CHEMISTRY 356
FALL 2011

Course Instructor:
Dr. A. Azadnia 355-9715, ex 114
Office: 128 Chemistry
Office Hours: M, Th 10:00-11:30 or by appointment
E-mail Address: azadnia@chemistry.msu.edu

Texts: The Systematic Identification for Organic Compounds: A Laboratory Manual, R. L. Shriner: R.C. Fuson; D. Y. Curtin; T. C. Morrill, 6th, 7th, or 8th ed. Operational Organic Chemistry, John Lehman, 3rd or 4th Ed. Allyn & Bacon, Boston, MA, 1981.

Suggested Supplemental Text: The Spectrometric Identification of Organic Compounds, R. M. Silverstein; G. C. Bassler; T. C. Morrill, 5th ed.

Microscale Organic Lab., D. W. Mayo; R. M. Pike; P. K. Trumper, Third ed.

Introduction to Organic Laboratory Techniques: A Microscale Approach, Pavia, Lampman, Kriz, and Engel, second ed.

Safety Items And Notebook: Approved splash proof safety goggles (ANSI 279.1 1979). A pair of rubber gloves and an apron are strongly encouraged. Any bound 9 X 12 book with duplicate prenumbered pages and carbon paper.

Lab Schedule

Experiment Title	**Points**	**Due Dates**	**Source**
Sulfanilamidopyridine	100	Sept. 29	Hand-out
Benzil and its Derivatives	150	Oct. 20	Lehman Ex. 56
Literature Assignments draft **(Dave Voss)**		Oct. 2	Hand-out
Final Literature Assignment **(Dave Voss)**	120	Nov. 4	Hand-out
One Component Unknown	130	Oct. 28	Shriner/Notes
Three Component Unknown	300	Dec. 9	Shriner/Notes

Total	**800**		
Optional Experiments*	50 each	Dec. 9	See Dr. Azadnia

See Dr. Azadnia when you are qualified for an Optional Experiment by no later than December 1, 2011 (see next page for details).

Penalties: Projects completed after their assigned due date will be assessed a 10 point penalty per week and after the third week or **December 9, 2011** (whichever comes first), a grade of zero will be assigned for them.

Open lab will begin on the second week of classes (After Labor day).

Performance and Grading: *No passing grade will be granted to anyone who does not complete the literature assignment and /or the three-component unknown.*

The laboratory schedule and grading scheme are designed to encourage speed and flexibility without sacrificing careful technique. The following grade scale will be used:

Points Earned	**Grade**
736--800	4.0
688--735	3.5
608--687	3.0
520--607	2.5
428--519	2.0
427 or below	0.0

This is a straight–scale, it will not be curved or modified in any way. Keep in mind that each completed optional experiment is worth up to 50 points. **However, students will not be allowed to do any optional experiments unless they have completed all the experiments (including the three component unknown) and the literature assignments, successfully.** On the following page is a complete breakdown of the grading for each experiment. No points will be granted for any unauthorized optional experiment(s) performed. See Dr. Azadnia when you are ready (qualified) for an optional experiment.

Everyone must attend one of the two lectures on:

Wednesday, September 7 at 7:30-9:30 p.m. in room 138 Chemistry.

Thursday, September 8 at 7:30-9:30 p.m. in room 138 Chemistry.

Mr. Dave Voss will go over Beilstein, Scifinder, and other tools used for literature search.

No labs on Tuesday, September 6 or Wednesday, November 23.

The following is a breakdown of the grading for each experiment:

Literature Assignments	**120**
Beilstein	60
Chemical Abstracts	60
Sulfanilamidopyridine	**100 pts**
Aniline	20
Acetanilide	20
Final Product	60
Benzil & Its Derivatives	**150**
Benzilic Acid	30
meso-Hydrobenzoin	30
cis-Stillbenediacetate	30
Tetracyclone	30
Heterocycle	30
One Component Unknown	**130**
NMR	30
IR	20
A Solid Derivative	40
Correct Identification	40
Three Component Unknown	**300, 100 points per component**
NMR	20
IR	10
A Solid Derivative	30
Correct Identification	40

Total	**800**

Note:
All NMR spectra must be fully interpreted and all peaks must be assigned correctly to the corresponding protons in order to obtain credit. For IR spectra, you must assign the peaks that correspond to the particular functional group(s). Failure to do so will result in low grades.

Optional experiments will be graded depending on the experiment. An additional one component unknown may also be used as an optional experiment. Turn the optional experiment results to Dr. Azadnia.

General Procedures

Organic chemistry laboratory can be an important and rewarding part of the training experience of a scientist. In addition to the obvious benefit of developing familiarity with equipment, methods, and technical skills necessary for a practicing chemist, there are many less well defined benefits. Thus, for many students the concepts of organic chemistry become more real when they are connected with things done in the laboratory. For some there is a real satisfaction in making substances which are beautifully crystalline or aesthetically pleasing in some other way. Development of the observational skills necessary to determine what has gone wrong and how to correct it can be especially easy in the laboratory and has obvious carry over to other problems. An important part of the community of scientists (indeed any community) is the sharing of methods, observations, ideas, and feelings in ways that others can reproduce or empathize with. In the laboratory there are many opportunities to develop these communication skills in exchanges with other students, grad assistants, and faculty; and in the write-up of the laboratory notebook. Remember that "chance favors the prepared mind," and in the laboratory you have another opportunity to prepare your mind to capitalize on those rare moments of intimacy when nature chooses to reveal her secrets to us.

Laboratory Notebook

This term you will be working at your own pace and frequently you will be doing operations that no one else in lab will be doing. Furthermore, the individual experiments will not always be completed in the same day or week. This applies with particular emphasis to your three component unknown, which usually requires the entire term to complete.

It is essential that your notebook be well organized and highly detailed. The notes should be completed as the individual operations are done. Try to make and record as many observations as possible. Did the color change? Was heat evolved when the reagent was added? Notes made after the lab--especially just before the following lab session--generally omit essential data such as heating or cooling times, modifications to the intended procedure, subtle color changes, unanticipated results, and especially, contents of flasks in lockers!

If you are making efficient use of your lab time this term, you will have several projects going at once. This means that you will have an assortment of solids and liquids stored in your locker. Unless they are clearly and specifically labeled, the samples invariably will all appear to be identical about the middle of October. This has happened in the past. These students have had to start over from the beginning. Any label should tell you not only what the product is, but also where it came from.

The notebook reference number--coupled with a continuously-up-to-date notebook--should prevent such crises. For example, RWG-II-34-D is material D as described on page 34 of notebook II of RWG. The same reference number may be put on spectra of the sample. The use of this numbering system permits rapid location of a substance, even if its structure or composition is not known. Remember, label everything as you do it. Otherwise you may have to **label it properly when you do it over**.

Reporting Results

All "preps" are to be turned in to your laboratory instructor in a stoppered, labeled bottle or vial. The label is to have clearly written on it: notebook reference number (see above), the compound's name, m.p. or b.p., tare weight, weight of the compound, % yield, student's name, and laboratory section. These instructions may be supplemented from time to time by your laboratory instructor.

For each unknown component, the report should include all spectra, all notebook pages (the carbon copies), and a standard cover sheet which summarizes your results and conclusions. A reference to a primary (research) journal - along with the Beilstein or CA cross reference - for the melting point of the derivative must be included. Melting points from handbooks and catalogs are useful but **not acceptable**. In the past this omission has been among the most common reason for lowered grades. Report both the literature and your experimental melting points. Submit only a sealed m.p. capillary of the unmelted derivative.

If you have not prepared a derivative, a reference to a reasonable proposed derivative must still be included, just as if the derivative was made. Include the literature melting point. The best derivatives are in Cheronis and Shriner; use Beilstein or Chem. Abstr. for the literature references though.

If you have not decided what the component is, give a reference for a derivative, with melting points, for your guess of the most likely structure. You should be able to identify at least the most reactive functional group from the ir spectrum.

Optional experiments may be started once sulfanilamidopyridine, benzil and derivatives, both literature assignments, one component unknown, and three component unknown experiments are completed. To do an optional experiment you must see Dr. Azadnia.

All reports must have your name and section present on each page. Staple all pages of a report together securely to prevent their becoming lost.

Housekeeping: Each of you is responsible for the general cleanliness of the lab. All common apparatus such as clamps, hoses, and heaters should be returned to the proper compartments at the end of each period. Steam baths are to be returned to the benches with a complete set of rings. **Hoarding essential equipment in your locker is considered grounds for a grade penalty.**

Broken glassware or stoneware, **except thermometers**, should be placed in the BROKEN GLASS bucket. Don't be responsible for an injured custodian. The thermometers contain mercury. If you break one, tell your instructor immediately. He or she will help you clean up the mercury. Waste mercury, including all thermometer parts, should be returned to the stockroom.

Common areas (balances, hoods, etc.) are to be kept clean. "Abused" balances will be removed. Your instructor will assign clean-up duties if the need arises. You are responsible for the condition of your benchtop.

A large assortment of reagents will be used this term. Returning the bottle to its proper place promptly will save everyone a lot of time and also prevents an occasional mistake.

You are personally responsible for all broken or missing items. Be sure to put everything away at the end of each period and to lock the drawers securely. Bills for breakage and loss will be issued at the end of the term. Some items may be repairable; check with your TA.

Safety Regulations

In order to avoid personal injuries and injuries to fellow students while performing experiments in your Chemistry Laboratory Courses, it is required that you read and understand the following regulations before performing any experiments. Please indicate that you have done so by signing and returning one copy to your instructor. The department reserves the right to exclude any person from the laboratory who endangers him/herself or others.

A. Personal Protection

1. Approved safety goggles (not sunglasses) must be worn at **all** times when in the laboratory. Soft contact lenses shall not be worn in the laboratory under any circumstances, even under goggles. Hard contact lenses are conditionally acceptable. Check with Dr. Azadnia.

2. If you get a chemical in your eye, immediate and extensive washing with water **only** is absolutely essential to minimize damage. Use an eye wash bottle, a hose, an eye fountain or an eye cup at once. If you spill any chemical on yourself, immediately wash with large amounts of water; then notify your instructor.

3. The wearing of rubber gloves and aprons is strongly advised when working with toxic and/or corrosive substances. However, gloves must never be a substitute for neatness and careful technique. Do not use organic solvents to remove organic compounds from the skin: they will only spread the damage over a wider area. Solvents also tend to penetrate skin, carrying other chemicals along. Soap and water are more effective.

4. Do not apply ointments to chemical or thermal burns. Use only cold water.

5. Do not taste anything in the laboratory. (This applies to food as well as chemicals. Do not use the laboratory as an eating place and do not eat or drink from laboratory glassware.) Do not use mouth suction in filling pipettes with chemical reagents. (Use a suction bulb.)

6. To minimize hazard, confine long hair securely when in the laboratory. (Also, a laboratory apron is essential when you are wearing easily combustible clothing, especially synthetics. Such an apron affords desirable protection on all occasions.) Shoes or sneakers must be worn in labs at all times.

7. Exercise great care in noting the odor of fumes and whenever possible avoid breathing fumes of any kind. See also C-6.

8. No drinking or eating in the laboratory.

9. You are advised to obtain medical attention for cuts, burns, inhalation of fumes, or any other laboratory incurred accident. If needed, your laboratory instructor will arrange for transportation to Olin Health Center. An accident report must be completed at the second floor stockroom for all injuries.

10. No earphones (e.g. Walkman) shall be worn in laboratories.

11. Material Safety Data Sheets (MSDS) for all chemicals you are going to be using in this course are available in the library. Prudent laboratory practices require one to study the MSDS of hazardous chemicals prior to the use. You should consider all chemicals that unknown to you as hazardous. Ask your instructor if you are not sure.

Major or continual violations of safety rules will result in dismissal from lab for the day in addition to a 50–point penalty per occurrence.

B. Property Protection

1. In case of fire, call the instructor at once. If you are near an extinguisher, bring the extinguisher to the fire, but let the instructor use it.

2. Know the location of all safety equipment: fire extinguisher, safety showers, fire blankets eyewashes (any water hose works in an emergency) and exits.

3. Treat all liquids as extremely flammable unless you know them to be otherwise.

4. Clean all spills promptly with water (except water-reactive substances) and paper towels. If you have any doubts about the proper clean-up procedure, ask your instructor.

5. Disposal of waste: dispose of all chemicals properly. For hazardous waste use the waste containers in your lab. Ask your instructor how to dispose of waste chemicals you are unsure about.

6. Place broken glass in the appropriate container. Do not put broken glass in the waste paper cans.

C. Laboratory Technique

1. Read the experiment before coming into the lab. This will allow you to plan ahead so that you can make best use of your time. The more you rush at the end of a lab, the greater your chance of having an accident.

2. Perform no unauthorized experiments. Do not remove any chemicals or equipment from the laboratories. You alone will bear the consequences of "unauthorized experimentation".

3. Never work in any laboratory alone!

4. Don't force glass tubing into rubber stoppers. (Protect your hands with a towel when inserting tubing into stoppers, and use a lubricant.)

5. When working with electrical equipment observe caution in handling loose wires and make sure that all equipment is electrically grounded before touching it. Clean up all puddles immediately.

6. Use hood facilities. Odors and gases from chemicals and chemical reactions are usually unpleasant and in many cases toxic.

7. View reactions from the side, keeping glass and safety glasses between you and the reactants. Do not look into the open mouth of a test tube or reaction flask. Point the open end of the tube away from you and other laboratory workers.

8. Be a good housekeeper. Order and neatness will minimize accidents.

9. Laboratory safety is the personal responsibility of each and every individual in the laboratory. Report unsafe practices.

10. Treat all chemicals as corrosive and toxic and all chemical reactions as hazardous unless you know them to be otherwise.

11. **Material Safety Data Sheets, MSDS** can be obtained from the chemistry department web page. First go to the safety page at: http://pittising.cem.msu.edu/Chem_main/Safety/Safety.html and then click on MSDS.

Literature Syntheses

The overall objective of this assignment is to introduce you to the chemical literature as a laboratory resource. Frequently a few hours spent in the library will replace several days spent in the laboratory. Efficient use of the library includes the ability to find information from both "old" and "recent" literature as well as proper use of electronic media. There are two parts to the literature assignment, each worth 60 points: the Beilstein/Reaxsys assignment and the Chemical Abstracts/Sci-FInder assignment. For each of these assignments you will be given a 3 x 5 card to copy from. Be sure you copy **all** of the information precisely as it is written on the card.

For the Beilstein literature assignment the card shows a structure along with some physical properties or, on occasion, an author's name. There is only one correct answer for each Beilstein card. The correct answer for each card is the one that not only is for the proper compound, but fulfils any additional requirements listed on the card. The report will include the Reaxsys registry number, the name of the compound, plus, a brief description of the synthesis of the compound and the citation to the original journal. For the Beilstein assignment you do not need to actually obtain the cited journal.

Preliminary Report Requirements Beilstein/Reaxsys:
1) Reaxys Registry Number
2) Name of compound (as referenced by Beilstein)

Final Report Requirements Beilstein/Reaxsys:
1) Preliminary report
2) Original journal reference in modern format {*ex. J. Org. Chem*., **61**, 820 (1996)}

For the Chemical Abstract/Sci-FInder literature assignment you will be given only a structure. Your assignment is to find the name and synthesis of the compound using Chemical Abstracts. All compounds on the list are selected from journal articles no older than 1957.

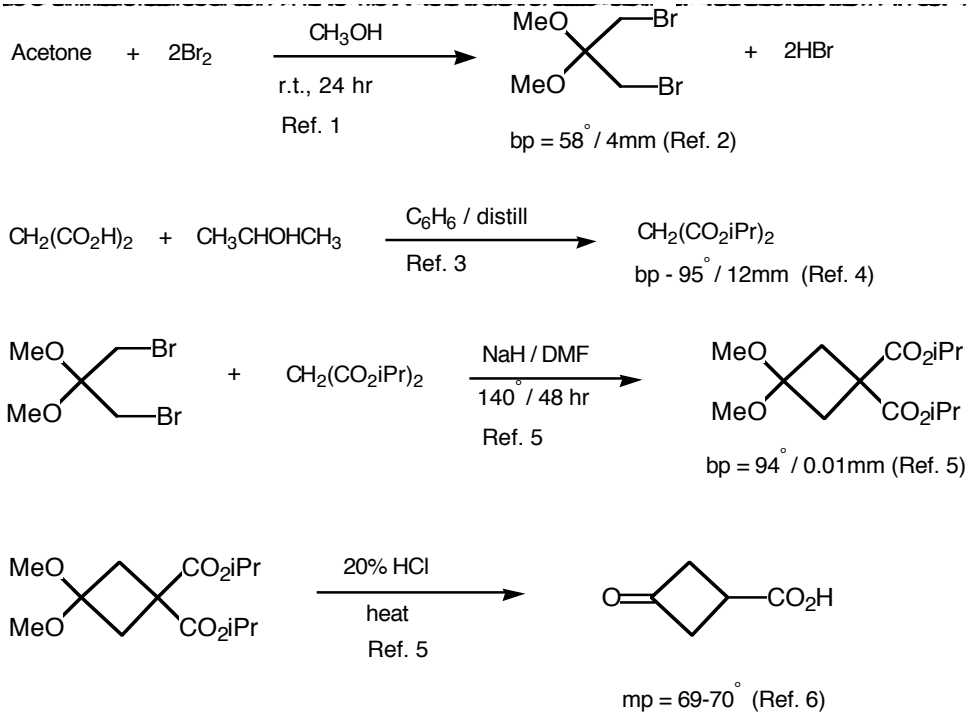
The report for this assignment will consist of the name of the compound, the CAS registry number, and the reference to the original paper containing the synthesis, plus a flow chart for the preparation of the compound from commercially available reagents. Literature references are required for each step, along with prices for all reagents and solvents. You may have to synthesize "starting material" as well. Therefore, there are multiple solutions to each Chemical Abstracts assignment. These secondary searches may be done in either Sci-Finder or Reaxsys. A sample flow chart is shown on the next page. Remember that a complete reference includes the author's name and initial, *the journal*, **volume**, pages, (year) in the acceptable format.

Preliminary Report Requirements Chemical Abstracts
1) CA registry number
2) Name of compound (as referenced by CA)

Final Report Requirements Chemical Abstracts
1) Preliminary report
2) Original journal reference(s) in modern format
3) A diagram of the synthesis of the final product, continuing backwards until a purchasable compound is found, each step must be referenced.
4) Price, grade, and supplier for **all** reagents used in the synthesis.

Sample Chemical Abstracts Assignment

Preparative Flow Chart for 3-Oxocyclobutanecarboxylic Acid (# C-000)
Joe Collij Sect. 0 Student No. 000001



Reagent Sources

acetone (reagent), Aldrich, $5.60 / 500ml
bromine (ACS), Aldrich, $18.00 / 100ml
methanol (ACS), Aldrich, $6.50 / liter
benzene (ACS), Aldrich, $56.00 / 4 liters
sodium hydride (60% dispersion), Aldrich, $60.00 / 100g
dimethylformamide (reagent), Spectrum, $45.00 / 4 liters
isopropanol (ACS), Aldrich, $8.80 / liter
malonic acid, Aldrich, $11.60 / 100g
hydrochloric acid, 20%, Baker, $15.00 / liter

References

1. Gallucci, R.R.; Going, R. *J. Org. Chem.*, **46**, 2532, (1981)
2. Hughes; Watson; Yates *J. Chem. Soc.*, 1215, (1932)
3. Paloma; Mikkila *Chem. Ber.,* **75**, 1666, (1942)
4. Caserio, M.; Roberts, J.D. *J. Amer. Chem. Soc.,* **80**, 5837, (1958)
5. Pigou, P.; Scheisser, C.H. *J. Org. Chem.*, **53**, 3841, (1988)
6. Avram, M; Nenitzescu, C.D.; Maxim, M. *Chem. Ber*, **90**, 1424, (1957)

Please note that the literature report must be typed and structures must be drawn via computers. Therefore, hand–written reports will not be accepted.

Sulfanilamidopyridine & Reduction of Nitrobenzene

In line with our policy of eliminating wherever possible the use of benzene, you will synthesize sulfanilamidopyridine starting from nitrobenzene. Please note that both nitrobenzene and aniline are toxic by inhalation or contact with the skin. Strong sodium hydroxide solutions will etch glass slowly and also tend to freeze standard taper joints by reprecipitating silicates. Prepare the sodium hydroxide solution on the day you plan to steam distill the free aniline. Be particularly careful to grease all joints completely and disassemble and clean the apparatus immediately after distilling the aniline. Before starting this reaction, review operation 15b on pages 614-616. The objective of a steam distillation is to remove all water-insoluble volatile components. No fractionation of these components is desired. Best results are obtained when the distillation is performed as rapidly as possible, consistent with the ability of the condensers to reliquify and cool the distillate. Mechanical carryover of the solid tin oxide or soluble salts is eliminated by using a Claisen stillhead.

1. ANILINE. The reduction of the nitrobenzene is carried out in a hood using a 500 mL round-bottomed flask suitable for steam distillation of the reaction product. Put 25 g of granulated tin and 12.0 g of nitrobenzene (bp = 211°) in the flask, make an ice-water bath ready, add 55 mL of concd. hydrochloric acid, insert a thermometer, and swirl well to promote reaction in the three-phase system. Let the mixture react until the temperature reaches 60° and then cool briefly in ice just enough to prevent a rise above 60°, so the reaction will not get out of hand. Continue to swirl, cool as required, and maintain the temperature in the range 55-60° for 15 minutes. Remove the thermometer and rinse it with water, fit the flask with a reflux condenser (to catch any nitrobenzene that may steam distill) and heat on the steam with frequent swirling until droplets of nitrobenzene are absent and the color due to an intermediate reduction product is gone (about 15 minutes). If metallic tin is still present add more HCl and continue mixing, with heat, until the metal is entirely consumed. During this interval dissolve 40 g of sodium hydroxide in 100 mL of water and cool to room temperature.

At the end of the reduction reaction, cool the acidic solution in ice (to prevent boiling and loss of aniline). When cool, slowly add, with mixing, the solution of alkali. A number of variables such as the rate of base addition, temperature, stirring, concentrations and carbonate content will affect the appearance of the inorganic precipitate. It's color may vary from jet black through various shades of grey to yellow or white. As long as the solution is highly alkaline (check a well-mixed sample with pH paper) no reduction in yield will occur.

Proceed to steam distill. Use the same apparatus that you used to collect crude 4-chlorotoluene (the Sandmeyer reaction) in CEM 355. Since aniline is fairly soluble in water (3.6 g/mL at 18°) the distillation should be continued somewhat beyond the point where the distillate has lost its original turbidity (50-60 mL more). The steam distilled aniline need not be isolated. Add 10 mL of concentrated hydrocloric acid and sufficient water to make 300 mL. (Good stopping place).

2. ACETANILIDE. The acidic solution of aniline from above may be decolorized with charcoal (OP-23) if it isn't water-white. Prepare a solution of 0.135 mole of sodium acetate in 60 mL of water. Premeasure 14 mL of acetic anhydride. Adjust the temperature of the acidified aqueous aniline solution to 50°C, add the acetic anhydride rapidly while swirling to mix and then immediately add the sodium acetate solution. The anhydride is rapidly hydrolyzed if the acidic solution is not promptly neutralized with the acetate, greatly reducing the yield. Amides hydrolyze much more slowly under these conditions, but they must still be collected the same day.

Cool the mixture by swirling in an ice bath. Collect the suction filtration and pump as dry as possible. Complete the drying by dissolving the white leaflets in methylene chloride, discarding the water layer, drying with sodium sulfate, decanting the dry solution and distilling off the solvent over steam.

3. 2-SULFANILAMIDOPYRIDINE

Caution: Chlorosulfonic acid is very toxic, corrosive, and a lactrymator. It reacts violently with water to form HCl-gas and sulfur oxides. Avoid contact and do not breath the vapors of chlorosulfonic acid since it will cause sever damage to skin and eyes. Also, its vapors are extremely dangerous to eyes and respiratory tract. Note also that chlorosulfonic acid rapidly degrades most types of rubber. Rubber gloves are a safety device, but they are not a substitute for neat, safe technique. **Caution**: Many corrosive fumes will be evolved. Perform the next three paragraphs in a hood. Report any spill of chlorosulfonic acid to your TA immediately. The spills need to be neutralized with sodium bicarbonate.

CHLOROSULFONATE: Place **no more than 25 mmole** of dry acetanilide in a dry 125-mL Erlenmeyer flask. Cautiously melt the acetanilide in the Erlenmeyer with a soft microburner flame. Swirl the melt as it cools to allow a thin film of solid to coat the bottom of the flask. Cool the acetanilide in an ice bath. Double check to verify that no water is present. WATER AND CHLOROSULFONIC ACID REACT VIOLENTLY. Measure 10 mL of chlorosulfonic acid into a DRY 100 mL graduated cylinder. Examine the bottle before you handle it. If it is wet or dirty, wipe it with a wet paper towel and then dry it. When you are done, wipe the bottle including the threads with a dry paper towel before you replace the cap. Soak the used towels in water before discarding them. Add the chlorosulfonic acid to the solid acetanilide. Drain the graduated cylinder thoroughly and then, working in a hood with the safety shield in front of your torso and face, cautiously add water with a wash bottle to the graduated cylinder. Wash the quenched acid promptly with tap water.

Remove the Erlenmeyer from the ice bath and swirl the contents to allow the contents to warm to room temperature. Once all of the solids have dissolved, heat the flask on a steambath for 30 minutes. Again clamp the flask and cool to below 20°C.

The next step is the most common source of failure in the sequence. Follow the procedure EXACTLY. If it fails, you will need to repeat some or all of the preceding steps, depending on how much "starting material" you have. Fill a large beaker with about 100 mL of cracked ice. Using a short Pasteur pipette (break of the fine part) and a glass-stirring rod, transfer the chlorosulfonic acid solution rapidly, but dropwise to the ice (pouring slowly usually results in a lousy yield). Stir the ice briskly as you add the liquid, crushing any lumps of product that may congeal. Immediately suction filter the precipitate and rinse with about 10 mL of ice cold water. Press the filter cake dry and add the solid - paper included - to 100 mL of ether. Triturate any remaining solid. If a solid residue remains, remove it by suction filtration. Rinse the solid with another 10 mL of ether.

Add a minute crystal of methyl red or methyl orange to the ether filtrate and swirl to dissolve the indicator in the residual water. Hold it up to the light and withdraw the now visible water with a Pasteur pipet. Dry the ether solution with sodium sulfate and decant it into a dry 125 mL Erlenmeyer flask. Add 5 mL of pyridine (hood) and proceed directly to the next step. Record all color changes.

Pour the above solution into a solution of 20 mmole of 2-aminopyridine in 10 mL of ether and 2.5 mL of dry pyridine. (For best results, this solution should be prepared in advance - while the chlorosulfonic acid mixture is being heated perhaps. Use a 250 mL Erlenmeyer flask and keep it stoppered until you need it.) Note any evidence of a reaction for the next 15 minutes. When things appear to have quieted down, stopper the flask and store if for at least 36 hours. Work on your benzil sequence or your one component unknown in the interim.

Thoroughly cool the mixture in an ice bath and collect the solid by vacuum filtration. Wash the solid free of pyridine with cold water. Adding water to the filtrate may yield a second

crop of product. Check the melting points. Hydrolyze the amide by refluxing the solid with 15 mL of 3M sodium hydroxide for 30 minutes (Steam isn't hot enough to boil aqueous solutions). Transfer the cooled reaction mixture to a 250 mL Erlenmeyer flask and add 3-4 drops of bromthymol blue solution to the flask. Using a Pasteur pipette, titrate (greenish-yellow, pH 6.8) the product with 6M of HCl. (Concentrated HCl is 12 M.) Considerable white precipitate (your product) should form. If the solid is so dense that you can't see the end point, do a preliminary filtration and continue adding HCl until you reach the end point. If you are having a hard time finding the end point you may also use bromthymol blue paper. This is easily prepared by "painting" a piece of filter paper with the indicator solution. Allow it to dry and transfer test droplets to the paper with a stirring rod. Cool thoroughly and collect the remaining crude product. Combine the various crops of product. What would be the result of adding too much HCl? Too little HCl? Justify your answers in relation to the structure of the product. If you pass the end point, add dilute NaOH to raise the pH back to 6.8.

Recrystallize the crude 2-sulfanilamidopyridine from ethanol. Add the alcohol sparingly, since the crude product may be contaminated with some NaCl which is quite insoluble in ethanol. Yes, steam is hot enough to boil ethanol, but isn't hot enough to ignite the alcohol fumes.

Benzil & Derivatives

1. BENZIL The oxidation of your entire sample of benzoin to benzil is to be done in a hood, using the procedure on page 454-455 of your text. Combine the cupric acetate, ammonium nitrate and acetic acid solution, bring the mixture to a boil, drop the heating mantle and finally add the benzoin slowly and resume heating. If the oxidation mixture doesn't stay green through the entire reaction time, precipitate the organic materials with 100 mL of water, collect the solids, filter well and repeat the oxidation. The oxidation may be started by heating and allowed to proceed overnight at room temperature. Complete the hour of heating the next period. Don't forget **WASH UP**. Use portions of the purified and dried product to prepare the following derivatives. Any excess benzil is to be submitted along with the derivatives. All six will be graded. Check the benzil m.p. before you attempt to prepare the derivatives (lit = 95 - 96°) and recrystallize if necessary. The benzil must be pure. From here on, label all flasks, etc.

2. BENZILIC ACID. Convert one gram of pure benzil into benzilic acid using the procedure in your text. (Experiment 56-c). Do not dilute beyond 100 mL. The hot charcoal filtration should remove the colloidal matter. Use cresol purple paper to test the pH (red<2, yellow>3). Some students have found use of a seed crystal or extraction helpful in forming a crystalline product. Some recrystallizations take days.

3. MESOHYDROBENZOIN. Reduce 500 mg of benzil in a 50 mL RB flask with this procedure: Dissolve the diketone in 5 mL of hot ethanol and cool rapidly in ice-water with swirling to form a fine suspension. Then add 100 mg of sodium borohydride (caution: hygroscopic). The benzil soon dissolves, the mixture warms up, and the yellow benzil is consumed in a few minutes. After 10 minutes, add 5 mL of water and heat to boiling with a heating mantle. Remove any suspended matter by gravity filtration, saturate the boiling filtrate with water and allow the solution to cool overnight. Complete the crystallization in ice-water and collect the product by suction filtration. This filtrate also goes to the USED ETHANOL bottle.

4. CIS-STILBENE DIACETATE. Reduce 1.0 g of pure, dry benzil in a fumehood with this procedure: acetyl chloride is a volatile corrosive liquid; pipet 2.0 mL of acetyl chloride (d = 1.1 g/mL) into a six-inch test tube. Cork the test tube and cool the contents thoroughly in an ice bath. Place 1.0 g of finely powdered benzil and 1.0 g of zinc dust in a 50 mL Erlenmeyer flask, mix intimately with a glass rod and also clamp in the ice bath. Wait 10 minutes. Add the **cold** acetyl chloride to the **cold** solids and **stir vigorously** and **continuously** with a glass rod for five minutes in the ice bath. Stir the tarry contents for another ten minutes outside the ice bath. The success of this procedure depends on keeping the zinc dust well suspended at all times. Hydrolyze the acetyl chloride to precipitate the crude product by adding 25 mL of ice water to the flask. Swirling and cooling will eventually precipitate a granular solid. If it looks bad, keep stirring. In difficult cases, it may be necessary to decant the water, add 10 drops of ethanol, stir well to break up the tarry mass, and then replace the water. Any lumps should be thoroughly crushed with a glass stirring rod (not a metal spatula) before the solid is collected by suction filtration. Rinse the flask and the crude product with 20 mL of cold water. This filtrate may go down the drain eventually. (Occasionally additional product separates slowly.) Return the solid to the same flask, add 20 mL of ethanol and heat to boiling over steam. Add some charcoal, swirl briefly, remove the solids by hot gravity filtration and then rinse the flask and residue with another 5 mL of hot ethanol. Precipitate the product by adding 20 mL of water and cooling thoroughly in an ice bath. Recrystallize the cis-stilbene diacetate from ethanol (**without** water). The alcoholic filtrates should go to the USED ETHANOL bottle.

5. TETRACYCLONE. Convert 1.0 gm of benzil to tetraphenylcyclopentadienone with this procedure: **Under a hood**, combine 1.0 gm of benzil, 1.0 gm of 1,3-diphenyl-2-propanone, and 5 mL of diethylene glycol (bp, 245) in a 6 inch test tube. Heat the mixture with a microburner until

the mixture is a homogeneous solution. Pipet 0.5 mL of benzyltrimethylammonium hydroxide (40% v/v in water) into a small test tube. Adjust the temperature of the benzil solution to **exactly 100°** and pipet the basic catalyst into it. Stir briefly and let the temperature drop to below 75°. Cool in ice water and add 5 mL of methanol to thin the slurry. Filter the suspension and wash with methanol until the washings are a clear magenta with no trace of brown. Pour the combined methanol washes into the USED METHANOL bottle. Pour the used ethylene glycol in the USED ETHYLENE GLYCOL bottle. Recrystallize the crude solid by heating it in 10 mL of diethylene glycol for each gram of product. Heat with stirring to 220° and allow the hot solution to cool undisturbed. Collect the product, wash with methanol, dry well and determine the yield and melting point.

6. A HETEROCYCLE. Dissolve 1.0 g of benzil and 0.60 g of urea in 10 mL of ethanol in a 25-mL round-bottom flask, and add to this a solution of 1.65 g of potassium hydroxide in 2 mL of water. This mixture is very alkaline. Grease the joint. After refluxing the mixture for 2.5 hours, the flask is cooled and the solids filtered off. The alkaline filtrate is cooled in an ice-water bath and slowly acidified with 6N sulfuric acid (cond. H_2SO_4 is 36N or 18 M) to pH 3, causing the heterocycle to precipitate out of solution. The product is filtered and air dried to yield the crude heterocycle ($C_{15}H_{12}N_2O_2$), mp >260°C with decomposition. Flush the aqueous filtrates down the drain. Recrystallization can be accomplished from 50mL of 95% ethanol. Remove any inorganic solids (What inorganic compounds might be present?) by hot filtration of the refluxing alcohol solution. A second crop may be isolated by evaporation of half of the ethanol. If time and instrument availability permits, the infrared spectrum of the final product can be recorded (Nujol or KBr). NMR: 10 H at 7.4 (s) and 2 H at 9.0 (s). The filtrates are to be placed in the USED ETHANOL bottle. Submit all product samples as well as all remaining benzil.

The following books are on reserve in the Chemistry Library for use in CEM 356:

Personal Copy	Aldrich	Catalog Handbook of Fine Chemicals
Personal Copy	Alfa	Alfa Catalog
QD 98 C45 1983	Cheronis, Entrikin, and Hodnett The earlier editions are also fine.)	Semimicro Qualitative Organic Analysis
QD 262 F5 v. 1-9	Fieser & Fieser	Reagents for Organic Synthesis
Personal Copy	Mayo, Pike, & Butcher	Microscale Organic Laboratory
Personal Copy	Williamson	Microscale Organic Experiments
Personal Copy	Pfalz & Bauer	P & B Research Chemical
QD 291 R3 1967	Rappoport	Handbook of Tables for Organic Compound Information
QD 272 f.S6 S55 1981	Silverstein & Bassler (The earlier editions are also fine.)	Spectrometric Identification of Organic Compounds
Folder	Folder	Optional Lab. Projects

Unknowns

The identification of substances is a common problem encountered in the final stages of structure determination of a compound of unknown structure. We have tried to set up this experiment as a realistic experience in identification subject to the limitation of time, materials, and pedagogy. Additional sample can be obtained, but a point charge will be assessed.

At the beginning of the term you will be given two, different semimicro scale pure unknowns plus a macroscale mixture of the three compounds of commercial purity. These compounds have been selected from a long list and not all of them are known to be completely safe. Remember that organic compounds can enter the body by breathing, by swallowing, through cuts and even directly through unbroken skin. Work neatly and treat all chemicals as if they are toxic. Most are.

In practical structure determination, substances are usually obtained as impure mixtures and must be separated and purified. You should determine and apply the applicable separation techniques you have learned (extraction, crystallization, distillation, chromatography). It is wise to follow the course of the separation by applicable analytical techniques (tlc, ir) to ensure that no chemical changes take place during the separation and purification procedure. For example, determining the ir spectrum of the mixture and then the ir spectra at successive stages serves as one useful check on the integrity of the components. Purification of the components is usually essential in order to avoid spurious results in the subsequent identification tests.

Once you have obtained acceptable spectra and determined the mp (± 5°) or bp (± 10°) of a pure component, you may request its elemental analysis. If all the data are acceptable, either a mass spectrum or a quantitative elemental analysis will be issued. Submit your labelled spectra with mp/bp to your T.A. You need not submit the entire set at once. Each component will be handled separately. If you need to resubmit your corrected data, attach the new work to the previous attempts.

It is expected that you will deduce the structure of each unknown from these data. To assist you in interpreting these data numerous copies of "Silverstein" are on reserve in the library. Learn this valuable skill now! It may be possible to discover the identity of your unknown by doing "hunt and peck" searches of published compilations of spectra. This approach is time consuming, non–instructive, and not guaranteed to succeed. Not all unknowns are in these collections. One objective of this course is for you to become competent at spectral interpretation.

Use any of the tests described in Lehman, Part III or any of the other experiments on qualitative organic analysis that will help you make a positive identification. Both Cheronis *et al*. and Shriner *et al*. have excellent discussions of separation and identification techniques. The sooner you start using Cheronis and Shriner, the easier this assignment will be.

The unknowns can be either aliphatic or aromatic, but will be found in the lists in Cheronis et al.; Rappaport; or Shriner, et al.

You will be expected to present a convincing case for the identification of the unknowns, including at least one derivative of well defined melting point, and several other pieces of supporting data for each compound by the end of the term. A reference to the primary literature must be given for each solid derivative. Attach all relevant notebook pages, spectra, **and earlier submissions** to the completed cover sheet.

Separation of the Mixed Unknown

Take extensive notes and label everything with a Notebook Reference Number. If you seek help, the quality of the help will be directly related to the quality of your recorded observations.

The following directions are general and should be modified based on your results and observations. Do not use your entire sample in any step until preliminary trials indicate that the procedure works. You should review Cheronis et al. (1965, Chapter 6 or 1957, Chapter 11), before proceeding with abandon. Your lab instructor also has a copy of the chapter for in-lab consultation. Remember, though, that lab time is expensive, especially at the end of the term.

1. If the unknown is heterogeneous, separate the two phases and treat them separately. Remember that all components probably will be present in both portions, but in different concentrations. Decant or gravity filter. Do NOT use vacuum filtration - you may lose a volatile component.
2. Take ir spectra of the portions or mixture and pmr of liquid portion(s).
3. Try distilling the liquid with a steam bath to isolate a low boiling component if present. The boiling point is a good indication of purity and structure. Bubbles on the boiling chip indicate a volatile component. Heating over 100° - i.e., using a burner or a heating mantle - frequently causes undesirable reactions or decompositions. It makes tar.
4. Dissolve the solid or liquid residue(s) in ether. Separate and evaporate the ether. Extract (both?) residues with water.
5. The ether soluble, water insoluble portion is then extracted first with dilute acid, and then dilute base.
6. Bromthymol blue and methyl orange test papers can be made by "painting" the indicator solutions onto filter paper pieces. Use these to separate A_2, A_1, and $A_{1'}$.

The interim report for each unknown mixture component will be a brief summary of the separation of the mixture and a tabulation of the physical properties of the purified component. Also suitable spectral data and a melting point or boiling point must be reported.

Note: See the last two pages for a possible separations flow chart and a table of solubility classifications. Keep in mind that many chemicals may hydrdyze in acid or base. Don't store mixtures in acidic or basic solutions overnight. It is best to do the extraction sequence for the first time "quick and dirty". Once you have a sense of where the components will appear, repeat the extraction sequence - working more carefully - with a larger portion.

Boiling Points of Micro Samples

The determination of a boiling point by distillation with ordinary apparatus requires that at least 5 mL of the liquid be available. Boiling points of smaller samples can be determined easily by the inverted capillary technique of Siwoloboff (Chem. Ber. **1886**, 19, 795). The apparatus for this technique is shown below and consists essentially of a boiler tube, 5 cm long and 4-5 mm in diameter (we use disposable culture tubes), that holds the sample and fine capillary thermometer sealed by fusion about 25 mm from the bottom. The boiler tube is affixed to a thermometer and heated in a Thiele melting point bath to secure the delicate control of temperature necessary for this technique. See also Mayo, Pike and Butcher for an even smaller scale version of this technique.

Sample area of a Thiele tube used for boiling points of microsamples

The laboratory procedure is to place 2-5 drops of the sample in the 4 mm boiler tube, giving a column of liquid 5-15 mm high into which the sealed capillary tube is dropped. The boiler tube is attached to the thermometer by means of a rubber band and the assembly supported in a melting point bath so that the top of the sample is at least 10 mm below the bath level. The bath is heated gradually with constant stirring until a rapid stream of bubbles emerges from the capillary. The temperature at which rapid bubbling occurs is a few degrees above the boiling point; the proper bubbling rate is easily recognized after gaining experience with a sample of known boiling point. Keep the rubber band above the expanding oil so that it won't dissolve.

The next step is to discontinue heating the bath and observe the boiling tube while the bath temperature drops about 10°. Bubbling ceases when the temperature approximates the boiling point of the sample, and as the temperature continues to drop, the liquid is drawn up into the capillary. The sequence of heating and cooling replaces most of the air in the capillary with vapor of the sample. Heating is now resumed and the temperature is raised at a rate of 2° per minute, with constant stirring, until bubbles once more emerge. The flame is removed and the exact temperature at which bubbling ceases is noted. This is the boiling point of the liquid, since it is the temperature at which the vapor pressure inside the capillary equals the external atmospheric pressure exerted on the top surface of the liquid in the boiler tube. For greater precision the heating and cooling may be repeated several times. Unlike ordinary distillation the Siwoloboff method gives merely the boiling point of the sample and provides no indication of the amount or type of impurity that may be present. Traces of volatile impurities will drop the boiling point significantly.

Spectroscopy

Infrared Spectroscopy

The operation of most infrared spectrometers is very simple. The crucial operation in obtaining quality infrared spectra is sample preparation. Spectra of solids are commonly obtained from solution (CCl_4, $CHCl_3$, or CS_2), potassium bromide wafers, and Nujol mulls.

Nujol mull: The traditional mulling technique involves grinding the sample in a small mortar. Place 5-10 mg of sample in one depression of a porcelain spot plate. Grind the dry sample with a 4" test tube for several minutes. Add one drop of mineral oil (Nujol) and grind several minutes more. The finished sample should have the consistency of toothpaste. If the mull is too thick, add another drop of oil and continue grinding. The secret to success is thorough grinding. An alternative procedure uses a pair of clean, standard taper joints for grinding. Place small amounts of sample and mineral oil inside a female joint. Place a glass stopper inside the joint with a twisting motion. Continue twisting and grinding until the proper consistency is achieved. A properly prepared mull has all particles ground smaller than 2 microns. Otherwise, excessive scattering will occur, and the peaks will have broad tails on the low frequency (wave number) side. The remedy is to grind the sample better. You may use whichever procedure works best for you. The salt plates are brittle, but soft and water soluble. Use a rubber policeman to transfer some of the mull to a salt plate. Place the other plate on the mull and press together gently. The mull should be slightly translucent and cover the entire window uniformly.

To use the FT-IR, select control panels from the tools menu. If the current background is older than 15 minutes take a new one. To do this set the control panel to background and click on scan.(make sure your sample is not loaded at this point) Next slide the cover back and place the salt plates (or the KBr press) in the sample holder. Close the cover and click on scan. If the spectrum is acceptable go to display, choose title and label your spectrum appropriately, then go to plot and print the spectrum out. If the spectrum is not acceptable go to math and choose auto baseline. If the spectrum now appears acceptable, go to title and proceed as before. If it is still not acceptable remove your sample and remake it. After you have plotted the spectrum, clean the plates and return them to the instructor. Wipe the bulk of the material off with a Kimwipe. **Do not wash the plates with water.** They are very soluble (35.7 g/100 mL) in water. Place a Kimwipe on 2-3 layers of paper towel. Put a few drops of ethanol on one part of the Kimwipe and rub the plate in the ethanol. **Dry the plate by sliding it onto a dry part of the Kimwipe**. Repeat this operation for the other three faces. Place the clean plates in the can between the foam and return them and the pen to the stockroom.

Potassium bromide wafer: The objective of this exercise is to learn how to make usable KBr wafers for IR spectroscopy. Obtain a minipress from your the stockroom. Weigh out less than 1 mg of sample on the analytical balance. Glassine weighing paper is in the drawer under the balance. Add 100 mg of ir grade KBr and immediately close the bottle; it is hygroscopic. Thoroughly grind the mixture on the white spot plate and prepare the wafer. Use less than half of the ground sample to make the actual pellet. (Lehman, OP-33). Use the controlled torque wrench attached to the bench in the lab. Remove the bolt and examine the results. If the wafer looks like waxed paper, run the spectrum. If it is opaque, pop out the wafer and try again, grinding more thoroughly. Potassium bromide spectra frequently display water peaks near 3450 cm^{-1} and 1640 cm^{-1}. The water may have been in the sample or the KBr, or may have been introduced during preparation of the wafer. Drying overnight at 120° will remove water from KBr. Many samples decompose under these conditions. Replace covers immediately after each use. The press is made from hardened steel bolts. They are not known for corrosion resistance and halides are very corrosive to steel. Wash the holder and bolts thoroughly with distilled water. Rinse away the residual water with acetone. For extended storage (i.e., overnight), a thin film of oil will be applied to the bolts. Return the cleaned and dried press and pen to the stockroom.

CEM 356 students frequently do not utilize ir data to the limit. The following pages list the generally most useful peaks. You should be very familiar with (memorize?) the data. All previously learned ir techniques are available.

NMR Spectroscopy

Sample Preparation:

As in infrared spectrometry, one of the most critical operations is sample preparation. A poorly prepared sample is a common cause for a poor spectrum. The NMR tube should be clean and free of any extraneous protons. Water can be removed only with difficulty from the long narrow tubes. Rinse a used tube with acetone and shake it as you would "shake down" a clinical thermometer. Remove the acetone by rinsing with several small portions of regular carbon tetrachloride, shaking out the liquid each time. Any unremoved acetone will produce a singlet at 2.0 ppm. NMR's must be run as solutions in ^1H free solvents. Some possibilities to consider are CCl_4, $CDCl_3$, D_2O and trifluoroacetic acid. The D_2O may be made basic with anhydrous K_2CO_3 or acidic with $SOCl_2$. Before preparing a solution with an expensive deuterated solvent- you should confirm the solubility with the corresponding proton version. Once you have verified the solubility, prepare the solution in a 3" or 4" test tube, centrifuge to settle any insoluble compounds and pipette the clear liquid into an NMR tube. Partially fill the cleaned tube (a trace of CCl_4 won't matter--Why?) with a solution of your compound in the appropriate solvent. A properly filled nmr tube has a **clear, solid-free** homogeneous solution in the bottom 1.5 to 2 inches. Less gives poor spectra; more only wastes solvent and sample.

Remember that although acetone is a good solvent for removing organic residues, it does have 6 protons that appear as a singlet at 2.05 ppm. Subsequent removal of acetone from nmr tubes requires some work. Drain the tube thoroughly after the rinse and place the NMR tube in a preheated oven (120^o C) for at least one hour and then blow dry air through it for about 5-10 minutes. A special assembly is set up in each laboratory. Ask your TA to show you the proper use of it. **Do not use the compressed air directly.**

D_2O is extremely hygroscopic. It invariably will have a peak at approximately 5.5 ppm., depending on the temperature, pH, polarity, etc. These protons come from H_2O in the air as well as any exchangeable protons (N-H and O-H) in your sample. CF_3CO_2H is also available for some hard to dissolve samples. This has a major peak above 10 ppm. Use it with caution since it is highly corrosive.

Sign the logbook before you place your sample in the spectrometer or adjust any controls. Failure to use the logbook will be viewed as irresponsible use of equipment, and appropriate penalties will be applied, including loss of sample and/or loss of machine use privileges. The absence of a log book entry also may be interpreted as a failure to do this experiment.

Cap the tube, wipe it clean, and carefully insert it into the plastic spinner. Use the depth gauge to set the proper immersion. Several samples may be preheated by storing them temporarily in the sample preheater to reduce drift while recording the spectrum. Watch the tube tops if you close the lid. There is a computer simulation program available in the Computer Assisted Instruction Facility (CAIF) in 120 CEM. You are strongly urged to practice there first. Actual NMR time is highly limited.

All CEM356 students are required to get trained/checked out on the 300 MHz NMR located in room 125 by one of the two NMR TA's. The training sign-up sheets are located outside room 125.

Everyone must get checked out by October 3, 2011, or there will be a 50-point penalty.

Summary of Major IR Peaks

Frequency (cm^{-1})	Functional Group	Comments
The 3m region (3600-2500 cm^{-1}).		Absorption in this region is associated with the stretching vibration of hydrogen atoms bonded to carbon, oxygen and nitrogen. Care should be exercised in the interpretation of very weak bands since these may be overtones (2m the frequency) of strong bands in the 6m region.
3600,3400 variable	O-H stretching	3600 cm^{-1} (sharp) unassociated O-H, 3400 cm^{-1} (broad) associated O-H [both bands frequently present in alcohol spectra], with strongly associated O-H (CO_2H or enolized b-dicarbonyl
3000 broad	acid O-H	compound) band is very broad (ca. 500 cm^{-1}) with its center at 2900-3000 cm-1.
3400-3200	N-H stretching	3400 cm^{-1} (sharp) unassociated N-H, 3200 cm^{-1} (broad) associated N-H, an NH_2 group usually appears as a doublet (separation ca. 50 cm^{-1}), the N-H of a secondary amine is often very weak.
3300	C-H stretching of an acetylene	
3080	C-H stretching of an olefin	The **complete** absence of absorption in this region (3000-3300 cm^{-1}) indicates the absence of hydrogen atoms bonded to C=C or C∫C and **usually** indicates the lack of unsaturation in the molecule. Since this absorption may be very weak in large molecules, some
3050	C-H stretching of an aromatic compound	care should be exercised in this interpretation. Compare these data with the pmr spectrum.
2980-2900	C-H stretching of an aliphatic compound	As in the previous entry, **complete** absence of absorption in this region (3000-2900 cm^{-1}) indicates the absence of hydrogen atoms bonded to tetravelent carbon atoms.
2900-2750	C-H stretching of an aldehyde	Either one or two bands may be found in this region for a single aldehyde function in the molecule.
2600-2550	S-H stretching	Usually weak. May be obscured by -CO_2H. Applies to thiols, thiophenols, and thiol acids (-COSH).

The triple-bond region (2300-2000 cm^{-1}). Absorption in this region is associated with the stretching vibration of triple bonds and cumulenes.

2250-2225 C∫N	2250 cm^{-1} unconjugated nitrile; 2225 cm^{-1} conjugated nitrile. Unless the spectrum has been calibrated in this region, it is often difficult to locate the band position with sufficient accuracy to decide whether or not the nitrile function is conjugated.
2150-2100 C∫C	This band will be either very weak or absent if the acetylene is approximately symmetrical.

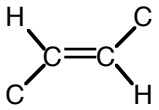
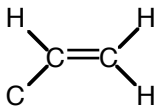
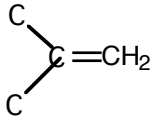
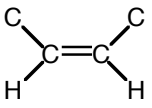
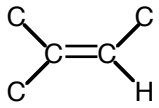
The 6m region (1900-1550 cm^{-1}). Absorption in this region is **usually** associated with the stretching vibration of carbon-carbon, carbon-oxygen, and carbon-nitrogen double bonds.

1710	C=O stretching of an aldehyde or ketone	This value refers to the carbonyl absorption frequency of an acyclic, non-conjugated aldehyde or ketone in which no electronegative groups are near the carbonyl group. Since this frequency is altered in a predictable way by structural alterations, the following generalizations may be drawn.
		I. Effect of Conjugation: Conjugation of the carbonyl group with an aromatic ring or carbon-carbon double or triple bond lowers the frequency by
	-30	about 30 cm^{-1}. If the carbonyl group is part of a cross conjugated system (unsaturation on each side of the carbonyl group), the frequency is lowered by
	-50	about 50 cm^{-1}. Thus, an alkyl aryl ketone or an alkyl vinyl ketone would absorb at about 1680 cm^{-1}, whereas a diaryl or divinyl ketone would absorb at about 1660 cm^{-1}.
		II. Effect of Ring Size: Carbonyl groups in 6-membered and larger rings exhibit approximately the same absorption as acyclic ketones.
	+35	The carbonyl absorption frequency is raised by about 35 cm^{-1} per atom decrease in ring size. Thus, a cyclopentanone absorbs at ca 1745 cm^{-1}, and a cyclobutanone absorbs at about 1780 cm^{-1}. The effects of conjugation and ring size are additive. For example, a 2-cyclopentenone absorbs at 1710 cm^{-1}.
		III. Effect of Electronegative Atoms: An electronegative atom (especially oxygen or halogen) bonded to the a-carbon atom of an aldehyde or ketone may raise the position of the carbonyl absorption
	+20	frequency by about +20 cm^{-1}. Since this effect is dependent on molecular conformation, such compounds may exhibit (a) normal absorption, (b) absorption at higher frequencies, or (c) both bands (a) and (b).

1740	C=O stretching of an ester or lactone	This band is subject to all of the structural effects discussed in the previous entry. Thus, a conjugated ester absorbs at ca. 1710 cm^{-1} and an a-lactone absorbs at ca. 1780 cm^{-1}. Esters also have strong (C-O) peaks for both the "acid" and "alcohol" fragments between 1050 and 1310 cm^{-1}.
1690	C=O stretching of an amide	This band is subject to the same structural effects Concentrated solutions or solids absorb closer to 1650 (primary) or 1640 (secondary) cm^{-1}. Amides also have a N-H bending band near 1630 (primary) or 1550 (secondary) cm^{-1}.
1800	C=O stretching of an acid chloride	As in the case of ketones, the frequency is lowered by conjugation.
1810 and 1760	C=O stretching of an acid anhydride	**Both bands** are present. **Each band** is altered by ring size and conjugation to approximately the same extent noted for ketones.
1700	C=O stretching of an acid	This absorption frequency is lowered by conjugation as noted for ketones.
1650-1550 and *ca.* 1400	C=O stretching of an acid salt	Both bands are present. The 1400 cm^{-1} band is usually weaker.
1680-1600	C=C stretching of an olefin	1680 cm^{-1} (usually weak) unconjugated olefin, 1610 cm^{-1} (medium to strong) conjugated olefin. The absorption frequencies of these bands are raised by ring strain but to a lesser extent than noted with carbonyl functions.
1640	C=N stretching	This band is usually weak.
1600,1580, 1500 and 1450	C=C aromatic stretching	Two, three or four bands will be detected in most benzenoid and many heteroaromatic compounds.

The finger print region (1600-600 cm^{-1}). Absorption in this region is usually associated with single bond stretching vibrations, with bending vibrations and with more complex molecular vibrations. The positions of absorption frequencies in this region are much less reliable than those frequently discussed. In addition, many bands interfere with one another. As a consequence, it is possible to interpret only a portion of the bands present in this region, and the reliability of this interpretation is often questionable.

1600	$-NH_2$	This band in conjunction with bands in the 3300 region is often used to characterize primary amines and unsubstituted amides. It is usually a doublet.
1540	-NH- bending	This band in conjunction with bands in the 3300 region is often used to characterize secondary amines and monosubstituted amides. In the case of secondary amines, this band, like the N-H stretching band in the 3300 region, may be very weak.
1520 and 1350	NO_2 coupled stretching bands	This pair of bands is usually very intense. Both will be present.
1465	$-CH_2-$ bending	
1410	$-CH_2-$ bending	Methylene group adjacent to a carbonyl group.
1450 and 1375	$-CH_3$	The band of lower frequency (1375 cm^{-1}) is usually used to characterize a methyl group. If two methyl groups are bonded to one carbon atom, a characteristic doublet (1385 and 1365 cm^{-1}) will be present.
1325	-CH- bending	This band is weak and often unreliable.
1330 and 1130	S=O stretching of a sulfone	Very intense. Both bands are frequently split for solid samples. Hydrogen bonding may lower the band frequencies somewhat.
1050	S=O stretching of a sulfoxide	Same as sulfone bands.

1200	C_6H_5-0-	It is not certain whether these strong bands arise from C-O bending or C-O stretching vibrations. One or more strong bands are found in this region of the spectra of alcohols, ethers and esters. The relationship indicated between structure and band location is only approximate, and any structural assignment based on this relationship must be regarded as tentative.
1150	-C-O-	
1100	-CH-O-	
1050	-CH_2-O-	
970 ± 10		This strong band is present in the spectra of *trans*-1,2-disubstituted olefins.
990 ± 5 and 910 ± 5		The lower-frequency band of these two strong bands is used to characterize a terminal vinyl group. Also, scissoring at 1415 cm^{-1}.
890 ± 5		This strong band, used to characterize a methylene group, may be raised by 20-80 cm^{-1} if the methylene group is bonded to an electronegative group or atom. Also, scissoring at 1415 cm^{-1}.
700 ± 30		This band, attributable to a *cis*-1,2-disubstituted olefin is unreliable because it is frequently obscured by solvent absorption or other bands. This also has a band near 1415 cm^{-1}.
840-810		
750 and 690	C-H bending	Monosubstituted benzene.
750	C-H bending	Ortho disubstituted benzene.
780 and 700	C-H bending	Meta disubstituted benzene.
825	C-H	Para disubstituted benzene.

bending

1100 and 1000	C-F	Multifluoro compounds have multiple bands between 1400-730 cm^{-1}.
850 to 550	C-Cl	These are generally intense. First overtones (2xu) may be observed.
690 to 520	C-Br	
600 to 500	C-I	

Regions of the infrared Obscured by Solvents and Other Media

Material	Region(s) Obscured
carbon tetrachloride	840-700 cm^{-1}
carbon disulfide	1600-1400 cm^{-1}
chloroform	3000 cm^{-1} 1200 cm^{-1} 840-700 cm^{-1}
Nujol, Lubriseal	3000-2900 cm^{-1} 1470-1440 cm^{-1} 1385-1365 cm^{-1}
potassium bromide	3500-3300 cm^{-1} if the pellet contains water. Since the water content may vary appreciably, the interpretation of the region of a spectrum determined in a potassium bromide pellet is **always** subject to error.

NOTE: In IR, negative evidence is the most reliable. For example, if there is no peak in the 1600-1800 region, your structure has no C=O of any type. It is positively absent.

Appendix A

Substances Posing a Potential Occupational Carcinogenic Risk

Substances Currently Regulated by the Occupational Safety and Health Administration as Carcinogens

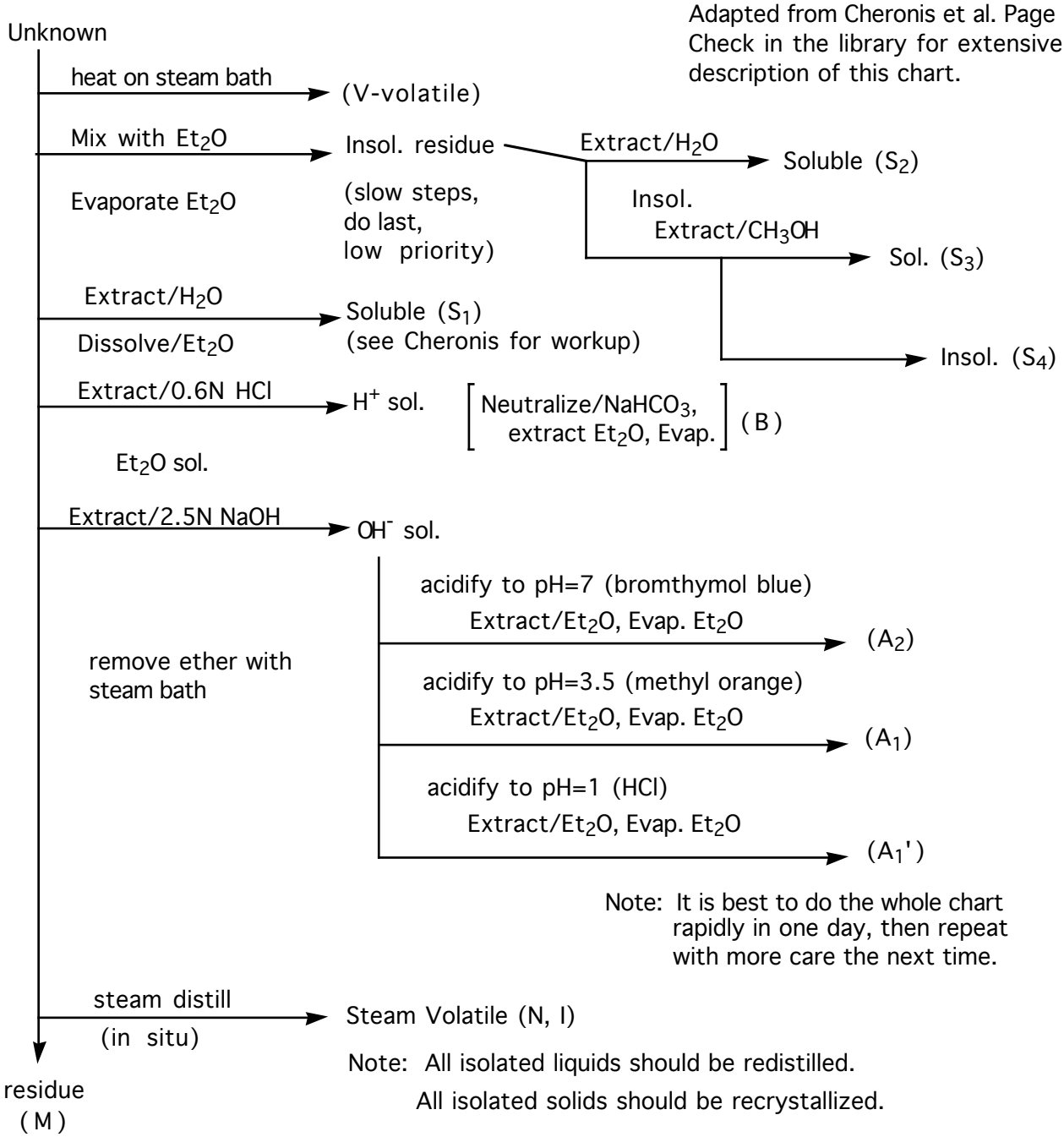
Asbestos
4-Nitrobiphenyl
alpha-Napthylamine
Methyl chloromethyl ether
3,3'-Dichlorobenzidine (and its salts)
bis-Chloromethyl ether
beta-Napthylamine
Benzidine
4-Aminodiphenyl
cigarette smoke
Ethylenimine
beta-Propiolactone
2-Acetylaminofluorene
4-Dimethylaminoazobenzene
N-Nitrosodimethylamine
Vinyl chloride
Inorganic arsenic
Benzene (some uses, not gasoline)
Coke oven emissions

Current List of Substances Selected by the DHEW Committee to Coordinate Toxicology and Related Programs for Inclusion Under these Guidelines (This list of substances is not to be considered all inclusive. Rather, it serves as a list of substances for which Safety Data Sheets are currently being prepared)

Benxo[a]pyrene
Benz[a]anthracene
3-Methylcholanthrene
N-Nitrosodiethylamine
N-Nitrosodi-n-propylamine
N-Nitrosodi-n-butylamine
N-Nitroso-N-methylurea
N-Nitroso-N-ethylurea
N-Nitroso-N-methylurethane
2-Aminofluorene
N-Hydroxy-2-acetylaminofluorene
N-Acetoxy-2-acetylaminofluorene
Dimethylethylenimine
3,3'-Dimethoxybenzidine
3,3'-Dimethylbenzidine
4,4'-Methylene bis-(2-chloroaniline)
m-Toluenediamine
Polychlorinated biphenyls
Diepoxybutane
p-Dioxane
Bromoethyl methanessulfonate
7,12-Dimethylbenz[a]anthracene
Dibenz[a,h]anthracene
N-Nitrosopiperidine
,4-Dinitrosopiperazine
N-Nitroso-N-ethylurethane
1-Methyl-3-nitro-1-nitrosoguanidine
1,1-Dimethylhydrazine
1,2-Dimethylhydrazine
Hydrazine
Methylhydrazine
Procarbazine
Chlorambucil
Uracil mustard
Carbon tetrachloride
Chloroform
1,2-Dibromo-3-chloropropane
Ethylene Dibromide
Propylennimine
4-Nitroquinoline-1-oxide
Urethane
Diazomethane

Ethyl methanesulfonate
Methyl methanesulfonate
1,3-Propane sultone
Ethionine
N-[4-(5-Nitro-2-furyl)-2-thiazoly]-formamide
Cycasin
o-Aminaazobenzene
3'-Methyl-4-aminoazobenzene
Aflatoxins

Adapted from Cheronis et al. Page 256. Check in the library for extensive description of this chart.



Note: It is best to do the whole chart rapidly in one day, then repeat with more care the next time.

Note: All isolated liquids should be redistilled.
All isolated solids should be recrystallized.

a Nitrogen, halogens, and sulfur are absent unless specified.

b Moderate-weight compounds with two or more polar groups, except for the sulfonic and sulfinic acids when only one polar group is necessary.

c Generally, mono functional compounds with 5 carbons or less.

d In this table, the more common classes are printed in SMALL CAPITAL letters.

e Amines with sufficiently strong negative substituents as well as diaryl and triarylamines fall in Division M.

f Generally with 10 carbons or less; many form colloidal soap solutions.

g High-molecular-weight acids form colloidal soaps.

h Including N-monoalkyl amides.

i Only the most common classes are listed.

j Halogens may be present at substituents.

k Noncyclic unsaturated hydrocarbons, and those unsaturated cyclics that are easily sulfonated, such as di- or polyalkyl-substituted benzenes.

l Char in the acid.

m Including most of the cyclic hydrocarbons, and all of the saturated, noncyclic hydrocarbons.

o Division M compounds are not present unless nitrogen and/or sulfur was found present on elemental analysis. distilling with steam does not give a "clean-cut" separation in these cases, since some Division M compounds do distill with the steam and because some Division N and I compounds do not distill, appreciably, with the steam.