Organic Laboratory
CH2360

Keep a Record!

Compiled by Al Scala, John C. MacDonald, Marion H. Emmert, and Uma Kumar
Department of Chemistry & Biochemistry
Worcester Polytechnic Institute
Worcester, MA
(rev 5/24/2016)

List of experiments

1. Simple Distillation and Boiling Point Determination.
2. Fractional Distillation of an Acetone-Toluene Mixture.
3. Melting Points and Mixed Melting Point Determination.
4. Esterification: Synthesis of *iso*Amyl Acetate.
5. Recrystallization: Purifying an Unknown by Recrystallization.
6. Dehydration of Cyclohexanol.
7. Thin Layer Chromatography.
8. Natural Products: Extraction of Caffeine from Tea.
9. Separation of a Mixture Using Column Chromatography.
10. Part A: Synthesis of Acetanilide
    Part B: Synthesis of Aspirin
11. Chlorination and Bromination of a Hydrocarbon: Reactivity Selectivity.
12. Part A: Reduction of Vanillin by Sodium Borohydride.
    Part B: Oxidation of Isoborneol.
13. Aldol Condensation: Dibenzal Acetone.
14. Grignard Reaction: Synthesis and Dehydration of 3-Methyl-3-pentanol.

Introduction to CH2360

This course corresponds to what is traditionally the laboratory accompanying a year-long course in Organic Chemistry. In CH2360, our attention will be focused on learning the experimental and analytical techniques used to synthesize, purify, and characterize solid and liquid organic compounds. Your goal is to be become knowledgeable and competent with those techniques, demonstrate care and efficiency in the laboratory, and learn to keep concise, detailed and accurate records of experimental work in your lab notebook so that you will be prepared for future laboratory work in organic chemistry and related areas in life and material sciences.

1. Notebooks. A lined notebook with a sewn binding is required (*loose-leaf and spiral notebooks are not acceptable*). A large format notebook with pre-numbered pages is preferable to a small format notebook. Read section G2 in *Experiments In Organic Chemistry* on (A) The Laboratory Notebook and (B) Lab Reports.

As in previous laboratory classes, you are expected to keep your experimental records up to date and to write all raw data and observations directly into your notebook. Raw data should be entered directly into the notebook on the left-hand page of the opened notebook. The right-hand page of the opened notebook should be reserved for your final record of the experiment. Each new experiment should be started on a new page of the notebook and all pages should be numbered and dated. Your experimental records should include a statement of the objective of the experiment (generally to synthesize a particular compound), a balanced equation showing the reaction to be carried out, a mole table of the reactants and products, a brief procedure section giving a concise but detailed account of the experiment, and a final statement of the result (i.e., amount, yield, % yield, description of the product obtained and the melting or boiling range recorded), as well as a brief, concise analysis of the purity of product. The procedure should be sufficiently detailed to allow you to repeat the experiment using only your notebook. The procedure should also include any important observations (e.g., color changes, evolution of heat, etc.). Finally, the procedure should be written in the third person past tense. For example, "…the solution of isoamyl alcohol, glacial acetic acid, and sulfuric acid was heated under reflux for 30 minutes..."

A recommended notebook format is as follows:

- Title and Date
- Reaction Scheme/Equation
- Mole Table
- Procedure & Observations
- Results & Conclusions

The first three items in this format must be done before you come to the lab to begin any synthetic experiment.

2. Evaluation of notebooks and products. Notebooks will be evaluated periodically either during lab, or they will be collected at the end of lab and returned at the start of the next lab period. Evaluation of experimental write-ups will be based on format, content, organization, completeness, and analysis of physical and analytical data. A summary of items to include in your lab

notebook is provided at the end of each experiment. Make sure you have included all items before turning in your notebook. Experiments involving synthesis of compounds frequently require that products be allowed to dry overnight, or that analytical data for products be collected the following lab period. Experimental write-ups should be completed on the day experiments are completed and all experimental and analytical data is obtained. Generally, you will be given several days to complete write-ups before notebooks are collected. You will be provided with an evaluation form for each experiment when your notebook is returned. The evaluation form is a check list of all experimental data, spectra, and products required for each experiment. When an item on the list is checked (✓), it has been accepted. If an X appears adjacent to the item with the date, the item either is missing or has not been accepted and must be improved and resubmitted by the next week. These evaluation forms will allow you to keep track of your progress on a weekly basis and to know what items to turn in with each completed experiment. Your grade for the course will be determined, in part, based on how complete your notebook is and whether items were included on time.

3. Labeling of compounds and spectra. During CH2360 you will synthesize a number of compounds. It is essential that those compounds be properly stored and labeled. Your products should be stored in a clean glass vial labeled with tape. Your name, the experiment number, and the name of the compound should be clearly written on the label. Compounds should be turned in the following lab period to be evaluated for purity and yield.

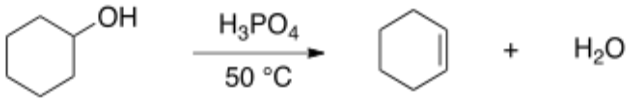
4. Mole Table. The mole table is a compilation of the physical properties, amounts, and toxicity of each reactant and product that appears in the balanced equation. The compilation should be tabulated using the headers shown below. The amounts of the reagents refers to the actual amounts used in the preparation, while the amounts of the products refers to the theoretically yield. Relevant data such as melting points or boiling points from the literature should be included along with references to the sources where the data was obtained.

A sample page from a lab notebook showing the information that should be entered prior to entering the lab is illustrated below.

……..
1/27/2010

Synthesis of Cyclohexene from Cyclohexanol

Objective: To synthesize cyclohexene via acid-catalyzed dehydration of cyclohexanol.



reagent	*moles*	*grams*	*mL*	*mol wt (g/mol)*	*Density (g/mL)*	*mp (°C)*	*bp (°C)*	*toxicity*
cyclohexanol	*0.20*	*20.0*	*21.0*	*100*	*0.96*	*25*	*161*	*irritant/ hygroscopic*
85% H_3PO_4	*-*	*-*	*5.0*	*98*	*-*	*-*	*dec.*	*corrosive/ hygroscopic*
cyclohexene	*0.20*	*16.4*	*20.2*	*82*	*0.81*	*-131*	*83*	*flammable/ irritant*
Water	*0.20*	*3.6*	*3.6*	*18*	*1.0*	*0*	*100*	

Procedure: Ault: Techniques and Experiments for Organic Chemistry, 2nd ed., Holbrook Press, Boston (1976) p.177.

Reference for physical constants: Sigma Aldrich 2010 catalog.

……..

5. Conferences. It is important that you attend all conferences and that you bring your laboratory and spectral notebooks with you. Each conference will begin with a review of the schedule for the coming week. It is particularly important that you know what you are expected to work on during each laboratory session. The remainder of the conference will be devoted to discussing the experimental details and theoretical background of coming experiments.

6. Attendance. It is absolutely essential that you attend the scheduled labs. The experimental Chemistry Laboratory is open during the scheduled lab period. The instructor and TA will be available during those times and normally will not be in the laboratory during other times. The instrument room will be open throughout the day on weekdays. You may use the instruments outside of the scheduled lab periods, but should not perform any synthetic experiments unsupervised for safety reasons.

7. Use of instruments. During CH2360 you will receive instruction on the proper use of the gas chromatograph. After you receive these instructions, you may use that instrument as needed during the lab period. You should regard this as a privilege and realize that you have a responsibility

to use the instrument safely and correctly and to keep the instrument in good working order. Always clean up after you are finished working so that we can keep our facilities in good condition.

8. Efficient Use of Time. You should use your laboratory time efficiently. Balanced equations and mole tables should be prepared ahead of time outside of the laboratory. Experimental procedures should be reviewed before you come to the lab so that you know in advance what you are going to do during each lab session. Many experiments involve periods of time when a solution is refluxing or a compound is crystallizing. During those times you should complete other work such as recording spectra or melting points, setting up an apparatus/glassware for the next stage of the experiment, or cleaning glassware. If you do not use your time efficiently, you will not be able to complete the required work in CH2360. It is generally acceptable to ask the instructor or TA to schedule extra time in the lab outside of the normally scheduled lab times. Lab periods occasionally may run slightly past the end of the scheduled time. If that happens, the instructor or TA will remain in the lab until experiments are complete.

9. Referencing melting and boiling points. Melting and boiling point ranges are reported to show the purity of a compound and to provide evidence of the identity of the synthetic product. To provide evidence for the identity of the compound the reported melting or boiling range must be compared to the accepted literature value. The literature value must be referenced properly. On the following page is a page copied from the experimental section of an article in the *Journal of the American Chemical Society* that illustrates how this is done. The *Sigma Aldrich Chemicals* catalog located in the lab is an excellent source for the physical constants of many organic compounds.

Required Materials

1. **Text.** *Experiments in Organic Chemistry*, R.K. Hill and J. Barbaro, Contemporary Publishing Company of North Carolina. Raleigh NC, 2005 (available on course site).

2. **Laboratory Notebook.** A lined notebook with a sewn binding is required (*loose-leaf and spiral notebooks are not acceptable*). Read section G2 in *Experiments In Organic Chemistry* on A. The Laboratory Notebook and B. Lab Reports.

3. **Safety Glasses.** Everyone must wear safety glasses meeting ANSI standard Z87.1. Such glasses may be purchased at the Chemistry stockroom or the WPI bookstore. These are *strictly* required and must be worn at all times in the lab. You will not be admitted into the laboratory without appropriate eye protection. *Contact lenses should not be worn in the laboratory*, even when worn under safety glasses.

4. **Clothing.** Clothing and shoes that leave no exposed skin must be worn in the lab as protection against spills and reagents that may splash if dropped. You will not be admitted into the laboratory if you are wearing open-toed shoes, shorts, or dresses that do not cover your legs completely.

Safety. Laboratory work necessarily involves use of hazardous materials periodically. In addition, some laboratory procedures can be dangerous if not carried out properly. General safety precautions and how to properly dispose of reagents and chemical waste are discussed on pp. G1-3 in *Experiments in Organic Chemistry*. *Please read this material carefully before doing any*

laboratory work. Hazards associated with particular experiments will be discussed in lecture, in pre-lab briefings, and in the Lab Manual of experiments. See Material Safety Data Sheets (MSDS) under *Useful References* (below).

Grading. Your grade in CH2360 will be based primarily on the quality of your laboratory work. Evaluation will be carried by observing your activities in the lab, examination of your lab notebook (e.g., content, completeness, analysis of products and analytical data, legibility, etc.), the results of your experiments, and grading your products both for yield and purity, as well as your demeanor in the lab. In addition, there will be two exams during the term that will examine your familiarity with the material covered in experiments and conference sessions, laboratory and analytical techniques, and laboratory procedures covered throughout the course. The breakdown for grading will be as follows:

Lab Notebook, 150 pts (60%) – 15 experiments x 10 pts/experiment

Lab Exams, 60 pts (24%) – 2 lab exams worth 30 pts each

Qualitative Assessment, 40 pts (16%) – preparedness, improvement, attitude, attendance, results

Experimental write-up from the Journal of the American Chemical Society

sulfur when the reaction is carried out in benzene–D_2O. This mechanistic view provides one coherent interpretation for the observed phototransposition and photodeuteration reactions.

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were recorded at 200 and 50.3 MHz on a Bruker FT-NMR system. ^1H and ^{13}C chemical shifts were measured relative to internal Me_4Si and $CHCl_3$, respectively. Infrared spectra were recorded on a PE-1620 FT spectrometer. GLC was performed on a PE-8500 FID instrument equipped with a 30 m × 0.25 μ Supelcowax 10 bonded phase. Mass spectra were recorded with an HP 5970B mass selective detector interfaced to an HP 5880 capillary gas chromatograph. Flash column chromatography was carried out on silica gel, 40 μ average particle size (J.T. Baker, Inc.). Preparative-layer chromatography was carried out on 20 × 20 cm glass plates coated with 2 mm of Kieselgel 60 F_{254} (Merck).

Synthesis of Phenylthiazoles and Phenylisothiazoles. Bromoacetaldehyde diethyl acetal, thiobenzamide, and thiourea were available from Aldrich Chemical Co.

2-Phenylthiazole (1). Bromoacetaldehyde diethyl acetal (11.8 g, 60.0 mmol) and dry tetrahydrofuran (50 mL) was added dropwise over 1 h to a stirred mixture of thiobenzamide (8.23 g, 60.0 mmol) in dry tetrahydrofuran (100 mL) while the temperature was maintained between 70 and 80 °C. The resulting mixture was stirred at this temperature for 8 h, cooled to room temperature, made basic with 50% aqueous sodium hydroxide, and steam distilled. The distillate (500 mL) was extracted with ether (5 × 100 mL). The ethereal extract was dried (Na_2SO_4) and concentrated by rotary evaporation. The yellow residual oil (5.71 g) was subjected to silica gel (40 g) flash column chromatography. The column (65 cm long × 1.5-cm diameter) was eluted with hexane–dichloromethane (3:7), and 10-mL fractions were collected. The fractions which showed only the desired product by TLC were combined and concentrated to give a colorless oil, which was distilled (Kugelrohr) to give 2-phenylthiazole (**1**) as a colorless oil:bp (oven temperature) 80 °C (0.2 Torr) (lit.[27] bp 135 °C at 18 Torr); 4.0 g (24.8 mmol, 41.3% yield); ^1H NMR ($CDCl_3$) δ 7.20–7.55 (m, 4H), 7.80–8.10 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 168.3 (C-2), 143.6 (C-4), 130.0 (C-5), 133.5 (Ph, C-1′), 128.9 (Ph, C-2′,2′), 126.5 (Ph, C-3′, 3′), 118.8 (Ph, C-4′); IR (neat) 3064, 1600, 1506, 1480, 1447, 1416, 1320, 1248, 1142, 1055, 1000, 971, 874, 762 cm^{-1}; MS *m/e* (%) 161 (44), 58 (100).

4-Phenylthiazole (2). Sodium nitrite (6.20 g, 0.090 mol) was added over a period of 45 min to a stirred solution of 2-amino-4-phenylthiazole[28] (10.0 g, 0.057 mol) dissolved in concentrated sulfuric acid (100 mL) which was maintained at 0 °C. The resulting mixture was added in small portions during a period of 1 h to a stirred solution of hypophosphorous acid (30%, 150 mL) containing Cu_2O (0.20 g) while maintaining the temperature at −5 °C. The solution was allowed to warm to room temperature and stirred until gas evolution ceased. It was then made basic with 50% aqueous sodium hydroxide and steam distilled. The distillate (500 mL) was extracted with ether (3 × 100 mL), and the ethereal extract was dried (Na_2SO_4) and evaporated. The residue was sublimed (40 °C, 0.5 Torr) to give 4-phenylthiazole (**2**) as white crystals: mp 55–56 °C (lit.[27] mp 52 °C); 1.83 g (11.0 mmol, 19.3% yield); ^1H NMR ($CDCl_3$) δ 7.25–7.40 (m, 3H), 7.45 (d, 1H, J = 2.0 Hz), 7.80–8.10 (m, 2H), 8.80 (d, 1H, J = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 152.8 (C-2), 156.4 (C-4), 128.2 (C-5), 134.2 (Ph, C-1′) 128.8 (Ph, C-2′, 2′), 126.4 (Ph, C-3′, 3′), 112.5 (Ph, C-4′); IR (KBr) 1474, 1410, 1069, 902, 884, 818, 770 cm^{-1}; MS *m/e* (%) 161 (92), 134 (100).

5-Phenylthiazole (3). 1,1-Dimethoxy-2-bromo-2-phenylethane[29] (33.6 g, 0.14 mol), thiourea (20.2 g, 0.26 mol), and aqueous HBr (48%, 0.30 mL) were heated at 100 °C for 2 h with continuous removal of methanol by distillation. The resulting mixture was allowed to cool to room temperature, acidified with aqueous HCl (6M, 60 mL), and extracted with chloroform (60 mL). The chloroform extract was discarded, and the aqueous layer was brought to pH 9 by the addition of concentrated aqueous ammonia. The yellow precipitate was collected by suction filtration, washed with water, and dried under vacuum to yield 2-amino-5-phenylthiazole (22.1 g, 0.12 mol, 89% yield), mp 180–182 °C (lit.[30] mp 207.5–208.5 °C).

Sodium nitrite (6.9 g, 0.10 mol) was added slowly in small portions with stirring to concentrated sulfuric acid (20 mL) at 0 °C. 2-Amino-5-phenylthiazole (10.4 g, 0.059 mol) was then added in small portions over 60 min while maintaining the temperature at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and added at 0 °C during a period of 30 min to a stirred suspension of Cu_2O (0.30 g) and hypophosphorous acid (30%, 130 mL) at −5 °C. The reaction mixture was allowed to warm to room temperature. After gas evolution ceased, the solution was brought to pH 9 by the addition of aqueous sodium hydroxide (25%) and steam distilled. The distillate (500 mL) was extracted with ether (5 × 100 mL). The ethereal extract was dried (Na_2SO_4) and concentrated by rotary evaporation. Distillation (Kugelrohr) of the residual solid gave 5-phenylthiazole (**3**), which solidified to a white solid: bp (oven temperature) 80 °C (0.2 Torr), mp 44–45 °C (lit.[27] mp 45 °C); 1.88 g (0.012 mol; 20.3% yield); ^1H NMR ($CDCl_3$) δ 7.20–7.65 (m, 5H), 8.05 (s, 1H), 8.70 (s, 1H), ^{13}C NMR ($CDCl_3$) δ 152.0 (C-2), 138.9 (C-4), 139.3 (C-5), 131.0 (Ph, C-1′) 129.1 (Ph, C-2′, 2′), 126.9 (Ph, C-3′, 3′), 128.6 (Ph, C-4′); IR (KBr) 3048, 1447, 1389, 1318, 1075, 908, 860, 830, 759, 688 cm^{-1}; MS *m/e* (%) 161 (91), 134 (100).

3-Phenylisothiazole (4). 3-Amino-3-phenyl-2-propenenitrile[31] (1.50 g, 10.4 mmol) dissolved in 2-propanol (15 mL) was added to diphenylphosphinodithioic acid[32] (6.93 g, 27.7 mmol), and the resulting mixture was stirred at 40 °C for 20 h. The resulting mixture was cooled to room temperature, 2-propanol (60 mL) was added, and the pale green diphenylphosphinodithioic acid thioanhydride was collected by suction filtration. The filtrate was cooled to −10 °C, and an additional small amount of this solid was collected by suction filtration. The filtrate was added to dichloromethane (300 mL), and the resulting solution was washed with water (3 × 100 mL), saturated aqueous sodium bicarbonate (1 × 100 mL), dried (Na_2SO_4), and evaporated to dryness by rotary evaporation. The resulting red semisolid (1.5 g) was recrystallized from benzene to yield 3-phenyl-3-iminothiopropionamide as yellow crystals: mp 171–173 °C (lit.[33] mp 169–171 °C); 0.48 g (2.70 mmol, 26.0% yield); ^1H NMR (DMSO-d_6) δ 5.42 (S, 2H), 7.42–7.56 (m, 5H), 7.79 (br s, 2H), 8.12 (br s, 1H); IR (KBr) 3420, 3339, 3274, 3173, 1604, 1544, 1492, 1470, 1379, 991, 769, 696, 538, 479 cm^{-1}.

3-Phenyl-3-iminothiopropionamide (2.70, 15.2 mmol) was treated with iodine in ethanol according to the procedure of Goerdeler and Pohland[34] to give 5-amino-3-phenylisothiazole as a yellow solid: mp 154–158 °C (lit.[34] mp 163 °C); 2.60 g (14.8 mmol, 97.4% yield); ^1H NMR (DMSO-d_6) δ 6.61 (br s, 2H), 6.71–6.74 (m, 1H), 7.31–7.45 (m, 3H), 7.79–8.84 (m, 2H); IR (KBr) 3427, 3266, 3167, 1611, 1527, 1460, 1413, 1389, 908, 798, 771, 692 cm^{-1}.

5-Amino-3-phenylisothiazole (2.60 g, 14.8 mmol) was diazotized and reduced according to the literature procedure[35] to yield 3-phenylisothiazole (**4**) as a pale yellow oil: bp (Kugelrohr oven temperature) 130 °C (2.0 Torr) (lit.[35] bp 65 °C at 0.2 Torr) 0.90 g (5.59 mmol, 37.7% yield); ^1H NMR ($CDCl_3$) δ 7.50–7.55 (m, 3H), 7.55 (d, 1H, J = 5.0 Hz), 7.85–8.05 (m, 2H), 8.65 (d, 1H, J = 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ 167.7 (C-3), 129.2 (C-4), 148.9 (C-5), 134.6 (Ph, C-1′), 128.8 (Ph, C-2′, 2′), 126.9 (Ph, C-3′, 3′), 121.2 (Ph, C-4′); IR (neat) 3066, 3034, 1059, 1483, 1451, 1379, 1306, 1085, 1068, 1026, 867, 836, 780 cm^{-1}; MS *m/e* (%) 161 (100), 58 (41), 53 (30).

4-Phenylisothiazole (5). 3-Chloro-2-phenylpropenal[36] (10.0 g, 0.060 mol) and ammonium thiocyanate (10 g, 0.13 mol) were refluxed in acetone (100 mL) for 6 h (CAUTION: HCN evolution).[37] The resulting mixture was allowed to cool, brought to pH 9 with 50% aqueous NaOH, and steam distilled. The distillate (2.0 L) was extracted with ether (3 × 150 mL). The ethereal extract was dried (Na_2SO_4) and concentrated by rotary evaporation. The yellow residual oil (8.0 g) was subjected to silica gel (100 g) flash column chromatography. The column (30 cm long × 2.7-cm diameter) was eluted with dichloromethane (300 mL), and 10-mL fractions were collected. The fractions which showed only the desired product by TLC were combined and concentrated to give a white solid, which was sublimed (40 °C, 0.2 Torr) to give 4-phenylisothiazole (**5**) as

(27) Vernin, G.; Aune, J. P.; Dou, H. J. M.; Metzger, J. *Bull. Soc. Chim. Fr.* **1967**, 4523–4533.
(28) Dodson, R. M.; King, L. C. *J. Am. Chem. Soc.* **1945**, *67*, 2242–2243.
(29) Bedoukian, P. Z. *J. Am. Chem. Soc.* **1944**, *66*, 1325–1327.
(30) Hurd, C. D.; Wehrmeister, H. L. *J. Am. Chem. Soc.* **1949**, *71*, 4007–4010.
(31) Kuthan, J.; Jehlicka, V.; Hakr, E. *Collect. Czech. Chem. Commun.* **1967**, *32*, 4309–4318.
(32) Benner, S. A. *Tetrahedron Lett.* **1981**, *22*, 1851–1854.
(33) Naito, T.; Nakagawa, S.; Tokahashi, K. *Chem. Pharm. Bull.* **1968**, *16*, 148–159.
(34) Goerdeler, J.; Pohland, H. W. *Chem. Ber.* **1961**, *94*, 2950–2959.
(35) Beringer, M.; Prijs, B.; Erlenmeyer, H. *Helv. Chim. Acta* **1966**, *49*, 2466–2469.
(36) Arnold, Z.; Zemlicka, *J. Proc. Chem. Soc.* **1958**, 227.
(37) Muehlstaedt, M.; Braemar, R.; Schulze, B. *J. Prakt. Chem.* **1976**, *318*, 507–514.

Useful References

1. Experiments in Organic Chemistry, R.K. Hill and J. Barbaro, Contemporary Publishing Company of North Carolina. Raleigh NC, 2005.

2. Handbooks for obtaining physical properties of compounds.

- *Aldrich Catalog -Handbook of Fine Chemicals*, Published annually by Aldrich Chemical Co., 1001 W. Saint Paul Ave., Milwaukee, WI 53233. (in lab) A very useful listing of physical properties and special hazards of many organic compounds. Also includes references to the Aldrich Libraries of IR and NMR Spectra, Merck Index, Beilstein, Fieser and Fieser. Copies of this handbook are available in the laboratory and stockroom. You can obtain a free copy by requesting one in writing from the Aldrich Chemical Co.

- *The Merck Index*, S. Budavarei, ed., Merck & Co., Rahway, NJ. This handbook provides information on many organic and inorganic compounds, including physical properties, medical uses, and toxicity information. This handbook includes a very useful extensive appendix of organic name reactions. This Reference is available in the Chemistry Stockroom and in the Reference Section of the Gordon Library: RS356 M526 12th 1996.

- *CRC Handbook of Chemistry and Physics*, R. C. Weast, ed., CRC Press, Boca Raton, FL. Revised annually. This text contains useful sections on the physical properties of common organic and inorganic compounds. There are useful tables of the densities of aqueous solutions of acids and bases. The 76th ed, 1986-87 is available in the Chemistry stockroom.

- *CRC Handbook of Table for Organic Compounds Identification*, 3rd ed., Z. Rappoport, ed., CRC Press, Boca Raton, FL, 1967. Over 8000 Compounds are listed by functional group. Within each group, tables are provided of solids and liquids in order of their increasing melting and boiling points respectively. This handbook is available in the Reference Section of the Gordon Library: QD 291 R28 1967.

3. Material Safety Data Sheets (MSDS). MSDS data are available on the internet at many locations including http://hazard.com/msds/index.php.

Laboratory Notebooks

Keeping an accurate and complete notebook is an essential part of any laboratory science. The format you should use for your notebook differs somewhat from that given in the text *Experiments In Organic Chemistry*, section G2. Please follow the instructions given in this section of the Lab Manual rather than those given in the text, in cases where the two are contradictory. In particular, each experimental write-up should begin as illustrated in the example on page 14. Be aware that no single notebook format is "correct"; everyone organizes their notebook slightly differently. What is essential is that all of the pertinent information be there.

General Considerations

1. A lined notebook with a sewn (not loose-leaf or spiral) binding is required.

2. The notebook should be written in black or blue indelible ink (not red), not in pencil. Entries of all original data should be made directly into the notebook rather than being transferred into it from scraps of paper. In order to make the notebook neater and more intelligible, *you should use the left-hand pages for recording data, notes, and calculations in preliminary form. The right-hand pages should be a complete, final, organized record of what you did along with your results/data, and analysis of your results/data. DO NOT scratch out, erase, or white out ANY mistakes or errors!! If you want to change something, simply draw a neat line through the item you wish to change and then write what you want your reader to see. The changed item should remain readable because, as often happens, today's big blunder sometimes turns out to be tomorrow's vital piece of information.*

3. Notebook pages must be numbered, and there should be a Table of Contents at the front. All entries must be dated.

4. A laboratory notebook should be legible, complete, and concise. Another laboratory worker should be able to repeat your experiments by referring only to your notebook and to any other printed materials (portions of your textbook, course handouts, journal articles, etc.) cited in your write-up. It is important to record accurately what *you* did and what *you* observed during the experiment. That information may be essential to the interpretation of your results.

5. Do not use the "Dear Diary" style in your write-ups; use the <u>past passive voice</u> instead. Words such as I, we, and my do not belong in a technical report. For example, state, "5.2 g of a white crystals were obtained," rather than "I obtained 5.2 g of white crystals."

Learning proper technique and operations in Organic Laboratory will enhance your capabilities in your other endeavors in science and engineering by training you in the fundamental procedures of experimentation, observation and record keeping that are common to all scientific investigation. Neatness and order, though important, are secondary to accurate information. Nevertheless, clear, unambiguous, and concise communication is required. Observations should be recorded directly into your lab note book immediately. Notes made on sheets of paper get misplaced and recall from memory is unreliable.

Follow directions carefully and be observant and you should achieve satisfactory results in each experiment. You are expected to work alone unless instructed to do otherwise. Questions should be addressed to the course instructor; but don't be afraid to consult your labmates.

General Content of experimental write-up.

1. **Prelab.** You should not begin an experiment until you have studied the reactions and their execution. Ask your instructor if you have any questions about the experiment before starting lab work. Read relevant sections from *Experiments in Organic Chemistry* as indicated at the start of each experiment as indicated in the lab manual.

2. **Procedure and Observations.** These are recorded in lab while the experiment is in progress.

3. Results. This section includes calculations, discussions, analysis of spectral or analytical data, conclusions, *etc*. This information is written after the lab is completed.

Specific Features of experimental write-up

1. **Pre-lab write-up.** You are required to write the first part of your experimental write-up before beginning the experiment. It is important that you carefully read the experiment before coming into lab both for reasons of safety and so that you use time in the lab efficiently. The pre-lab write-up for each new experiment should include:

   a. The **date** the experiment is started.

   b. The **title** of the experiment.

   c. A balanced equation for the main reaction (when applicable). Quantities of reagents and products in grams and moles should appear in a Mole Table following the balanced equation. (see section e. below) In experiments where you are learning a technique and do not carry out a chemical reaction, omit the mole table. Instead write a *brief* statement of purpose telling why you are doing the experiment. In experiments involving an isolation rather than a chemical reaction, give the structure(s) of the compounds you are going to isolate.

   d. Literature reference. Give pertinent pages of the text or URL, or indicate **"**Handout**"** if one was used that you followed for a given experiment. If you are synthesizing a known compound, include its physical properties (e.g., m.p., b.p., density, formula weight, etc.) as given in the corresponding reference source.

   e. **Mole table.** A mole table is a table of physical properties, amounts, and toxicity of each reactant and product *that appears in the balanced equation.* Also included in the table should be any solvents or catalysts used in the experiment, along with their quantities and toxicities. The compilation should be tabulated as follows:

Mole Table

Substance	mol.wt.	grams	moles	mLs	density	m.p./b.p.	toxicity

The amounts of the reactant refers to the actual amounts used in the preparation while the amounts of the products refer the quantities theoretically possible based on the stoichiometry, the limiting reagent and the quantities you used in your experiment, not those in the manual. It is not necessary to fill in every entry in the mole table. If you are weighing a liquid and know the mass, listing the density is not necessary. If you are adding a liquid by volume, it is useful to include the density to calculate the number of moles. It is for you to determine what significant information to include in your mole table. Remember, the mole table is a compilation of useful information that allows you to quickly determine the number of moles (i.e., mol. wt., grams, mLs,

density), know the physical properties (e.g., m.p. or b.p.), and be aware of the toxicity (for safety) of substances you work with. It's easier to look that information up ahead of time and have it at hand rather than having to look up that information piece meal during an experiment. See the sample pages from lab notebooks that follow this section.

2. **Procedures and Observations.** Following the mole table, you should record in the past passive voice the exact step-wise procedures (order of operations) used in setting up, carrying out, monitoring and working up reactions, as well as for isolating/purifying and characterizing compounds. It is not sufficient or desirable to simply copy the procedures described in the lab manual, which generally are too lengthy and provide too much detail to include in your procedure. Instead, *write in your own words a concise description of what you did (all operations and observations at each step of the experiment)in enough detail that you could repeat the experiment without the lab manual using just your notebook*. Include any observations (e.g., **"…**the reaction mixture changed from colorless to purple after 10 minutes**…"**, **"…**a white precipitate formed immediately when the reactants were mixed that slowly dissolved over 20 minutes as the reaction was heated to reflux**…"**). That information is important because certain observations may explain your experimental results. Also, record anything that appeared to beunexpected. That information is particularly important for others who might need to repeat the experiments you did.

   For example, you might observe that "after being heated at reflux for 30 minutes, the initially colorless reaction mixture turned dark brown." It is useful and customary to describe the appearance of reaction mixture, products, etc. A solid should be described by its color (if none, describe as white or colorless)* and form (needles, plates, amorphous, etc.). A liquid may be clear (not the same as colorless)* or cloudy, and colorless or colored. For example, you might describe a product as a clear, pale yellow liquid. Melting point or boiling point *ranges* (starting and ending temperatures) should be given for all products, both crude and purified.

***** *NOTE: The terms "white" and "colorless" are not synonymous. Neither are the terms "clear" and "colorless".*

   Any procedure such as analysis by thin layer chromatography (TLC) or gas chromatography (GC) that was used either to monitor a reaction and/or to characterize product(s) should be described in this section. The description of any TLC experiment must include identities of the solid phase and solvent system, method used to visualize spots, appearance of spots including color and intensity, and a sketch of the plate. Similarly, the description of a GC analysis should include the material analyzed, the type and size of the column, the carrier gas flow rate, temperatures of the column, injector and detector, as well as any method used to establish the identities of peaks. The chromatogram itself should be taped in your notebook.

   The procedure and observations generally can be described concisely in just a few sentences. For example, in Experiment #4, the entire procedure in the lab manual (and corresponding observations) could be condensed to *four* sentences in your lab notebook as follows: *"A 25 mL round-bottom flask containing a boiling stone was equipped with isoamyl alcohol (2.9 g, 0.033 mole) and glacial acetic acid (4.8 g, 0.080 mole), followed by concentrated H_2SO_4 (1.0 mL). The reaction mixture was heated to reflux for 30 minutes, during which the initially clear solution turned deep red. After cooling the reaction to RT, the solution was poured over*

20 mL of 5% aq. $NaHCO_3$ with bubbling. The organic phase was then washed with 5% aq. $NaHCO_3$ (2 x 1 mL) and water (1 x 1 mL), dried over anhydrous $CaCl_2$, then purified by simple distillation (b.p. 141-142 °C) to yield isoamyl acetate (3.5 g, 0.027 mole, 83% yield) as a clear, colorless liquid."

Compare the text above carefully to the procedure in the lab manual. Many of the details described in the manual are omitted on purpose. You may assume that anyone who has taken a lab in organic chemistry will know (1) what reflux means and that it requires heating the reaction mixture to boiling with a reflux condenser attached to prevent loss of reagents, (2) that adding an acidic solution to aqueous base such as sodium bicarbonate will release CO_2 gas, (3) how to use a separatory funnel and that washing an acidic organic phase with aqueous sodium bicarbonate in a closed system such as a separatory funnel will require venting the funnel periodically to release pressure created by the buildup of CO_2 gas, (4) what a drying agent such as anhydrous calcium chloride is and the procedure for removing residual water with a drying agent, and (5) how to purify a liquid by simple distillation (as you will do in Exp. 1). You do not need to describe all of the nitty-gritty details of the procedure in your lab notebook for standard synthetic techniques. You will learn the procedures for those techniques from the lab manual and by using them repeatedly in different experiments throughout the term. If you are unsure of what to include in writing the procedure and observations in your lab notebook, err on the side of including more details. As you become more familiar with the procedures for standard lab techniques, strive to write as concisely as possible when recording experiments in your lab notebook.

3. **Results.** Analyze your experiment and data. Calculate the percent yield, determine R_f values (TLC) and retention times, calculate relative areas of GC peaks, assign IR bands, *etc.* Comment on the m.p. or b.p. range of your product and provide the literature values and references if available. What conclusion may be drawn from your experimental results? Did the product or products form? Does your data indicate the product was pure? If the experiment did not turn out as expected, try to explain what went wrong. In many cases, the results section is quite brief.

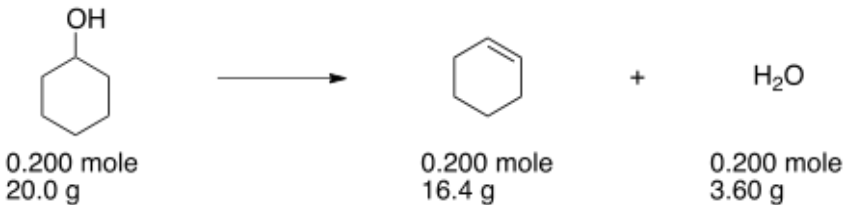
4. **Product Labels.** All products should be turned in to your instructor for evaluation after the experiment is completed. Product labels should contain the name and structure of the material, the net weight of the product contained within, the appropriate physical properties of the product (e.g., m.p. range), along with your name and the experiment number

Example of a pre-lab writeup

9/15/2011

Syntheses of Cyclohexene from Cyclohexanol

Purpose: To convert cyclohexanol to cyclohexene via acid-catalyzed dehydration by heating the alcohol with 85% H_3PO_4.



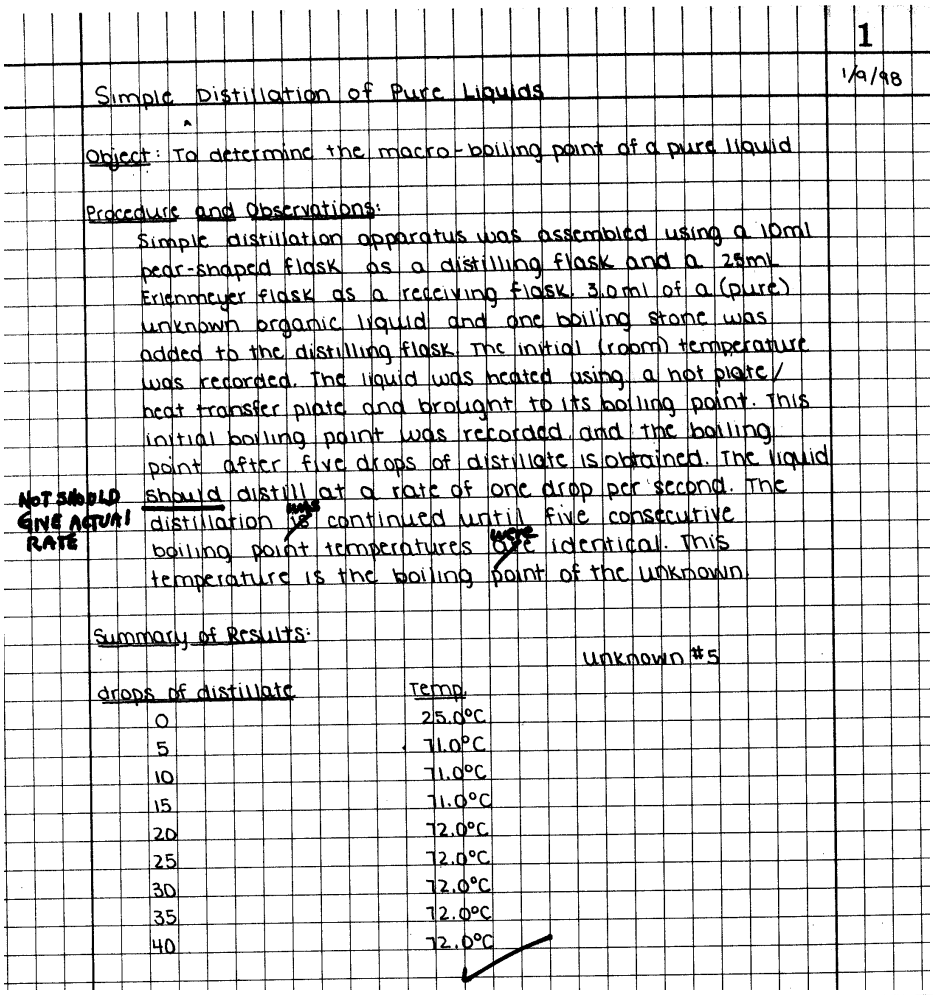
The product will be isolated by distillation.

Mole Table

Substance	Amount							Toxicity/care
	moles	grams	mL	mol. wt	density	mp	bp	
Cyclohexanol	0.20	20.0	21.0	100	0.96	25	161	Irritant/ hygro-scopic
85% H_3PO_4			5.0	98		liq	dec	Corrosive/ hygro-scopic
Cyclohexene	0.20	16.4	20.2	82	0.81	-131	83	Flammable/ irritant
Water	0.20	3.6	3.6	18	1.0	0	100	

Procedure: Ault: Techniques and Experiments for Organic Chemistry, 2nd ed., Holbrook Press, Boston (1976) p.177.

Example of a completed experimental writeup from a lab notebook where no mole table is required (no reaction is carried out).



1

1/9/98

Simple Distillation of Pure Liquids

Object: To determine the macro-boiling point of a pure liquid

Procedure and Observations:

Simple distillation apparatus was assembled using a 10ml pear-shaped flask as a distilling flask and a 25ml Erlenmeyer flask as a receiving flask. 3.0ml of a (pure) unknown organic liquid and one boiling stone was added to the distilling flask. The initial (room) temperature was recorded. The liquid was heated using a hot plate/heat transfer plate and brought to its boiling point. This initial boiling point was recorded and the boiling point after five drops of distillate is obtained. The liquid should distill at a rate of one drop per second. The distillation was continued until five consecutive boiling point temperatures were identical. This temperature is the boiling point of the unknown.

NOT SHOULD GIVE ACTUAL RATE

Summary of Results:

Unknown #5

drops of distillate	Temp.
0	25.0°C
5	71.0°C
10	71.0°C
15	71.0°C
20	72.0°C
25	72.0°C
30	72.0°C
35	72.0°C
40	72.0°C

2

Experiment 2 : Data

10ml pear-shaped (distilling) flask Preweigh: 18.112g
+ 7.0mL of acetone-toluene mixture: 23.866g
acetone-toluene mixture only 5.754g

Preweighed: Vial #1 : 21.475g
Vial #2 : 21.442g
Vial #3 : 21.411g

Vial #1 boiling range: 58.0°C - 58.0°C Temp ↓ to 43.0°C
clear, colorless liquid

Vial #3 boiling range: 108.5°C - 109.0°C Temp ↓
clear, colorless liquid

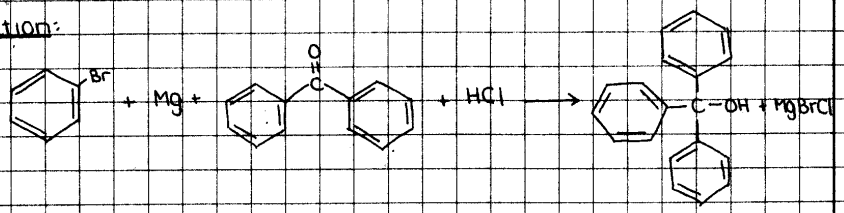
Post-weight:		mass of fraction
Vial #1 :	22.705g	1.280g
Vial #2 :	21.674g	0.232g
Vial #3 :	24.485g	3.019g

Example of a completed experimental writeup from a lab notebook where a mole table is required (i.e., a reaction was carried out).

45

Experiment 10: Grignard Reaction- Synthesis of Triphenylmethanol — 2/16/98

Equation:



Mole Table:

Compound	mp/bp	Mol. Wt (g/mol)	Density (g/mL)	grams	mLs	moles	Toxicity
bromobenzene	bp=155°C	157.01	1.495	0.94	0.63	0.0060	combustible
magnesium	mp=650°C	24.305		0.18		0.0075	flammable
benzophenone	mp=48.5°C	182.22		0.36		0.0020	irritant
hydrochloric acid	mp=-114.24°C bp=-85.05°C	36.461				Excess	corrosive, irritant
Triphenyl-methanol	mp=161°C	260.33		0.52		0.0020	irritant
magnesium ~~bromide~~ chloride							

Object: To synthesize Triphenylmethanol by way of a Grignard reaction.

Procedure and observations: — 2/19/98

Magnesium turnings (0.18g) were placed in a clean, dry 25mL ~~Erlenmeyer~~ round-bottom flask. A stir bar was added and the flask was equipped with a Claisen adapter, a ground glass stopper, and a condenser. The condenser was fitted with a calcium chloride drying tube. The apparatus was gently flamed to remove any water vapor from the system.
A solution containing 0.63mL of bromobenzene in 2mL of anhydrous ether was prepared in a centrifuge tube and corked. The ground glass stopper was removed from the apparatus and 2mL of anhydrous ether and 5 drops of Newman's reagent was added to the round bottom flask, with stirring. The clear, colorless solution began to boil and turned cloudy. Once this reaction had started, the ethereal bromobenzene solution is added to the flask along with a small, dry ether rinse. The solution turned orange

Expt. 1b (cont'd) 2/19/98

Procedure and Observations (cont'd):

and then a lime-green color. The reaction was allowed to proceed with stirring for 30 minutes.

Once the reaction was complete, 0.31g of benzophenone dissolved in 2-3mL of anhydrous ether was added to the flask as well as a small dry ether rinse. The reaction mixed was allowed to stir for one hour. The white, opaque mixture was cooled by means of an ice-water bath. 3mL of 2M HCl was added dropwise down the condenser until the reaction with the alkoxide has ceased. The reaction mixture was filtered into a separatory funnel using approximately two 10mL portions of solvent ether to rinse the round bottom flask. The aqueous layer was discarded and the ether layer was washed with small volumes of cold water, 10% aqueous Na_2CO_3, and aqueous brine. The resulting ether layer was dried over anhydrous Na_2SO_4 and then concentrated to dryness in a round bottom flask by rotary evaporation. The crude product (0.549g) was recrystallized with methanol in a 10mL Erlenmeyer flask. Triphenylmethanol (0.0160g) was collected as a white crystalline solid by suction filtration. The product was isolated in a yield of 11.5% theoretical. The melting point of the triphenylmethanol was determined to be 160.0-161.0°C. (Lit. mp 163°C, ChemFinder, Feb. 16, 1998).

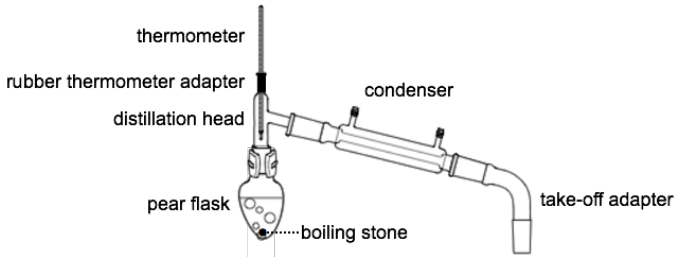
good 2/21/98

Experiment #1: Simple Distillation and Boiling Point Determination

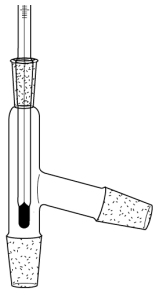
Assigned Reading: *Experiments in Organic Chemistry*, section T4 1-10.

Simple distillation is a commonly used method to purify a liquid that involves vaporizing the liquid and then condensing the pure vapor in a different location. Simple distillation can be used to purify a liquid by removing other non-volatile components (e.g., salts, polymers, compounds with high molecular weights, etc.). Simple distillation also can be used to determine the boiling point of a pure liquid that is volatile.

Procedure. Set up a simple distillation apparatus as shown below. A sample apparatus will be set up in the lab. *The apparatus must be dry to avoid contamination by water*. Check that the thermometer reads room temperature correctly and that there are no breaks in the mercury. Use a pear-shaped flask (10 mL) as the distillation flask and a small Erlenmeyer flask (~10 mL) as the receiver to collect the distillate. Record the number of your unknown in your notebook. Record the mass of unknown liquid placed into the distillation flask and also the mass of the distillate collected in order to determine the percent of distillate recovered based on the masses. Place the unknown, flammable organic liquid (~3.0 mL) and a boiling chip into the distillation flask. Using a heating mantle containing some sand to promote heat transfer as the heat source, distill the liquid at a rate of approximately one drop per second. Record the initial boiling temperature and then continue recording the temperature after every five drops of distillate. Make a table of temperature vs. volume in your notebook. Record the appearance of the distillate (e.g., clear, cloudy, colorless, light yellow, dark yellow, etc.).



Simple distillation set-up



correct thermometer placement

Stop the distillation *before* the distillation flask has run dry (~ 0.5 mL left in the flask). Pour the distillate and residue into the appropriate chemical waste container. Construct a graph using the data collected in your table of b.p. data. Determine the boiling point of your unknown and determine its identity from the list of compounds shown below.

Compound	Boiling point (°C)	Compound	Boiling point (°C)
methylene chloride	40	ethyl acetate	77
acetone	56	isopropyl alcohol	82
chloroform	61	n-propyl alcohol	97
methanol	65	toluene	111
hexane	69	butyl alcohol	117

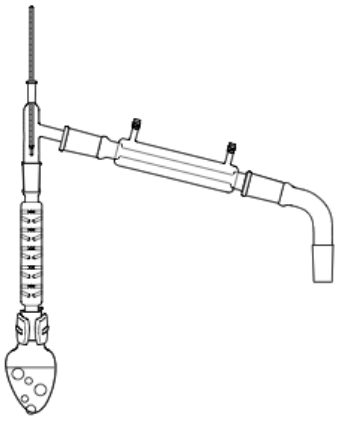
Summary of items to include in your lab notebook: 1) unknown #, 2) table of temperature vs. volume, 3) b.p. range of unknown liquid, and 4) identity of unknown liquid.

Experiment #2: Fractional Distillation of an Acetone-Toluene Mixture. Analysis of Distillate Fractions by Gas Chromatography.

Assigned Reading: *Experiments in Organic Chemistry*, sections T4 1-10 and T8 1-10.

The goal of this experiment is to fractionally distill a mixture of acetone and toluene in order to obtain pure samples of both compounds with maximum recovery.

Procedure - Part A. Assemble a fractional distillation apparatus as shown in Figure 3 of section T4 (see below), using a 10 mL pear-shaped flask as the distilling flask, a 4-inch Vigreux column, and a tared 2-dram glass vial as a receiver instead of a round bottom flask. Have 3 or 4 tared 2-dram glass vials available at the start of the distillation.



Fractional distillation set-up

Weigh the 10 mL pear-shaped distilling flask. Introduce 5.0 mL of the acetone-toluene mixture into the flask and weigh again to determine the mass of the mixture. Add one boiling stone to the flask and attach the flask to the distillation apparatus. Heat the distilling flask with a heating mantle containing some sand to aid in heat transfer, and distill the mixture at a rate of ~one drop per second. Note the initial temperature and continue to collect the distillate until you see evidence that the first fraction is exhausted (*i.e.*, the distillation stops and/or the temperature decreases). Note the temperature range over which the first fraction was collected. Change collecting vials and cap the first vial tightly in order to prevent evaporation (note: acetone is quite volatile). C continue heating until the second fraction begins to distill by incrementally increasing the temperature of the heating mantle. Note the temperature. Collect several drops of the distillate to wash residual acetone out of the condenser (fraction 2), then change vials and continue to collect the distillate until the higher-boiling fraction is exhausted (fraction 3). *Do not distill the mixture to dryness—leave ~0.5 mL of liquid in the distillation flask.* Note the temperature range over which the higher-boiling fraction was collected and cap the vial. Label the three vials as fraction 1, fraction 2, and fraction 3.

Re-weigh each vial to determine the mass of each fraction. Analyze the original mixture and each fraction by gas chromatography.

Procedure - Part B. Analysis of Distillates by Gas Liquid Chromatography

Click on Sample Info in the GC software and enter your name as operator and then click OK. It is important that you enter your name prior to injecting samples to ensure the printout of your data includes your name and not the name of the previous user. *GC traces with your name hand written on the trace will not be accepted.*

The sample size is 0.2 μL measured using a 0.5 μL syringe. It is important to rinse the syringe by taking up and then ejecting 0.3 μL of your sample *before* taking up and injecting your sample into the GC. The GC method is set to run at 140° C for 6 minutes, during which time you will inject all three of your fractions serially at 2 minute intervals. Under those conditions, it takes less than 2 minutes for acetone and toluene to elute from the column; therefore you can analyze all three of your fractions in one GC trace. Start by injecting 0.2 μL of fraction 1 and pressing the start button on the front of the GC instrument. Do not click the "Start" button on the computer screen. As soon as you have injected fraction 1, immediately rinse the syringe with fraction 2, and load the syringe with 0.2 μL of fraction 2. At exactly 2.0 minutes, inject fraction 2 and immediately rinse the syringe with fraction 3, and load the syringe with 0.2 μL of fraction 3. At exactly 4.0 minutes, inject fraction 3.

After 6.0 minutes, the run is automatically terminated and the results are displayed on the screen and automatically sent to the printer. *Print a second copy of your GC trace and data before exiting the software.* Give one copy to the TA, and save one copy to include in your lab notebook. Include the entire printout in your lab notebook (i.e., do not cut out the trace and table of data to save space). Close the results screen, and then click on the MENU item (top) called Run Control. Click on Sample Info and the GC is ready for the next operator.

The printed results give you among other things a table of retention times, areas, and area percents for each peak in the GC chromatogram. You should use the raw peak areas to determine the percentage of each compound by weight present in each fraction. The flame ionization detector used in our GC instruments has sensitivity that generally varies from compound to compound. In other words, the response of the detector to equal amounts of two different compounds may give peaks with different areas. Therefore, you will need to correct the areas of the peaks to account for differences in sensitivity using the procedure described below. Label the peaks for acetone and toluene directly on your GC trace and also in the table of GC data. Ignore any spurious peaks that do not correspond to acetone or toluene.

A reliable experimental method for determining the relative quantities of different compounds in a mixture from an integrated gas chromatogram involves four steps: (1) obtain pure samples of each compound present in the mixture, (2) inject an equal volume of each compound (e.g., 0.2 μL) to obtain GC traces of the pure compounds, (3) examine the detector response to each pure compound on the basis of *weight* to determine a weight response factor by comparing the areas of the peaks, and (4) correct the raw peak areas in the GC trace of the *mixture* using the weight response factor from the pure compounds to account for differences in detector response.

For this experiment, you will be provided with GC traces for pure acetone and pure toluene showing three peaks corresponding to three separate injections of 0.2 μL of each pure compound on each GC instrument. Note which instrument you use since the detector response may be different for the two instruments. Determine the average area for the three peaks in each GC trace. Calculate the area per gram of acetone and toluene using the density for each compound. You

should find that the detector gives a greater response (area) to a given weight of toluene compared to acetone. To determine the weight response factor, divide the area per gram of toluene by the area per gram of acetone. Correct the areas for all peaks corresponding to acetone in the GC trace of your three fractions by multiplying the peak area (or area percent) for acetone by the weight response factor to adjust the areas upward to account for the lower sensitivity of the detector to acetone. Finally, calculate the composition of each fraction by determining the percent of acetone and toluene in each fraction by weight. For example, to calculate the weight percent of acetone in a given fraction, divide the adjusted peak area for acetone by the sum of the areas for acetone and toluene in that fraction and multiply by 100. Show your calculations in your lab notebook.

Summary of items to include in your lab notebook: 1) b.p. ranges over which the fractions distill, 2) mass of fractions, 3) GC instrument used (left or right), 4) average peak area per gram of pure acetone and toluene, 5) GC weight response factor for acetone (peak area/g A ÷ peak area/g T), GC trace & data for fractions 1 & 3 (tape or staple whole pages into notebook), 6) corrected peak areas for acetone, 7) weight % of acetone and toluene in fractions 1 & 3, and 8) analysis of the purity of fractions 1 & 3. Were you successful in obtaining pure samples of acetone and toluene by fractional distillation? If not, why?

Experiment #3: Melting Point and Mixed Melting Point Determinations

Assigned Reading: *Experiments in Organic Chemistry*, sections T2 1-6, T3 1-6 and E1.

The goal of this experiment is to determine the melting points (ranges) for three unknown crystalline solids (vials A, B and C) and to determine which of the solids are the same substance. You will use melting point analysis in a slightly different context to determine the purity of an unknown solid that you recrystallize in Experiment #5.

Although called melting point, you should always report the *range* of temperature over which a solid melts rather than a single temperature. A melting range is defined by the initial onset temperature at which the solid starts to melt and the final temperature at which the last of the solid melts (i.e. only liquid remains). If the solid decomposes (turns brown or black) before melting or melting completely, that should be recorded. The range over which a solid melts indicates the purity of the solid. Pure solids generally melt over a 1-2 degree (°C) range. Impurities in a solid will cause both the onset melting temperature to be lower and the range over which the solid melts to be broader when compared to the pure solid.

Melting points should be determined by heating the solid at a rate no greater than 5 degrees per minute; it takes time for heat to transfer from the Mel-temp apparatus through the glass capillary tube to the solid. Heating at more than 5 °C per minute generally gives melting data ranges that are inaccurate (onset melting temperature is too high) and broad. Do not repeat the determination of a melting point more than twice, as you will run out of time if you do so.

Procedure. You will receive three vials labeled A, B and C. Each vial contains a pure crystalline substance. Two vials contain the same substance. Place a small amount (enough to see by eye) of each solid into separate glass capillary melting point tubes, then tap the tubes on the lab bench until the solid rests at the bottom. Place the tubes into a Mel-temp apparatus and determine the melting point range for each solid. Next, make three different binary mixtures containing approximately equal amounts of A:B, A:C, and B:C, respectively, on a piece of wax weighing paper or watch glass. Mix the solids thoroughly with a spatula, taking care to grind the solids together by pressing them flat with the head of the spatula and then mixing. Place a small amount of each binary mixture into separate glass capillary melting point tubes, tap the solids to the bottom, and then determine the melting point ranges of the mixtures. Record that melting data for A, B, C, A:B, A:C, and B:C in a table, identify which two solids are the same substance, and clearly explain the reasoning for your conclusions.

Summary of items to include in your lab notebook: 1) unknown #, 2) table of melting point ranges for solids A, B and C, and binary mixtures A:B, A:C, and B:C, 3) identification of which two solids are the same substance.

Experiment #4: Esterification - Synthesis of Isoamyl Acetate

Assigned Reading: *Experiments in Organic Chemistry*, sections E18 1-6, T4, T5, T6, T8 and T9.

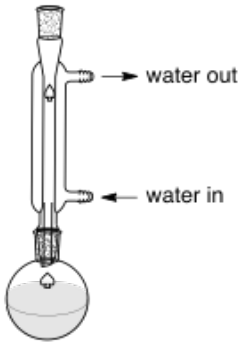
Introduction. Isoamyl acetate is the substance that gives a banana its distinctive odor. Isoamyl acetate also is an alarm pheromone secreted by honeybees in times of distress to signal other bees to aggressively attack an intruder.

In this experiment, isoamyl acetate will be synthesized by allowing isoamyl alcohol to react with acetic acid according to the reaction below. To drive this reversible equilibrium reaction toward production of the ester via Le Chatelier's Principle, an excess amount of isoamyl alcohol or acetic acid is required. Acetic acid will be used in excess because it is less expensive and easier to remove from the reaction mixture. The excess acetic acid will be removed by aqueous extraction with sodium bicarbonate and any unreacted alcohol will be removed using anhydrous calcium chloride ($CaCl_2$).

Be cognizant of your time management in this lab! Three different glassware set-ups (reflux condenser with flask; separatory funnel; simple distillation) are required, so choose well when you set up each part and when to wash your dirty glassware.

CAUTION: Sulfuric acid (H_2SO_4) is very corrosive. If spilled on the skin, dilute with large amounts of water and wash with copious amounts of water. When diluting concentrated H_2SO_4, add H_2SO_4 slowly to water with stirring. Do not add water to concentrated H_2SO_4.

Procedure. Place 2.9 g (? mL) of isoamyl alcohol and 4.8 g (? mL) of glacial acetic acid into a dry 25 mL round-bottom flask containing a boiling chip. Carefully add 1.0 mL of concentrated H_2SO_4 to the flask and swirl. Attach a condenser to the flask (below) and reflux the reaction for 30 minutes by heating the reaction mixture with a heating mantle until it starts to boil. Record your observations of the reaction. Allow the mixture to cool to room temperature, then pour the mixture into a beaker containing 20 mL of 5% aqueous sodium bicarbonate. After all of the carbon dioxide (CO_2) gas has been released, pour the mixture into a small separatory funnel.



Reflux set-up

Remove the aqueous layer, then wash the organic layer with 5% aqueous sodium bicarbonate (2 x 1 mL). To prevent build-up of any CO_2 (g) in the separatory funnel: 1) swirl the unstoppered funnel gently until no more CO_2 (g) is released, 2) stopper the funnel, 3) shake the funnel once or twice, and 4) vent the funnel. Continue shaking and venting until all of the CO_2(g) has been removed. Remove the aqueous layer, then wash the organic layer with water (1 mL). Transfer the organic layer to a centrifuge tube and dry the organic layer over anhydrous $CaCl_2$(s). After 10 minutes, pipettete the crude dry ester into a *tared* pear-shaped flask. Record the weight of the crude ester. Purify the ester by simple short-path distillation using a *tared* clean glass vial as a receiver. Collect the purified product and record the boiling range. Distill all of the product, leaving just a trace of residual liquid in the distillation flask. Take care not to pyrolize (decompose by overheating) the residue in the distillation flask. Determine the yield and percent yield of the product, assuming that it is pure. You will then analyze the product by GC to determine its purity.

Gas Chromatographic Analysis. The GC procedure for the analysis of your isoamyl acetate is similar that for Experiment 2. Enter your name, then inject 0.2 uL of your sample into the GC. The run for isoamyl acetate takes 2.5 minutes. Your GC report will be printed automatically once the run is over. *Print a second copy of your GC trace and data before exiting the software.* Give one copy to the TA, and save one copy to include in your lab notebook. Include the entire printout in your lab notebook (i.e., do not cut out the trace and table of data to save space). The GC trace should contain peaks for isoamyl alcohol and the ester product. Assume that the response of the detector (sensitivity) is the same for the alcohol and the ester such that you do not need to correct the areas of the peaks. Label the peaks for the alcohol and ester on your GC trace, calculate the weight % of alcohol and ester using the corresponding densities, analyze the purity of your ester product, and report your conclusions. Your entire GC trace and tabulated data (if more than one page, include both pages) should be neatly taped into your lab notebook.

Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) yield and % yield of isoamyl acetate, 4) GC trace and data for the product with peaks labeled as isoamyl acetate or isoamyl alcohol, 5) weight % of isoamyl acetate in your product on the basis of GC peaks corresponding to isoamyl acetate and isoamyl alcohol (*see note below), 6) analysis of the purity/composition of your product. Were you successful in obtaining a pure sample of isoamyl acetate?

*Note: You can assume the response of the GC detector is the same for isoamyl alcohol and isoamyl acetate—that is, the areas of the peaks directly reflect the volumes of alcohol and ester.

Product: Turn in your product in a vial labeled with your name, experiment number, and compound name.

Experiment # 5: Recrystallization: Purification an unknown by recrystallization

Assigned Reading: *Experiments in Organic Chemistry*, sections T2 1-6, T3 1-6 and E1.

In this experiment, the technique of recrystallization will be used to purify an unknown solid. You will have to decide which of four solvents is best for recrystallizing your unknown. Choosing a solvent that exhibits appropriate behavior for recrystallization is a crucial step because the choice of solvent will determine both the purity and the percent recovery of the purified solid.

Keep the following in mind: the solubility of solutes (solids) in a given solvent increases as the temperature of the solvent is raised, and decreases as the temperature of the solvent is lowered. Recrystallization takes advantage of that variation in solubility for purification by dissolving the compound and any impurities at elevated temperature, and then driving recrystallization (purification) of just the compound upon cooling. An ideal solvent for recrystallization is one in which the solid has high solubility at elevated temperature and low or no solubility at low temperature. Therefore, determining the correct solvent is essential. Once an appropriate solvent has been determined, the general procedure for recrystallizing a solid involves dissolving the solid *in the minimum amount of hot solvent*, then cooling the resulting solution slowly to room temperature to initiate crystallization, followed by cooling the solution to 0 °C in an ice bath to maximize recovery.

You will be given an unknown solid. Record the number in your lab notebook. Determine a suitable solvent with which to recrystallize the unknown. The procedure and attached flowchart (below) shows the steps necessary for choosing an appropriate solvent for recrystallization.

Recrystallizing the unknown sample

1. A good solvent for recrystallization is one that will not dissolve the unknown sample at room temperature but that will dissolve all of the sample at elevated temperature. Solvent choices are: methanol, ethanol, water, cyclohexane or any mixture of those solvents.

2. To begin, measure into four test tubes ~0.1 g of the unknown sample. Add 1.0 mL of each solvent to the appropriately labeled test tube. Stir each solvent and note the solubility of the solid. If the unknown solid does not dissolve, warm the test tube and note the solubility. If the unknown sample does dissolve upon heating, cool the sample in an ice-bath and note the solubility. If crystals do not form, scratch the inside of the test tube with a glass rod to facilitate the recrystallization. Crystallization from the cold solvent may indicate a reasonable solvent for the recrystallization.

3. If none of the solvents were found to be appropriate, experiment using either 1.5 or 2.0 mL of each solvent or experiment with 1 mL of a mixed-solvent system (a mixture of two different solvents) at room temperature (see flowchart). When testing a mixed-solvent system, be sure to note the exact ratio of solvents used. For the mixed solvent system, follow the same steps—examine solubility at room temperature, elevated temperature, and cold temperature (see flowchart).

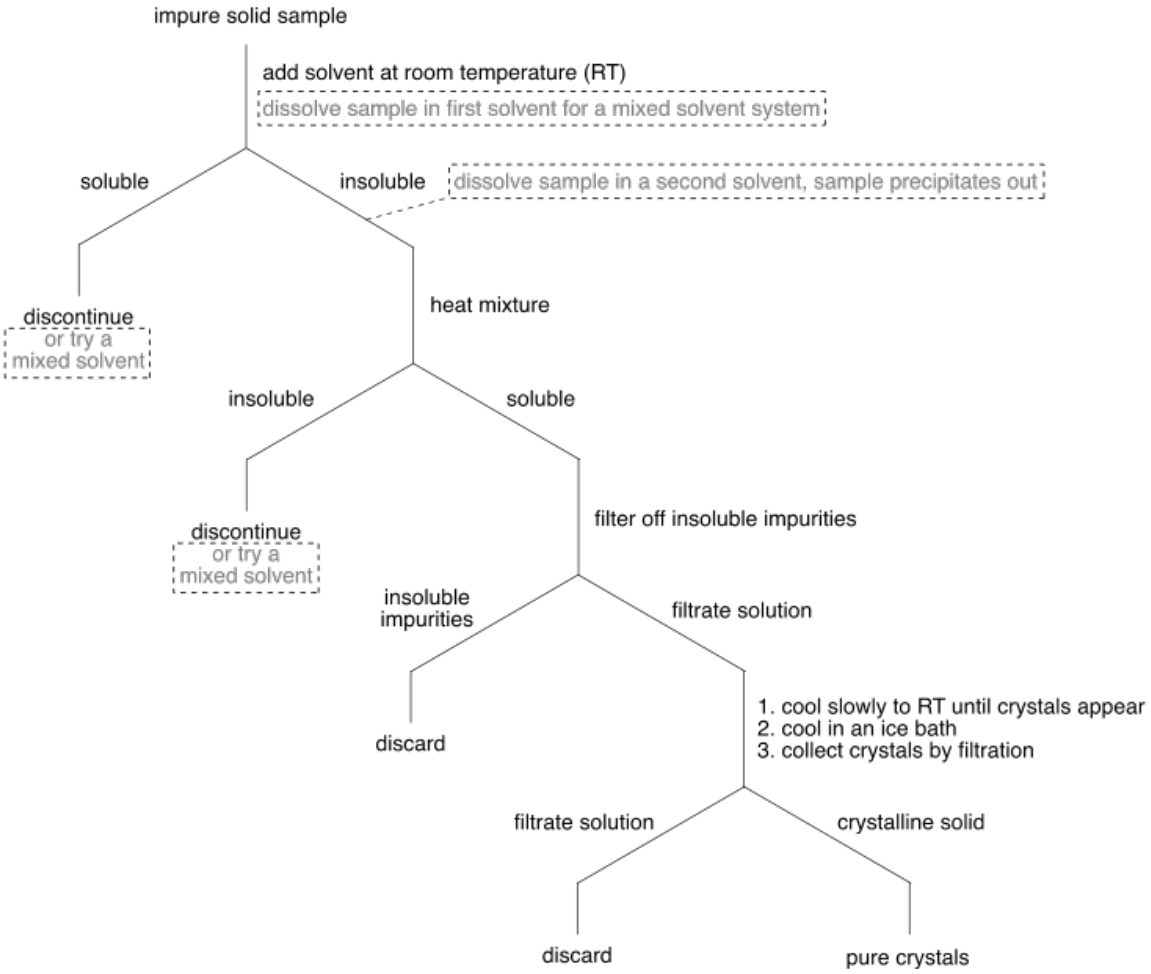
4. After an appropriate solvent system has been determined, purify 0.5 g of the unknown sample by recrystallization, and then analyze the purity of the recrystallized solid using melting point determination.

5. To purify the 0.5 g sample of the unknown, weigh 0.5 g of the unknown sample into an Erlenmeyer flask. Measure out the appropriate amount of solvent (use the same ratio of solvent to solid that was determined previously). Add the solvent to the solid in small increments and heat continuously while swirling the solution until the solid just dissolves. If insoluble impurities are present, a hot filtration will be required (see flowchart). If no insoluble impurities are visible, place the flask on the lab bench and let the solution slowly cool to room temperature. When cool to room temperature, place the flask in an ice-bath. If crystals have not formed, scratch the inside of the flask with a glass stirring rod. Once the crystals have formed (~15 minutes in an ice bath), collect the product by suction filtration in a Buchner funnel. While the crystals are still in the Buchner funnel, wash the crystals with a small quantity of cold solvent to remove traces of the recrystallizing solvent, which will contain residual impurities. When the crystals are *completely dry*, determine the melting point (range) of both the crude and the purified crystals. The crystals must be dry and you should have evidence that they are dry before determining the melting point or the residual solvent act as an impurity and lower the melting point. Transfer crystals to a tared vial and calculate the % recovery (% recovery = mass of crystals recovered/mass of crude crystals before recrystallization).

Summary of items to include in your lab notebook: 1) unknown #, 2) analysis of solvents, 3) m.p. ranges for both the crude and recrystallized solid, 4) % recovery of recrystallized solid, 5) analysis of purity of the recrystallized solid based on m.p. data.

Product: Turn in your product in a vial labeled with your name, experiment number, and unknown #.

Scheme for determining a solvent system for recrystallization



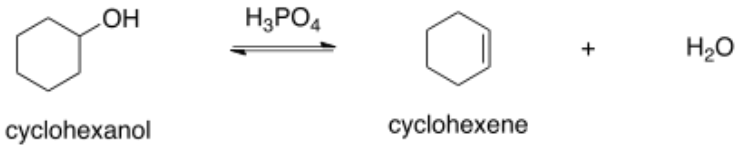
Experiment #6: Dehydration of 2-Methylcyclohexanol

Assigned Reading: *Experiments in Organic Chemistry*, sections **E5A at ½ scale**, T4-T6 and T8.

In this experiment, a mixture of *cis*- and *trans*-2-methylcyclohexanol will undergo a dehydration reaction with the aid of a strong acid (H_3PO_4) to produce a mixture of alkenes and water. The products obtained will be quantitatively analyzed by gas chromatography (GC).

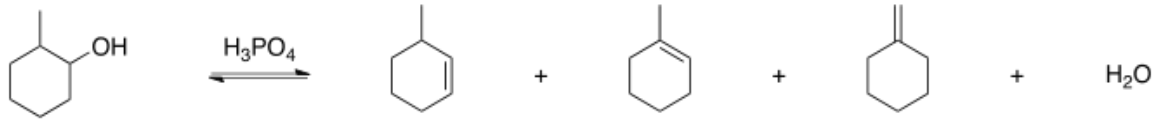
Introduction. Treating cyclohexanol with a strong acid results in the elimination of water (referred to as dehydration) and the production of cyclohexene, as shown in Scheme 1. Only one product is produced because cyclohexanol is a symmetrical molecule. This equilibrium reaction is reversible and favors the alcohol, which has a structure that is lower in energy than the alkene. To shift the equilibrium toward the production of the alkene via Le Chatlier's Principle, the alkene can be removed by continuous steam distillation.

Scheme 1. Synthesis of Cyclohexene

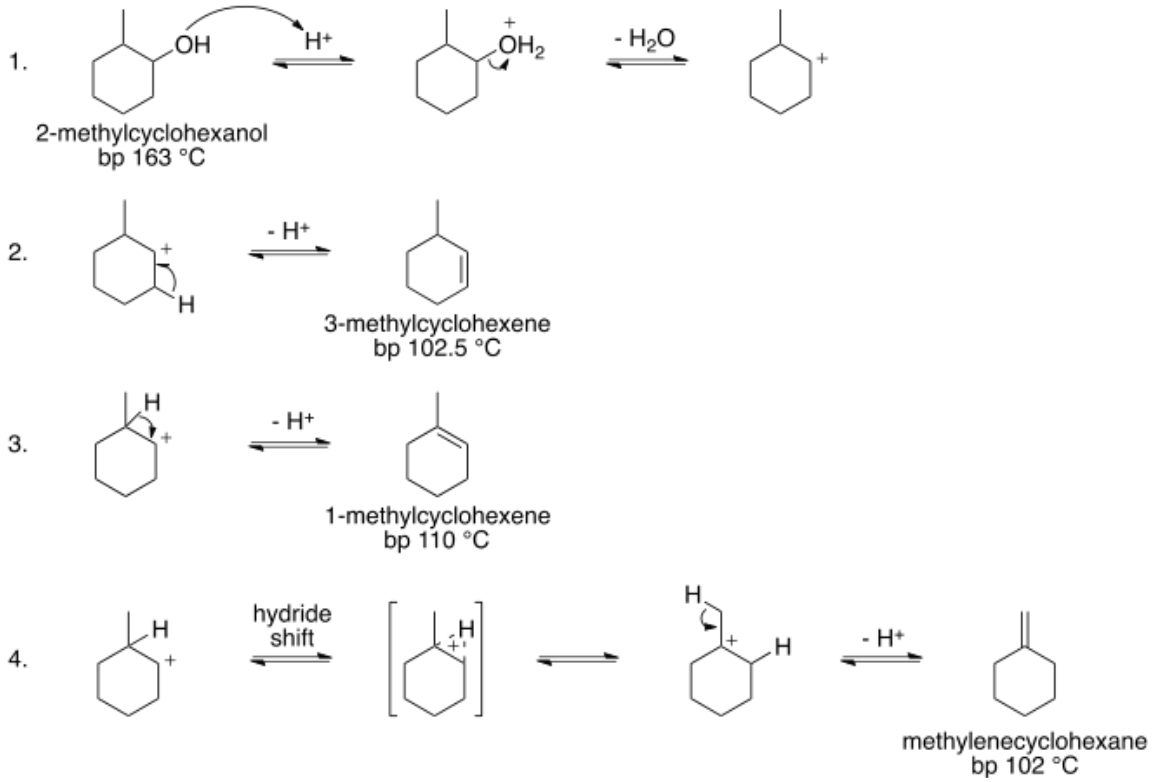


Scheme 2 shows the dehydration reaction of 2-methylcyclohexanol. Considering that 2-methylcyclohexanol is not a symmetrical molecule, dehydration via E1 elimination leads to three possible alkenes as products. Mechanistic pathways accounting for formation of the possible products from dehydration are shown in Scheme 3. As part of the pre-lab to this experiment, predict the major and minor products in the dehydration of 2-methylcyclohexanol on the basis of the relative energetic stability of alkenes. You may assume that methylene cyclohexane will be produced only in trace amounts (why?). In your analysis of the experimental results, discuss if your prediction was correct or incorrect and explain why.

Scheme 2. Dehydration of 2-Methylcyclohexanol



Scheme 3. Plausible Mechanisms for the Dehydration of 2-Methylcyclohexanol



Procedure - Part A. Into a 25 mL round-bottom flask place the *cis- ,trans*-2-methylcyclohexanol mixture (0.035 mol), 85% phosphoric acid (~1.0 mL) and a boiling stone. Attach the flask to a distillation apparatus equipped with a Vigreux column (4 inch, used in case of severe bumping), a heating mantle and a centrifuge tube as the receiver. Heat the mixture *gently* to slowly distill (short-path) the alkenes, which will co-distill with water from the reaction flask. Stop the distillation when there is ~0.5 mL left in the reaction flask and/or when the rate of distillation is very slow.

Use a pipette to remove the aqueous phase from the organic phase in the centrifuge tube. Then wash the crude mixture of products with 5% aqueous $NaHCO_3$ (2 x 3 mL) and water (2 x 3mL). Washing should be carried out in the centrifuge tube. Use a pipette to mix the two phases and to remove the aqueous layer after the phases have separated. All visible water should be removed mechanically via pipette. Dry the remaining organic layer over anhydrous $CaCl_2$ or Na_2SO_4 for about 5 minutes. Transfer the dried organic layer via pipette to a clean centrifuge tube and dry it a second time over Na_2SO_4 for an additional 5 minutes (why?). Transfer the product mixture into a clean dry tared screw-capped vial. Determine the mass of the product mixture. Cap the vial tightly and wrap it with parafilm. Store the tube securely upright in a beaker until GC analysis can be carried out.

Alkene Tests (optional). In a small test tube, add 5 drops of your mixture of alkene products to:

1. 1 mL of 0.5% aqueous potassium permanganate solution
2. 1 mL of a 2% solution of bromine in carbon tetrachloride (CCl_4)

For both tests, shake the mixture carefully and record your observations.

Procedure - Part B. Analysis by Gas Chromatography. Analyze your sample by gas chromatography, injecting 0.20 μL as usual. *Print a second copy of your GC trace and data before exiting the software.* Give one copy to the TA, and save one copy to include in your lab notebook. Include the entire printout in your lab notebook (i.e., do not cut out the trace and table of data to save space). You should expect to find two major peaks for alkene products in your GC trace. What are they? You may also find a minor peak for a third alkene, as well as a peak for the starting alcohol. You can expect the compounds to elute from the GC column according to their boiling points (roughly) with the compound having the lowest boiling point eluting first. Determine the composition of your product mixture on the basis of weight. Assume the detector response is the same for all products—you do not need to calculate a detector response factor and adjust the peak areas.

Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) b.p. range of the distillate, 4) mass of the product mixture, 5) GC trace and data for the product mixture with peaks labeled for each alkene and starting alcohol if present, 6) weight % of each alkene and starting alcohol if any, and 7) analysis of the composition of your product mixture.

Product: Turn in your product mixture in a vial labeled with your name and experiment number.

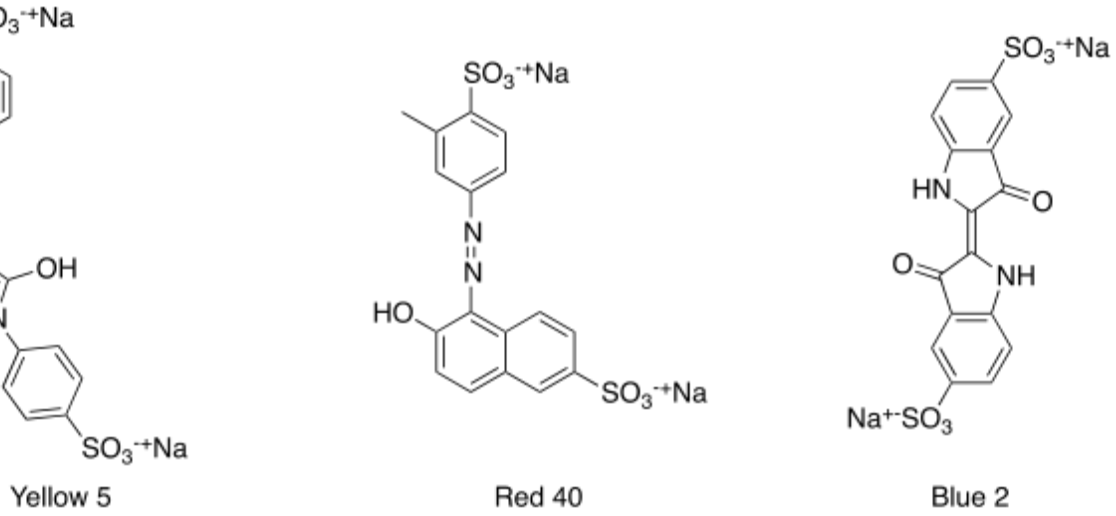
Experiment #7: Thin Layer Chromatography (TLC)

Reference: This experiment was adapted, in part, from a write-up prepared by K. J. Williamson at Mount Holyoke College.

Assigned Reading: *Experiments in Organic Chemistry*, section T7.

Part A. Separation of Food Colors

A limited number of dyes have been approved by the FDA for use in coloring food, drugs and cosmetics. Dyes that are used for food, drugs and cosmetics (FDC) are commonly given numbers, such as FDC Red 40 (below), because their chemical names are complicated. The structures of three commonly used commercial dyes—Yellow 5, Red 40 and Blue 2 are shown below.



Structures of commercial dyes Yellow 5, Red 40 and Blue 2

In the first part of this experiment, you will use thin layer chromatography (TLC) to analyze the composition of dyes that are commonly used in food coloring.

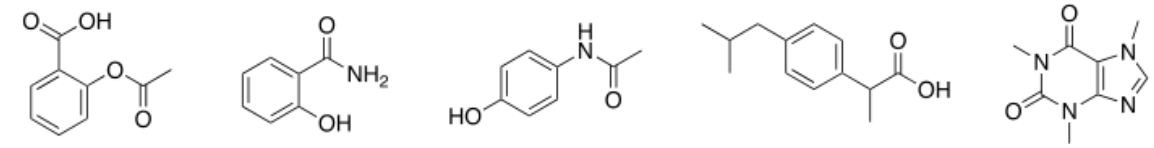
General procedure for carrying out TLC. Using a ruler, draw a horizontal baseline in *pencil* (do not use pen—why?) on a TLC plate 1 cm from the bottom edge of the plate. Apply solutions of samples onto the plate at the line as small spots with a glass capillary TLC spotting tube. Food dyes must be diluted at least 10:1 before being spotted on the TLC plate. Use a new spotting tube for each different sample to avoid cross-contamination of spots and the solutions of compounds. Draw an identifying label in pencil underneath each spot. Label the solvent system used in pencil at the top of the plate. Place the TLC plate upright into a glass developing chamber containing ~0.5 cm of the developing solvent and cover the chamber. Spots at the bottom of the TLC plate should not come into contact with the developing solvent or the compound will dissolve off the plate into the developing solvent. Allow the solvent to wick up the plate until near the top. Do not allow the solvent to reach the top of the plate. If that happens, the spots of compounds will continue to move up the plate as solvent evaporates off the top of the plate. Remove the plate and mark the solvent front in pencil. Allow the plate to dry. Observe the plate under a 254 nm UV lamp (avoid looking directly into the lamp) and trace the outer edges of any spots observed.

Visualization under UV light is not necessary if the compounds are colored and visible to the eye. Determine the distance each spot moves by measuring from the baseline to the center of the spot. Determine the distance the solvent moves from the baseline. Calculate the R_f values for all spots (R_f = distance a spot moves/distance the solvent moves. Record R_f values to two decimal places.

Procedure - Part A. Using a TLC glass capillary spotting tube, apply (spot) solutions containing red, blue, green and yellow food coloring and a mixture of the four colors on silica gel TLC plates. To ensure proper resolution, apply no more than three equally spaced spots per plate to prevent adjacent spots from overlapping. Be sure keep the size of the spots small when applying each sample. *Small spots are essential!* Use wide-mouth glass jars with screw caps as the chambers for developing the TLC plates. To develop your food coloring TLC plates use a mixture of the following four solvents, 1-butanol, ethanol, water, and ammonium hydroxide (v:v, 50:25:25:10). After the solvent has advanced close to the top of the plate, remove the plate from the jar and allow the solvent to evaporate until the plate appears dry. Examine the TLC plate under visible light and note the number and positions of spots that appear and calculate the R_f values. Draw an *accurate* sketch of each TLC plate in your notebook. Alternatively, you may tape your TLC plates into your notebook *(Note: the layer of silica gel on TLC plates is somewhat fragile and can detach from the plastic backing due to mechanical abrasion or bending of the plate. Cover TLC plates entirely with tape to prevent silica gel from detaching).* Tabulate and record all data including compounds spotted, solvent system used, R_f values (to two decimal places) for all spots, and the color and intensity of spots.

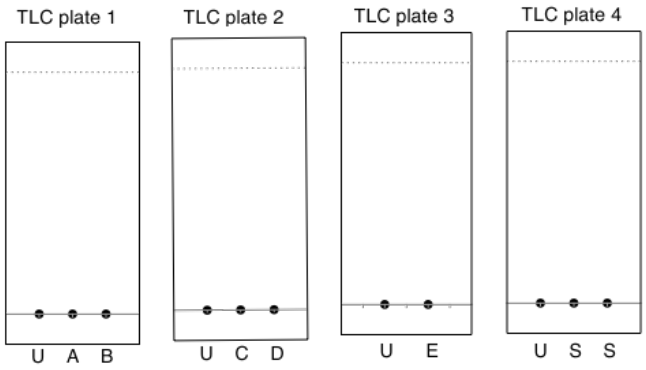
Part B. Separation and Identification of the Components of Common Analgesics

Many of the common non-prescription analgesics (pain killers) such as Aspirin, Empirin, Anacin, Medipren, Tylenol and Advil are composed of one to four different active ingredients that include acetylsalicyclic acid, salicylamide, *p*-hydroxyacetanilide and ibuprofen. Stimulants such as caffeine often are added to painkillers to counteract their sedative effects. The structures of those compounds are shown below.



In this part of the experiment, you will identify an unknown pain-killer using TLC by comparing the R_f values of spots from the unknown to those from known pain-killers. *Spotting TLC plates with small spots is essential to be able to distinguish compounds having R_f values that are close to one another.*

Procedure - Part B. Obtain an unknown sample of a crushed analgesic and record the number. Place a small quantity of the crushed tablet (~2-3 mg on the tip of a microspatula) into a centrifuge tube and add methanol (0.3 mL). The binder, which is an additive that holds the tablet together (e.g., talc, cellulose), will not dissolve. Apply a spot of the solution of unknown, as well as spots of the known analgesics onto TLC plates (2 or 3 spots per plate) as shown below.

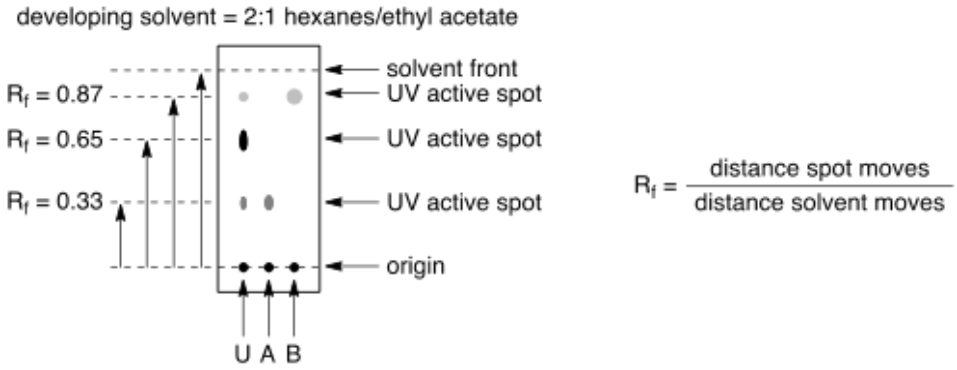


Example of how to apply and compare an unknown (U) with known compounds (A, B, C, D, E, S=suspected compound).

Develop the TLC plates using a solvent mixture containing 1-butanol, 2-butanone, ethyl acetate, hexane (v:v, 2:9:9:20). After the solvent has evaporated from the developed TLC plates, examine the plates under UV light. Mark the position of all the UV active spots on the plate with pencil (circle spots by tracing the outer edges). Draw an *accurate* sketch of each TLC plate in your notebook. Alternatively, you may tape your TLC plates into your notebook. Tabulate and record all data including compounds spotted, solvent system used, R_f values (to two decimal places) for all spots, and the color and intensity of spots. Identify the compound or compounds in the unknown sample.

Proper Method for Recording of TLC Data When Monitoring Reactions

For any reaction (or unknown) monitored by TLC, the data should be recorded in your lab notebook as follows. All TLC plates of reactions should to be carried out by spoting each of the reactants, the reaction mixture and the expected product if it is available. R_f values should be recorded for each compound as well as the solvent system used. Note: it is important to record the solvent system used because R_f values will differ for a given compound developed in different solvents. In addition, data on the shape and UV characteristics (e.g., color, whether the spot is UV active, if the spot streaks, intensity, etc.) for each compound observed should be recorded. Shown below is an example of a TLC plate developed in 2:1 hexanes/ethyl acetate as the solvent system. The reaction mixture (U) on the left shows three spots with R_f values of 0.33 (dark grey), 0.65 (black), and 0.87 (light grey). Reactant A corresponds to the spot at R_f 0.33 and reactant B corresponds to the spot at R_f 0.87. The spot at R_f 0.65 corresponds to the product that was formed by the reaction. The presence of the spots for reactants A and B indicates that the reaction had not gone to completion at the time the reaction mixture was spotted.



The most common error in TLC is spotting too much sample on the plate.

Example of a developed TLC plate with one unknown mixture of compounds (U) and two known compounds (A and B) visualized under UV light. R_f values for the three different spots indicate the distance the compounds moved relative to the solvent front on the TLC plate.

Summary of items to include in your lab notebook: 1) labeled TLC plates (sketches or actual plates) of dyes, 2) R_f values and other data for spots from dyes, 3) unknown #, 4) labeled TLC plates (sketches or actual plates) of analgesics, 5) R_f values and other data for spots from analgesics, 6) identity of the unknown analgesic, 7) Solvent system used for each TLC plate.

Experiment #8: Natural Products: Extraction of Caffeine from Tea

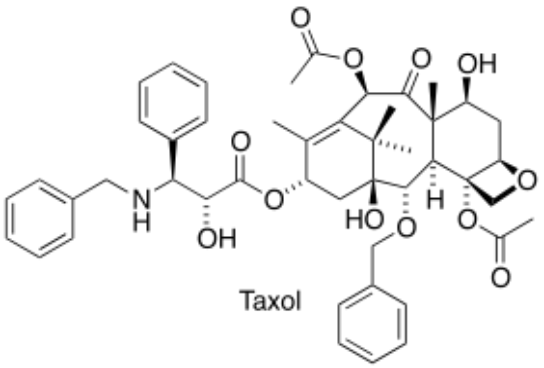
Reference: K. J. Williamson, *Macroscale and Microscale Organic Experiments*, D. C. Heath, Lexington, MA, pp 116-137.

Assigned Reading: *Experiments in Organic Chemistry*, E4A, T5 and T6.

Introduction. A variety of medicinally active compounds occur as natural products in plants and can be extracted in the laboratory from plant material.

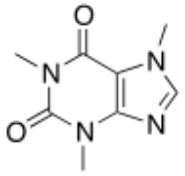
The pharmaceutical industry has found that for certain drugs that are difficult to synthesize in the laboratory, it sometimes is easier to grow the plants that produce the drug and then isolate the drug via extraction. One disadvantage to using natural products in organic syntheses is that the drugs often are present in plants only in very small quantities, requiring many plants to be grown and harvested.

The anti-cancer drug Taxol (below) is found in the bark of the Pacific Yew tree in very small quantities. Harvesting of that drug from yew trees has led to severe deforesting, and new trees take years to grow. Although many research groups have attempted to prepare Taxol in the laboratory, synthesis of the complex structure of that compound has proven particularly challenging. Organic chemists who have been the most successful have relied on using precursors extracted from the leaves of the tree as their starting material.



Taxol

In this laboratory, the natural product caffeine (below) will be extracted from tea leaves. The process of sublimation will then be used to purify the caffeine. Hill and Barbaro describe a similar procedure in *Experiments in Organic Chemistry* in section E4A that uses ethyl acetate as the extracting solvent.



Caffeine

Procedure. Obtain 4 tea bags and record their combined mass. Add H_2O (~ 30 mL), sodium carbonate (Na_2CO_3, ~ 2 g) and a boiling chip into a beaker (~150 mL) and bring the solution to a boil. Remove the beaker from the heat source and let two tea bags steep in the basic solution for 5 minutes. Upon removing the tea bags from the hot solution, carefully squeeze as much liquid as possible from each tea bag. Add water (10 mL), again bring the solution to a boil, remove the

beaker from the heat, add two more tea bags, let them steep for 5 minutes, and again squeeze out any excess liquid. Add ice (~20 mL) and once the solution has cooled to room temperature, carefully pour the solution into a separatory funnel. Extract the caffeine from the aqueous layer using methylene chloride (CH_2Cl_2, 5 x 5 mL). *Do not shake the separatory funnel, rather swirl it. Vigorous shaking will lead to an emulsion that takes hours to separate.* Combine the organic layers in an Erlenmeyer flask (25 mL). Dry the organic layer over anhydrous sodium sulfate (Na_2SO_4). Transfer the dried organic layer into a 50 mL round-bottom flask, attach it to a simple distillation apparatus, and distill off the CH_2Cl_2 using a beaker of warm water as the heat source. Using a small amount of methylene chloride, quantitatively transfer the residue of caffeine to a *tared* watch glass. Allow the methylene chloride to evaporate, taking care to avoid spilling the solution. Record the appearance of the crude solid product (e.g., color, consistency, etc.) that remains after evaporation of the solvent is complete. Determine the melting point (range) and yield of the crude solid. Compare your experimental m.p. range to that of pure caffeine reported in the literature to assess the purity of the product you isolated. Calculate the mass % of caffeine contained in the 4 tea bags [mass % = (mass of crude caffeine recovered/mass of 4 tea bags) x 100].

Note: CH_2Cl_2 is referred to either as methylene chloride or dichloromethane. What is the density of CH_2Cl_2?

After recording the m.p. and mass, turn in your sample of caffeine to the instructor or TA. The samples of caffeine will be combined and then purified by sublimation. Caffeine can be purified readily by sublimation because the solid has a reasonably high vapor pressure. You will be given a small sample of pure caffeine after sublimation is completed so that you can determine the melting point and compare it that of your crude product and the literature value.

Note: Caffeine has two different crystalline forms: (1) an anhydrous form in which the crystals contain just caffeine; and (2) a monohydrate form in which water and caffeine are present in a 1:1 ratio. The melting point ranges for the two crystalline forms of caffeine are different. Look up both and make note of which form the m.p. data for sublimed caffeine most closely corresponds to.

Summary of items to include in your lab notebook: 1) mass of crude caffeine isolated and % mass recovery from the 4 tea bags, 2) m.p. data for crude caffeine, 3) m.p. data for caffeine purified by sublimation, 4) literature m.p. data for the anhydrous and monohydrate forms of caffeine, 5) analysis of caffeine content of the tea you isolated caffeine based on % mass recovery, 6) purity and crystalline form of the pure sublimed caffeine based on m.p. analysis.

Product: You do not need to turn in your product.

Experiment # 9: Separation of a Mixture Using Column Chromatography

Assigned Reading: *Experiments in Organic Chemistry*, sections T3 and T7.

Thin layer chromatography is a useful technique for separating the components of mixtures on an analytical scale. Because only a very small quantity of the mixture is placed on the TLC plate, the technique is not suitable for separating and then isolating milligram or gram quantities of pure compounds. When it is necessary to separate larger quantities of material, the technique of column chromatography is used. In this technique, silica gel is packed in a column containing solvent, and the sample is placed on the top of the column. The sample is then moved through the silica gel by passing solvent through the column. Column chromatography uses much larger amounts of silica gel than TLC, and therefore is useful for separating gram quantities of material.

In this experiment, column chromatography will be used to separate a mixture containing two compounds, naphthalene and β-naphthol (below), and then isolate the pure compounds. Although naphthalene and β-naphthol are both aromatic compounds with similar structures, the phenolic OH group on β-naphthol makes that compound more polar than naphthalene. Given the polar nature of silica gel resulting from OH groups exposed on the surface of the SiO_2 particles, polar β-naphthol will interact more strongly with silica gel than nonpolar naphthalene, and therefore will elute from the column more slowly. As the two compounds are moved through the silica gel (stationary phase) by the solvent (mobile phase), β-naphthol forms weak van der Waals and stronger dipolar hydrogen-bonding interactions with silica gel, whereas naphthalene forms only weak van der Waals interactions.

Note: Items 1,2 & 3 below are to be carried out simultaneously, not sequentially.

1. **Preparing the sample.** Measure a sample (200 mg) of the mixture of naphthalene and β-naphthol into a small test tube. Add the solvent mixture 1:12:12 CH_3OH/CH_2Cl_2/hexane (v:v) drop-wise until the sample is *just* dissolved. It is important to use only a *minimum* amount of solvent to dissolve the sample.

2. **Analysis of the sample by TLC.** Analyze the solution of the sample on separate TLC plates using 1:1 methylene chloride/hexane and 1:1 ethyl acetate/hexanes as the developing solvents. Determine which solvent mixture is more effective for separating the components of the mixture. You should use this solvent to analyze the individual fractions as they elute from the column.

3. **Packing the column.** Place a small piece of glass wool in the chromatography column (25 mL burette with a Teflon stopcock) and *gently* push it to the bottom with a glass rod. The glass wool is needed to prevent sand from exiting the bottom of the column. Take care not to pack the glass wool too tightly as this would restrict the flow of solvent. Securely clamp the column in a vertical position using two clamps. Check that the column is aligned perfectly vertical to ensure good separation. Pour enough sand into the column to make a layer about 1 cm deep on top of the plug of glass wool. The surface of the sand must be level (if necessary, level the sand by tapping gently on the side of the column with a rubber stopper or cork ring). With the stopcock closed, fill the column halfway with the solvent 1:1 methylene chloride/hexane. If necessary, tap the column gently to re-level the sand and to remove any bubbles. Weigh 5 grams of silica gel (i.e., 2.5 g of silica gel for every 100 mg of sample) into a beaker.

Alternatively, in order to save time waiting for a balance, you may measure the silica gel volumetrically. Note that 5.0 g of silica gel occupies 14.0 mL. Add 20 mL of the solvent 1:1 CH_2Cl_2/hexanes and stir to make a slurry. Place a glass funnel on top of the column, swirl the silica gel to make a slurry, and quickly add the slurry to the column. Partially open the stopcock and slowly drain the solvent into an Erlenmeyer flask. Stir the remaining slurry and add it to the column. The column should be tapped during the packing process to prevent cracks or channels. When all of the slurry has been added, tap the column and pour additional solvent through until the packing is completely settled. Finally, add a ~1 cm layer of sand to the top of the packing to protect the silica gel from being disturbed when additional solvent is added to the top of the column. Drain the solvent until it is even with the *top* of the sand. Never allow the level of the solvent to fall *below* the top of the sand to avoid introducing air into the silica gel that can crack the packing.

4. **Loading the sample (a mixture of naphthalene and β-naphthol).** Using a pipette, carefully transfer the sample onto the column. To achieve a good separation, the sample must be applied to the column carefully and evenly so that it travels down the column in a narrow band that is perpendicular to the column axis. A narrow band on a column is analogous to making a small spot on a TLC plate. After the addition of the sample to the column, drain the solution until the solution on top of the column is level again with the top of the sand. Close the stopcock and add ~0.5 mL of the solvent 1:1 methylene chloride/hexanes to the top of the column in order to wash any residual sample on the glass onto the column. Again drain the solvent until the level is at the top of the column. Repeat that process once more by adding an additional ~0.5 mL of solvent to the column. After dropping the level of the solvent even with the top of the sand, the band of sample will sit on top of the silica gel below the sand.

5. **Elution of the sample from the column.** Carefully add 10 mL of the solvent 1:1 methylene chloride/hexanes to the column by pipetteting ~4 mL of solvent onto the column without disrupting the packing, and then slowly pour the remaining ~ 6 mL of solvent onto the column. Open the stopcock and collect two ~ 5 mL fractions in separate Erlenmeyer flasks. *CAUTION: do not allow the top of the solvent to go below the top level of the column.* Analyze each fraction by TLC. If fraction 2 contains the nonpolar naphthalene, continue to elute the column with the same solvent and collect two additional fractions. Continue this until the TLC shows all of the napthalene has been removed from the column (i.e., the last fraction does not contain naphthalene). Now change to the more polar solvent 1:1 ethyl acetate/hexanes and proceed as above to collect 5 mL fractions until TLC shows that the more polar β-naphthol has been eluted from the column.

6. **Sample collection.** Into two separate, clean, *tared (record the weight in your notebook)*, round-bottom flasks, combine the fractions containing the same compound. Do not fill the round-bottom flasks more than half full. Analyze the contents of each flask by TLC, then remove the solvents using rotary evaporation to isolate the pure crystalline solids. When the crystals appear completely dry, remove the flask from the rotary evaporator and dry the outside of the flask with a paper towel to remove any water.

7. **Analysis.** Re-weigh the flasks to determine the masses of naphthalene and β-naphthol recovered from the column. Use those masses to determine the % recovery and the composition of the original mixture. Note: it can be difficult to recover all of the solids using a spatula to scrape the solid out of the flask. Determine the melting point of both solids. Record the masses

of both solids and any observations. Calculate the yields and % recovery, and determine the composition of the original mixture. Transfer the solids to clean, properly labeled vials and turn them in. If you care to, you may recrystallize your compounds and see what kind of a recovery you get and how the melting point changes.

Chromatographic separation of organic compounds can be carried out using a variety of techniques, two of which are TLC and column chromatography. Additional chromatographic techniques that may be used are summarized in the table below.

Summary of Different Types of Chromatography

Type	Moving Phase	Stationary Phase	Detection?	Quantification?	Isolation?	Indentifcation?
GC	He gas	Liquid in column	Electronic	Yes	No/Yes	Retention GC/MS
TLC	Solvent	SiO_2/slide	Visual	No	No	R_f
Column	Solvent	SiO_2/buret	Visual/Evaporation	Weigh	Yes	Isolated Material
Paper	Solvent	Cellulose	Visual	No	No	R_f
HPLC	Solvent	Solid in column	Electronic	Yes	Yes	Retention LC/MS
Electrophoresis	Solvent (buffer) Electric potential	Gel (agar/agar)	Visual/assisted	Yes/No	No	R_f
Capillary electrophoresis	Solvent (buffer)	Gel/in column	Electronic	Yes	No	R_f

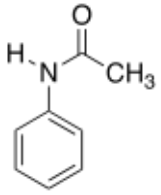
Summary of items to include in your lab notebook: 1) TLC plates (both solvent systems), 2) yields for both compounds, 3)% recovery, 4) melting point data, 5) analysis of the composition of the original mixture, 6) analysis of purity of naphthalene and β-naphthol based on m.p.

Product: Turn in the two products in vials labeled with your name, experiment number, and compound name.

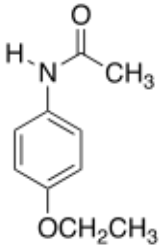
Experiment # 10A: Synthesis of Acetanilide

Assigned Reading: *Experiments in Organic Chemistry*, section E20B.

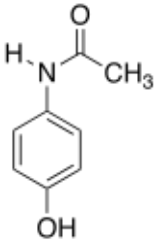
Introduction. Aromatic amines acylated on nitrogen have been used extensively as non-prescription analgesics (pain relievers) and antipyretics (fever reducers). Examples of such compounds that have been used for those purposes include acetanilide, phenacetin and acetaminophen as shown below. Acetanilide and phenacetin no longer are sold commercially because they were found to cause a serious blood disorder called methemoglobinemia. Today, acetominophen is used widely, marketed under the trade names Tylenol and Datril.



acetanilide

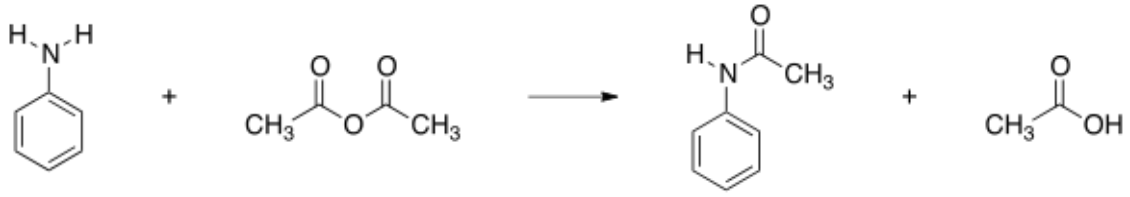


phenacetin



acetaminophen
(Tylenol)

Acetic anhydride is a good acylating agent and can be used to acetylate nitrogen, oxygen and carbon. In this experiment, crude aniline (contains small amounts of impurities that give it a yellow color; pure aniline is a colorless liquid) will be treated with acetic anhydride as shown below. The N-acetylated product, acetanilide, will be purified by treatment with decolorizing carbon and recrystallization.



aniline acetic anhydride acetanilide acetic acid

CAUTION: Aniline is highly toxic on ingestion and is a suspected carcinogen upon long-term exposure to high concentrations. Avoid breathing aniline vapor or contact with skin. Acetic anhydride is corrosive and a lachrymator (a reagent that irritates the eye).

Procedure. In the hood, add 6.5 mmol of aniline to 15 mL of water in a 25 or 50 mL Erlenmeyer flask. Swirl the mixture thoroughly and add 7.9 mmol of acetic anhydride. At your bench, continue to swirl the solution for 10 minutes, then cool the flask in an ice bath. Collect the product by vacuum filtration using a Buchner funnel. Return the crude acetanilide to a 50 mL Erlenmeyer flask. Start to dissolve the solid in a minimum amount of boiling water by adding 15 mL water and a boiling stone, and then bring the mixture to a boil. Add a minimum amount of additional *hot* water to the boiling solution of acetanilide until the acetanilide just dissolves. *Note: the total amount of water in the solution should not exceed 20 mL or else recrystallization will be difficult*

and the yield of pure product will be low. Add some activated charcoal (a spatula tip full, ~ 0.3-0.4 g) and perform a hot gravity filtration through a pre-heated funnel containing fluted filter paper. The solution should be cooled to room temperature, then chilled in an ice bath. Collect the crystalline product by vacuum filtration. Wash the crystals with a small amount of cold water. If the product still appears to be impure (colored), an additional recrystallization should be performed; otherwise allow the product to thoroughly dry overnight. Determine the melting point, yield and percent yield of the *dried* product.

Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) yield and % yield of acetanilide, 4) m.p. of acetanilide, 5) analysis of purity based on m.p.

Product: Turn in the product in a vial labeled with your name, experiment number, and compound name.

Experiment # 10B: Synthesis of Aspirin (small scale)

Assigned Reading: *Experiments in Organic Chemistry*, section E19.

Follow the directions for the "small scale" preparation of acetylsalicylic acid as described in section E19 of *Experiments in Organic Chemistry*.

Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) yield and % yield of aspirin, 4) melting point (range) of your aspirin, 5) analysis of purity based on comparison of melting point data to literature melting point for pure aspirin.

Product: Turn in the product in a vial labeled with your name, experiment number, and compound name.

Experiment #11A: Free Radical Chlorination.

Reference: This experiment was adapted from Experiment 6 in *Experimental Organic Chemistry* J. R. Mohrig, C. N. Hammond, T. C. Morrill and D. C. Neckers. W. H. Freeman & Co., 1998.

Discussion. Hydrocarbons are generally chemically "inert" because of the absence of a functional group. The only reactions which aliphatic hydrocarbons undergo, which are of any significance, are combustion and halogenation. In this experiment you will generate Cl_2 gas in the presence of a hydrocarbon, isopentane, to generate a mixture of monochlorinated products. The Cl_2 is generated by the action of HCl on sodium hypochlorite, NaOCl, present in commercial bleach. Note: commercial bleach is an aqueous solution containing approximately 5% NaOCl.

$$NaOCl + HCl \longrightarrow HOCl + NaCl$$

$$HOCl + HCl \longrightarrow Cl_2 + H_2O$$

The following is the net reaction for monochlorination of methane:

$$Cl_2 + CH_4 \longrightarrow CH_3Cl + HCl$$

The mechanism of that reaction involves a series of free radical steps shown below:

Initiation: $Cl_2 \longrightarrow 2\ \cdot Cl$

Propagation: $Cl\cdot + CH_4 \longrightarrow HCl + \cdot CH_3$

$\cdot CH_3 + Cl_2 \longrightarrow CH_3Cl + \cdot Cl$

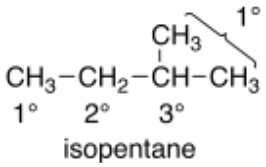
Termination: $\cdot CH_3 + \cdot CH_3 \longrightarrow CH_3CH_3$

$\cdot CH_3 + \cdot Cl \longrightarrow CH_3Cl$

$\cdot Cl + \cdot Cl \longrightarrow Cl_2$

The two propagation reactions constitute a chain reaction because the reactive species, the free radicals •Cl and $\cdot CH_3$, are not depleted and the two reactions sum to the net reaction.

Chlorinations usually lead to a mixture of products because, for most hydrocarbons, there are different types of hydrogen (i.e., methyl, methylene and methine). In the chlorination of propane, two different isomers of monochloropropane are formed. The major factors that control the preference for formation of isomers are the strength of the C-H bond and the statistical factor due to the number of hydrogens available for reaction. In the case of isopentane (below), there are nine equivalent primary (1°) methyl C-H bonds, which are stronger than the two secondary (2°) methylene C-H bonds, which in turn are stronger than the one tertiary (3°) methine C-H bond. The normal textbook ratios of reactivity in the gas phase at 25° C for 1°vs. 2°vs. 3° C-H bonds are 1:3.8:5.0 for chlorination and 1:82:1600 for bromination. What would you expect for the product distribution from monochlorination of isopentane? What about monobromination?



isopentane

Procedure. You will carry out only the free radical chlorination of isopentane. As part of your pre-lab preparation, draw out the structures of all of the possible monochlorinated isomers of isopentane and name each according to IUPAC rules. You also should record the boiling points for each isomer. The boiling points provide an indication of the order of elution of those isomers from a nonpolar GC column, with the lowest boiling isomer eluting first.

Prepare two 16 mL (5 dram) centrifuge tubes with screw caps with Teflon-lined screw caps. Place 2 mL of isopentane into each tube. Working in the hood, add 2 mL of 5% aqueous NaOCl solution to each tube and followed by 1 mL of 3M HCl. Immediately cap the tubes tightly and mix them well, until the yellow chlorine color has moved into the organic phase (about 30 seconds). Observe the yellow color disappearing from the organic phase. Periodically shake each vial and observe a new supply of chlorine in the organic phase. The reaction should be complete (i.e., no yellow color in the organic phase immediately after shaking) in a few minutes. If the yellow color persists for more than 2 minutes, treat the solution with some UV light by holding a 254 nm UV lamp next to the vials and shake them gently.

Note: Isopentane has a b.p. of only 30 °C and is highly volatile. Do not allow it to evaporate out of the centrifuge tubes.

Working with both tubes at the same time, wash the organic layer two times with 1 mL of water. Be sure to mix the phases well using a pipettete. Allow the phases to separate, then draw out the aqueous layer (bottom layer) with a pipettete. Add about 100 mg of anhydrous sodium sulfate to each tube and allow the solutions to dry for at least 5 minutes. Transfer the dried product mixtures to clean, dry, labeled glass vials. Analyze the product mixtures of both samples using gas chromatography. The instructor or TA will assist you in identifying the peaks for products in the GC traces.

Note: If one mole of NaOCl ultimately gives one mole of chlorinated hydrocarbon, what is the maximum conversion of your hydrocarbon that you can expect? Be sure to consider this when evaluating the GC analysis. Also, what is the maximum amount monochlorinated product(s) you can expect based on the amounts of reagents that were used? Determine the limiting reagent and calculate the theoretical yield for chlorination. Which peak in your GC traces do you expect to have the greatest area?

GC Analysis. Determination of the relative molar amounts of the various monochlorinated products based on areas under the GC peaks requires that you make one assumption which, though reasonable, would have to be verified if this were a serious research study. The assumption is that the sensitivity of the detector is the same for each product. The sensitivity of the detector is similar enough for the different products that the assumption is valid in this case.

Analyze *both* of your samples by gas chromatography, injecting 0.20 µL as usual. *Print a second copy of both GC traces and data before exiting the software.* Give one copy of both GC traces to the TA, and save one copy of both GC traces to include in your lab notebook. Include the entire

printout in your lab notebook (i.e., do not cut out the trace and table of data to save space). You should expect to find one peak for the starting material isopentane and four peaks for monochlorinated products in your GC traces. You can expect the compounds to elute from the GC column according to their boiling points, with the compound having the lowest boiling point eluting first. *You may assume the response of the detector in the GC is the same for all of the isomers—that is, the areas of the peaks directly reflect the relative volumes of the different alkenes*. Determine the composition of both product mixtures and compare the relative *molar* amounts of each isomer in each mixture. Hint: you will need to use densities (g/mL) and molecular weights (g/mol) to determine the relative molar amounts of each isomer by converting from area/mL to area/mole.

One may be skeptical about the results of a single analysis. This skepticism, which is healthy, can be lessened somewhat if it is demonstrated that the analysis is repeatable. Repeatability gives a greater confidence in the outcome of the experiment, although it does not deal with the issue of systematic errors. How repeatable is your analysis of the distribution of products based on composition of the two different product mixtures?

Disposal: The aqueous phase may be flushed down the drain. All organics must be disposed of in the *haloginated organic waste container*.

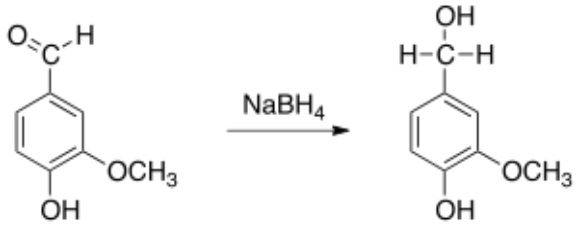
Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) calculations for limiting reagent and theoretical yield of monochlorinated products, 4) GC trace and data for both product mixtures with peaks labeled for each monochlorinated isomer and starting material, 5) analysis of the molar composition of both product mixtures based on the GC data, and 6) conclusions regarding the reproducibility of the reaction (product distribution) based on your data.

Product: You do not need to turn in the product mixtures.

Experiment # 12A: Reduction of Vanillin by Sodium Borohydride

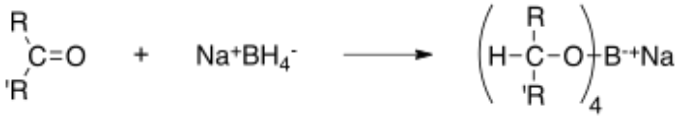
Reference: David Todd, Experimental Organic Chemistry, Prentice-Hall, Engelwood Cliffs, NJ, 1979, Experiment 21.

Introduction. In this experiment, vanillin (4-hydroxy-3-methoxybenzaldehyde) will be reduced using sodium borohydride to produce vanillyl alcohol (4-hydroxy-3-methoxybenzyl alcohol) as shown below. The length of time the reaction should be allowed to continue will be determined by monitoring the reaction mixture by TLC. The reaction will discontinued when TLC analysis shows that all of the vanillin has been consumed and converted to vanillyl alcohol.



vanillin vanillyl alcohol

Sodium borohydride is an efficient and specific reducing agent for aldehydes, ketones and acid chlorides, converting those functional groups to the corresponding alcohols. Other reducible groups such as carbon-carbon double or triple bonds, nitro or cyano groups, and other functional groups containing carbonyl groups such as esters or lactones and amides generally are not reduced by sodium borohydride. Sodium borohydride is a solid that is fairly soluble in water, methanol, and ethanol. In those solvents and in the presence of base, sodium borohydride hydrolyzes to form nucleophilic hydride (H^-) very slowly; addition of acid, however, deactivates sodium borohydride and leads to rapid evolution of hydrogen (H_2) gas. The reduction reaction proceeds by *hydride* transfer from the borohydride ion to the carbonyl group as shown below. Each mole of borohydride delivers four moles of nucleophilic hydride that will reduce four moles of the carbonyl compound.



The borate ester can then be hydrolyzed by addition of water to release the corresponding alcohol:

General procedure for monitoring a reaction by TLC. The length of time that a reaction should be carried out often can be determined by TLC analysis. TLC is used to monitor the

disappearance of reactant(s) and/or appearance of product(s). In the reaction in this experiment, the disappearance of vanillin and the appearance of vanillyl alcohol will be followed.

Procedure for picking a TLC solvent system for monitoring reduction of vanillin by TLC. To monitor a reaction by TLC, spot solutions of the reactant and product separately about 1 cm apart on four separate TLC plates. A suitable solvent system for developing the plates should now be determined. Reactant and product spots must be well separated and all spots of interest should have R_f values should be around 0.5; neither component should remain at the origin or follow the solvent front. Develop one plate in each of the four solvent mixtures supplied and visualize the spots using UV light.

Procedure for carrying out the reaction. Add 2.6×10^{-2} mole of vanillin and 29.0 mL of 1 M aqueous NaOH solution (2.90×10^{-2} mole of NaOH) to a 250 mL Erlenmeyer flask. Using a magnetic stirring bar and stirring plate, stir the solution to dissolve the vanillin, and then cool the contents of the flask by placing the flask in an ice bath. Analyze the mixture by TLC using the solvent mixture that gives the best separation of reactant and product. Spot the pure reactant in one lane, the reaction mixture in the second lane and the pure product in the third lane.

Add 0.5 g (1.3×10^{-2} mole) of sodium borohydride in several portions over a period of 5 minutes while stirring (magnetic stirrer). Continue stirring the solution until all $NaBH_4$ has dissolved, which occurs slowly. Allow the flask to stand at room temperature until the reaction is complete. Monitor the reaction by TLC at 10-minute intervals until the reaction is complete. Take a very small amount of your reaction mixture (tip of a pipette) and dilute it at least 5-10 fold with ethanol. Record your TLC data in your notebook.

Upon completion of the reaction, as judged by TLC analysis, cool the contents of the flask by briefly placing it in an ice bath. Add 5.0 mL of a solution of concentrated HCl (0.060 mole of HCl) in 5 mL of water to the reaction in several 1-2 mL portions, stopping when the solution in the flask is acidic (i.e., pH is less than 7) to a pH indicator strip. If at this point the solid product has not separated from the solution, scratch the walls of the flask near the bottom with a stirring rod to induce crystallization. Thoroughly cool the contents of the flask and then collect the solid vanillyl alcohol by vacuum filtration. Wash the crystals with a small amount of cold water to remove contaminants contained in any residual solution from the reaction. Press the crude product as dry as possible in the funnel (use the bottom of a small flask or beaker) to make recrystallization easier. Spread the crude solid on a large piece of filter paper, break up any lumps, and allow it to dry overnight in your drawer. *Save a small portion (~2-3 mg) of the crude product for melting point determination.*

Recrystallize the dried vanillyl alcohol from ethyl acetate (b.p. 77 °C) using the *minimum* amount of hot solvent; pre-heat the ethyl acetate in a beaker in a hot water bath. A persistent cloud in the ethyl acetate solution is an indication that there is water in your sample. If water is present, it should be removed by treating the solution with anhydrous sodium sulfate. It *may* be necessary to filter the hot solution in order to remove insoluble material. Determine the melting points of the crude and pure products and compare them to the literature value for pure vanillyl alcohol. Calculate the percent yield of both the crude product and the pure product recovered after recrystallization.

Note: D. Todd, pp 138-139. Vanillin is a breakdown product of lignin and is isolated as a by product of paper manufacture. The colorless "artificial" vanilla extract in supermarkets is a solution of pure vanillin in ethanol-water and, as such, is a good deal "purer" than the brown extract of the bean of the vanilla plant—originally an obscure orchid grown in Mexico. The product that you make is a normal metabolite of vanillin that you eat.

Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) yield and % yield of recrystallized vanillyl alcohol, 4) melting point data for the crude and recrystallized vanillyl alcohol, 5) analysis of purity based on comparing the melting point data for recrystallized vanillyl alcohol to the literature melting point.

Product: Turn in the product in a vial labeled with your name, experiment number, and compound name.

Experiment # 12B: Oxidation of Isoborneol to Camphor.

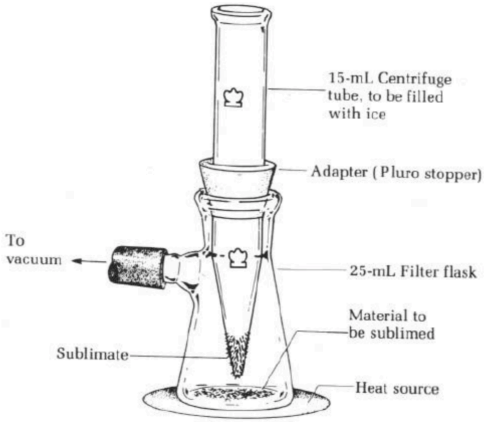
Assigned Reading: *Experiments in Organic Chemistry*, section E11.

Follow the directions for the preparation of camphor as given in section E11 p. 3 at ***3/5 of the scale indicated in the prep***. Be sure to adjust the amounts of all reagents accordingly.

Note: you will not carry out the KI Starch Test indicated in the prep in E11.

After recovering the camphor from methylene chloride and determining the mass and % yield of the crude product, you will purify a small sample of your camphor by sublimation. It is possible to purify camphor via sublimation because the solid has an appreciable vapor pressure when the solid is heated. *Note that applying too much heat will cause the solid to decompose (turns brown). Take care to heat crude camphor very gently over low heat to initiate sublimation and avoid decomposition.*

Procedure for purifying the crude camphor by sublimation. Weigh out approximately 0.5 g of crude camphor (record the mass) and place it into a 25 mL side-arm filter flask that is clamped securely on top of a hot plate to prevent it from tipping over. Insert a centrifuge tube through a rubber adapter—make sure the tube fits snugly enough to create a tight seal—and place the centrifuge tube/adapter into the flask (see setup below). Adjust the height of the tube so that the tip rests on the bottom of the filter flask (Note: application of vacuum will pull the tube down if it rests above the bottom of the flask, potentially causing the tube or flask to break). Fill the centrifuge tube with ice to form a condenser. Connect the flask to the vacuum spigot with vacuum tubing, turn on the vacuum, then gently warm the flask on the hot plate to initiate sublimation. Continue heating gently until most or all of the crude camphor sublimes onto surface of the centrifuge tube. Turn off the vacuum, break the seal by removing the vacuum tubing from the spigot, and remove the centrifuge tube and adapter together. Recover the pure crystals of camphor by scraping them onto a piece of weighing paper with a spatula. Record the mass and melting point (range) of pure camphor recovered. Determine the melting points (ranges) of the crude and pure camphor, and analyze the purity of both by comparing the melting point data to that of pure camphor reported in the literature.



glassware setup for sublimation

Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) yield and % yield of crude camphor, 4) yield and % yield of pure camp recovered via sublimation (based on the mass of crude camphor used for sublimation), 5) melting point data for the crude and sublimed camphor, 6) analysis of purity based on melting point.

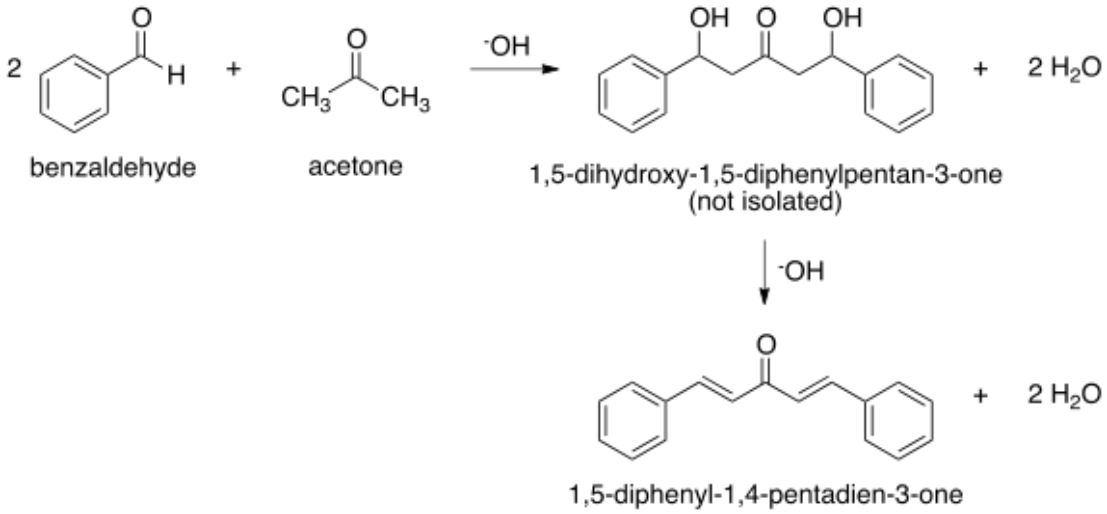
Product: Turn in your crude and purified product in vials labeled with your name, experiment number, and compound name.

Experiment #13A: Aldol Condensation: Dibenzal Acetone

Reference: L. F. Fieser, K. L. Williamson, *Organic Experiments*, 6th edition, Heat, 1987, Chapter 25.

Assigned Reading: *Experiments in Organic Chemistry*, section E12.

Introduction. In the presence of a base, non-enolizable aldehydes will react with enolizable ketones to undergo a mixed aldol reaction, commonly referred to as a Claisen-Schmidt reaction. The initial product of the reaction, a ®-hydroxyketone, frequently undergoes base-catalyzed dehydration to give an ⟨,®-unsaturated ketone. In this experiment, dibenzal acetone (1,5-diphenyl-1,4-pentadiene-3-one) will be prepared by condensation of one molar equivalent of acetone (enolizable) with two molar equivalents of benzaldehyde (non-enolizable), as shown below.



Procedure for TLC analysis. Solutions of benzaldehyde and dibenzal acetone will be available as chromatographic standards (acetone is too volatile to analyze by TLC). Use a 4:1 (v:v) mixture of hexane and ethyl acetate as the developing solvent. Spot benzaldehyde (reference) in the first lane, a co-spot (separate spots of both reagents spotted on top of one another) of the benzaldehyde and dibenzal acetone in the middle lane, and the dibenzal acetone in the third lane. Examine your test plates under UV light and record the visualized TLC plate in your lab notebook.

Procedure for carrying out the reaction. In an Erlenmeyer flask, mix 0.030 mole of benzaldehyde with acetone (determine the appropriate number of moles) and cover the flask to prevent evaporation of acetone. In a separate flask, prepare a solution of 3.0 g of sodium hydroxide dissolved in 30 mL of water and 25 mL of 95% ethanol. Since dissolving NaOH in water/ethanol is an exothermic process, cool the flask to room temperature in a water bath if necessary (see note below). Stir the solution of aldehyde and ketone with a magnetic stirrer at room temperature and add the sodium hydroxide solution.

Note: Addition of a hot solution to acetone will cause acetone to evaporate.

Note: Stoichiometry and quantitative transfer is very important in this experiment. Any deficiency of either reactant not only may lower the theoretical yield, but may lead to contamination

of the product by excess benzaldehyde or mono-benzalacetone, which may make the isolation of pure dibenzal acetone difficult.

Follow the course of the reaction by TLC. Spot the benzaldehyde reference in the first lane, the dibenzal acetone reference in the third lane, and the reaction mixture in the middle lane. Note that there are several transient intermediates in this reaction, which may be possible to detect by TLC. Since the product precipitates from the reaction mixture as an insoluble solid, a small aliquot of the reaction mixture containing the solid product must be transferred via pipettete into a clean vial (or clean small test tube) and the solids dissolved in 1-2 drops of methylene chloride. The resulting solution of dissolved product may then be used for the TLC analysis. Take a very small amount of your reaction mixture (tip of a pipette) and dilute it at least 5-10 times. Reactant and product do not need to be co-spotted every time. Repeat that process for each TLC plate, as the reaction progresses. Run a TLC plate every 10 minutes until the reaction is complete. Do not overload the spot containing the product!

Once the reaction is complete, collect the solid product by vacuum filtration. Wash the product with ice-cold EtOH (3 x 5 mL) to remove residual sodium hydroxide. Leaving the crystals in the Buchner funnel, remove as much water as possible by pressing the solid with the bottom of an Erlenmeyer flask. To further remove any residual water, remove the filter cake from the Buchner funnel and press the crystals dry between two sheets of filter paper taking care to minimize loss of product that may stick to the filter paper. Recrystallize the solid product from ethanol using approximately 2.5 mL of ethanol for each gram of product. Transfer the *dried* crystals into a tared vial, determine the yield, % yield and the melting point (range).

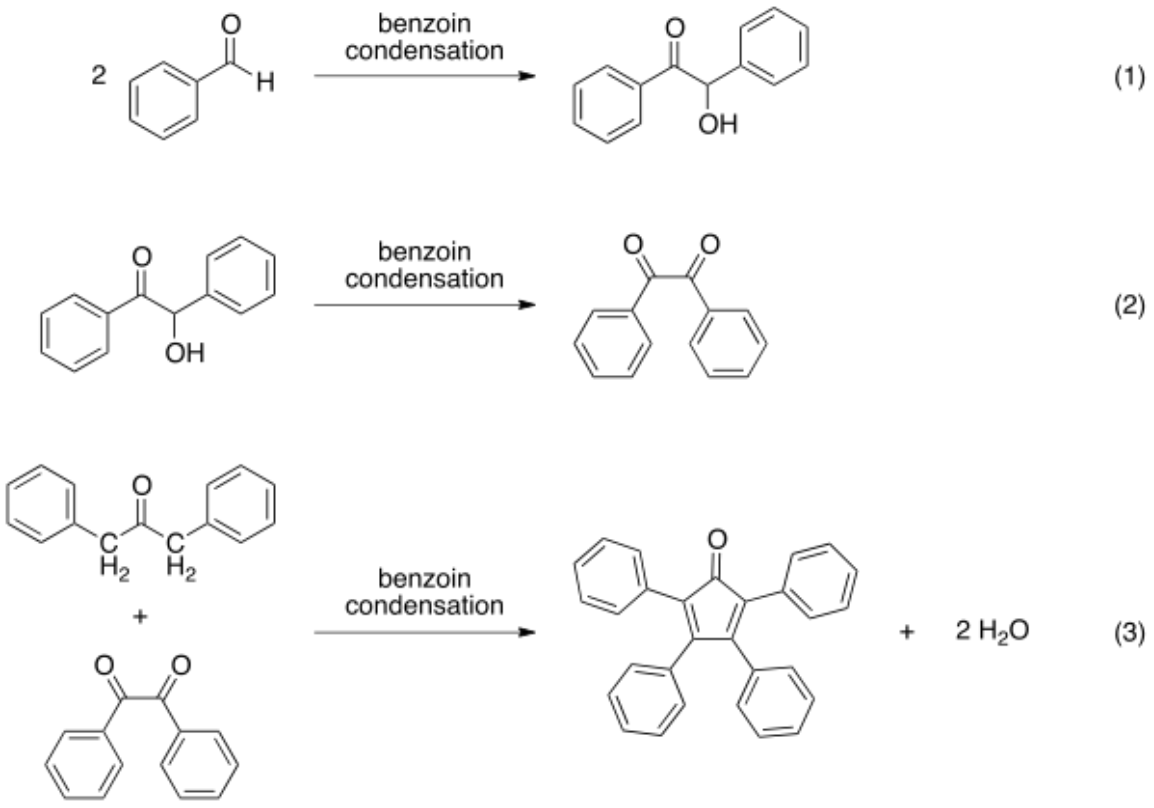
Summary of items to include in your lab notebook: 1) reaction scheme, 2) mole table, 3) TLC data (draw the TLC plates in your notebook and determine R_f values for all spots), 4) yield and % yield of dibenzal acetone, 5) melting point data for dibenzal acetone, 6) analysis of purity based on melting point.

Product: Turn in your dibenzal acetone in a vial labeled with your name, experiment number, and compound name.

Experiment #13B: Multi-step synthesis of tetraphenylcyclopentadienone (tetraphenylcyclone).

Assigned Reading: Look up the three reactions described below in your organic textbook and review the reaction mechanisms.

Introduction. In this experiment, three reactions will be required in order to produce the product tetraphenylcyclopentadienone via the following reaction sequence: (1) a benzoin condensation of benzaldehyde; (2) oxidation of benzoin to benzil; (3) aldol condensation of benzil with 1,3-diphenylacetone. The three steps of the reaction sequence are shown below.



Procedure. Determine appropriate conditions for following the course of the reaction by TLC. Solutions of benzaldehyde, benzoin, and benzil will be available as chromatographic standards. Start with a 3:1 (v:v) mixture of hexane and ethyl acetate as the developing solvent. Examine your test plates under UV light. Each plate should be spotted with the reactants and the products.

Benzoin condensation. Place 0.35 g of thiamine hydrochloride, 0.90 mL of water, and 3.0 mL of ethanol in a 25 mL Erlenmeyer flask. Cool the solution in an ice bath. Over a few minutes, slowly add 0.75 mL of cooled 3M NaOH to the flask. Add 2.0 mL benzaldehyde to the cooled solution and check the pH, which should be between 8 and 9. Place the Erlenmeyer flask into a water bath at 70 °C and let it stand at 70 °C for approximately 30 minutes. TLC analysis in 3:1 hexanes/ethyl acetate should be performed at 15 and 30 minutes to monitor the reaction. If the reaction is not complete at 30 minutes, check the temperature of the water bath and continue

running the reaction for no more than 45 minutes. Cool the reaction mixture to room temperature and then place it in an ice bath. The product should form a yellow precipitate. Isolate the benzoin by vacuum filtration and recrystallize the crude solid from ethanol/water. Determine the yield and % yield of the dry product as well as the melting point.

Oxidation of benzoin to benzil. Place 0.50 g of your benzoin and 3.50 mL of acetic acid onto a 10 mL round bottom flask. Use a vacuum adapter and a short hose to the vent the vapors from the flask to an aspirator through which water is flowing. Add 1.75 mL of concentrated nitric acid, swirl the flask carefully, and place it in a hot water bath at ~85-95° for 15-20 minutes. Monitor the reaction by TLC using methylene chloride as the developing solvent. When the reaction is complete, cool the reaction mixture and then carefully add 10 mL of cold water. Mix the mixture well and cool in an ice bath. The benzil should precipitate and may be collected by vacuum filtration of the cold mixture. Wash the benzil with cold water to remove any residual nitric acid. Recrystallize the benzil from ethanol/water. Determine the yield, % yield and melting point of the dry product.

Aldol condensation. Weigh out 1.0 mmole (*millimoles not moles*) each of benzil (your product from the previous reaction) and 1,3-diphenylacetone* (*see note below*) and combine the two in a small test tube (9.5 cm x 1.5 cm). Add 1.0 mL of triethylene glycol. Heat the solution in a sand bath until homogeneous. Continue heating until the temperature reaches 100 °C, then add 0.1 mL of 40% benzyltrimethylammonium hydroxide (a basic catalyst). After heating 5 minutes in the sand bath, remove the test tube and allow it to cool to near room temperature. Add 1 mL of methanol and mix the reaction well. Isolate the precipitate by vacuum filtration. Wash the solid product with cold methanol. Determine the yield, % yield, and melting point of the dry product.

** Note: If the 1,3-diphenylacetone is a liquid (m.p. 32-34 °C) or semi-liquid, weigh it directly into the test tube first, then weigh and add an equimolar amount of benzil to the 1,3-diphenylacetone in the test tube.*

Summary of items to include in your lab notebook: 1) reaction schemes, 2) mole table of reagents for all reactions, 3) TLC data for benzoin and benzil (draw the TLC plates in your notebook and determine R_f values for all spots), 4) yield and % yield for benzoin, benzyl and tetraphenylcyclopentadienone**,** 5) melting point data for benzoin, benzyl and tetraphenylcyclopentadienone, 6) analysis of purity of the three products based on melting point data.

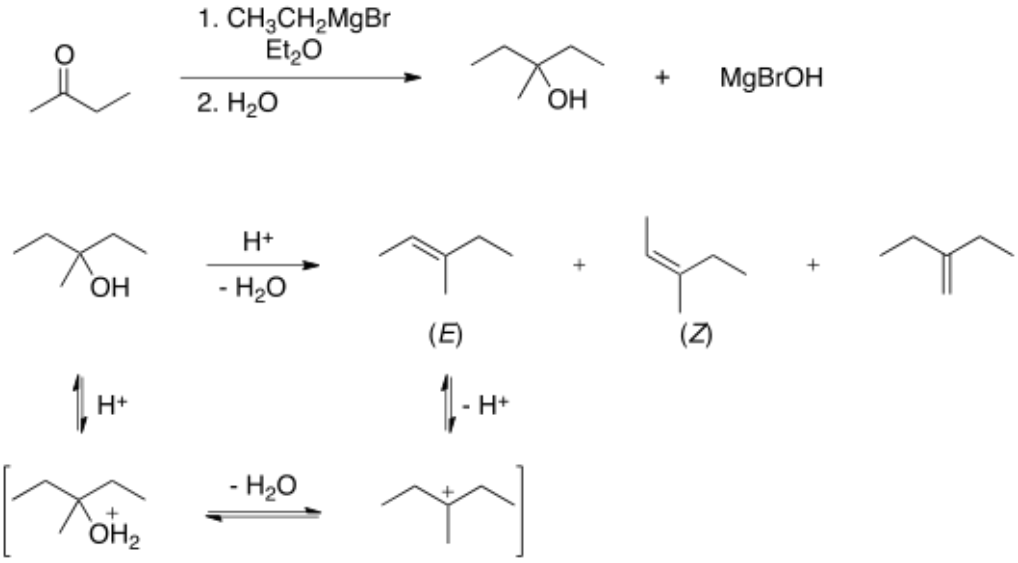
Product: Turn in your three products in vials labeled with your name, experiment number, and compound name.

Experiment #14: Grignard Reaction of a Ketone; Alcohol Dehydration.; Alkene Stability

Reference: This experiment was originated by Professor Alfred A. Scala at WPI.

Assigned Reading: *Experiments in Organic Chemistry*, sections E16 1-3 and E5B.

Discussion. Organic syntheses seldom involve single reactions that give single products. The majority of syntheses involve multiple reactions, any one of which may produce more than one product. In this experiment, 3-methyl-3-pentanol will be synthesized by reaction of 2-butanone with ethyl magnesium bromide (a Grignard reaction). The alcohol will then be subjected to acid-catalyzed dehydration to give a mixture of the alkenes consisting of (*E*)-3-methylpent-2-ene, (*Z*)-3-methylpent-2-ene, and 2-ethylbut-1-ene, as shown below.

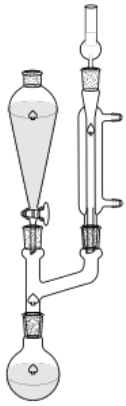


Acid-catalyzed dehydration of the alcohol proceeds via a carbocation intermediate that undergoes elimination to produce three different alkene isomers as products. If the dehydration reaction is irreversible, the yield of each isomer will be dependent upon the relative rates of formation for each alkene (kinetic control). If formation of the alkenes is reversible such that they can interconvert through the carbocation, then the yields of each isomer will reflect the equilibrium concentrations (thermodynamic control) rather than the rates of formation (kinetic control).

Procedure for the Grignard reaction. Assemble a glassware setup featuring a 50 mL round-bottom flask, a magnetic stir bar, a Claisen head, an addition funnel (to add solutions of reagents), a reflux condenser, and a drying tube as shown below. Disassemble the entire apparatus and dry it in the oven. ***Note: It is important to dry all of the glassware required for this setup overnight in the oven prior to coming to the lab so you can get started immediately***. The condenser jacket does not need to be dry where the water passes through the condenser. Remove the apparatus from the oven and reassemble it while the glassware still is hot using an oven mitt to protect your hand. Prepare 25 mmoles (*millimoles)* of ethylmagnesium bromide as follows. Add 0.028 moles of magnesium into the round-bottom flask while it is still hot. After the flask has cooled to room temperature, add approximately 2 mL of anhydrous ether to the magnesium. Place 25 mmoles (*millimoles*) of ethyl bromide (*see note below*) into the addition funnel, along

with 3 mL of anhydrous ether. Add approximately 0.5 mL of the ethyl bromide solution to the magnesium and look for signs (e.g., bubbling) of reaction. Ask the instructor to confirm the start of the reaction. Once the reaction has started, add another 3 mL of dry ether to the round-bottom flask and slowly add the remaining ethyl bromide solution to the reaction drop-wise from the addition funnel at a rate such that the ether gently refluxes. The magnesium should slowly dissolve as the reaction proceeds and only the excess magnesium should remain in the flask. When the reaction is complete, allow the solution to stand for about 15 minutes. Prepare a 1:1 (v:v) solution of 25 mmoles of 2-butanone in anhydrous ether in the addition funnel, and then carefully add the solution drop-wise to the solution of Grignard reagent in the round-bottom flask. This reaction also is exothermic and the addition should be at a rate that allows the ether to reflux gently. After addition is completed, gently reflux the reaction mixture for 30 minutes using a warm water bath as the heat source.

Note: Ethylbromide has a relatively high vapor pressure (b.p. 37 °C) and is toxic. Be sure to measure out ethylbromide in the hood.



glassware setup

You are now ready to hydrolyze the magnesium salt of 3-methyl-3-pentanol, which also is an exothermic reaction. Place 10 mL of 10% (v:v) sulphuric acid into the addition funnel and add it to the reaction mixture at a rate that allows the ether to reflux gently. If any solid persists when the hydrolysis is complete, add enough extra acid or DI water to dissolve most of the solid, as big pieces of crystals or of Mg turnings will complicated your phase separation by separatory funnel. If large pieces of precipitate persist, filter the solution into the separatory funnel through a glass funnel containing a fluted filter paper or a small piece of cotton. Separate the aqueous phase from the ether phase in a separatory funnel and save both phases. Pour the aqueous phase back into the separatory funnel and extract any remaining product with 2 x 5 mL of ether. If the second ether extraction is yellow, then a third 5 mL extraction with ether may be necessary for complete recovery of the product. Combine the ether solutions and wash them successively with 2 x 5 mL water, 1 x 5 mL 10% Na_2CO_3 (*Note: take care because the reaction may foam*), and 2 x 5 mL water. Dry the ether solution over anhydrous Na_2SO_4. Transfer the solution to a tared flask and distill the ether off using a hot water bath as a heat source. Alternatively, you may remove the ether using a rotary evaporator. After all of the ether has been removed, weigh the flask and its contents and determine the yield and % yield of crude 3-methyl-3-pentanol.

Carry out the dehydration in the next step below with the crude 3-methyl-3-pentanol in the same flask. Normally, it would be desirable to purify the crude alcohol by distilling it to remove trace

amounts of ether before moving onto the next step. You will not perform a distillation in this case to ensure you have enough crude alcohol for the next step. Residual ether will not interfere with the dehydration reaction. That said, you should expect to find some residual ether in your alkenes.

Procedure for dehydration of 2,3-dimethyl-2-butanol. Place 0.5 g of *p*-toluenesulfonic acid into the 25 mL flask containing your crude 3-methyl-3-pentanol. Equip the flask for simple distillation *except* with a vacuum adapter in place of the condenser and a 10 mL round-bottom flask immersed in an ice/water bath as a receiver (*Note: do not use a glass vial as the receiver because the alkene products are volatile*). Heat the contents of the flask in a water bath to approximately 95° for 30 minutes (i.e. heat water bath to boiling without cooking over) during which some of the alkenes will steam distill and collect in the receiving flask. If you have a significant amount of material remaining in the distillation flask, add ~1 mL of water to the distillation flask, raise the temperature (not above 100°), and make certain that all of the alkenes have distilled (Note: a similar process was employed for dehydration of 2-methylcyclohexanol in Exp 6). Separate the water (if any) from the distillate and dry the product over a small amount of anhydrous sodium sulfate. If you need to store your product, add a few crystals of hydroquinone to your product and store cold, in a sealed container. Hydroquinone acts as a radical scavenger that prevents oxidation of alkenes by oxygen (O_2).

Run a gas chromatogram of the mixture of alkenes. *Print a second copy of your GC trace and data before exiting the software.* Give one copy to the TA, and save one copy to include in your lab notebook. Include the entire printout in your lab notebook. Determine the relative concentrations of the different isomers that are present. *You may assume the response of the detector in the GC is the same for all of the isomers—that is, the areas of the peaks directly reflect the relative volumes of the different alkenes.* The instructor will assist you in identifying the peaks. Label each peak in the GC trace with the structure of the isomer it corresponds to.

Disposal. The aqueous phase may be flushed down the drain. All organics must be disposed of in the *appropriate organics waste container*.

Summary of items to include in your lab notebook: 1) reaction schemes for both reactions, 2) mole table of all reagents, 3) b.p. range of the distillate from dehydration, 4) yield and % yield for both products, 5) GC trace and data for the alkene product mixture with peaks labeled for each alkene and starting alcohol if present, 6) weight % of each alkene and starting alcohol if any, and 7) analysis of the composition of the alkene isomers present in the product mixture.

Product: Turn in your products in vials labeled with your name, experiment number, and compound name.