help you dry your stuff by use of a heat guy.
   - Note: if you can see solid material in some of your test tubes, try to use acetone to dissolve this and rinse them into your Erlenmeyer.

9. Once dry, weigh to determine your mass recovery, and run a melting point to identify the unknown.

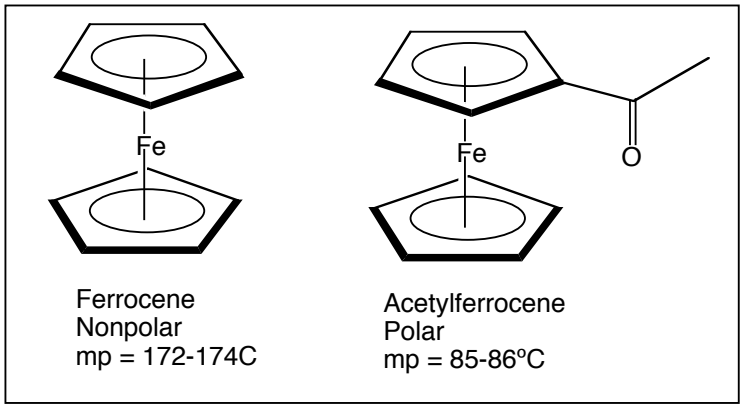
10. Test tubes that had solvent but no sample should be poured out into the solvent waste and returned to the Combiflash tray. Test tubes that did have sample should be rinsed with acetone before being returned to the Combiflash tray.

Part II: COLUMN CHROMATOGRAPHY

Separation of nonpolar Ferrocene(mp 172-174ºC) from polar Acetylferrocene (mp 85-86ºC).

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.



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.
    - 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. (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 your 50-mL 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.

- 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.

8. Concentrate the solution by adding a boiling stick and carefully boiling the solvent off in a hot water bath.

9. 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:

10. Clamp down your 25-mL round-bottomed flask, or if working with a partner use your partner's 50-mL Erlenmeyer.

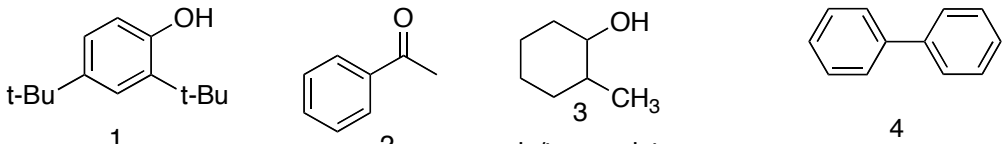
11. Now use 10-15 ml of 50/50 diethyl ether/petroleum ether solvent to wash the more polar acetylferrocene off of the column and into your second round-bottomed flask. You should be able to see the colored band as it moves through the column. There will be some residual gray or brown color that will not wash off; these are impurities that we don't want anyway.

12. Concentrate the solution by adding a boiling stick and carefully boiling the solvent off in a hot water bath.

13. Take a melting point for your actylferrocene. (You may need to use a bent microspatula to scrape off enough solid material to do the melting point.

Part III: TLC (Thin Layer Chromatography)

4 Substrates, Unknown Candidates



Goals

1. 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).

2. Determine how each substrate can be visualized. Which are UV active, and which appear only when using a visualizing "dip"?

3. Observe the dependence of TLC mobility on solvent polarity.

4. Calculate R_f values

5. Identify two unknowns by TLC.

6. 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 Rf'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 Chromatography

Sample Mix: (A, B, C, or D…)_____ Fraction (1, 2, or 3…): _____

Melting range: _____ Identification of unknown (see Table): _____

Table 1: "Combiflash" Candidates:

Melting Range	Name	Melting Range	Name
56-60	Dimethoxybenzene	121-122	Stilbene
69-72	Biphenyl	133-134	cinnamic acid
78-80	Methyl 3-nitrobenzoate	148-150	4-nitroaniline
98-99	Benzotriazole	160-165	triphenylmethanol
104-107	Dibenzylacetone	179-182	Camphor

Part 2: Column Chromatography

1. Part 1 Yields and Melting Ranges:

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

Part 3: TLC

2. Fill out the Rf data in the chart below for the two columns that you ran yourself (either first two, or last two).
   - An eyeball estimate of Rf is satisfactory; one sig. fig. is probably appropriate (0.2, 0.3...)
   - Remember that the Rf value for a spot will be fall somewhere from $0.0 \leq Rf \leq 1.0$, 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 Rf data from partner and fill in those two columns.
   - Note: You and your partner's Rf's may differ, but the relative ordering should be analogous.

Substrate	2% Ethyl Acetate/Hexane R_f	10% Ethyl Acetate/Hexane R_f	10% Ethyl Acetate/Hexane R_f	20% Ethyl Acetate/Hexane R_f
2,4-di-t-Butylphenol **1**				
Acetophenone **2**				
2-Methylcyclohexanol **3** (cis/trans, may give two spots)				
Biphenyl **4**				
First Unknown				
Second Unknown				

3. 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

4. Identify your two TLC Unknowns:

   First Unknown: Letter _____ Identity_____

   Second Unknown: Letter _____ Identity_____

5. Did increasing the polarity of your eluent increase or decrease your Rf's?

6. Given that the solid surface is polar, explain <u>why</u> polar **<u>samples</u>** have lower Rf values than less polar ones.

7. Explain <u>why</u> increasing **<u>eluent</u>** polarity increases the Rf value for a given sample?

8. In what order, from <u>top to bottom</u>, would you expect to see the spots for naphthalene ($C_{10}H_8$), butyric acid ($CH_3CH_2CH_2CO_2H$), and phenyl acetate ($CH_3CO_2C_6H_5$)?

   Top

   Middle

   Bottom

9. In what order, from <u>top to bottom</u>, would you expect to see the spots for the following:

- acetic acid=CH_3CO_2H
- butanal=$CH_3CH_2CH_2CHO$;
- 2-octanone=$CH_3COCH_2CH_2CH_2CH_2CH_2CH_3$
- decane=$C_{10}H_{22}$;
- 1-butanol=$CH_3CH_2CH_2CH_2OH$

Top

2^{nd}

3^{rd}

4^{th}

Bottom

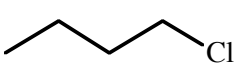
10. If an eluent of too low polarity is used for the development of a TLC plate, will the sample spots be somewhere in the middle, way at the bottom, or way at the top of the plate?

11. If a 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?

Chem 355-Jasperse

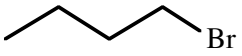
STRUCTURAL EFFECTS ON SUBSTITUTION REACTIONS

Structures:



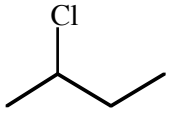
1-chlorobutane

1



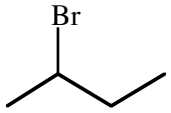
1-bromobutane

2



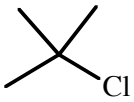
2-chlorobutane

3



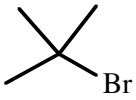
2-bromobutane

4



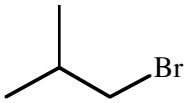
2-chloro-
2-methylpropane

5



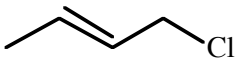
2-bromo-
2-methylpropane

6



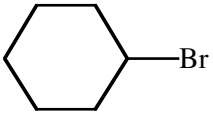
1-bromo-
2-methylpropane

7



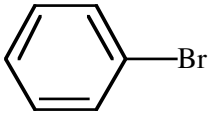
1-chloro-2-butene

8



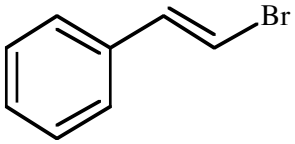
bromo-
cyclohexane

9



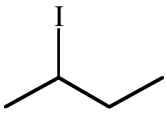
bromobenzene

10



ß-Bromostyrene

11



2-iodobutane

12

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, $AgNO_3$/ethanol for the S_N1 reactions), [stopper the tube in the case of **8**, which is smelly], mix by swirling vigorously (for NaI reactions, if you get a precipitate at first make sure you shake it/mix it initially; sometimes an initial false precipitate forms and persists that would dissolve if you swirl well), and watch for the formation of precipitate. For the NaI experiments, after 3 minutes warm test tubes in a 50° water bath if neither of them react; keep heating until at least one of them gives precipitate.

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

Notes

1. Crotyl chloride **8** is a lachrymator (makes you cry). Do not spill it, 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 it's 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 REACTIONS

Part 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 ($AgNO_3$/ethanol)

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

Run **12** vs **3** vs **4**

2. Primary/Secondary/Tertiary: (Record $1^{st}/2^{nd}/3^{rd}$ 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?

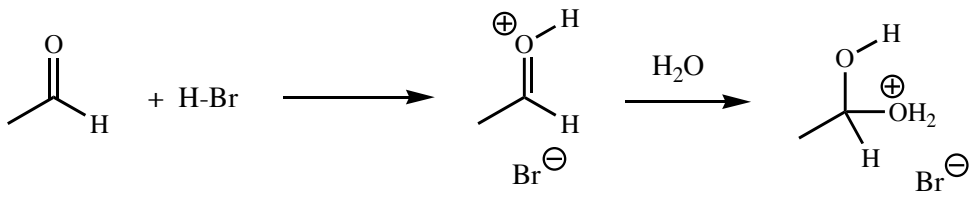
5. Both **2** and **7** are primary bromides. Can you explain the difference in their S_N2 reactivity, if there was any?

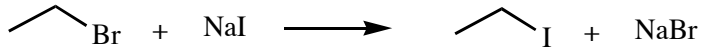
6. What would be the specific mathematical effect on the reaction rate if you carried out the sodium iodide-in-acetone reactions on the alkyl halides using an iodide solution half as concentrated? ("Slower" or "faster" is not specific enough.)

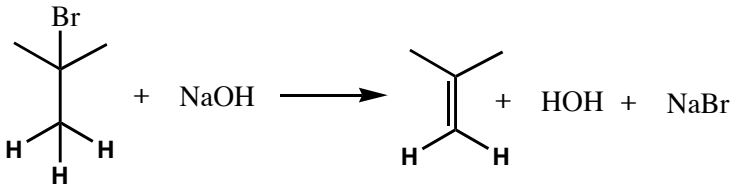
Name:

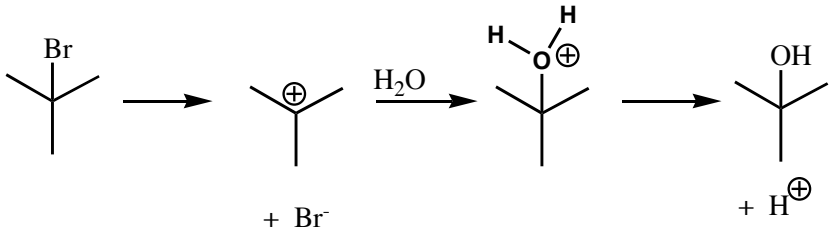
Arrow-Pushing Practice:

- 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.

1. (Old Test) 

2. S_N2 

3. E2 

4. S_N1 

5. E1