THE COMPLETE HANDOUT FOR THE LABORATORY EXPERIMENTS AND OTHER COURSE MATERIALS MAY BE ACCESSED THROUGH THE BLACKBOARD SITE FOR CHEM 225LB THROUGH Hunter Blackboard (https://hunter.cuny.edu/quick-links/**)**

HUNTER COLLEGE
Department Of Chemistry
Organic Laboratory II
Hybrid Chemistry 225

TEXT: Pavia, Lampman, Kriz and Engel, A Small Scale Approach to Organic Laboratory Techniques, Fourth Edition, Cengage Learning, 2015.

This short version of Lab Manual will help you prepare for lab with additional reading from the Pavia text and any Organic Chemistry textbook.

You have learned the basic laboratory techniques in organic chemistry-I lab. Now you should be able to work more independently than in the first-semester. **You will work individually during all in-person Experiments 1-4 (Week 1 – 7).** The key to success is planning your work carefully before you enter the laboratory! The total number of hours allotted for the lab is may not be exceeded for any student who gets behind in the work (2 hours and 45 minutes). You must finishing cleaning and leave the lab to allow staff to prepare for the next lab. **No work will be allowed out-side the scheduled time period including washing glassware and taking melting points.**

For safety reasons you must remain outside the laboratory until your lab instructor has entered the lab. You must bring your own gloves, safety glasses, paper towel and masks. Your online Pre-lab quiz should be submitted and Pre-lab write up must be uploaded on BB via the link set up by your lab instructor (check for instructions from your lab instructor).

Your total grade will be assigned on a 1200 point scale which will be explained to you by your lab instructor and recitation instructor. Your point total will be based upon recitation examinations, Quizzes, laboratory technique, the products you hand in, the organization of your work, your write-up of experiments, safe lab practices, cleanliness, and certainly on how well you have planned your work before hand and how well you understand the chemical processes occurring as you work. When you hold a flask in front of your instructor to ask him or her a question about the contents you must tell exactly what you put in the flask, and the exact sequence of operations you have carried out in arriving at that point. Your instructor will not tell you the solutions but provide ideas to help you problem solve. Maintain social distance at all times.

Pre-lab quizzes (online from BB)
Pre-lab write up for weeks 1 – 13 (uploaded on BB)
Lab participation both in person and during BB Collaborate sessions (Kahoot Polling & Discussions)
Lab reports (uploaded on BB)
PowerPoint Presentation (week-14)

Recitation class assessments (exams)

Online Safety Quiz	10 points * 1 week	10 points
Online Pre-lab Quizzes	10 points * 13 weeks	130 points
Online Pre-lab Writeup	10 points * 13 weeks	130 points
Online Lab Participation (Kahoot Online Polling)	10 points * 6 weeks	60 points
Lab Participation In-person and (Synchronous Discussion BB Collaborate) OR (Discussion Boards)	10 points * 13 weeks	130 points
In-person Lab Report for Expt- 1 – 4	40 points * 7 weeks	280 points
Online Lab Report for Expt- 5 – 10	30 points * 6 weeks	180 points
PP presentation (week 14)	30 points * 1 week	30 points
Recitation Exams & assessments	250 points	250 points
TOTAL		1200 points

The importance of studying the recitation material and applying what you have learned cannot be exaggerated. Don't let yourself become one of the disappointed students who receive a low grade in the entire course due to low scores on their recitation examinations.

In addition to carrying out several organic syntheses you will identify a functional groups in unknown compounds as well as separate and identify the compounds in an unknown binary mixture. These identifications will require the use of both chemical and spectroscopic methods. You will be required to consult other sources in addition to your laboratory text in this endeavor.

In the synthesis experiments you may not be given the procedure in complete detail. You will incorporate information from the recitation and textbook to fill in the details and modify the procedure as needed before you enter the laboratory. You will have to plan your own allotment of time. In order to avoid falling behind you will have to carry out some (previously planned) reactions at the same time you are continuing work on earlier experiments.

RECITATION. Attendance at recitation is a most fundamental requirement. If you should be forced to miss a recitation class you must obtain the class notes from another student. Failure to attend recitation and understand the material presented does more than subject your experiments to the risk of failure. It is essential from a viewpoint of laboratory

safety alone to attend all the recitation classes. **Attendance will be taken.**

NOTEBOOK. Your notebook should be bound - not loose-leaf, and have numbered **duplicate** (carbon copy) pages. The original copy is to remain attached to the notebook. The carbon copy is to be removed and submitted to your instructor for grading. Refer to your Organic Laboratory I (Chem. 223) notes and to the laboratory text (Pavia, technique 2, p 566-573) for details. **Use ink only. Never use "White-out".**
Pre-lab and data collected during in-person lab must be on lab notebook. The Report - Discussion can be typed and must include chem draw structures where appropriate.

PLANNING. We stress again the importance of studying and planning your work before you start the experiment! Students who really understand what they are doing in lab will enjoy the work and will look back on their organic chemistry laboratory as a really pleasurable learning experience. Those who do not understand the experiments they are doing will experience frustration and likely fail in addition to exposing themselves and others to the risk of a serious laboratory accident. We will do our best to help you enjoy the course and achieve successful results, but if you don't do your homework and planning, no one will be able to help you. If a laboratory instructor determines that a student has not adequately prepared an experiment, the student will be sent away from the laboratory and will not be allowed to do make-up work in another section. Pre-lab write up must be uploaded on BB from links set by your lab instructor. Pre-lab should describe your plan and preparation for the experiment. **Points for pre-lab write-up will be awarded at the start of each experiment.**
Review all the appropriate laboratory techniques (recrystallization, distillation, filtration, extraction etc.) before you start.

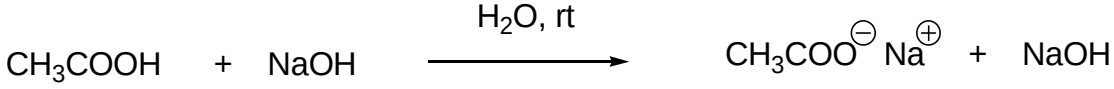
Preliminary Write-Up for Synthesis Labs:

Use the format explained in detail last semester (Chem 223). For each preparative reaction, you are to carry out a separate preliminary write-up which must be entered in your notebook before you start. **Points for pre-lab write-up will be awarded at the start of each experiment (they should be uploaded on BB via link posted by your lab instructor).** All equations must be balanced! Here is a somewhat trivial example for illustration:

1. TITLE OF EXPERIMENT: Neutralization of Aqueous Acetic Acid

2. OBJECTIVE: BRIEFLY describe or list the aim(s) of the experiment.

I. Main Reaction



II. Side Reactions

(Balanced equations for any known side reactions.)

3. TABLE OF SAFETY HAZARDS & PHYSICAL CONSTANTS

#1-3 & other specific prelab exercises must be completed before starting the experiment. Prelab preparation will be considered in determination of your final grade.

III. Table of Reactants and Products. Solvent Data. Hazards

Compound	Mol. Weight.	Grams Used	Moles Used	Mole Theor.	Mole Used / Mole Theor	Hazards/ Physical Props
CH_3CO_2H	60.0	6.50 g	0.11	0.10	1.1	List hazards & relevant physical Properties
NaOH	40.0	4.0	0.10	0.10	1	As above
CH_3CO_2Na	82.0	--	--	0.10	--	As above
H_2O		--	--		--	As above

Solvent: H_2O, bp 100°C; mp 0°C; density 1.00 g/ml, nontoxic.

IV. Procedure

Steps required for the experiment or flow chart (should demonstrate you have critically thought about the experiment, calculated the reagents you will need, have listed the equipments and supplies that will be required, know the reaction conditions

Theoretical Yield: (show all calculations)

V. Observations

(to be entered during the lab period) along with any changes you may have made the the above procedure.

METHODS / PROCEDURE: Describe any changes to the procedure as outlined in the lab handout. **There is no need to rewrite the procedure in the handout or textbook. Cite the relevant pages.**

RESULTS & OBSERVATIONS: Record your observations in a clear fashion, and in sufficient detail such that it can be easily understood by anyone. Tabulation of data is usually the most efficient way of doing this. **The carbon copies of the original data from your lab note book must be attached as an appendix to your write up.**

TREATMENT OF RESULTS: Calculations, Graphs, etc. Summarize your results. Whenever possible, use a table format. This will be very helpful in planning your discussion.

Please note that you should enter "1" for the limiting reagent in both Mole Ratio columns. For liquid reactants it is convenient to enter both the mass (g) and volume (mL) in the table using the densities which you also enter in the table.
Review all the appropriate laboratory techniques (recrystallization, distillation, filtration, extraction etc.) before you start.

This exercise will continue even when lab sessions are held remotely.

SAFETY. Students are responsible for knowing the proper safety practices for every experiment, including safety information on all chemicals and procedures used in the experiment.
This information can be obtained by reviewing the safety video from Organic Chemistry I laboratory (Chem 223), from the laboratory text (Pavia, technique 1, p 548-565), and from the following handbooks available in the stockroom room 1414 north: Dangerous Properties of Industrials by Irving Sax; Handbook of Chemistry and Physics; Merck Index and Aldrich Chemical Catalog; Webpage www.sigmaaldrich.com. For the safety and convenience of students taking Organic Chemistry I and II the chemicals in room 1404 north have been organized according to the individual experiment.

Please return chemicals to their correct positions.

You are to supply your own safety glasses, disposable gloves, paper towels and masks.

Required Reading for Imporatant Techniques (for different experiments): Pavia, 4th Edition (Listed from page 548 onwards)
Essay-Aspirin (pg 47)
Essay- Analgesics (pg 53)
Essay- Caffeine (pg 67)
Essay: Green Chemistry (218-223
Technique 1: Laboratory Safety
Technique 2: Laboratory Notebook
Technique 3: Laboratory Glass ware Care and Cleaning (pg 578-579 for names of glassware)
Technique 4 : How to find data for Compounds: Handbooks and Catelogs
Technique 5: Heating and Cooling
Technique 7: Assembling Reactions (pg 610-615) (different clamps & set up for distillation and reflux)
Technique 8: Filteration
Technique 9 : Melting Points (pg 650-651)
Technique 10: Solubility
Technique 11: Crystallization- choosing solvent and drying (pg 664)
Technique 12: Extraction (separatory funnel and drying agents) (pg 668)
Technique 13: Physical Constancts of Liquids: Boiling Point and Density Chart Part A. "Boiling Point and Temperature Corrections"
Technique 14: Simple Distillation
Technique 15: Fractional Distillation
Technique 25: Infrared Spectroscopy and Appendix 3 (pg 998)
Technique 26 and 27: NMR (^{1}H and ^{13}C) and Appendix 3 (pg 999)
Technique 29: Guide to Chemical Literature
Appendix 1 (pg 960 – 993) – Table of Unknowns and Derivatives
Appendix 2: Procedure for preparing derivatives (pg 994 – 997)
Last page of the text book has – NMR shifts
First page has a list of common solvents

EXPERIMENT 1: REACTIONS OF DIAZONIUM IONS (IN-PERSON WEEK – 1)

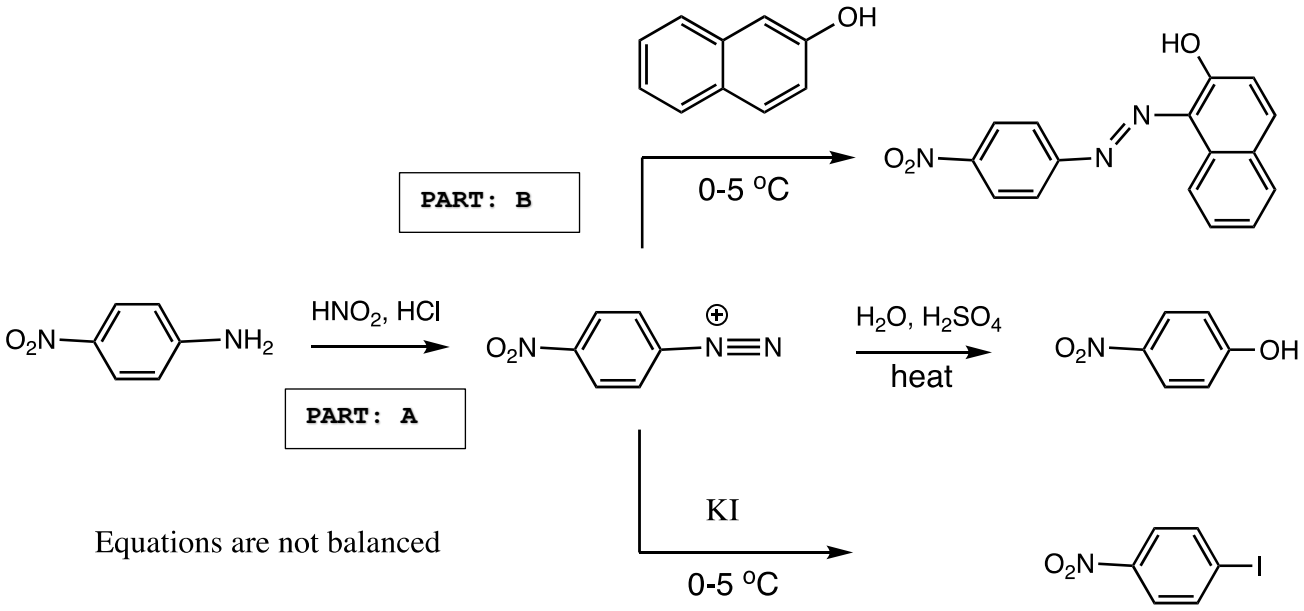
Experiment 1 requires careful planning as the reactions and must be carried out in one laboratory period. Recrystallization and melting points of reaction products may be performed in the same lab period.

References
Klein, Organic Chemistry, 3rd Ed.: Chapter 18 (aromatic substitution), Chapter 22 (Amines): Sec 22.10, 22.11 (diazonium ions)

Related Topics: Pavia: Experiment 44, p 345, 55G, p 493-495; Essay, p 340, 374

Aromatic diazonium ions, delivered by nitrosation of aromatic amines, are reactive species which generally are stable for short periods of time at ice bath temperatures. These compounds enter into a variety of reactions, including nucleophilic substitution to give benzene derivatives which otherwise are difficult to prepare, and coupling reactions to yield highly colored materials used as dyes and titration indicators. Reactions of these types are summarized.

The tables of reactants and products for part B may be filled out by assuming that the yield of the diazonium salt in part A is quantitative.



The first commercially important synthetic dye (Mauve- Aniline purple) was synthesized by William Henry Perkin in 1856. Perkin made this serendipious discovery while he was attempting to synthesize Quinine-the anti malarial drug. In this experiment, you will only synthesize the azo dye Para Red (once called American Flag Red -used to dye cloth for the stripes of American Flag) from part B.

Azo dyes are prepared by reacting a diazonium salt (the diazo part) with an activated aromatic compound (the coupling reagent.The coupling reaction is a Electrophilic Aromatic Subsititution reaction (EAS). The color of the dye depends on the lenghth of conjugation in the chromorphore (the light absorbing part). The benzene ring and the naphthalene rings form the 21 atom long chromophoric system of Para Red. Increasing the conjugation decreases the pi to pi* gap for electronic transitions and molecule absorbs at long wavelenghts (wavelength of light absorbed is inversly proportional to energy).

You should wear <u>disposable</u> gloves in this experiment since some of the reagents and products are quite toxic.

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)

Follow the guidelines discussed earlier.

Part A. <u>Diazotization of *p*-Nitroaniline</u>

Dissolve 0.012 mole *p*-nitroaniline in 2.5 mL conc. HCl diluted with 4 mL water in an appropriate flask, warm if necessary. Add an additional 1 mL conc. HCl and pour into a 250 mL Erlenmeyer flask containing approximately 10 g chopped ice. Swirl the mixture vigorously to obtain a fine suspension of crystals of *p*-nitroaniline hydrochloride.

Before moving to the next step you should prepare all the materials you need for the subsequent reactions. Therefore, make sure you read and understand the directions in advance.

To the vigorously agitated suspension of *p*-nitroaniline hydrochloride, maintained at 5-10°C (ice bath-use a thermometer immersed in the liquid) add as quickly as possible a cold (ice bath) solution of 0.015 mole sodium nitrite in 5 mL of water **(CAUTION: sodium nitrite is highly toxic. DO NOT get on hands, and wash hands thoroughly when finished with experiment)**. Swirl the flask until most of the amine hydrochloride dissolves (about 3 min.) and allow it to stand 15 minutes (cold) until diazotization is complete. Vacuum filter through an ice filled Buchner funnel into an ice cooled Erlenmeyer flask. Proceed to next step as quickly as possible keeping all the solutions cold in the ice bath.

Part B. <u>2-Naphthol Coupling</u> (Synthesis of para-red).

Dissolve 0.0167 mole 2-naphthol in 30 mL 2M NaOH. Some heating may be required to completely dissolve the 2-naphthol. Cool this solution to about 5°C, then, quickly add with thorough mixing one of the p-nitrobenzenediazonium chloride portions and let stand for 10 minutes (cool). Check the pH, and adjust to 8-10 if necessary. Filter using the vacuum (this may take a long time, use of a large Buchner funnel is recommended) and then break into finely divided

clumps. **Let dry** and determine the melting point of the product (Lit mp 257°C-258°C).

If necessary recrystallize a small amount of the product (approx. 0.50 g) from 1:1 toluene:ethanol. (check with lab instructor)

Show / Submit a properly labelled sample to your instructor and properly dispose the product after approval.

(Check with lab instructor. Maintain all social distance guidelines)

Report Write-UP: (40 points)
Appendix I in this manual

As part of your write-up, describe all the steps (step A and step B) of the experiment (in third person, past tense). Add reaction mechanisms at appropriate positions. Use chemdraw to draw structures. Do not share chemdraw drawings with other students. Comment on yields (with reason), Color of compounds (with reason), Compare the melting points of your products from parts B with reported values, Discuss purity (with reason), and Discuss any problems that you encountered (with reason).

Include the literature references for the melting points and other information that need referencing (PP slides and this lab manual are not literature references).

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EXPERIMENT 2: QUALITATIVE ORGANIC ANALYSIS (IN-PERSON WEEKS – 2)

References: Pavia: Experiment 58 (from p 458 – 58 A, 58 B, 58 C, 58 D, 58 E, 58 F, 58 G)
Shriner, Fuson, and Curtin, *The Systematic Identification of Organic Compounds*.
Fieser and Williamson, *Organic Experiments*, 4th Ed.

Klein, Organic Chemistry, 3rd Ed.: For Functional group tests: Chapter 14 (IR), Chapter 15 (NMR), Chapters (7 (Alkyl halides), 8 (Alkenes), 12 (Alcohol & Pheols), 19 (Carbonyl Chemistry: Aldehyde & Ketone), 20 (Acids and Acid Derivatives), 21 (Carbonyl Chemistry-Enols and Enolates), 22(Amines)

Classification Tests:

One way of identifying the major functional groups in your compounds is by performing a series of Classification Tests. Since most of you have no familiarity with this type of test, **we have set up a series of preliminary experiments for** you to perform on known compounds. The tests listed below are by no means the only classification tests that you should perform on your unknowns. Also, they do not cover all of the possible functional groups that may be present in your unknown.

Preliminary Write-Up:

Write balanced equations for all of the tests indicated. Record the physical properties and possible hazards for all the substances you will be working with.

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)- Document that you have read all the tests using balanced reactions using any one compound from the list.

General Instructions:

Most tests can be run in test tubes. Run the same test on all the different compounds supplied for that test at the same time. In this way you can see the differences in appearance for the various types of compounds. Be sure to label your test-tubes carefully so as to not get confused. Record all observations in your notebook. You may use tabular form for this. You can use your phone to take pictures and include in your lab report.

Part A. Carbonyl Compounds

Ref: Pavia, Experiment 58D, p 482

You are to carry out tests i, ii, & iii (indicated below) on the following compounds:

1. Heptaldehyde (heptanal)
2. Acetone (dimethyl ketone)
3. Benzaldehyde
4. Ethyl acetate
5. Benzoic acid

(i) 2,4-Dinitrophenylhydrazone (2,4-DNP) Test:
Use the procedure in Pavia p 483. **NOTE: The reagent has been prepared for you.**

(ii) Tollen's Test:
NO STEPWISE Mechanism needed in report
Use the procedure in Pavia (p.484). NOTE: Tollen's A and B are already made for you. Take careful note of the possible explosion hazard indicated in the procedure. If the test tube is not clean, you may observe a dense, dark precipitate but no silver mirror. **Do not use the bis(2-ethoxyethyl)ether. In its place use a minimum amount of 1,2-dimethoxyethane. Never heat the Tollen's test experiment, as this will cause in a false positive result.**

The Chromic Acid Test can be used as an alternative test for aldehydes (See later)
NO STEPWISE Mechanism needed in report

(iii) **Iodoform Test:**
Use the procedure in Pavia p. 486. **NOTE: The reagent has been prepared for you.**

Part B: Amines

Ref: Pavia,Experiment 58G, p 493
The Hinsberg Test is a good method of differentiating among primary (1°), secondary (2°), and tertiary (3°) amines. Amines in general are characterized by their solubility in dilute acid solution. (Why?)

Run the Hinsberg Test on:
1. Aniline
2. N-ethylaniline
3. N,N-dimethylaniline

Hinsberg Test

NO STEPWISE Mechanism needed in report

Procedure. Place 0.1 mL of a liquid amine or 0.1 g of a solid amine. 0.2 g of *p*-toluenesulfonyl chloride (*p*-TsCl), and 5 mL of 10% potassium hydroxide (KOH) solution in a small test tube. Stopper the test tube tightly and shake it intermittently for 3 to 5 minutes. Remove the stopper and warm the test tube, with shaking, on a steam bath for 1 minute. Cool the solution and test a drop of it with pH paper to see whether it is still basic; if it is not, add more 10%

KOH. If a precipitate has formed, dilute the basic mixture with 5 mL of water and shake it well. If the precipitate is insoluble, a disubstituted sulfonamide is probably present, which indicates that the unknown was a 2°amine. (**NOTE: the precipitate may also be unreacted *p*-TsCl, leading to confusing results**).

If no precipitate remains after you dilute the mixture, or if none formed initially, carefully add 5% hydrochloric acid until the solution is just acidic to litmus (avoid excess acid). If a precipitate forms at this point, it should be the monosubstituted sulfonamide, indicating that the original compound was a 1° amine. If no reaction was apparent during the test, the original compound was probably a 3°amine.

If the above procedure gives confusing results(!), the procedure can be repeated, using 0.2 mL of benzenesulfonyl chloride instead of *p*-toluenesulfonyl chloride. However, this reagent is likely to lead to the production of oils instead of solids.

Summary of the Hinsberg test

Primary amine + *p*-TsCl	KOH →	Clear Solution	HCl →	Precipiate
Secondary amine + *p*-TsCl	KOH →	Precipitate	HCl →	No Change
Tertiary amine + *p*-TsCl	KOH →	No apparent rxn	HCl →	Clear Solution

Two cautions should be observed when you are performing the Hinsberg test. First, these tests work well with reagent-grade amines. However, practical grades often contain impurities. For instance, secondary amines are often made from primary amines that may be contaminants. Similarly, tertiary amines may contain traces of secondary amines. Therefore, trace precipitates should not be considered as definitive results. Second, reaction times should be short, and any heating should be gentle, many tertiary amines will react under more vigorous conditions.

C: Alcohols

Ref: Pavia, Experiment 58H, p 497

(i) The Lucas Test is often a good means of distinguishing among 1°, 2° and 3° alcohols of fairly low molecular weight. Generally the Lucas test does not work well with solid alcohols or liquid alcohols containing six or more carbons.

Run the Lucas Test on:

1. Benzyl alcohol
2. 1-Butanol
3. Cyclohexanol
4. Tert butyl alcohol
5. Allyl Alcohol

Follow Pavia, p 499; the test reagent has been prepared.

(ii) The Chromic Acid Test is an alternative test for primary and secondary alcohols and aldehydes. Follow Pavia, p 485, 500; the test reagent has been prepared. **The chromic acid reagent is very corrosive and may be carcinogenic. Wear gloves to avod contact with the reagent.** A positive test is the production of an opaque suspension with a green to blue color. Note that enols may also

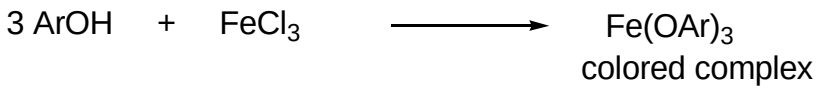
give a positive test, and that phenols give a dark colored solution which is not blue-green like a positive test.
NO Mechanism needed in report

Run the Chromic Acid Test on:

1. Heptaldehyde
2. 1-Butanol
3. Cyclohexanol
4. Tert butyl alcohol

D: Phenols
NO Mechanism needed in report

Ref: Pavia, Experiment 58F, p 490



The Iron (III) Chloride Test for Water-Soluble Phenols. Follow Pavia, p 491.

The Iron (III) Chloride Test for Water-Insoluble Phenols. For water-insoluble or less reactive phenols. less reactive phenols, dissolve or suspend 50 mg of the unknown in 1 mL of methylene chloride. Add several drops of the the Iron (III) chloride solution. Add a drop of pyridine and stir. Addition of pyridine will produce a color if phenols or enols are present.

Run the Iron (III) Chloride Test on :
1.Phenol
2.Cyclohexanol

E. Nitro Groups
NO Mechanism needed in report

The Iron (III) Hydroxide Test for Nitro Groups. Follow Pavia, p 475. The presence of a nitro group in an unknown compound is determined most easily by IR spetroscopy. Generally nitro compounds give a positive test within 30 seconds. Hoever, the speed with the reaction occurs depends on the solubility of the test compound. Unfortunately, functional groups other than the nitro group may also give a positive result. You shopuld interpret the results of this test with caution.

Run this test on 2-nitrotoluene

F: Esters: You will not perform this test

Ref: Pavia, Experiment 58I, p 501

Feric Hydroxamate Test (Pavia, p 502). You will not perform this test as part of Experiment 2. Keep this test in mind, should you need to test for an ester in experiments 3.

G: Halides: You will not perform this test

The Beilstein Test is one of the simplest and most reliable tests for halogens (not including fluorine). However, it does not differentiate among chlorine, bromine and iodine, anyone of which will give a positive test, and it does not detect fluorine (Why?). Note also that because the test is very sensistive, halogen containing impurities may give misleading results. The procedure in Pavia, p 472 will be demonstrated to you by your instructor.

Test compounds:

1. 1-bromobutane
2. 1-chlorobutane
3. 1-butanol

You should be familiar with other tests for halogens from Organic Chemistry I Laboratory (Chem 223, Pavia, p 152-154, 472-474). Tests for specific halides are also described in the textbook. Review this material as these tests may be useful in Experiment 5 (Pavia, p. 464).

H: Test for Multiple Bonds: You will not perform this test

You should be familiar with these tests from Organic Chemistry I Laboratory (Chem 223). Review this material (Pavia, p. 478-480).

Keep this test in mind, should you need to test for an ester in experiments 3.

Report Write-Up: 40 points

Follow the format posted on Bb (check with lab instructor)

EXPERIMENT 3: AN UNKNOWN BINARY MIXTURE

(IN-PERSON WEEKS – 3, 4, 5)

References: In addition to the SDBS site for IR and NMR spectra and other references listed in experiments 3, please note the more extensive listings of organic compounds in:

1. Chemical Rubber Publishing Co., Handbook of Chemistry and Physics and Handbook of Tables for Organic Compound Identification. Pavia: technique 4, p 581.

2. Dictionary of Organic Compounds, Heilbron, Cook, Bunbury, and Hey, Editors.

3. Sigma-Aldrich Chemical Co. Catalogue (www.sigmaaldrich.com)

Klein, Organic Chemistry, 3rd Ed.: Chapter 14 (IR),Chapter 15 (NMR)

Review all of the references in experiments 2. **You must know this material.** Pavia: Experiment 58 (from p 458 – 58 A, 58 B, 58 C, 58 D, 58 E, 58 F, 58 G)

You will first separate the two components in your unknown mixture. Then you will purify each of them. You will identify the type of compound you have by using a combination of classical methods (solubility test, classification tests) and more modern techniques (IR and NMR). Once you have properly identified the functional groups in your compounds you will fill out and give to your teacher an NMR Spectrum Request Form for each of the two unknowns. Your instructor will keep the forms but will not give you the spectra if you have made a major error in your prior analysis. You will use the NMR spectrum together with the rest of your data to identify your unknown. Take pictures of separation & interesting tests for PP presentation and report!!!

During Online Lab -9 you will learn how prepare one or more derivatives to positively identify your compound. Use of the chemical literature to identify unknown using dericatives will be discussed.

Power Point Presentation (Week-14)

You will be presenting how you separated and analysed your of unknown binary mixture (NMR, IR, tests) during week -14. You will talk about which derivatives you could have prepared and how it would help you identify your unknown

Pre-lab Quiz (10 points * 3 weeks = 30 points)

Pre-lab Write-Up (10 points * 3 weeks = 3 points)

Week: 3 (pre-lab should include all the different possible methods of separation – solid-solid; solid-liquid; liq-liq from your readings)

Week: 4 (pre-lab should include the tests you plan on to do based on IR data)

Week: 5 (pre-lab should include your plan with list of things that need to be done, like MP, repeating tests)

NOTE: As soon as your are provided with your unknown compound, take note of the sample number on the vial.

References: Classification tests listed in the previous experiment and in Pavia.

A data base of IR spectra is freely accessible via the Spectral Data Base System (SDBS) maintained by the Japanese National Institute of Advanced Industrial Science and Technology at:

http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/cre_index.cgi?lang=eng

or by searching 'SBDS' in any search engine.

IR Spectroscopy: Pavia: Technique 25, p 854, Appendix 3, p 998

You will identify the functional groups in two unknown compounds by using a combination of IR spectroscopy and classical methods (solubility tests, classification tests.

NOTE: As soon as you are provided with your unknown, take note of the sample numbers on the vials. Take care that a possibly volatile unknown does not evaporate on storage!

You will first separate the compounds and obtain the IR spectra for the two unknown samples and then perform solubility and classification tests to help with the identification of the functional groups in each unknown.

A: Preliminary Examination (WEEK-3)

Note the state, odor, color and solubility characteristics of your mixture as a whole. Take care that a possibly volatile component does not evaporate on storage.

Solubility Tests

Solubility Tests are easily performed on small amounts of sample and are extremely important for determining the main functional groups of an unknown sample, particulary acidic and basic groups. Perform the Solubility Tests as described in the textbook (Experiment 58A, p 465).

Note: Many carboxylic acids are soluble in $NaHCO_3$ solution only after prolonged standing or heating. Do not let this mislead you. Correlate this data with other classification tests and with your IR Spectrum.

B: Separation (WEEK-3)

You will be using one of the following techniques. Review the relevant literature and your recitation notes before you begin. The general order of preference is:

1. Acid-Base Extraction - Pavia, Technique 12, p 683
2. Fractional Distillation - Pavia, Technique 15, 733
3. Fractional Crystallization - Pavia, Technique 11, p 664

General Notes:

1. Acid-Base extraction cannot be used if either compound is soluble in water.

2. Acid-Base extraction cannot be used unless the compounds differ in their acidity or basicity.

3. You should not distill at atmospheric pressure at temperatures > 220°C. This may result in decomposition of one of your samples. Distillation under vacuum is advised.

4. In many cases fractional distillation cannot be used because the boiling point ranges of the two components are too close (whether under vacuum or not).

(IR & NMR can be done as soon as you have separated the compounds and are sure they are sufficiently pure)

Infrared Spectroscopy (I.R spectra)

Pavia: Technique 25, p 854; Appendix 3, p 998.

Run an IR spectrum of your pure unknown. If the unknown is liquid, you may run the spectrum neat (no solvent). If you have a solid, run the spectrum using the dry film method, as a Nujol mull on NaCl discs, or as a KBr pellet. If necessary, your instructor will show you how to prepare a KBr pellet of your solid. Signed and dated spectra are to be taped in your notebook. Interpret your spectra.

NMR Sample Preparation. Submit a sample to your instructor in a NMR tube labeled with your initials and sample I.D..(check with instructor on how to label) The sample should contain 0.003 g of your unknown (1 small drop of liquid) in 0.7 ml of $CDCl_3$. The NMR data will be obtained by a T.A. and returned to you.

C: Purification. (WEEK-4 and 5)

All solids must be **recrystallized** (Pavia, p 664); All liquids must be distilled (Pavia, p 733).

When you have both unknowns purified, refer to them as follows: If one is a solid and one a liquid (at 25 ^{o}C), call them "S" and "L" respectively. If both are solids, call them "S_H"for the higher-melting solid, and "S_L" for the lower-melting solid. If both are liquids, call them "L_H" for the higher-boiling liquid, and "L_L" for the lower-boiling liquid. This will facilitate discussion and notebook grading later.

D: Physical Examination of Each Pure Compound (Pavia, p 461)

Keep accurate, complete and dated records in your notebook! Take care that a possibly volatile unknown does not evaporate on storage!

1. Note the mp range or bp. (Pavia, Technique 9, p 645; Technique 13, p 711.
2. Note the color, state, odor (carefully!).

E: Determination of the Functional Groups in Each Compound from Solubility and Classification Tests and IR Spectroscopy. (WEEK-4 and 5)

Run the appropriate Classification Tests on each unknown. Refer to Shriner and Fuson for additional tests (check with your lab instructor). In some cases Pavia has insufficient detail. Information obtained for your IR spectrum and solubility tests should provide guidance as to what tests you to perform. We cannot guarantee that your unknown will be of high purity. In many cases traces of impurities may give misleading results. **Perform appropriate positive and negative control experiments with known compounds to confirm your resiults.**(check with your lab instructor)

For each compound, follow the exact procedures in Sections A – D of Experiment 2.
Remember the Beilstein Test must be performed under supervision of the instructor (we will not need this test this semester).

F: NMR Analysis (Pavia, Technique 26, p 888; Appendix 3, p 992

Enter your analysis for the identification of the functional groups in each of your unknown compounds in your notebook and fill out the NMR Spectrum Request Form. If you are on the right track, your instructor will give you NMR tubes to prepare NMR samples. If you analysis is flawed, you will be asked to redo your analysis until you get it right, before you can get your NMR data.

Interpret the N.M.R. spectrum completely.

Write-Up
From the data in A – F, construct a clear logical analysis for the identification of the functional groups in your two unkown compounds. A flow chart is an effective way of summarizing your discussion on acid-base

separation. Write reactions for all the key chemical reactions. Discuss any observations that do not agree with your conclusions, and provide possible explanations for these inconsistencies.

Report Write-Up: 40 points (Separation)

A good story about your mixture and how it was separated. Purity of compounds and justification

Report Write-Up: 40 points(IR and Classification Tests explained for two compounds)

IR information explained and Tests explained positive and negative(2 compounds * 20 points)
IR bands must be labelled. Attach IR or add picture within report.

Report Write-Up: 40 points. (NMR analysis of two compounds)

NMR Sample Preparation
NMR peaks must be labelled and described (shielded, deshielded, integration (2 compounds * 20 points)
MP or BP of each compound
Table with structure and physical properties

EXPERIMENT 4: A MULTI STEP SYNTHETIC SEQUENCE: SYNTHESIS OF DIMETHYL 3,4,5,6 TETRAPHENYLPHTHALATE

(IN-PERSON WEEK- 6 AND 7)

References: Pavia: Oxidation,Exp 32B, p. 269

Related reading:
Aldol condensation: p. 306-312
Diels-Alder Reaction, p 404-405, 411-414; 416-423

Klein, Organic Chemistry, 3rd Ed.: Chapter 12 (Alcohols) Sec 12.10 (alcohol oxidation), Chapter 15 (NMR), Ch 16 (Pericyclic reactions) Sec 16.7 (Diels Alder), Chapter 21 (enolates)Sec 21.3 (Aldol Condensation)

You will note that some of the steps of this experiment are similar to corresponding preparative experiments in your lab text, and may wonder why we don't just use the procedures in the textbook. The reason is that the experiments in these notes have been thoroughly tested.

This synthetic sequence illustrates a variety of reaction types that are frequently used in organic synthesis. You must thoroughly study the procedures before you start the experiment. You must plan your time so that you utilize it efficiently. If you don't do this you won't be able to finish the experiment.

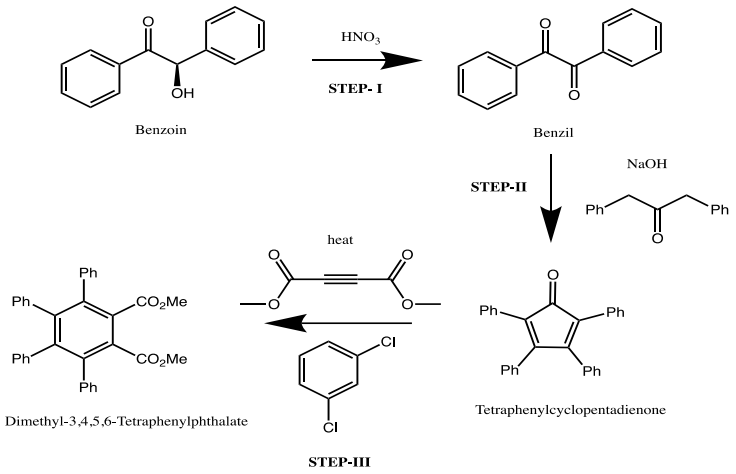
Week -6 Prelab Quiz: (10 points)

Week -7 Prelab Quiz: (10 points)

Week -6 Prelab : Steps I and II (10 points)

Week -7 Prelab : Steps III and MP (10 points)

Outline of reactions (not balanced):



Step 1: <u>The Oxidation of Benzoin to Benzil</u>

You must carry out the oxidation and the initial precipitation of the product in the fumehood. Once the brown fumes are gone, you may filter the product at your lab bench. Place 5.0 g of benzoin in a small flask, add 15 ml of conc. nitric acid (HNO_3) (how many moles?) and heat the flask, with occasional swirling, for 30-40 minutes on the steam bath.

After cooling the flask in an ice bath, pour the contents into 100 mL of water containing a few chunks of ice. Break up the lumps of yellow benzil and filter under vacuum. Wash the benzil with a little ice cold 95% ethanol, press the solid with a clean glass stopper, and spread the product out to dry on a piece of paper. Recrystallize the product from a minimum amount of **methanol**. The melting point of the dry material may be a few degrees below the literature mp (94-95°C). Save portions of the product for Step 2 and **submit the remainder of the product to your instructor in a test tube labeled with your name, the date, name of compound, yield, and melting point.**

Step 2: <u>The Aldol Condensation - Synthesis of Tetraphenylcyclopenta-dienone.</u>

Into a 50 mL Erlenmeyer flask place exactly 0.01 mole benzil and 0.01 mole dibenzyl ketone (1,3-diphenyl-2-propanone or diphenylacetone), and 10 mL triethylene glycol, using the solvent to wash down the walls. Swirl the mixture on a hot plate until the benzil is dissolved, then remove from heat.

Have ready in a test tube 1 ml of a 40% solution of benzyl trimethyl ammonium hydroxide (in CH_3OH, S. G. 0. 92g/mL). Place a thermometer into the benzil-dihenzylketone mixture, adjust the temperature with stirring to exactly 100°C and then add the base. Swirl once to mix, and remove from heat. Crystallization should start in 10-15 minutes. Let the temperature drop to ≈ 80°C, then cool under the tap and add 10 mL methanol. Stir or

swirl to a slurry, collect the product and wash with cold methanol until the filtrate is dark purple-pink. Dry and record the mp and yield (Lit. mp 219°C). If the product is impure it can be crystallized from triethylene glycol by heating in a tenfold excess (w/v) of solvent to 220°C and letting cool.

Submit the product to your instructor in a test tube labeled with your name, the date, name of compound, yield, and melting point.

Step 3: <u>Synthesis of 3,4,5,6-Dimethyl Tetraphenylphthalate</u>

Measure into a 25 mL round-bottom flask 0.50 g of tetraphenylcyclopentadienone, 2.5 mL of o-dichlorobenzene and 0.25 mL of dimethylacetylenedicarboxylate and add a boiling chip.**(SEE NOTE AT END).** Attach an air condenser (i.e. an ordinary condenser with no water flowing through it) and boil very gently in the fumehood (CO evolution: highly toxic!) until there is no more color change; 10 - 15 min. should be enough. Do not let the vapor rise very high into the condenser. The pure adduct is white, and if the starting material is adequately pure, the color changes from purple to pale tan. Cool to 100°C (thermometer), slowly stir in 15 mL of methanol, and let crystallization proceed. Cool and collect the product, washing with cold methanol. Record the yield, appearance, and mp. **Turn in a properly labeled sample in a melting point tube.** Lit. mp 258°C- 259°C.

<u>NOTE</u>: Dimethylacetylenedicarboxylate is a powerful lachrymator. Handle with extreme caution in the fumehood. Even a trace on the skin should be washed off with plenty of soap and water. Dimethyl acetylenedicarboxylate is also very expensive. Your instructor will dispense this compound (you should use around 0.25 mL).

Report Write-Up

Week -6: Steps I and II (40 points)

Week -7: Steps III and MP and NMR analysis (40 points)

Follow the guidelines discussed from Experiment 1 and in Appendix I in this manual.

Write up must describe steps-I, II and II in a correct logical order so the reader understands the entire multistep reaction. The more creative you are in your story telling by providing justifications, observations, mechanisms along the way the better your discussion with be.

Your write-up must include reaction mechanisms for the reactions in Steps 1 and 2 (Chem draw), show calculation of the percentage yields of all products.

Show your calculations for yields at each step.

Discuss any procedure modifications or problems with the individual steps (change in reaction conditions, low yield, etc)in each step.

Interpret both the ^{1}H and ^{13}C NMR spectra for the reactants and the product posted on Blackboard. Label the different types of protons and carbons for each compound and locate the signals for these nuclei on the spectra. Use the chemical shift and the integral ratio to help with your peak assignments. Because of signal overlap, you may not be able to assign individual protons/carbons in a compound to a separate signal in the spectrum. In these cases unseparated peaks in the spectrum are to be assigned to groups of protons/carbons. Explain how you arrived at your peak assignmnts.
Write reactions for all the key chemical reactions. Discuss any observations that do not agree with your conclusions, and provide possible explanations for these inconsistencies.

EXPERIMENT 5: REDUCTION OF CAMPHOR TO BORNEOL AND ISOBORNEOL

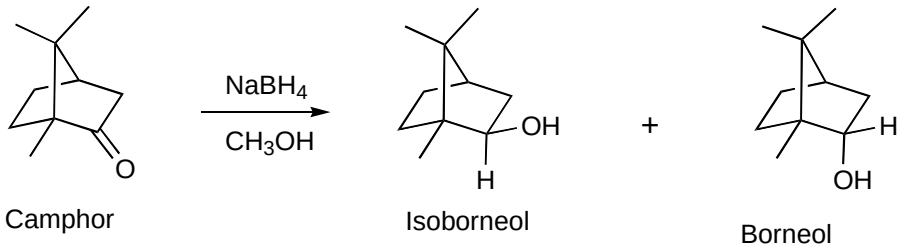
WEEK 8: ONLINE VIA BB COLLABORATE DISCUSSIONS& VIDEOS

References: Pavia: Exp 31B, p 248-252; 254-261; Technique 25: Infra Red (IR)Spectroscopy, p 854; Technique 26: Nuclear Magnetic Resonance (NMR) Spectroscopy, p 888

Klein, Organic Chemistry, 3rd Ed.: Chapter 12 (Sec 12.4, alcohols from reduction of ketones); Sec 12.11 (Biological Redox reactions), Chapter 14 (IR), Chapter 15 (NMR).

There are many reagents that are useful for the reduction of various carbonyl compounds. Metal hydride reagents such as sodium borohydride and lithium aluminum hydride act as hydride donors, which undergo nucleophilic addition reactions with aldehydes and ketones to yield alcohols.

In this experiment, you will reduce camphor, a naturally occurring ketone, using sodium borohydride. You will isolate the product, calculate the percentage yield and analyze it by NMR.



Camphor Isoborneol Borneol

Review all the appropriate laboratory techniques (recrystallization, distillation, filtration, extraction etc.) before you start.

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)

Follow the guidelines discussed earlier.

Procedure:

In a 50 mL Erleneyer flask dissolve 250 mg of camphor in 1.5 mL of methanol. Stir with a glass stirring rod until the camphor has dissolved. Weigh out 250 mg of $NaBH_4$, and add this in four portions to the camphor solution over the course of five minutes, stirring the reaction mixture during the addition. When all the borohydride is added, boil the contents of the flask on a water bath for 2 minutes. After cooling the reaction

mass to room temperature, carefully add 10 mL of ice-cold water. Collect the crude product by vacuum filtration. Allow the vacuum to pull for about 10 minutes to dry the solid. Transfer the solid to a dry Erlenmeyer flask. Dissolve the solid in 10 mL of dichloromethane and dry the solution with about 0.5 g of anhydrous Na_2SO_4. When dry the solution should not be cloudy. If the solution is still cloudy, add some more granular anhydrous Na_2SO_4. Transfer the solution from the drying agent into a preweighed dry flask. Gently evaporate the solvent using a hot water bath under the hood.

Analysis of the product

Determine the weight of the dry solid and obtain the melting point, IR and NMR spectra. Signed and dated spectra are to be taped in your notebook. Indelible ink only, **no "white-out"!**
Obtain the IR spectrum by using the dry film method described in Technique 25 in you textbook (Pavia, Sec 25.6, p. 863. (Infrared spectroscopy will also be used in experiments 5 and 6, where other methods for preparing your sample may be necessary).

A: Infrared Spectroscopy (I.R spectra)

Pavia: Technique 25, p 854; Appendix 3, p 998.

Run an IR spectrum of your pure unknown. If the unknown is liquid, you may run the spectrum neat (no solvent). If you have a solid, run the spectrum using the dry film method, as a Nujol mull on NaCl discs, or as a KBr pellet. If necessary, your instructor will show you how to prepare a KBr pellet of your solid. Signed and dated spectra are to be taped in your notebook. Interpret your spectra.

NOTE: Both the IR Spectrometers and the IR discs are expensive and delicate. Never use force in assembling the discs, inserting it in the instrument or in making any adjustments. (Our new IR Spectrometer has a replacement costs $10,000.00!) If you use force on the discs they will be scratched and neither you or anyone else will be able to obtain good spectra. These discs are brittle and very expensive. Be careful.

Submit a sample to your instructor for the NMR. The sample should contain 0.003 g of your unknown (1 small drop of liquid) in 0.7 ml of $CDCl_3$. The NMR data will be obtained by a T.A. and returned to you.

You must also submit a sample to your instructor in a melting point tube labeled with your name, the date, name of compound, yield, and melting point.

(See NMR on Pavia page 260 – Mixture of products in NMR after camphor reductiona and understand how you will use it to find product ratio)

Report Write-Up (30 points)

(Follow the format for write-up of synthesis experiments in Appendix I in this manual)

Write up must describe details of why each step was done in a correct logical order so the reader understands the entire reaction. The more creative you are in your story telling by providing justifications, observations, mechanisms along the way the better your discussion with be.

Your write-up must include reaction mechanisms for the reactions in Steps 1 and 2 (Chem draw), show calculation of the percentage yields of all products.

(i) Calculation of the percent yield of your product (show the calculation)

(ii) Interpretation of the IR spectrum of your product by comparing with IR spectra for camphor, borneol and iso-borneol in the textbook (Pavia, p. 255 – 259). Make note of the presence and absence of any significant absorptions and what they indicate as to the success of the reaction. Determine the ratio of isoborneol to borneol from the 1H-NMR spectrum of your product. Refer to the textbook (Pavia, p 255) for guidance in interpreting the NMR data.

EXPERIMENT 6: SYNTHESIS OF BENZOIC ACID WITH A GRIGNARD REACTION

WEEK 9: ONLINE VIA BB COLLABORATE DISCUSSIONS & VIDEOS

References: Pavia: Exp 33B, p 278-283; 286-288; Technique 25: Infra Red (IR) Spectroscopy, p 854

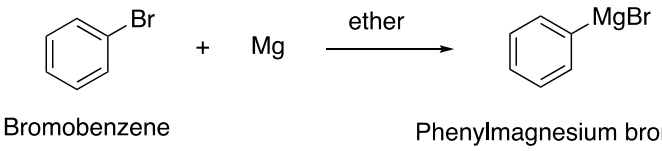
Klein, Organic Chemistry, 3rd Ed.: Chapter 12 (Sec 12.6, alcohols via Grignard Reagents), Chapter 14 (IR), Chapter 15 (NMR).

The alkyl portion of the Grignard reagent behaves as if it had the characteristics of a carbanion. We may write the structure of the reagent as a partially ionic compound. This partially bonded carbanion is a Lewis base. It reacts with strong acids to give an alkane. Any compound with a suitably acidic hydrogen will donate a proton to destroy the reagent, water, alcohols, terminal acetylenes, phenols, and carboxylic acids are all acidic enough to bring about this reaciton.

The Grignard reagent also functions as a good nucleophile in nucelophilic addition reactions of the carbonyl group. The carbonyl group has an eletrophilic character at its carbon atom (due to resonance), and a good nucleophile seeks out this center for addition.

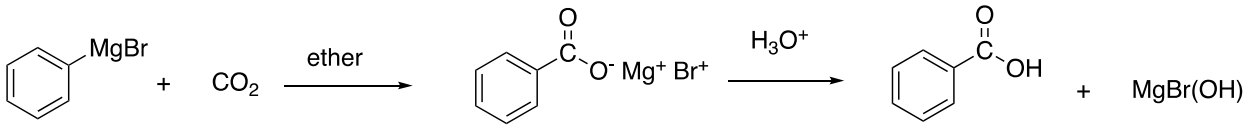
The Grignard reaction is used synthetically to prepare secondary alcohols from aldehydes and tertiary alcohols from ketones. The Grignard reagent will react with esters twice to give tertiary alcohols. Synthetically, it can also be allowed to react with carbon dioxide to give carboxylic acids and with oxygen to give hydroperoxides.

In this experiment, you will prepare a Grignard reagent (organomagnesium reagent). The reagent is phenylmagnesium bromide. It will then be converted to a carboxylic acid upon reaction with dry ice.



Bromobenzene

PhenylImagnesium bromide



Benzoic acid

Because the Grignard reagent reacts with water, carbon dioxide, and oxygen, it must be protected from air and moisture when it is used. The

apparatus in which the reaction is to be conducted must be scrupulously dry and the solvent must be free of water (anhydrous). During the reaction, the flask must be protected by a calcium chloride drying tube. Oxygen should also be excluded. In practice, this can be done by allowing the solvent ether to reflux. This blanket of solvent vapor keeps air from the surface of the reaction mixture.

In the experiment described here, the principal impurity is biphenyl. Which is formed by a heat- or light-catalyzed coupling reaction of the Grignard reagent and unreacted bromobenzene. A high reaction temperature favors the formation of this product. Biphenyl is highly soluble in petroleum ether, and it is easily separated from benzoic acid by extraction.

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)

Follow the guidelines discussed earlier.

Procedure:

Part I: Preparing the Grignard Reagent

Preparation of Glassware
If necessary, dry all the pieces of glassware (no plastic parts) in an oven at 110$_{\circ}$C for at least 30 minutes or flame dry it with a bunsen burner. All glassware used in your Grignard reaction must be scrupulously dried. Surprisingly, large amounts of water adhere to the walls of the glassware, even when it is apparently dry. Glassware washed and dried the same day, if it is to be used, can still cause problems in starting a Grignard reaction.

Apparatus
Add a clean, dry stirring bar to the 100-mL round bottom flask and assemble the apparatus as shown in the figure for this experiment in the Pavia textbook. Place drying tubes (filled with fresh calcium chloride) on both the separatory funnel and on the top of the condenser. A stirring hot plate will be used to stir and heat the reaction. Make sure that the apparatus can be moved up and down easily on the ring stand. Movement up and down relative to the hot plate will be used to control the amount of heat applied to the reaction.

Formation of the Grignard Reagent
Using smooth paper or a small beaker, weigh about 0.5 g of magnesium turnings (AW=24.3) and place them in the 100-mL round-bottom flask. Using a preweighed 10-mL graduated cylinder, measure approximately 2.1 mL of bromobenzene (MW=157.0), and reweigh the cylinder to determine the exact mass of the bromobenzene. Transfer the bromobenzene to a stoppered 50-mL Erlenmeyer flask. Without cleaning the graduated cylinder, measure a 10-mL portion of anhydrous ether and transfer it to the same 50-mL Erlenmeyer

flask containing the bromobenzene. Mix the solution (swirl) and then, using a dry, disposable Pasteur pipet, transfer about half of it into the round-bottom flask containing the magnesium turnings. Add the remainder of the solution to the 125-mL separatory funnel. Then add an additional 7.0 mL of anhydrous ether to the bromobenzene solution in the separatory funnel. At this point, make sure all joints are sealed and that the drying tubes are in place.

Position the apparatus just above the hot plate, and stir the mixture gently to avoid throwing the magnesium out of the solution and onto the side of the flask. You should begin to notice the evolution of bubbles from the surface of the metal, which signals that the reaction is starting. It will probably be necesssary to heat the mixture, using your hot plate, to start the reaction. The hot plate should be adjusted to its lowest setting. Because ether has a low boiling point (35^{o}C), it should be sufficient to heat the reaction by placing the round-bottom flask just above the hot plate. Once the ether is boiling, check to see if the bubbling action continues after the apparatus is lifted above the hot plate. If the reaction continues to bubble without heating, the magnesium is reacting. You may have to repeat the heating several times to successfully start the reaction. After you have made several attempts at heating, the reaction should start, but if you are still experiencing difficulty, proceed to the next paragraph.

Optional Steps

You may need to employ one or more of the following procedures if heating fails to start the reaction. If you are experiencing difficulty, remove the separatory funnel. Place a long, dry, glass stirring rod into the flask, and gently twist the stirring rod to crush the magnesium against the glass surface. Be careful not to poke a hole in the bottom of the flask; do this gently! Reattach the separatory funnel and heat the mixture again. Repeat the crushing procedure several times, if necessary, to start the reaction. If the crushing procedure fails to start the reaction, then add one crystal of iodine to the flask. Again, heat the mixture gently. The most drastic action, other than starting the experiment over again, is to prepare a small sample of the Grignard reagent externally in a test tube. When this external reaction starts, add it to the main reaction mixture. This 'booster shot' will react with any water that is present in the mixture and allow the reaction to get started.

Completing the Grignard Preparation

When the reaction has started, you should observe the formation of a brownish-gray, cloudy solution. Add the remaining solution of bromobenzene slowly over a period of 5 minutes at a rate that keeps the solution boiling gently. If the boiling stops, add more bromobenzene. It may be necessary to heat the mixture occasionally with a hot plate during the addition. If the rection becomes too vigorous, slow the addition of the bromobenzene solution, and raise the apparatus higher above the hot plate. Ideally, the mixture will boil without the application of external heat. It is important that you heat the mixture if the reflux slows or stops. As the reaction proceeds, you should observe the gradual disintegration of the magnesium metal. When all the bromobenzene has been added, place an

additional 1.0 mL of anhydrous ether in the separatory funnel to rinse it and add it to the reaction mixture. Remove the separatory funnel after making this addition, and replace it with a stopper. Heat the solution under gentle reflux until most of the remaining magnesium dissolves (don't worry about a few small pieces). This should require about 15 minutes. Note the level of the solution in the flask. You should add additional anhydrous ether to replace any that is lost during the reflux period. During this reflux period, you can prepare any solution needed for the second part of the experiment. When the reflux is complete, allow the mixture to cool to room temperature.

Part II: Making Benzoic Acid

Addition of Dry Ice

Be careful with dry ice, as contact with skin can cause severe frostbite. Always use gloves or tongs. The dry ice is best crushed by wrapping large pieces in a clean, dry towel and striking them with a hammer or wooden block. Use as soon as possible to avoid contact with atmospheric moisture.

When the phenylmagnesium bromide solution has cooled to room temperature, pour it as quickly as possible onto 10 g of crushed dry ice contained in a 250-mL beaker. The dry ice should be weighed as quickly as possible to avoid contact with atmospheric moisture. It need not be weighed precisely. Rinse the flask, in which the phenylmagnesium bromide was prepared, with 2 mL of anhydrous ether and add it to the beaker. Cover the reaction mixture with a watch glass, and allow it to stand until the excess dry ice has completely sublimed. The Grignard addition compound will appear as a viscous, glassy mass.

Hydrolysis

Hydrolyze the Grignard adduct by slowly adding approximately 8 mL of 6M hydrochloric acid to the beaker and stirring the mixture with with a glass rod or spatula. Any remaining magnesium chips will react with the acid to evolve hydrogen. At this point, you should have two distinct liquid phases in the beaker. If you have solid present (other than magnesium), try adding a little more ether. If the solid is insoluble in ether, try adding a little more 6M hydrochloric acid solution or water. Benzoic acid is soluble in ether, and inorganic compounds (MgX_2) are soluble in the aqueous acid solution. Transfer the liquid phases to an Erlenmeyer flask, leaving behind any residual magnesium. Add more ether to the beaker to rinse it, and add this additional ether to the Erlenmeyer flask. You may stop here. Stopped the flask with a cork, and continue with the experiment during the next laboratory period.

Isolation of the Product

If you stored your product and the ether layer evaporated, add several milliliters of ether. If the solids do not dissolve on stirring or if no water layer is apparent, try adding some water. Transfer your mixture to a 125-mL separatory funnel. If some material remains undissolved or if there are three layers, add more ether and hydrochloric acid to the separatory funnel, stopper it, shake it, and allow the layers to separate.

Continue adding small portions of ether and hydrochloric acid to the separatory funnel, and shake it until everything dissolves. After the layers have separated, remove the lower aqueous layer. The aqueous phase contains inorganic salts and may be discarded. The ether layer contains the product benzoic acid and the by-product, biphenyl. Add 5.0 mL of 5% sodium hydroxide solution, restopper the funnel, and shake it. Allow the layers to separate, remove the lower aqueous layer, and save this layer in a beaker. This extraction removes the benzoic acid from the ether layer by converting it to the water-soluble sodium benzoate. The by-product biphenyl stays in the ether layer along with some remaining benzoic acid. Again, shake the remaining ether phase in the separatory funnel with a second 5.0 mL portion of 5% sodium hydroxide, and transfer the lower aqueous layer into the beaker with the first extract. Repeat the extraction process with a third portion (5.0 mL) of 5% sodium hydroxide, and save the aqueous layer as before. Discard the ether layer, which contains the biphenyl impurity, into the waste container designated for nonhalogenated organic wastes.

Heat the combined basic extracts while stirring on a hot plate (100$_{\circ}$C-120$_{\circ}$C) for about 5 minutes to remove any ether that may be dissolved in this aqueous phase. Ether is soluble in water to the extent of 7%. During this heating period, you may observe slight bubbling, but the volume of liquid will not decrease substantially. Unless the ether is removed before the benzoic acid is precipitated, the product may appear as a waxy solid instead of crystals.

Cool the alkaline solution, and precipitate the benzoic acid by adding 10.0 mL of 6M hydrochloric acid while stirring. Cool the mixture in an ice bath. Collect the solid by vacuum filtration on a Büchner funnel. The transfer may be aided and the solid washed with several small portions of cold water. Allow the crystals to dry thoroughly at room temperature at least overnight. Weigh the solid, and calculate the percentage yield of benzoic acid (MW=122.1)

Crystallization
Crystallize your product from hot water. Set the crystals aside to air-dry at room temperature before determining the melting point of your purified benzoic acid (literature value, 122$_{\circ}$C) and the recovered yield in grams.

Spectroscopy
Determine the IR spectrum of the purified material in a KBr pellet.

You must also submit a sample to your instructor in a melting point tube labeled with your name, the date, name of compound, yield, and melting point.

Crude yield (---g, ----%); Recrystallized yield (---g, ----%) and Melting point range:----

(yields will be provided by your lab instructor so you can calculate yield)

(MP range will be provided by your lab instructor so you can comment on purity)

IR data:

Find IR for both Starting Material and Product and identify the significant bands. Decribe how IR can be used to determine if the reaction worked.

Report Write-Up (30 points):

Write-Up (Follow the format for write-up of synthesis experiments in Appendix I in this manual)
In addition to the requirements in Appendix I, your write-up must include the following:
(i) Calculation of the percent yield of your product (show the calculation)
(ii) Interpretation of the IR spectrum of your product by comparing with IR spectra for benzoic acid. Refer to the textbook for guidance in interpreting the IR data.

EXPERIMENT 7:
IR AND NMR WORKSHOP
WEEK 10: ONLINE VIA BB COLLABORATE DISCUSSIONS & VIDEOS

You will identify the functional groups and structure of three unknown compounds by using a combination of IR & NMR spectra.

Klein, Organic Chemistry, 3rd Ed.: Chapter 14 (IR), Chapter 15 (NMR)

References: Classification tests listed in the previous experiment and in Pavia.

IR Spectroscopy: Pavia: Technique 25, p 854, Appendix 3, p 998

A: I.R & NMR

Your instructor will give your IR and NMR's of 3 compounds. Label all peaks chemical shifts, integration and propose how your arrived at your structure.

Report Write-Up (30 points):

Construct a clear logical analysis for the identification of the functional groups & structure in your unkown compounds.

Label the three IR and NMRs and include them in the report.

Indicate the chemical shifts, area under curve & splitting as indicated below

^{1}H NMR (----- MHz, solvent) Chemical shift δ (ppm): --- (----H, multiplicity)

Provide justification for most sheilded, deshielded and splittings.

****

EXPERIMENT 8: SEPARATING THE COMPONENTS OF PANACETIN
WEEK 11: ONLINE VIA BB COLLABORATE DISCUSSIONS

References: Related reading:
Pavia: Experiment-3B, 3C, 3D, 4A
Distribution of a solute between two immisible solvents
How do you determine which is Organic layer?
Use of extraction to Isolate Neutral
Compound
Separation with a separatory funnel
Essay: Analgesics (pg 55)

Klein, Organic Chemistry, Chapter 3 (Acids-Bases), Chapter 20 (Carboxylic acids)

Panacetin – analgesic drug contains aspirin, sucrose and acetaminophen. Aspirin and acetaminophen are the active ingredients. Counterfeit drugs may contain less % of an active ingredient or no active ingredient.

Panacetin – batch your are testing analgesic drug contains aspirin, sucrose and an unknown component that can be acetanalide or phenacetin. The unknown components in your batch (acetanalide or phenacetin) are cheically related to acetaminophen and have similar pain releiving properties like acetaminophen. However, acetanalide and phenacetin more toxic and banned in the USA. In this experiment, you will separate the components of Panacetin batch under study using their solubility and acid-base properties and find the % of aspirin, sucrose and the unknown component it contains. You will use spectroscopy to confirm the identity of your unknown.

Sucrose is insoluble in Organic Solvents (Dichloromethane, CH_2Cl_2 or diethyl ether)- {which is the greener solvent??? How does use of diethyl ether change the layers during extraction Organic layer – top layer or lower layer???}

Aspirin, acetanalide or phenacetin are soluble in Dichloromethane, CH_2Cl_2 or diethyl ether but relatively insoluble in water

Aspirin (Acetylsalicylic acid) reacts with bases (NaHCO3 – aqueous sodium bicarbonate) to form a salt, sodium acetylsalicylate, which is insoluble in Dichloromethane, CH_2Cl_2 or diethyl ether but soluble in water {why are salts more soluble in water}

Acetanalide or phenacetin are not converted to salts and acetanalide or phenacetin

Experiment: In this experiment you are only provided with the reagents and supplies you have in lab. You will devise the separation and write

the experiment. Record the % of each component (mass will be provided by your lab instructor) and use spectroscopy to identify the unknown.

Panacetin Batch: 3.00 gm
Dichloromethane (50 mL) or Diethyl ether (50 mL)
Aqueous $NaHCO_3$ (60 ml; for 2 extractions with 30 mL portions)
6 M HCl (10 mL)

Glass ware & Supplies:
Round bottom flask (50 mL, 100 mL, 250 mL)
Erlenmeyer flask (25 mL, 125 mL, 250 mL)
Separatory funnel with stopper
Buchner funnel and supplies for vaccum filteration
Filter paper (different sizes)
Litmus paper
Stem funnel
Powder funnel
Glass rod
Vials
Labels
Rotary evaporator

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)

Follow the guidelines discussed earlier.

Draw the structures of aspirin, sucrose, acetaminophen, acetanalide, phenacetin and any other solvents / reagents you will need.

Draw the flow diagram to summarize the extration.

Report Write-Up (30 points): Write the detailed steps you will use (in past tense). Also use a flow chart to help with your discussion. Follow the guidelines in Experiment 3 for the discussion on the identification of each unknown.

Write the experimental details for:

A) Separation of Sucrose:

B) Separation of Aspirin (with reactions):

C) Isolation of Unknown:

D) Identification using spectroscopy:

EXPERIMENT 9:
LEARNING ABOUT DERIVATIVES
WEEK 12: ONLINE VIA BB COLLABORATE DISCUSSIONS & VIDEOS

Identification of Unknown using physical properties of the derivative.

A "Derivative" is a crystalline solid that can be synthesized by the functional group transformation or organic compounds using simple reactions The derivative after purification must have a sharp melting point. The melting points of derivatives are reported in literature and can be used to identify the compound from which the derivative was prepared.

For example, Amides are derivatives of Carboxylic acids. Unknown carboxylic acids can be converted to amide by reacting the acid with thionyl chloride and ammonia.

From Literature you can find the melting points of various amides.

If the amide synthesized from unknown acid melts at 101 -102 ₀C you can conclude the amide is hexamide. Looking backward you can propose the unknown acid that was used should be hexanoic acid (Boiling Point: 205 – 206 ₀C). Just comparing boiling points of the unknowns may not help one identify the unknown because there can be another acid with similar boiling point range. Amide derivative of 2-bromopropanoic acid (Boiling Point: 205 – 206 ₀C)melts at 123 -124 ₀C. Ofcourse, because NMR is so readily available derivatives are not made very often. However, this was a method to confirm identity of compounds when spectroscopic tools were not readily available. While selecting a derivative you would like to prepare you must look at which derivatives are reported in literature so you can compare the Melting point of your derivative with compounds from literature.

For information on how to find data for compounds, tables of unknowns and the preparation of derivatives, see Pavia: Technique 4, p 581; Appendix 1, p 980; Appendix 2, p 994.

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)

Follow the guidelines discussed earlier.

Preparation of Derivatives (See Shriner and Fuson as additional reference)

Propose Preparation of one derivative of each purified unknown (from experiment 3)in order to positively identify it.

Report the expected mp of all derivatives (literature values) and how MP can help identify the unkown.

Report Write-Up (30 points):

Discuss how you decided on the method used for separation of your mixture. If appropriate, use a flow chart to help with your discussion. Follow the guidelines in Experiment 3 for the discussion on the identification of each unknown.

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EXPERIMENT 10:
GREEN CHEMISTRY
THIAMINE-MEDIATED BENZOIN TYPE CONDENSATION OF FURFURAL

WEEK 13: ONLINE VIA BB COLLABORATE DISCUSSIONS & VIDEOS

References: Related reading:
Pavia: Thiamine catalyzed benzoin condensation: Exp 32A, p 263
Essay: Green Chemistry (218-223)
Experiment: 53 (pg 421)

R. Breslow, *J. Am. Chem. Soc.* 1958, 80, 3719

C. K. Lee, M.S. Kim, J. S. Gong, and L-S. H. Lee, *J. Heterocyclic Chem.* 1992, 29, 149

Klein, Organic Chemistry, Chapter 19 (Aldehyde and Ketones) Sec 20.10 (Carbon nuceleophiles & cyanohydrins),

In Experiment-4, you performed oxidation of Benzoin. Benzoin is synthesized from benzaldehyde using Benzoin condensation reaction. Two chemists Friedrich Wohler and Justus von Liebig, discovered this cyanide catalyzed reaction of benzaldehyde. Aldehydes that have no alpha hydrogen undergo this condensation reaction. A new C-C bond is formed when two equivalents of benzaldehyde combine to form one equivalent of benzoin.

However, cyanide salts are toxic and acidic conditions converts them to volatile toxic hydrogen cyanide (HCN) gas.

A century after the discovery of benzoin condensation, it was found that Vitamin B_1 (thaimine) hydrochloride salts can effectively catalyze the benzoin condensation reaction. The use of a biologically derived reagent for Organic syntehsis allowed for chemists to develop environmentally friendly techniques for Organic Chemistry. A safe compound Thymine replaced the very toxic cyanide salts.

In this experiment, you will discuss the "Green Chemistry" aspects of this reaction. You will discuss the Green Chemistry Principles and other reactions where such green chemistry approaches (cofactors) have been used in organic synthesis.

The thymine mediated condensation can be carried using other aldehydes like furan-2-carboaldehyde which you will discuss in this experiment (Part B). The reaction is too slow to allow completion in a single lab session. Normally, the reaction is set up during the first session followed by isolation, purification and characterization done one week later.

Pre-lab Quiz (10 points)

Pre-lab Write-Up (10 points)

Follow the guidelines discussed earlier.

Part A: <u>The Benzoin Condensation of benzaldehyde using Sodium Cyanide:</u>

Read and understand the procedure to synthesize Benzoin using traditional Cyanide method. Draw the mechanism and understand the role of cyanide.

Part A:

Dissolve 1.0 g potassium cyanide (KCN) in 20 mL distilled water in a 250 mL round bottom flask (rbf). **<u>Ensure that the rbf has no cracks or chips</u>.** Add 40 mL 95% ethanol, 20 mL pure benzaldehyde (freshly opened or distilled) (Why???), and one or two boiling chips. (Why???)

(CAUTION: DO NOT ALLOW KCN TO COME IN CONTACT WITH ACID! DO NOT TOUCH WITH BARE HANDS!)

Reflux gently over a heating mantle for 45 min. Allow the reaction to cool. If crystals do not appear within a few minutes withdraw a drop of the reaction mixture on a stirring rod and induce crystallization by scratching it against the neck of the flask. When crystallization is complete, collect the product and wash it free of the yellow mother liquor with a 1:1 mixture of cold ethanol-water. The cyanide containing mother-liquor should be discarded ONLY in the waste bottle marked **'CYANIDE WASTE'** and it must be washed down thoroughly with a lot of water. NO ACID should ever be poured in that sink. Check to see that the fumehood is turned on.(Why???)

Your benzoin crystals should be white, melting point (mp) 134-135°C. Determine the mp and yield of your product.

Discuss how Melting Point can help you identify the purity of your compound.

PART B: <u>The furoin Condensation of furfural using Thiamine hydrochloride:</u>

Read and understand the procedure for furoin condensation and discuss the Green aspects of the reaction.

Calculate atom economy.

Calculate the theoritical yield.

Calculate % yield from information provided by lab instructor. If yield is low, provide plausible reason for low yield.

Compare melting point range of your recrystallied compound (data shared by instructor) with reported melthing point of compound in literature and determine the purity of your compound.

Find the IR of the starting material and product and identify the significant bands. Decribe how IR can be used to determine if the reaction worked.

Part B: Reaction:

Thiamine hydroochloride (0.30 g) was added to a round bottom flask (25 mL) equipped with a magnetic stirring bar and dissolved with a mixture of water (0.45 mL) and 95 % ethanol (3 mL). Aqueous NaOH (0.90 mL, prepared from dissolving 8.0 g of NaOH in 100 mL of water)is added dropwise to the contents of the round bottom flask. A light yellow color should persist when all of the NaOH solution is added. If the reaction mixture is colorless more NaOH should be added. Furfural (0.73 mL) is added and the reaction mixture is allowed to stir vigorously for 15 minutes. The round bottom flask is sealed with a septum and stored in your drawer until next lab period.

Part B: Work up and Purification

Water is added to the cold reaction mixture (ice bath)to precipitate the product from the reaction mixture. The crude solid is isolated by buchner filteration and air dried. The crude product is recystallized form 95% ethanol.

Part B: Characterization:

Crude yield (---g, ----%); Recrystallized yield (---g, ----%) and Melting point range:----

(yields will be provided by your lab instructor so you can calculate yield)
(MP range will be provided by your lab instructor so you can comment on purity)

IR data:

Find IR for both Starting Material and Product and identify the significant bands. Decribe how IR can be used to determine if the reaction worked.

Report Write-Up

Part A and B (30 points)

Follow the guidelines discussed from Experiment 1 and in Appendix I in this manual.

Write up must describe steps in a correct logical order so the reader understands the reaction. The more creative you are in your story telling by providing justifications, observations, mechanisms along the way the better your discussion with be.

Your write-up must include reaction mechanisms for the reactions in Steps A and B (Chem draw), show calculation of the percentage yields of products.

Show your calculations for yields at each step.

Discuss any problems (change in reaction conditions, low yield, etc) and Green Chemistry aspects in the reaction.

Interpret both the IR spectra for the reactants and the product.

Write reactions for all the key chemical reactions. Discuss any observations that do not agree with your conclusions, and provide possible explanations for these inconsistencies.

APPENDIX I

REPORTS FORMAT: GENERAL WRITE-UP FORMAT FOR SYNTHESIS EXPERIMENTS

DATE:

1. TITLE OF EXPERIMENT

2. OBJECTIVE: BRIEFLY describe or list the aim(s) of the experiment. (include reactions)

3. INTRODUCTION: CONCISELY describe the theory behind the experiment.

4. DISCUSSION/CONCLUSION:

This should be a nice story in a logical order.
Discuss all steps of the reaction, show mechanisms, discuss yield purity Calculations, Graphs, etc.
Summarize your results. Whenever possible, use a table format.
How the experiment concurs or disagrees with the theory. Sources of error.
(Use past tense and do not say "I" weighed)

Late notebooks will be penalized. Organize and format your report so that it is easy to read. Leave adequate space between sections. You may use a word processing program to prepare your report but the carbon copies of the original data from your notebook must be submitted as an appendix. **Enquire with your instructor if he/she has any other specific write-up requirements.**

LABORATORY NOTEBOOK

Your notebook should contain in the very least #1-3, listed for the write-up. along with For notebook keeping, a convenient practice is to use the left side of your notebook as a worksheet for initial recording of observations/results, calculations, TLC plates etc, and the right hand side for more complete documentation of procedures and results. Do not use loose papers for recording data. All entries must be recorded in ink. The use of white-out is strictly prohibited. If you make an error, strike it out with a single line such that this action cannot be construed as an attempt to falsify data.

Lab reports should be uploaded on BB via link posted by your instructor and check using safe-assign for plagerism.

Cheating will be reported to the course coordinator and the Dean of Students.