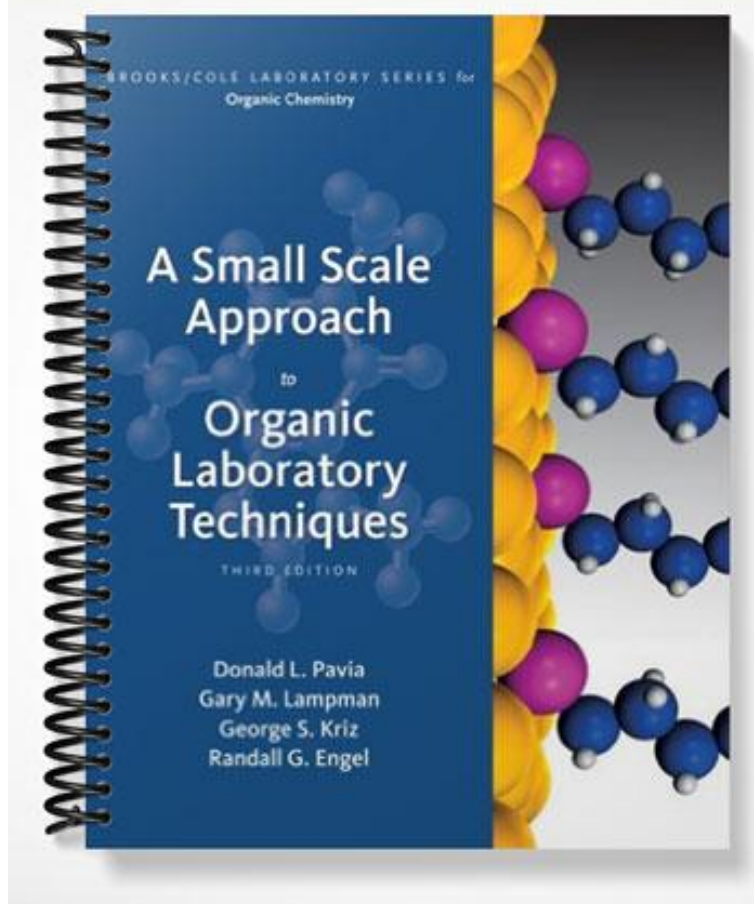
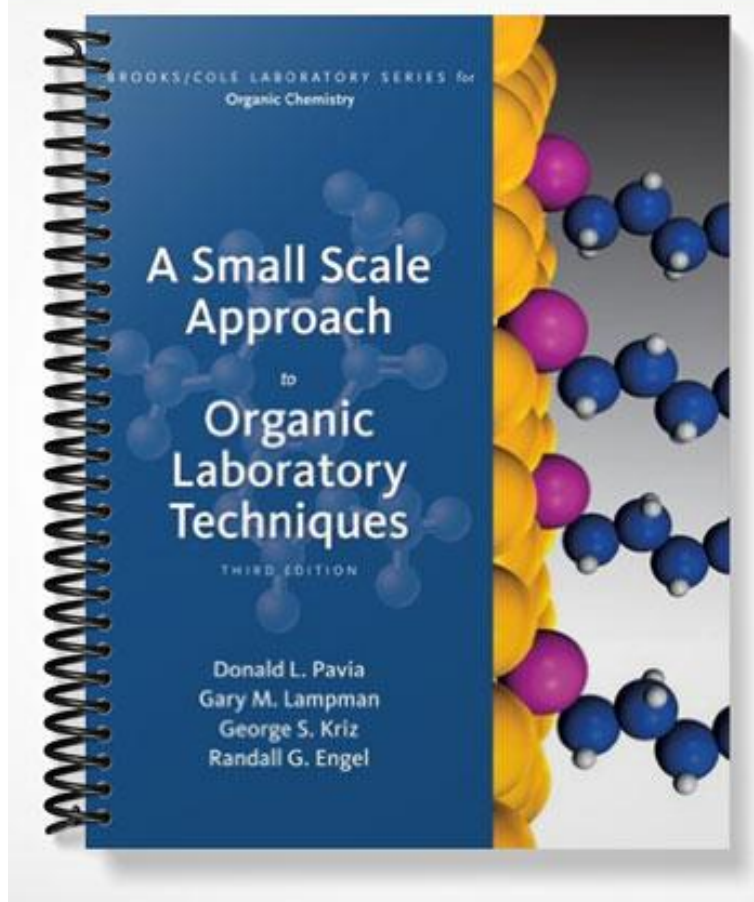


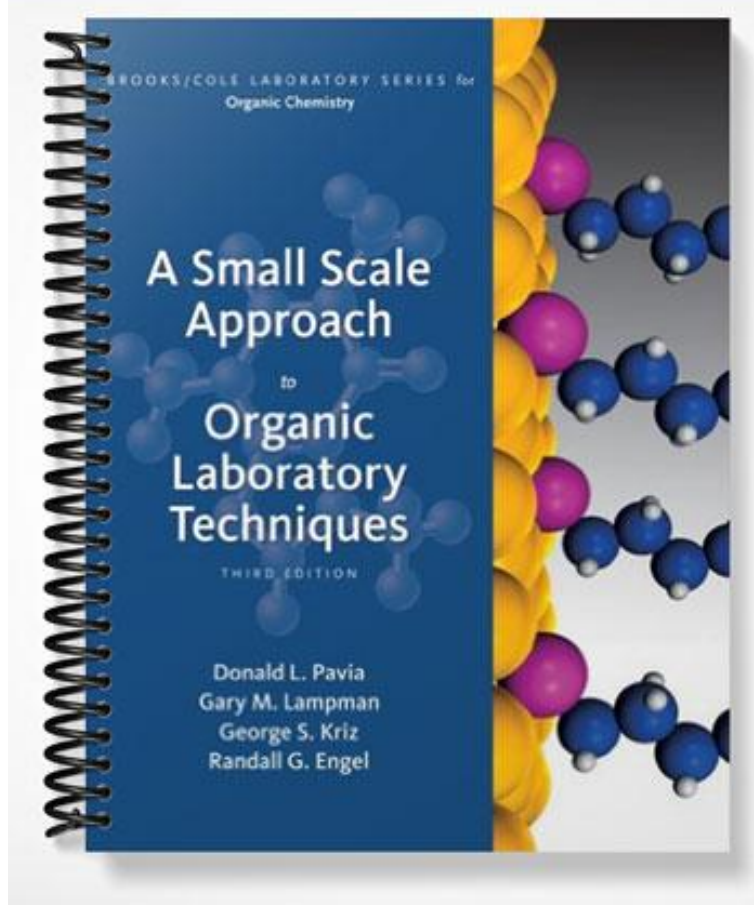
# SOLUTIONS MANUAL



# SOLUTIONS MANUAL



# SOLUTIONS MANUAL



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## Experiment 1

### SOLUBILITY

TIME ESTIMATE: Parts A-D (3 hours); Part E (1 hour); Part F (1 hour)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### Part A

Benzophenone (Grind up the flakes into a powder)	0.5 g
Malonic acid	0.5 g
Biphenyl	0.5 g
Methyl alcohol	40 mL
Hexane	40 mL

#### Part B

Methyl alcohol	13 mL
1-Butanol	13 mL
1-Octanol	13 mL
Hexane	40 mL

#### Part C

Ethyl alcohol	13 mL
Diethyl ether	13 mL
Methylene chloride	25 mL
Hexane	13 mL

#### Part D

Benzoic acid	1.2 g
--------------	-------

Ethyl 4-aminobenzoate	1.2 g
1M NaOH	25 mL
1M HCl	25 mL
6M NaOH	6 mL
6M HCl	6 mL
Litmus paper	

#### Part E

- |         |       |
|---------|-------|
| Acetone | 25 mL |
| Hexane  | 13 mL |
- We give each pair of students two mixtures. Each mixture contains 2 mL of each liquid and about 0.1 g of the dissolved solid. There are many possible combinations of substances to use. The mixtures we have used contain one of the following combinations of solid and liquids (the solid is listed first): fluorene, methylene chloride, water; triphenylmethanol, diethyl ether, water; salicylic acid, methylene chloride, 1M NaOH; ethyl 4-aminobenzoate, diethyl ether, 1M HCl; naphthalene, hexane, water; benzoic acid, diethyl ether, 1M NaOH; *p*-aminoacetophenone, methylene chloride, 1M HCl. The mixtures containing ethyl 4-aminobenzoate and *p*-aminoacetophenone should be made up fresh on the same day as the lab, otherwise the solutions become colored.
- |                              |       |
|------------------------------|-------|
| Tetraphenylcyclopentadienone | 0.3 g |
| Methyl alcohol               | 13mL  |

#### Part F

Self-Assembled Monolayer Demonstration Kit  
 Available from Asemblon, Inc., 15340 N.E. 92nd St., Suite B,  
 Redmond, WA 98052; phone 425-558-5100; [asemblon.com](http://asemblon.com).  
 Instructions for filling the Asemblon pen with the thiol are provided  
 with the kit.

If done as a demonstration, one kit is sufficient. Otherwise one kit for every 4 students works well.

Butane to fill the torch for erasing the gold slide

Methyl alcohol 10 mL

Acetone 10 mL

**CAS Registry numbers:**

Benzophenone	119-61-9
Malonic acid	141-82-2
Biphenyl	92-52-4
Hexanes	73513-42-5
Methyl alcohol	67-56-1
1-Butanol	71-36-3
1-Octanol	111-87-5
Ethyl alcohol (ethanol), 95%	64-17-5
Diethyl ether	60-29-7
Methylene chloride	75-09-2
Benzoic acid	65-85-0
Ethyl 4-aminobenzoate	94-09-7
Acetone	67-64-1
Fluorene	86-73-7
Triphenylmethanol	76-84-6
Salicylic acid	69-72-7
Naphthalene	91-20-3
<i>p</i> -Aminoacetophenone	99-92-3
Tetraphenylcyclopentadienone	479-33-4

**SPECIAL NOTES**

In Part A, it is very important that students follow the instructions carefully for stirring the mixtures. The bigger spatula shown in Figure 12.10 on page 697 of the Textbook is very effective in achieving consistent stirring from one mixture to another.

We have found that some students have difficulty performing Critical Thinking Application #2 (p. 9 of the Text) on the same day that they complete the rest of this experiment. Many students need time to assimilate the material in this experiment before they can complete this exercise successfully. One approach is to assign Critical Thinking Applications from several technique experiments (for example, Experiments 1 - 3) on a laboratory period following

the completion of the individual technique experiments. This provides an effective way of reviewing some of the basic techniques.

Part A (expected results)

Compound	Water	Methyl alcohol	Hexane
Benzophenone	Insoluble	Soluble in about 25 sec	Soluble in about 60 sec
Malonic acid	Soluble in about 10 sec	Soluble in about 10 sec	Insoluble
Biphenyl	Insoluble	Partially soluble	Soluble in about 40 sec

Part B (expected results)

Compound	Water	Hexane
1-Octanol	Insoluble	Soluble
1-Butanol	Partially soluble	Soluble
Methanol	Soluble	Insoluble

Part F

In Part F, a butane torch is used to erase the gold slide. It is best that this be done by the instructor. When erasing the slide, keep the torch moving and do not hold it in one spot on the slide. Heating one spot for too long can cause the slide to shatter.

ANSWERS TO QUESTIONS

- yes
  - no
  - yes
  - no
  - no
  - yes
  - no
- miscible
  - miscible
  - miscible
  - immiscible
  - miscible
  - miscible

3. Ibuprofen is a carboxylic acid which is converted to a water-soluble salt in 1.0M NaOH.
  4. Thymol has a phenolic OH group which is acidic. In 1.0M NaOH, thymol is converted into a water-soluble salt.
  5. Cannibinol is only slightly soluble in methyl alcohol because the large hydrocarbon component of cannibinol negates the fact that they belong to the same family.
  6. When you write on the slide, a monolayer of thiols is deposited on the slide. The OH groups will be located at the top surface of the coated area. Since hydroxyl groups are hydrophilic, water is attracted to the part of the slide that was written on. The rest of the surface is coated with hydrocarbons from the air and is hydrophobic, so the water rolls off and does not stick.
  7. Water adheres to the gold surface immediately after flame cleaning because the gold surface is a high-energy surface that attracts water molecules. Within several minutes, the surface becomes coated with hydrocarbons from the air, making the surface hydrophobic.
  8. A methyl group on the end of the thiol molecule would make the surface nonpolar or hydrophobic.
  9. Heating the slide with a butane torch burns off the thiols.
  10. When you write on a glass surface with a crayon or wax pencil, you are transferring a thick layer of material rather than a monolayer. You can even see this difference since you can see the film made by the wax, but you cannot see the monolayer after it forms on the gold slide.
  11. This is caused by the very high surface tension of water that allows water molecules to span the gap of the hole in these letters.
-



## Experiment 2

### CRYSTALLIZATION

TIME ESTIMATE: Parts A and B (3 hours), Parts C (about 1 hour)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### Part A

Impure sulfanilamide (5% fluorenone the impurity) 10 g  
Grind thoroughly to make homogeneous.

95% Ethyl alcohol 250 mL

Filter paper for Büchner funnel

Melting point capillary tubes

Waste container for non-halogenated organic wastes.

#### Part B

The appropriate solvent for crystallizing the impure fluorene is methyl alcohol. Fluorene is too soluble in toluene and insoluble in water at all temperatures.

Impure fluorene (5% fluorenone as the impurity) 10 g  
Grind thoroughly to make homogeneous.

Methyl alcohol 300 mL

Toluene 25 mL

Waste container for non-halogenated organic wastes.

#### Part C

Acetylsalicylic acid 5 g

Benzoic acid 5 g

Benzoin 5 g

Dibenzoyl ethylene 5 g

Succinimide 5 g

*o*-Toluic acid

5 g

Prepare unknowns consisting of pure samples of the above 6 compounds; about 0.2 g for each unknown sample.

Part D (Answers)

1. Phenanthrene  
95% ethyl alcohol - best solvent  
water - not soluble  
toluene - too soluble
2. Cholesterol  
ether - too soluble  
95% ethyl alcohol - best solvent  
water - not soluble
3. Acetaminophen  
95% ethyl alcohol - too soluble  
water - best solvent  
toluene - not very soluble
4. Urea  
Water - too soluble  
95% ethyl alcohol - best solvent  
Hexane - not very soluble

**CAS Registry numbers:**

Sulfanilamide	63-74-1
Acetanilide	103-84-4
95% Ethyl alcohol (Ethanol)	64-17-5
Fluorene	86-73-7
Fluorenone	486-25-9
Methyl alcohol (methanol)	67-56-1
Toluene	108-88-3
Acetylsalicylic acid	50-78-2
Benzoic acid	65-85-0
Benzoin	119-53-9
Dibenzoyl ethylene	4070-75-1
Succinimide	123-56-8
<i>o</i> -toluic acid	118-90-1

SPECIAL NOTES

In the Pre-lab Calculations for Part A, students calculate the amount of sulfanilamide which will remain in the mother liquor. If they perform the Optional Exercise in Part A, they determine the weight of solid in the mother liquor. However, the actual weight of solid in the mother liquor is usually much greater than the amount calculated in the Pre-lab Calculations. This is because the calculation does not take into account the impurity, which ends up in the mother liquor. Also, the calculation assumes that a minimum amount of solvent is used to dissolve the impure sulfanilamide at 78 °C. It is likely that most students use more than the minimum amount.

#### ANSWERS TO QUESTIONS

1. Too much solvent was added. Since 10 mL of 95% ethyl alcohol will dissolve 0.14 g of sulfanilamide at 0 °C, none of the 0.1 g of sulfanilamide will crystallize when the solution is cooled. To make the crystallization work, the excess solvent must be evaporated.
2. The boiling point of the solvent is higher than the melting point of fluorenone. While performing this crystallization, it is possible that the fluorenone would melt rather than dissolve, thus forming an oil which could be difficult to crystallize.
3. Biphenyl is highly soluble in both hot and cold benzene. The solubility curve would look like C in Figure 11.1 on page 663 of the Textbook.

---

### **Experiment 3**

#### **EXTRACTION**

TIME ESTIMATE: Parts A-D (3-4 hours); Part E (30 minutes)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### **Part A**

Caffeine	2.2 g
Methylene chloride	200 mL

Anhydrous sodium sulfate (granular) 38 g

Evaporation station in a hood (optional)

Waste containers for aqueous and non-halogenated organic wastes (note: there will be some methylene chloride in the aqueous waste)

### Part B

(These quantities are based on the assumption that each student does this part with only one of the compounds.)

Benzoic acid 0.4 g

Succinic acid 0.4 g

Sodium benzoate 0.4 g

Methylene chloride 25 mL

Anhydrous sodium sulfate (granular) 5 g

Evaporation station in a hood (see “Equipping the Organic Chemistry Laboratory” earlier in this manual).

Waste containers for aqueous and non-halogenated organic wastes (note: there will be some methylene chloride in the aqueous waste)

### Optional Exercise in Part B

Caffeine 1.0 g

Methylene chloride 30 mL

Anhydrous sodium sulfate (granular) 5 g

### Part C

We give a set of all three mixtures to each pair of students. Each mixture contains about 2 mL of each liquid. The three mixtures are: (1) water and n-butyl chloride; (2) water and n-butyl bromide; and (3) n-butyl bromide and saturated aqueous sodium bromide. It is best if the aqueous sodium bromide is not quite saturated. Otherwise, it may salt out when mixed with n-butyl bromide. Do not dilute it too much, however, since it should be more dense than n-butyl bromide. Each mixture should be prepared in a stoppered

test tube or centrifuge tube.

Waste container for halogenated organic wastes.

#### Part D

Each student receives an unknown which contains 0.24 g of a neutral compound and 0.12 g of benzoic acid, the acid impurity. The neutral compound should be one of the following: fluorenone, fluorene, 1,2,4,5-tetrachlorobenzene, or triphenylmethanol.

1.0M NaOH	120 mL
6.0M HCl	12 mL
Saturated aqueous NaCl	60 mL
Diethyl ether	120 mL
Anhydrous sodium sulfate (granular)	10 g
Litmus paper	

Evaporation station in a hood (see “Equipping the Organic Chemistry Laboratory” earlier in this manual).

Waste containers for aqueous, non-halogenated and halogenated

#### Optional Exercise in Part D

Each student receives an unknown which contains 0.24 g of a neutral compound and 0.12 g of ethyl 4-aminobenzoate, the base impurity. The neutral compound should be one of the following: fluorenone, fluorene, 1,2,4,5-tetrachlorobenzene, or triphenylmethanol.

1.0M HCl	120 mL
6.0M NaOH	12 mL
Saturated aqueous NaCl	60 mL
Diethyl ether	120 mL
Anhydrous sodium sulfate (granular)	10 g

Litmus paper

Evaporation station in a hood (see “Equipping the Organic Chemistry Laboratory” earlier in this manual).

Waste containers for aqueous, non-halogenated and halogenated organic waste

### Part E

Methylene chloride 25 mL

Solution A: Mix 25 mg of 2,6-dichloroindophenol (sodium salt) with 50 mL of water and 1 mL of 1M NaOH. This solution should be prepared the same day it is used.

1M HCl 2 mL

1M NaOH 4 mL

Waste container for halogenated organic wastes.

### **CAS Registry numbers:**

Caffeine	58-08-2
Methylene chloride	75-09-2
Diethyl ether	60-29-7
sodium sulfate	7757-82-6
Benzoic acid	65-85-0
Succinic acid	110-15-6
Sodium benzoate	532-32-1
Ethyl 4-aminobenzoate	94-09-7
Fluorenone	486-25-9
Fluorene	86-73-7
1,2,4,5-Tetrachlorobenzene	95-94-3
Triphenylmethanol	76-84-6
2,6-dichloroindophenol (sodium salt)	620-45-1

### SPECIAL NOTE

In Parts A and B, it is essential that students make all weighings very carefully on balances that weigh to the nearest 0.001 g. In Part B, it is still likely that results will vary a lot. However, definite trends will be seen when students average their results. In Part E, students may require some help in interpreting the results. It is helpful for them to read about acid/base indicators in their general chemistry book. This experiment is described in the reference given at the end of Experiment 3 in the Textbook.

## ANSWERS TO QUESTIONS

$$1. \quad \frac{52 - x/2}{x/2} = 4.6$$

$$52 - x = 4.6x$$

$$52 = 5.6x$$

$$x = 9.3 \text{ mg in the aqueous phase; } 42.7 \text{ mg in the organic phase}$$

---

### Experiment 4

#### A SEPARATION AND PURIFICATION SCHEME

TIME ESTIMATE: 1-2 Periods

Students must be told the composition of their mixture well in advanced of the laboratory period so that they have sufficient time to devise a procedure. It is advisable to require that students turn in a copy of their procedure at the beginning of the lab period. It is also helpful if they draw a flow chart before they begin the experimental work. You may wish to allow enough time so that students can repeat the experiment if their procedure doesn't work the first time or if they want to improve on their percentage recovery and purity. We have found that many students benefit from doing this experiment a second time, even if their first attempt is somewhat successful.

We have used the following mixtures in this experiment (percent by mass):

- (1) 50% phenanthrene, 40% *o*-toluic acid, 10% 1,4-dibromobenzene
- (2) 50% phenanthrene, 40% methyl 4-aminobenzoate, 10% 1,4-dibromobenzene
- (3) 50% phenanthrene, 40% 2-chlorobenzoic acid, 10% 1,4-dibromobenzene
- (4) 50% phenanthrene, 40% 4-aminoacetophenone, 10% 1,4-dibromobenzene
- (5) 50% benzoin, 40% 4-aminoacetophenone, 10% 1,4-dibromobenzene
- (6) 50% 1,2,4,5-tetrachlorobenzene, 40% *o*-toluic acid, 10% 1,4-

dibromobenzene

(7) 50% 1,2,4,5-tetrachlorobenzene, 40% 2-chlorobenzoic acid, 10% 1,4-dibromobenzene

(8) 50% 4-aminoacetophenone, 40% 1,2,4,5-tetrachlorobenzene, 10% 1,4-dibromobenzene

(9) 50% methyl 4-aminobenzoate, 40% 1,2,4,5-tetrachlorobenzene, 10% 1,4-dibromobenzene

(10) 50% methyl 4-aminobenzoate, 40% benzoin, 10% 1,4-dibromobenzene

(11) 50% benzoic acid, 40% benzoin, 10% 1,4-dibromobenzene

(12) 50% fluorene, 40% *O*-toluic acid, 10% 1,4-dibromobenzene

(13) 50% benzoin, 40% benzil, 10% 1,4-dibromobenzene

(14) 50% ethyl 4-aminobenzoate, 40% benzoin, 10% 1,4-dibromobenzene

(15) 50% ethyl 4-aminobenzoate, 40% benzil, 10% 1,4-dibromobenzene

When you prepare these mixtures, it is important that the relative amounts be accurate, especially if you will be grading them on % recovery. One way to do this is to prepare each student mixture individually. For example, one sample of the first mixture would consist of 0.5 g phenanthrene, 0.4 g *o*-toluic acid, and 0.1 g 1,4-dibromobenzene. If you have a large class, however, this may require too much time. An alternative method is to weigh out a larger amount of the three compounds in a mixture according to the relative percentages given above. Make sure that each compound is a fine powder and then place them into a large enough bottle so that you can shake the mixture in the bottle thoroughly. Shake vigorously for several minutes. Another option is to place the powdered compounds in an Erlenmeyer flask and place the flask on a laboratory shaker for 1-2 hours. Individual samples of 1.0 g can then be weighed out either by the lab prep person or by the students.

**Additional comment about these mixtures:** In this experiment, students must find a solvent in which to crystallize the compounds that they isolate. Some of the compounds in the above mixtures are found in other experiments in this textbook, along with instructions on how to crystallize them. If students find these procedures, the task of crystallizing the compounds in this experiment becomes relatively easy. Depending on your goals in this experiment, you may or may not want to assign compounds that are found in other experiments in the book. The compounds above that are found in the



book are: benzoin, benzil, 4-ethyl aminobenzoate, and fluorene.

#### OTHER CHEMICALS AND SUPPLIES PER 10 STUDENTS

The actual amounts needed are difficult to estimate, since students will be developing their own procedures. The suggested amounts should be more than sufficient for 10 students.

1M NaOH	200 mL
1M HCl	200 mL
6M NaOH	50 mL
6M HCl	50 mL
1M NaHCO <sub>3</sub>	100 mL
Saturated aqueous sodium chloride	200 mL
Diethyl ether	200 mL
95% Ethanol	100 mL
Methanol	50 mL
Isopropyl alcohol	50 mL
Acetone	50 mL
Hexane	50 mL
Toluene	50 mL
Methylene chloride	100 mL
Anhydrous sodium sulfate (granular)	25 g
Other solvents may be needed for crystallization	
Melting point capillary tubes	
Filter paper for Büchner or Hirsch funnels	

## TABLE OF CONTENTS

Preface	4
Equipping the Organic Chemistry Laboratory	7
Waste Management Guidelines	12
Laboratory Equipment and Supplies	17
Organic Laboratory Techniques Practical Exams	
Organic lab practical exam advice for instructors	21
Organic lab practical exam instructions for students	22
Organic lab practical exam instructions and report sheet for crystallization	23
Organic lab practical exam instructions and report sheet for extraction	24

### Chemicals and Supplies for Each Experiment Answers to Questions

Experiment 1	Solubility	25
Experiment 2	Crystallization	30
Experiment 3	Extraction	32
Experiment 4	A Separation and Purification Scheme	36
Experiment 5	Chromatography	39
Experiment 6	Simple and Fractional Distillation	44
Experiment 7	Infrared Spectroscopy and Boiling-Point Determination	47
Experiment 8	Acetylsalicylic acid	49
Experiment 9	Acetaminophen	51
Experiment 10	TLC of Analgesic Drugs	53
Experiment 11	Isolation of Caffeine	57
Experiment 12	Isopentyl Acetate (Banana Oil)	61
Experiment 13	Isolation of Eugenol from Cloves	63
Experiment 14	Spearmint and Caraway Oil: (+)- and (-)-Carvones	66
Experiment 15	Isolation of Chlorophyll and Carotenoid Pigments from Spinach	71
Experiment 16	Ethanol from Sucrose	73
Experiment 17	An Introduction to Molecular Modeling	75
Experiment 18	Computation Chemistry	75
Experiment 19	Reactivity of Some Alkyl Halides	76
Experiment 20	Nucleophilic Substitution Reactions: Competing Nucleophiles	80
Experiment 21	Synthesis of <i>n</i> -Butyl Bromide and <i>t</i> -Pentyl Chloride	85
Experiment 22	4-Methylcyclohexene	89
Experiment 23	Methyl Stearate from Methyl Oleate	91
Experiment 24	Gas Chromatographic Analysis of Gasolines	95
Experiment 25	Biodiesel	97
Experiment 26	Ethanol from Corn	100
Experiment 27	Chiral Reduction of Ethyl Acetoacetate; Optical Purity Determination	102
Experiment 28	Nitration of Aromatic Compounds Using a Recyclable Catalyst	105
Experiment 29	Reduction of Ketones Using Carrot Extract	106
Experiment 30	Resolution of $\alpha$ -Phenylethylamine and Determination of Optical Purity	107
Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol	112

Experiment 32	Multistep Reaction Sequence: The Conversion of Benzaldehyde to Benzilic Acid	116
Experiment 33	Triphenylmethanol and Benzoic Acid	122
Experiment 34	Aqueous-Based Organozinc Reactions	128
Experiment 35	Sonogashira coupling of Iodoaromatic Compounds with Alkynes	131
Experiment 36	Grubbs-Catalyzed Metathesis of Eugenol with <i>cis</i> -1,4-Butenediol	135
Experiment 37	The Aldol Condensation: Preparation of Benzalacetophenones (Chalcones)	137
Experiment 38	A Green Enantioselective Aldol Condensation Reaction	139
Experiment 39	Preparation of an $\alpha,\beta$ -Unsaturated Ketone <i>via</i> Michael and Aldol Condensation Reactions	141
Experiment 40	Preparation of Triphenylpyridines	142
Experiment 41	1,4-Diphenyl-1,3-Butadiene	143
Experiment 42	Relative Reactivities of Several Aromatic Compounds	146
Experiment 43	Nitration of Methyl Benzoate	148
Experiment 44	Benzocaine	150
Experiment 45	<i>N,N</i> -Diethyl- <i>m</i> -Toluamide: The Insect Repellent “OFF”	155
Experiment 46	Sulfa Drugs: Preparation of Sulfanilamide	156
Experiment 47	Preparation and Properties of Polymers: Polyester, Nylon, and Polystyrene	165
Experiment 48	Ring-opening Metathesis Polymerization using a Grubbs Catalyst	169
Experiment 49	The Diels-Alder Reaction of Cyclopentadiene with Maleic Anhydride	173
Experiment 50	Diels-Alder Reaction with Anthracene-9-methanol	174
Experiment 51	Photoreduction of Benzophenone and Rearrangement of Benzpinacol to Benzopinacolone	175
Experiment 52	Luminol	179
Experiment 53	Carbohydrates	180
Experiment 54	Analysis of a Diet Soft Drink by HPLC	190
Experiment 55	Identification of Unknowns	191
Experiment 56	Preparation of a C-4 or C-5 Acetate Ester	205
Experiment 57	Isolation of Essential Oils from Allspice, Cloves, Cumin, Caraway, Cinnamon, Fennel or Star Anise	207
Experiment 58	Competing Nucleophiles in $S_N1$ and $S_N2$ Reactions: Investigations Using 2-Pentanol and 3-Pentanol	210
Experiment 59	Friedel-Crafts Acylation	213
Experiment 60	The Analysis of Antihistamine Drugs by Gas Chromatography-Mass Spectrometry	225
Experiment 61	Carbonation of an Unknown Aromatic Halide	226
Experiment 62	The Aldehyde Enigma	229
Experiment 63	Synthesis of Substituted Chalcones: A Guided-Inquiry Experience	230
Experiment 64	Green Epoxidation of Chalcones	234
Experiment 65	Cyclopropanation of Chalcones	235
Experiment 66	Michael and Aldol Condensation Reactions	237

Experiment 67	Esterification Reactions of Vanillin: The Use of NMR to Determine a Structure	239
Experiment 68	An Oxidation Puzzle	240

### Answers to Problems in the Techniques Section

Technique 1	Laboratory Safety	241
Technique 2	The Laboratory Notebook, Calculations, and Laboratory Records	241
Technique 3	Laboratory Glassware: Care and Cleaning	241
Technique 4	How to Find Data for Compounds: Handbooks And catalogs	242
Technique 5	Measurement of Volume and Weight	
243		
Technique 6	Heating and Cooling Methods	244
Technique 7	Reaction Methods	245
Technique 8	Filtration	
247		
Technique 9	Physical Constants of Solids: The Melting Point	248
Technique 10	Solubility	248
Technique 11	Crystallization: Purification of Solids	249
Technique 12	Extractions, Separations, and Drying Agents	252
Technique 13	Physical Constants of Liquids: The Boiling Point and Density	255
Technique 14	Simple Distillation	256
Technique 15	Fractional Distillation, Azeotropes	257
Technique 16	Vacuum Distillation, Manometers	260
Technique 17	Sublimation	260
Technique 18	Steam Distillation	261
Technique 19	Column Chromatography	262
Technique 20	Thin-Layer Chromatography	264
Technique 21	High-Performance Liquid Chromatography (HPLC)	265
Technique 22	Gas Chromatography	266
Technique 23	Polarimetry	267
Technique 24	Refractometry	268
Technique 25	Infrared Spectroscopy	269
Technique 26	Nuclear Magnetic Resonance Spectroscopy	270
Technique 27	Carbon-13 Nuclear Magnetic Resonance Spectroscopy	271
Technique 28	Mass Spectrometry	271
Technique 29	Guide to the Chemical Literature	271
Correlation of Experiments with Lecture Topics		273

## PREFACE

*Introduction to Organic Laboratory Techniques: A Small Scale Approach (Third Edition)* continues our dedication to the teaching of the organic chemistry laboratory. As we have gathered experience with microscale techniques in the organic laboratory through the development of experiments and methods for the microscale versions of our textbook, we have discovered that students *can* learn to do careful work in the organic laboratory on a small scale. They do not have to consume large quantities of chemicals, and they do not have to work with very large flasks to learn the standard laboratory techniques. Furthermore, we recognize that many instructors do not wish to abandon the traditional-scale approach to their courses, and many colleges and universities cannot afford to convert all of their glassware to microscale.

In the traditional approach to teaching this subject, the quantities of chemicals used were on the order of 5-100 grams. The approach used in this textbook differs from the traditional laboratory in that nearly all of the experiments use smaller amounts of chemicals (1-10 grams). However, the glassware and methods used in this approach are identical to the glassware and methods used in traditional-scale experiments. The advantages of the small-scale approach include improved safety in the laboratory, reduced risk of fire and explosion, and reduced exposure to hazardous vapors. This approach decreases the need for hazardous waste disposal, leading to reduced contamination of the environment.

In this edition we have devoted considerable effort toward improving the safety of all of the experiments. Technique Chapter 1, "Laboratory Safety," places strong emphasis on the safe use and disposal of hazardous chemicals. We have included information on Material Safety Data Sheets (MSDS) and Right-to-Know laws. We have continued to update and improve instructions for the handling of waste products that are produced in the experiments. We recommend that virtually all waste, including aqueous solutions, be placed into appropriate waste containers.

The new experiments are listed in the Preface of the Textbook. These include several "green" chemistry experiments and some project-based experiments. In the latter experiments, students must either solve a significant problem or they must generate all or part of the experimental procedure. A Green Chemistry essay has been added and some of the experiments have been modified to make them more "green." We have significantly increased the number of unknowns listed in Appendix 1. We also offer an alternative way of solving unknowns using mainly spectroscopy.

We hope that this instructor's manual will assist you in preparing solutions, chemical reagents, supplies, and equipment necessary for each experiment that you choose to do. The lists of chemicals and equipment required for each experiment are based on the amount required for ten students. For chemicals, the amounts indicated include at least a 25% excess. At the end of the manual we have included a section that correlates the experiments with topics presented in standard organic lecture courses.

The time required for each experiment is given in laboratory periods. It is assumed that a laboratory period is about three hours in length. For laboratory periods that are either shorter or longer, appropriate adjustments must be made.

The technique chapters of the textbook are designed to stand independently from the experiments. You may have a favorite experiment that you like to do in your course. If this is the case, you can freely add your experiment and still take advantage of the technique chapters in the textbook. Since both standard-scale and microscale techniques are described in the technique chapters, you may even add some microscale experiments and still be able to refer your students to the appropriate sections in these chapters for information on each technique.

The publishers have made available videos to accompany the Textbook. These videos can be studied by students in advance of the laboratory session. They show the various steps for assembling an apparatus and carrying out a technique. See the Preface to the Textbook for more information. Students may purchase access to the website: [www.cengagebrain.com](http://www.cengagebrain.com)

A new feature of the Instructor's Manual is the inclusion of some laboratory practical exams that test students on two basic organic laboratory techniques: crystallization and extraction. You may find these exams to be a useful way of evaluating student technique. The idea is to have students perform techniques without the textbook and without looking over another student's shoulder for help!

If you encounter problems with any of the experiments in the Textbook or if you need help in setting up your laboratory, please contact us. We would also like to hear from you if you have any suggestions for improvements in techniques or in any of the experiments.

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## EQUIPPING THE ORGANIC CHEMISTRY LABORATORY

This section includes some suggestions for equipping a macroscale laboratory using a reduced scale approach. In addition, this section provides information for all instructors on some of the laboratory requirements for doing the experiments found in the textbook.

Although some experiments involve microscale techniques, they do not require special equipment. These experiments can be conducted with flasks, beakers, test tubes and other simple equipment.

### Dispensing and Measuring Liquids

Where possible liquid reagents and solvents should be stored in a hood in small glass or plastic bottles. To avoid waste, the exact amount of liquid should be transferred to the student's container by one of the methods described below. Students should not pour an approximate amount of liquid into one container and then measure the required volume, leaving some excess liquid behind which must be discarded.

When accuracy is not important, one-piece polyethylene transfer pipets or calibrated Pasteur pipets shown in Technique 5, Figures 5.6B and 5.6C, provide an efficient method for delivering liquids, especially solvents to be used for extractions or crystallizations. We tape a test tube to the bottle containing the liquid in order to hold the pipet. It is easy for students to use one of these pipets to transfer liquid to a graduated cylinder for more careful measurement. If one of these techniques is used for measuring a limiting reagent, students need to be strongly encouraged to weigh the liquid following transfer.

Dispensing pumps (Technique 5, Figure 5.2) may be used to deliver larger amounts (more than 0.5 mL) of liquid. They are especially useful in dispensing solvents or non-limiting reagents. *Care must be taken to ensure that the tip is filled with liquid and that no air bubbles are observed in the tubing.* These units easily lose their "prime" especially with more volatile solvents. We have observed that some solvents swell the plastic plunger such that it can not be pulled up easily. If this happens to you, remove the solvent from the unit. After drying out thoroughly, the unit can be used again (with another solvent!). We have found that waste has been significantly reduced with dispensing pumps. They can be set individually for a particular solvent. Students simply raise the pump and dispense exactly the right amount of solvent thus eliminating waste.

If you plan to do some microscale experiments, it is useful to have available several adjustable 100-1000  $\mu\text{L}$  automatic pipets for dispensing very small amounts (less than 1 mL) of liquids used as limiting reagents. They are also useful for measuring densities of liquids. The automatic pipet is very accurate



with aqueous solutions, but it is not as accurate with organic liquids. With all limiting reagents, it will be necessary to obtain the weight in order to determine accurately the amount of substance used. Since most of the errors that occur in the laboratory may be attributed to "sloppy" transfers, you should give a thorough demonstration of how to use the automatic pipet. They should be cautioned about not allowing the plunger to snap back rapidly. The automatic pipet should be placed near the appropriate reagent and supported in a vertical holding device. Automatic pipets should never be used with corrosive or caustic liquids.

A graduated 1 or 2-mL one-piece polyethylene pipet should be used to dispense small amounts of corrosive or caustic liquids, such as sulfuric acid, hydrochloric acid, or sodium hydroxide. Alternatively, a graduated pipet and pipet pump can be used. When using graduated pipets, we prefer the pipet pump shown in Technique 5, Figure 5.3B in the Textbook. The top of the pipet fits more securely in a pipet pump of this style than in a pump similar to the one shown in Figure 5.3A. To avoid contamination of the stock reagent and to minimize waste, we provide a graduated pipet and pipet pump with the reagent for community use. A pint bottle is a convenient container for holding the pipet when it is not in use.

For most procedures one of the above methods will work well to deliver the volumes of liquid required in the experiments in the Textbook. Even when more than 2 mL of liquid is required, we prefer to use one of the pipet methods for transferring the liquid, rather than having the students pour an approximate amount of liquid from the original container into their own.

The instructor should place the appropriate measuring device with each reagent and solvent. In most cases, the device will be a one-piece polyethylene pipet, a graduated pipet with a pipet pump, or dispensing pump. *The person who prepares the laboratory for an experiment should read the procedure in order to determine which device is appropriate.*

### **Dispensing Solids and Weighing Reagents**

Four top-loading balances that read to 0.01 or 0.001 gram are required for a class of 20 students. The balances should be used with draft shields to improve accuracy. It is convenient to store solids in containers near the balances. To avoid the possibility of contamination, we provide a community spatula with the reagent.

### **Evaporating Solvents**

Ideally, students should remove solvent by heating at a low temperature and by directing a stream of nitrogen or air through a Pasteur pipet into a flask in order to evaporate a solvent. This procedure gives a student complete control of

the evaporation process, but only works well in a laboratory with many individual hoods. In laboratories where there are only a few hoods it becomes necessary to have a permanent community evaporation station assembled in the hood. A community station may consist of aluminum heating blocks on hot plates (see Ludwig, S.N. "The Use of Solid Aluminum Heat Transfer Devices in Organic Chemistry Laboratory Instruction and Research," *Journal of Chemical Education*, 66 (1989): 77). Hot plates with containers filled with small pebbles or sand may also be used to heat the samples. The station is equipped with multiple outlets using Y-connectors and screw clamps with flexible tubing. In this way, several students can evaporate solvents using one air or nitrogen source.

The N-EVAP evaporator is a commercially available unit which is useful for larger classes. Several commercial models are available from Organomation Associates, Inc., 266 River Road West, Berlin, MA 01503-1699. Phone: (888) 838-7300. These units consist of an electrically heated water-bath container and a gas manifold equipped with blunt-end, stainless-steel needles. The holders are made with 6, 12, 24, 36 or 45 positions and will accept a variety of containers including test tubes and Erlenmeyer flasks. The 12 position model provides an exceptionally efficient means of evaporating solvents in a lab with 20 students.

### **Rotary Evaporators**

It is becoming more common to equip the laboratory with rotary evaporators to avoid some environmental problems with evaporating solvents in the hood. We suggest systems that have coolers attached to the evaporators to improve solvent recovery thereby making the laboratory a greener environment for students and instructors. You may want to continue evaporating small amounts of solvents, approximate 10 mL or less, as indicated in the above section. Use a rotary evaporator for larger amounts, about 25 mL or more. The use of a rotary evaporator can create a large student backup unless reserved for evaporating large volumes of solvent.

A "rotacool" model rotary evaporator is available from Heidolph-Brinkmann for about \$10,000. It is equipped with vacuum pump, condensation cooler and rotacool circulating chiller. This is a very efficient system that does a great job of collecting even the most volatile solvents. If you can afford to buy a rotary evaporator with a cooler, you won't regret it!

### **Heating Mantles and Hot Plates**

For most applications involving reflux and distillation, we recommend that you use a heating mantle equipped with a temperature controller, such as the one shown on page 610 of the Textbook (Thermowell mantle with Powermite controller). These mantles employ a ceramic heating shell with electric heating coils embedded within the shell. The ceramic shell protects the mantle from

damage caused by chemical spills. A 100-mL mantle will heat 25, 50, and 100 mL flasks, and should be sufficient for most experiments in this Textbook.

Hot plates are very useful for heating solvents required for crystallization. In some cases, reaction mixtures need to be stirred as well as heated. For this reason, we suggest purchasing combination stirrer/hot plate units. If the hot plate is used for refluxing a mixture in a round-bottom flask, it is best to use a hot plate with an aluminum top and an aluminum block as a heating source. *You should not use hot plates with ceramic tops unless you are certain that the tops will withstand high temperatures without cracking.* The holes that have been drilled in the aluminum block easily support and accommodate smaller round-bottom flasks and a thermometer. The aluminum block is especially useful when temperatures above 200 °C are required. The stirrer/hot plate units should provide a temperature range of about 60 to above 250 °C. Reaction mixtures which boil at less than about 100°C can usually be heated under reflux with only a hot plate without an aluminum block.

*If you wish to monitor the temperature of aluminum blocks, we recommend that you not employ mercury thermometers, especially those inserted in the aluminum blocks.* Glass thermometers break too easily. We suggest that you use metal dial thermometers rather than mercury thermometers. They are sufficiently accurate for monitoring the temperature of the aluminum blocks.

### **Melting Point Apparatus**

Four electrically-heated melting point apparatus should be provided for a class of 20 students (Mel-Temp or Electrothermal). A Thomas-Hoover Uni-Melt apparatus should be considered if the class is determining micro boiling points. This device has a rapid temperature response. The Mel-Temp or Electrothermal units are less expensive and more serviceable alternative, but the temperature response is not as rapid and micro boiling point determinations may be more difficult to perform. You should try several different melting point units before buying them to see which one is the best for you.

### **Gas Chromatographs**

At least two gas chromatographs should be provided for every 20 students, if students are expected to perform their own injections. Conditions for running samples on the Gow-Mac 69-350 or Hewlett Packard 5890 gas chromatographs are given in this Textbook. If students are expected to collect samples from a chromatograph, Gow-Mac models 69-350 or 580 can be equipped with a convenient sample collection device. Gow-Mac instruments should be equipped with an 8-foot column packed with Carbowax 20M and an 8-foot column containing 20% DC-710. Columns required for the Hewlett Packard chromatographs are given in the Textbook or in this manual.

## **Spectrometers/Polarimeters**

The laboratory should have at least one FT-infrared spectrometer for every 20 students. The FT-infrared instruments increase the through-put of students in the laboratory. If you can afford it, an FT instrument with ATR (attenuated total reflectance) accessory is highly recommended. Use of this accessory makes analysis of solids totally trivial! Otherwise, you will need to make do with determining a spectrum using the dry film method or with a KBr pellet. For conventional IR spectroscopy we have available two of the hand press units for solids. NMR spectroscopy is important in the modern organic chemistry laboratory and you should make this available to your students, if possible. The availability of both proton and carbon NMR increases student interest especially when solving unknowns. The laboratory should be equipped with one polarimeter for use by the class.

## **Centrifuges**

Several experiments or experimental techniques require the use of a centrifuge. They are very useful for breaking emulsions. One or two "clinical" centrifuges are adequate for 20 students. They should hold 15 mL centrifuge tubes.

## **Vortex Mixer**

Extractions can be carried out conveniently in a 15-mL centrifuge tube. Although the tube can be stoppered and shaken to mix the layers, mixing can be accomplished efficiently with a vortex mixer. This method eliminates the problems of pressure buildup and leakage. One mixer easily serves 20 students.

## **Syringes and Rubber Septa**

In some experiments a syringe is used to add reagents to a reaction mixture. A 1 or 2-mL glass or plastic syringe should be provided to allow use with organic solvents without contamination occurring. The plastic syringes are readily available and are much cheaper and durable than glass syringes. Disposable hypodermic needles may be used for most applications. We recommend 1 1/2- or 2-inch needles (21 or 22 gauge). When the experiment is completed, they should be saved for reuse.

## **Plastic Joint Clips ("Blue Clips")**

It is essential that the lab be supplied with plastic joint clips to secure the 19/22 ground glass equipment (Technique 7, Figure 7.3). Breakage is dramatically reduced when they are used to secure equipment. At least 3 should be included in each laboratory locker.

## **Monometers**

Several monometers should be available in the laboratory for use in vacuum distillations. A simple U-tube manometer is shown in Technique 16, Figure 16.9 of the Textbook.

## **Sublimation Equipment**

It is suggested that the laboratory be supplied with microscale sublimation equipment such as that shown in Technique 17, Figure 17.2 A or B. This apparatus is equipped with 14/10 joints and can be used to perform all sublimation procedures described in this Textbook. We suggest 5 complete units as part of the community equipment.

## **Washing Glassware and Equipment**

A plastic dishpan provides a convenient container in which to soak and wash dirty glassware. You may want to consider buying an ultrasound cleaner (sonicator) cleaner for the laboratory. Especially dirty glassware can often be effectively cleaned with one of these devices. There are some disadvantages: they are noisy and students often forget to retrieve their glassware.

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## **WASTE MANAGEMENT GUIDELINES**

These guidelines are intended for schools where the chemistry department is responsible for its own waste management. Although most of this information should apply to your situation, specific waste management practices will depend on the size of your program, other hazardous wastes generated on your campus, and state and local regulations. This information may not cover everything you need to know; however, it can help you get started or may provide some new ideas that will improve your existing waste management program.

To get started, you need to determine who regulates hazardous waste in your state. The U.S. Environmental Protection Agency (EPA) has ultimate responsibility for regulating hazardous waste in all 50 states plus the District of Columbia, Puerto Rico, and the Virgin Islands. Many states have been delegated the authority to regulate their own hazardous waste by the EPA. States which have the authority to regulate their own hazardous waste must have regulations that are as strict as the federal laws. If you operate in a state that has a hazardous waste regulating agency, then you must follow the regulations for your state rather than the federal regulations. The EPA has a home page (<http://www.epa.gov>) and ten regional offices that can help you find out if there is a state program in your area.

Region	States in the Region	Telephone Number
1	ME, NH, VT, MA, RI, CT	617-565-3423
2	NY,NJ,PR,VI	212-637-5000
3	PA,DE,DC,MD,VA,WV	800-438-2474
4	KY, TN,NC,SC,MS,AL,GA,FL	800-241-1754
5	MN,WI,IL,MI,IN,OH	800-621-8431
6	NM,TX,OK,AR,LA	214-665-2200
7	NE,KS,IA,MO	913-551-7000
8	MT,ND,WY,SD,UT,CO	800-227-8917
9	CA,NV,AZ,HI	415-744-1500
10	WA,OR,ID,AK	800-424-4372

You must obtain a Resource Conservation and Recovery Act (RCRA) site identification number if your campus does not already have one. This number identifies your site and all the waste generated there. This identification number is obtained through the agency that regulates hazardous waste in your state. You must supply this number to waste disposal firms when you ship waste off site, and it identifies your site on your annual hazardous waste report.

We collect all chemical waste generated in student laboratories, and we make a serious attempt to teach students that waste management is important. Therefore, students do not dispose of any chemical materials down the drain or in the trash. We find that labeling waste containers with the experiment name and a list of the chemicals that should be placed in the container greatly increases the chances that students will put wastes into the correct containers. We will use our "Isolation of Caffeine from Tea" experiment to give an example. The students generate an aqueous layer contaminated with methylene chloride. Unfortunately, the small amount of methylene chloride that dissolves in water renders the entire aqueous solution hazardous waste. The waste bottle would be labeled as follows:

Isolation of Caffeine from Tea  
Hazardous Waste  
Aqueous layer contaminated w/ methylene chloride  
Suspect Human Carcinogen

Note that "Hazardous Waste" must be included on the label, as required by law. Also, the primary hazard of the waste, the last entry on this label, is required by law. Refer to the material safety data sheet (MSDS) for the primary or most hazardous constituent of the waste to determine an appropriate warning.

Wastes collected from student labs are consolidated by waste type or treated, if it is safe and legal to do so. We find that all wastes we generate fit into one of the following categories:

**Nonhazardous Solids** such as paper, tea bags, and corks are disposed of with the ordinary trash.

**Broken Glassware** is disposed of in a container designated for this purpose. When the container is full, it is packaged securely and disposed of with the ordinary trash.

**Organic Solids** with halogens are consolidated with our halogenated organic solvents, and those without halogens are consolidated with our non-halogenated organic solvents.

**Inorganic Solids** such as alumina and drying agents are accumulated together and disposed of as hazardous waste.

**Non-Halogenated Organic Solvents** such as alcohols, toluene, hexane, and diethyl ether are disposed of as hazardous waste. Intentional evaporation or drain disposal of these materials is illegal. However, evaporation of these solvents as part of the workup in an experiment *is legal*, since the material is not yet waste and the evaporation is a legitimate part of the procedure.

**Halogenated Organic Solvents** such as dichloromethane (methylene chloride), chloroform, and carbon tetrachloride are disposed of as hazardous waste. Intentional evaporation or drain disposal of these materials is illegal. However, evaporation of these solvents as part of the workup in an experiment is legal, since the material is not yet waste and the evaporation is a legitimate part of the procedure.

**Inorganic Acids** without heavy metals or halogenated solvent contamination are neutralized and discharged to the sewer. A log of these treatment activities is maintained.

**Inorganic Bases** without heavy metals or halogenated solvent contamination are neutralized and discharged to the sewer. A log of these treatment activities is maintained.

**Aqueous Solutions Contaminated with Halogenated Solvents** are disposed of as hazardous waste. Intentional evaporation or drain disposal of these materials is illegal.

**Aqueous Solutions with Heavy Metals** may either be treated to remove the heavy metal or disposed of as hazardous waste. If you treat these wastes, you

must test the pH and metal levels before discharge of the treated waste to the sewer to confirm successful treatment. In most states, the water may be legally evaporated to reduce the waste volume, and the remaining metal sludge treated as hazardous waste. The original amount of waste including water must be reported on your annual hazardous waste report.

Most states allow some forms of treatment by the waste generator without the need for special permits. Before you treat a waste you must make sure that your regulators allow the treatment practice. Prior to waste treatment, all of the constituents of the waste, such as heavy metal, solvent content, and low or high pH must be determined. You also need to contact your local sewer district to find out if they have limits on what may be discharged to their system. In many cases a material may not be considered hazardous waste by the EPA or a State Environmental Regulatory Agency, but is restricted from disposal to the sanitary sewer. Treatment and discharge of waste is not recommended if you are on a septic system.

If you elect to treat waste, you are required to test the treated waste for each constituent that made the untreated waste hazardous before you discharge it to the sewer. For example, if you treated an aqueous waste that contained silver, barium, and chromium by precipitating the metals, you would have to check the barium, silver, and chromium levels of the treated waste before discharge to the sewer. Because of this burden, we limit our treatment to neutralization of non-heavy-metal-bearing aqueous wastes that have a low or high pH. Also, remember that intentional evaporation of solvents, and dilution and drain disposal of hazardous wastes not only violates EPA regulations but is also harmful to the environment.

Maintain a log of all wastes treated on site. At a minimum this log should include: a description of the waste, the amount of waste treated, the name of the person treating the waste, the treatment method, and the treatment date. Hazardous wastes that are treated on site must be "counted" and reported on your annual hazardous waste report.

Maintain a waste generation log, which includes the total amount of waste treated and generated. At a minimum this log should include: date, description of the waste, amount, and identity of generator. This log must be included in the annual hazardous waste report that is described below.

We recommend that you limit the amount of waste you accumulate not only to simplify your regulatory requirements, but also to minimize the risk of leaks and spills. In most states, by accumulating less than 55 gallons of each type of waste you simplify the storage and record keeping requirements associated with waste storage. Larger waste accumulation areas must be inspected weekly and equipped with emergency response supplies. Waste must be stored in a secure



(locked) area, segregated by type, capped when not in use, and provided with secondary containment (several bottles of the same type of waste can be placed in a tray or individual bottles may be stored in pails). We recommend hazardous waste shipments at intervals as dictated by your operation to limit the amount of waste stored.

At smaller schools you may find that annual waste shipments are a good management practice. At larger schools shipments each semester, quarterly, or even monthly may be required. At Western Washington University, the motor pool and the physical plant operations generate far more waste than the chemistry department. You may find it worthwhile to coordinate your waste disposal with other departments or operations within your school.

If you elect to ship your own waste, you must learn and follow all of the mandated procedures. As a simpler alternative, there are private contractors who will consolidate, treat, package, and ship your waste for you. However, this alternative does not keep you from having to keep good records.

Contact your local fire department to find out about requirements concerning hazardous material storage. Often these agencies require chemical inventory and storage information about your site so that they can respond appropriately in the event of an emergency.

Establish written hazardous waste management procedures for your campus and communicate these procedures to those involved with waste handling. Also, assure that the person on your campus who signs manifests has received Department of Transportation training on hazardous material shipping.

Retain copies of all manifests and land disposal restriction certifications, sometimes known as "land bans", of waste sent off site for disposal. Manifests can be thought of as the shipping papers for hazardous waste shipments. Land disposal restriction certifications accompany manifests and document disposal and treatment restrictions based on the characteristics of the waste being sent for disposal.

Complete an annual hazardous waste report for all hazardous waste activities on your campus. This report is required by law and must be submitted to the agency that regulates hazardous waste in your area. The report summarizes your hazardous waste activities for the previous calendar year. To complete this report you will need: your RCRA site identification number, copies of all manifests for the past year and your treatment and generation logs.

## LABORATORY EQUIPMENT AND SUPPLIES

- A. Individual student glassware and equipment contained in the locker
1. Organic Chemistry Kit (19/22 joints)
    - 500 mL 3-Neck round bottom flask
    - 250 mL Round-bottom flask with side tubulation
    - 25, 50, and 100 mL Round-bottom boiling flasks
    - Stoppers (2)
    - Thermometer adapter
    - Rubber thermometer holder
    - Bleed tube (ebulliator tube)
    - Claisen head
    - Distilling head
    - Vacuum adapter
    - Condenser
    - Fractionating column (packed with steel wool)
    - 125 mL Separatory funnel, Teflon stopcock
  2. Other individual glassware
    - Beakers; 50 mL (2), 100 mL (2), 250 mL (2), 400 mL (1)
    - Graduated cylinders; 10 mL and 100 mL
    - Drying tubes (2)
    - Evaporating dish, size 00
    - Erlenmeyer flasks; 25 mL (2), 50 mL (2), 125 mL (1), 250 mL (1), 500 mL (1)
    - Filter flask; 125 mL
    - Aspirator trap bottle (part of community equipment)
    - Conical funnel (stemless), 50 mm
    - Powder funnel
    - Büchner funnel; size 0
    - Büchner funnel; size 2A (optional)
    - Hirsch funnel, plastic preferred
    - Test tubes or culture tubes; 10 x 75 mm (6); 16 x 100 mm (5); 15 x 125 mm (3)
    - Thermometer, non-mercury; 360°
    - Watch glasses; 50 mm (2) and 100 mm (2)
    - Small ground glass bottles for submitting liquid samples (2)
    - Small vials for submitting solid samples to the instructor (2)
    - 4 oz. Screw cap bottles (2)
    - Centrifuge tubes, glass, screw cap with Teflon liner; 15 mL (2) or Centrifuge tubes, polypropylene, screw cap, 15 mL (2), VWR 20171-010

Centrifuge tubes, plastic (no screw cap), 15 mL (2)  
2 mL Glass or plastic syringe (Luer lock and Teflon plunger  
tip preferred)  
Needles to fit syringe

3. Individual equipment

Plastic joint clips to fit 19/22 joints (3)  
Condenser clamp, 3-prong with holder  
Utility clamps (2)  
Screw clamp  
Dropper bulbs, latex, 2 mL (4)  
Rubber policeman  
Stirring rod  
Neoprene adapters, nos. 2, 3, and 4  
Rubber serum bottle stopper to fit over 19/22 joint  
Brushes, small and large  
Microburner and chimney (optional)  
Wire gauze (optional)  
Test tube holder  
Spatula  
Stir bar  
Test tube block  
Rubber tubing  
Pressure tubing  
Scorer or file  
Safety glasses  
Aluminum blocks (optional)  
Metal thermometer to measure temperature when accuracy  
is not required (optional)

B. Community Equipment

The following equipment should be available in the laboratory or nearby.  
(Numbers in parentheses indicate requirements for 20 students)

Hot plate/stirrer (20)  
Ring stands (40)  
Iron rings to hold separatory funnels (20)  
Heating mantles with controllers, two sizes (20 each)  
Wooden blocks to support glassware  
Automatic pipets; 100 - 1000  $\mu$ L (optional)  
Dispensing pumps; 2 and 5 mL sizes (optional)  
Pipet pumps (optional)  
Sponges (10)  
Screw cap bottles for chromatography (40)

Ice buckets (5)  
Filter flasks; 500 mL (optional)  
Separatory funnels, 500 mL (optional)  
Microscale sublimation apparatus, with 14/10 joints (optional, 5)  
Melting point apparatus (4)  
Top-loading balances with draft shields, 0.001 g (4)  
Refractometer (1)  
Polarimeter (1)  
Centrifuges (2)  
Gas Chromatographs, Gow-Mac, model 69-350  
Equipment required for optional collection of liquids from Gow-Mac chromatographs: metal adapter for collection of samples (2), 1 mL conical reaction vials with 5/5 joint (2) and collection tubes with 5/5 joint (2)  
Vortex mixer (optional, 1)  
Infrared Spectrometer (2)  
Potassium bromide hand press (2)  
Salt plates for infrared spectroscopy (2 pairs)  
NMR spectrometer  
Ovens (2)  
Glass working bench with burners and supply of glass tubing  
Matches or gas lighters for burners  
Scissors (2)  
Handbook of Chemistry and Physics (mounted on board)  
Handbook of Tables for Organic Compound Identification  
Merck Index (mounted on board)  
Rotary Evaporators (recommended)

## C. Community Supplies

### 1. Chemicals and supplies

The following materials should be available at all times on the side shelves or desks.

Gloves, disposable  
Pasteur pipets; 5 3/4-inch and 9-inch sizes  
Graduated one-piece polyethylene transfer pipets  
Applicator sticks  
Decolorizing carbon, pelletized and powdered  
Sample vials for submitting products  
Filter paper to fit Büchner and Hirsch funnels  
Filter paper for gravity filtrations  
Stopcock grease  
Glycerol in dropper bottle  
Boiling stones, inert such as corundum

Corks, assorted  
pH paper  
Red and blue litmus paper  
Copper wire  
Capillary tubes, sealed on one end for melting points  
Capillary tubes, open on both ends for TLC chromatography  
Glass wool  
Cotton  
Labeling tape  
Soap  
Celite (Filter Aid)  
Rock salt  
Anhydrous magnesium sulfate (powdered)  
Anhydrous calcium chloride (4-20 mesh)  
Anhydrous sodium sulfate (granular)

2. Acids and bases  
The solutions and reagents should be placed in one area of the laboratory on a chemically resistant surface.  
Acids need to be separated from bases.  
Sodium hydroxide solutions; 5%  
Sodium bicarbonate solution, 5%  
Hydrochloric acid solutions; concentrated and 5%  
Sodium chloride solution, saturated  
Nitric acid, concentrated  
Ammonium hydroxide, concentrated  
Sulfuric acid, concentrated

3. Common solvents  
These solvents should be placed in a hood during use and stored in a special cabinet at other times (see below).

Hexane  
Petroleum ether (various boiling ranges)  
Acetone  
Methanol  
Toluene  
Methylene chloride  
95% Ethanol (5 % water)  
Diethyl ether  
Carbon tetrachloride and methylene chloride, kept in a hood near the infrared spectrometer, with a Pasteur pipet attached.

4. Test reagent shelves  
We usually keep the reagents and known compounds for

Experiment 55 (qualitative analysis) in a designated area of the laboratory at all times. The noxious chemicals are kept in a hood.

D. Safety

Storage cabinet for flammable organic solvents  
Fire extinguishers  
Eye wash fountains  
Showers  
Fire blankets  
Solvent waste containers (see individual experiment)

E. Safety References and MSDS sheets (Technique 1)

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## ORGANIC LABORATORY TECHNIQUES PRACTICAL EXAMS

Some instructors may desire to test students on two very basic organic laboratory techniques: crystallization and extraction. We call this a laboratory practical exam. With the technique exam, you can determine who really has the best technique and who the leaders and followers are in your laboratory course. Students do their work without a textbook in front of them. They are prohibited from looking at what other students are doing.

### Organic lab practical exam advice for instructors

You may desire to give this test to students at the end of the first organic laboratory course. Each student will be required to purify a compound either by acid-base extraction or crystallization. These students have completed Experiment 2 (Crystallization) and Experiment 3 (Extraction). They have also completed Experiment 4 (A Separation and Purification Scheme).

Several days before the exam they are given the handout titled “Organic Lab Practical Exam Instructions for Students”. At this point they don’t know if they will be doing an extraction or crystallization. Therefore, they must prepare for both possibilities. On the test day, they are given either the sheet titled “Extraction” or “Crystallization” and a sample of an impure compound. They have three hour to complete this assignment, but most students are done after two hours.

We make up the samples for crystallization by mixing thoroughly 12 g of urea and 0.53 g of trans-cinnamic acid. Each student is given 1.0 g of the mixture. We don’t tell them the actual weight and they are told not to weigh it. For the extraction, dissolve 3.0 g of fluorene and 0.75 g of benzoic acid in 60

mL of methylene chloride. Each student is given 4.0 mL of this solution. Students should use a centrifuge tube to perform the extraction procedure.

Because of the way this test is designed, students do not know how much of the compound they start with or the melting point. Therefore, it is impossible for them to change their data to get a better grade.

### **Organic lab practical exam instructions for students**

For this lab practical exam you will be given an impure sample of a compound to be purified either by acid/base extraction or crystallization. You are to carry out this task without the aid of other students or any written or electronic resources.

When you arrive in lab, you will be given an impure sample and an instruction sheet that will inform you whether the compound is to be purified by acid/base extraction or crystallization. You will be told the structure of the compound, but not the melting point.

**Extraction.** On the instruction sheet for the acid/base extraction purification you will be told the structure of the neutral compound, the approximate weight of the compound, and what organic solvent it is dissolved in (the compound and impurity will already be dissolved in an appropriate solvent to do the extraction). The volume of this solution will be 4.0 mL. Therefore, you should use a centrifuge tube to perform the extraction. You will also be told whether the impurity is an organic acid or base (amine) and how much 1M NaOH or 1 M HCl you should use for the extraction step. You do not have to isolate the acid or base impurity. You must decide whether to use NaOH or HCl to extract the impurity.

Your goal will be to separate the neutral compound from the acid or base impurity, isolate it in a pure form, and determine the weight recovered and the melting point. You will **not** know exactly how much of the neutral compound is in the original sample or the melting point.

**Crystallization.** For the crystallization purification, you will be told the structure of the impure compound and the approximate weight of the sample. You will also be given three suggestions as to which solvent could be used for crystallization. One of these solvents will be suitable for crystallizing this compound. The compound will be too soluble in one of them and not soluble enough in the third solvent. Your goal will be to determine the best solvent, purify your sample by crystallization, and determine the weight recovered and melting point. You will **not** know the exact amount of the compound that you start with or the literature melting point of the compound

**General comments and grading procedures.** You may **not** use your textbook, handbooks, or any other resources (written or electronic) while completing this exercise. You may not talk to other students and you should refrain from looking at the set-ups used by other students. This exam will be worth 20 points and will be based on the weight recovered of the purified material and the purity based on melting point. You will also be graded on how your sample looks and whether or not the sample is dry. You may have a second sample, but it will cost you 2 points. If you take a third sample, this will cost you an additional 3 points.

### Organic lab practical exam instructions and report sheet for crystallization

\_\_\_\_\_ Name

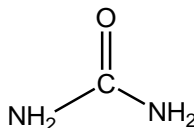
\_\_\_\_\_ Tube Number

You may **not** use your textbook, handbooks, or any other written material while completing this exercise. You may not use any electronic resources. However, you may take down notes on this sheet of paper. You may not talk to other students during this exercise and you should refrain from looking at the set-ups used by other students. If you have questions during the lab, **ask your instructor.**

There will be a 2-point subjective grade. The subjective grade will be determined by the instructor's assessment of such things as whether or not you talk to other students or if you obviously look at what other students are doing. You may have a second sample, but it will cost you 2 points.

**Instructions.** You will be given a sample of impure urea that has a weight between 0.8 – 1.2 g. **Do not weigh the sample.** You should crystallize the entire sample. **Write down the number of the tube and your name in the space above.**

The structure of urea is:



Urea can be crystallized from one of the three following solvents: 95% ethyl alcohol, water, or hexane. You may determine which solvent to use either by experimentation or by making an educated guess.

After crystallizing the sample of impure urea, determine the weight and melting point of the dry crystals. The melting point should be between 120 - 140° C. Turn in this sheet and your sample in a vial labeled as follows: your name, the name of the compound, weight of sample, and melting point. You



will be graded on the recovery and purity, as determined by appearance and melting point. Record the recovery and melting point below:

Recovered weight of sample \_\_\_\_\_

Melting point of sample \_\_\_\_\_

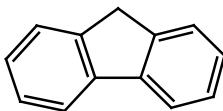
### Organic lab practical exam instructions and report sheet for extraction

\_\_\_\_\_ Name

You may **not** use your textbook, handbooks, or any other written material while completing this exercise. You may not use any electronic resources. However, you may take down notes on this sheet of paper. You may not talk to other students during this exercise and you should refrain from looking at the set-ups used by other students. If you have questions during the lab, **ask your instructor.**

There will be a 2-point subjective grade. The subjective grade will be determined by the instructor's assessment of such things as whether or not you talk to other students or if you obviously look at what other students are doing. You may have a second sample, but it will cost you 2 points.

**Instructions.** You will be given 4.0 mL of a methylene chloride solution containing fluorene (a neutral compound) and an **acid** impurity. The weight of fluorene will be between 0.15 - 0.25 g. Your goal is to isolate the neutral compound and determine its weight and melting point. To remove the impurity, you should extract the methylene chloride solution with two 2-mL portions of either 1.0M NaOH or 1.0M HCl. After drying the organic layer, evaporate off the methylene chloride. Weigh the solid and determine the melting point. The melting point should be between 105-125 °C.



Fluorene:

Turn in this sheet and your sample in a vial labeled as follows: your name, the name of the compound, weight of sample, and mp. You will be graded on the recovery and purity, as determined by appearance and melting point. Record the recovery and melting point below

Recovered weight of sample \_\_\_\_\_

Melting point of sample \_\_\_\_\_

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## Experiment 1

### SOLUBILITY

TIME ESTIMATE: Parts A-D (3 hours); Part E (1 hour); Part F (1 hour)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### Part A

Benzophenone (Grind up the flakes into a powder)	0.5 g
Malonic acid	0.5 g
Biphenyl	0.5 g
Methyl alcohol	40 mL
Hexane	40 mL

#### Part B

Methyl alcohol	13 mL
1-Butanol	13 mL
1-Octanol	13 mL
Hexane	40 mL

#### Part C

Ethyl alcohol	13 mL
Diethyl ether	13 mL
Methylene chloride	25 mL
Hexane	13 mL

#### Part D

Benzoic acid	1.2 g
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Ethyl 4-aminobenzoate	1.2 g
1M NaOH	25 mL
1M HCl	25 mL
6M NaOH	6 mL
6M HCl	6 mL
Litmus paper	

#### Part E

- |         |       |
|---------|-------|
| Acetone | 25 mL |
| Hexane  | 13 mL |
- We give each pair of students two mixtures. Each mixture contains 2 mL of each liquid and about 0.1 g of the dissolved solid. There are many possible combinations of substances to use. The mixtures we have used contain one of the following combinations of solid and liquids (the solid is listed first): fluorene, methylene chloride, water; triphenylmethanol, diethyl ether, water; salicylic acid, methylene chloride, 1M NaOH; ethyl 4-aminobenzoate, diethyl ether, 1M HCl; naphthalene, hexane, water; benzoic acid, diethyl ether, 1M NaOH; *p*-aminoacetophenone, methylene chloride, 1M HCl. The mixtures containing ethyl 4-aminobenzoate and *p*-aminoacetophenone should be made up fresh on the same day as the lab, otherwise the solutions become colored.
- |                              |       |
|------------------------------|-------|
| Tetraphenylcyclopentadienone | 0.3 g |
| Methyl alcohol               | 13mL  |

#### Part F

Self-Assembled Monolayer Demonstration Kit  
 Available from Asemblon, Inc., 15340 N.E. 92nd St., Suite B,  
 Redmond, WA 98052; phone 425-558-5100; [asemblon.com](http://asemblon.com).  
 Instructions for filling the Asemblon pen with the thiol are provided  
 with the kit.

If done as a demonstration, one kit is sufficient. Otherwise one kit for every 4 students works well.

Butane to fill the torch for erasing the gold slide

Methyl alcohol 10 mL

Acetone 10 mL

**CAS Registry numbers:**

Benzophenone	119-61-9
Malonic acid	141-82-2
Biphenyl	92-52-4
Hexanes	73513-42-5
Methyl alcohol	67-56-1
1-Butanol	71-36-3
1-Octanol	111-87-5
Ethyl alcohol (ethanol), 95%	64-17-5
Diethyl ether	60-29-7
Methylene chloride	75-09-2
Benzoic acid	65-85-0
Ethyl 4-aminobenzoate	94-09-7
Acetone	67-64-1
Fluorene	86-73-7
Triphenylmethanol	76-84-6
Salicylic acid	69-72-7
Naphthalene	91-20-3
<i>p</i> -Aminoacetophenone	99-92-3
Tetraphenylcyclopentadienone	479-33-4

**SPECIAL NOTES**

In Part A, it is very important that students follow the instructions carefully for stirring the mixtures. The bigger spatula shown in Figure 12.10 on page 697 of the Textbook is very effective in achieving consistent stirring from one mixture to another.

We have found that some students have difficulty performing Critical Thinking Application #2 (p. 9 of the Text) on the same day that they complete the rest of this experiment. Many students need time to assimilate the material in this experiment before they can complete this exercise successfully. One approach is to assign Critical Thinking Applications from several technique experiments (for example, Experiments 1 - 3) on a laboratory period following

the completion of the individual technique experiments. This provides an effective way of reviewing some of the basic techniques.

Part A (expected results)

Compound	Water	Methyl alcohol	Hexane
Benzophenone	Insoluble	Soluble in about 25 sec	Soluble in about 60 sec
Malonic acid	Soluble in about 10 sec	Soluble in about 10 sec	Insoluble
Biphenyl	Insoluble	Partially soluble	Soluble in about 40 sec

Part B (expected results)

Compound	Water	Hexane
1-Octanol	Insoluble	Soluble
1-Butanol	Partially soluble	Soluble
Methanol	Soluble	Insoluble

Part F

In Part F, a butane torch is used to erase the gold slide. It is best that this be done by the instructor. When erasing the slide, keep the torch moving and do not hold it in one spot on the slide. Heating one spot for too long can cause the slide to shatter.

ANSWERS TO QUESTIONS

- yes
  - no
  - yes
  - no
  - no
  - yes
  - no
- miscible
  - miscible
  - miscible
  - immiscible
  - miscible
  - miscible

3. Ibuprofen is a carboxylic acid which is converted to a water-soluble salt in 1.0M NaOH.
  4. Thymol has a phenolic OH group which is acidic. In 1.0M NaOH, thymol is converted into a water-soluble salt.
  5. Cannibinol is only slightly soluble in methyl alcohol because the large hydrocarbon component of cannibinol negates the fact that they belong to the same family.
  6. When you write on the slide, a monolayer of thiols is deposited on the slide. The OH groups will be located at the top surface of the coated area. Since hydroxyl groups are hydrophilic, water is attracted to the part of the slide that was written on. The rest of the surface is coated with hydrocarbons from the air and is hydrophobic, so the water rolls off and does not stick.
  7. Water adheres to the gold surface immediately after flame cleaning because the gold surface is a high-energy surface that attracts water molecules. Within several minutes, the surface becomes coated with hydrocarbons from the air, making the surface hydrophobic.
  8. A methyl group on the end of the thiol molecule would make the surface nonpolar or hydrophobic.
  9. Heating the slide with a butane torch burns off the thiols.
  10. When you write on a glass surface with a crayon or wax pencil, you are transferring a thick layer of material rather than a monolayer. You can even see this difference since you can see the film made by the wax, but you cannot see the monolayer after it forms on the gold slide.
  11. This is caused by the very high surface tension of water that allows water molecules to span the gap of the hole in these letters.
-

## Experiment 2

### CRYSTALLIZATION

TIME ESTIMATE: Parts A and B (3 hours), Parts C (about 1 hour)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### Part A

Impure sulfanilamide (5% fluorenone the impurity) 10 g  
Grind thoroughly to make homogeneous.

95% Ethyl alcohol 250 mL

Filter paper for Büchner funnel

Melting point capillary tubes

Waste container for non-halogenated organic wastes.

#### Part B

The appropriate solvent for crystallizing the impure fluorene is methyl alcohol. Fluorene is too soluble in toluene and insoluble in water at all temperatures.

Impure fluorene (5% fluorenone as the impurity) 10 g  
Grind thoroughly to make homogeneous.

Methyl alcohol 300 mL

Toluene 25 mL

Waste container for non-halogenated organic wastes.

#### Part C

Acetylsalicylic acid	5 g
Benzoic acid	5 g
Benzoin	5 g
Dibenzoyl ethylene	5 g
Succinimide	5 g

*o*-Toluic acid

5 g

Prepare unknowns consisting of pure samples of the above 6 compounds; about 0.2 g for each unknown sample.

Part D (Answers)

1. Phenanthrene  
95% ethyl alcohol - best solvent  
water - not soluble  
toluene - too soluble
2. Cholesterol  
ether - too soluble  
95% ethyl alcohol - best solvent  
water - not soluble
3. Acetaminophen  
95% ethyl alcohol - too soluble  
water - best solvent  
toluene - not very soluble
4. Urea  
Water - too soluble  
95% ethyl alcohol - best solvent  
Hexane - not very soluble

**CAS Registry numbers:**

Sulfanilamide	63-74-1
Acetanilide	103-84-4
95% Ethyl alcohol (Ethanol)	64-17-5
Fluorene	86-73-7
Fluorenone	486-25-9
Methyl alcohol (methanol)	67-56-1
Toluene	108-88-3
Acetylsalicylic acid	50-78-2
Benzoic acid	65-85-0
Benzoin	119-53-9
Dibenzoyl ethylene	4070-75-1
Succinimide	123-56-8
<i>o</i> -toluic acid	118-90-1

SPECIAL NOTES



In the Pre-lab Calculations for Part A, students calculate the amount of sulfanilamide which will remain in the mother liquor. If they perform the Optional Exercise in Part A, they determine the weight of solid in the mother liquor. However, the actual weight of solid in the mother liquor is usually much greater than the amount calculated in the Pre-lab Calculations. This is because the calculation does not take into account the impurity, which ends up in the mother liquor. Also, the calculation assumes that a minimum amount of solvent is used to dissolve the impure sulfanilamide at 78 °C. It is likely that most students use more than the minimum amount.

#### ANSWERS TO QUESTIONS

1. Too much solvent was added. Since 10 mL of 95% ethyl alcohol will dissolve 0.14 g of sulfanilamide at 0 °C, none of the 0.1 g of sulfanilamide will crystallize when the solution is cooled. To make the crystallization work, the excess solvent must be evaporated.
2. The boiling point of the solvent is higher than the melting point of fluorenone. While performing this crystallization, it is possible that the fluorenone would melt rather than dissolve, thus forming an oil which could be difficult to crystallize.
3. Biphenyl is highly soluble in both hot and cold benzene. The solubility curve would look like **C** in Figure 11.1 on page 663 of the Textbook.

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### Experiment 3

#### EXTRACTION

TIME ESTIMATE: Parts A-D (3-4 hours); Part E (30 minutes)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### Part A

Caffeine	2.2 g
Methylene chloride	200 mL

Anhydrous sodium sulfate (granular) 38 g

Evaporation station in a hood (optional)

Waste containers for aqueous and non-halogenated organic wastes (note: there will be some methylene chloride in the aqueous waste)

### Part B

(These quantities are based on the assumption that each student does this part with only one of the compounds.)

Benzoic acid 0.4 g

Succinic acid 0.4 g

Sodium benzoate 0.4 g

Methylene chloride 25 mL

Anhydrous sodium sulfate (granular) 5 g

Evaporation station in a hood (see “Equipping the Organic Chemistry Laboratory” earlier in this manual).

Waste containers for aqueous and non-halogenated organic wastes (note: there will be some methylene chloride in the aqueous waste)

### Optional Exercise in Part B

Caffeine 1.0 g

Methylene chloride 30 mL

Anhydrous sodium sulfate (granular) 5 g

### Part C

We give a set of all three mixtures to each pair of students. Each mixture contains about 2 mL of each liquid. The three mixtures are: (1) water and n-butyl chloride; (2) water and n-butyl bromide; and (3) n-butyl bromide and saturated aqueous sodium bromide. It is best if the aqueous sodium bromide is not quite saturated. Otherwise, it may salt out when mixed with n-butyl bromide. Do not dilute it too much, however, since it should be more dense than n-butyl bromide. Each mixture should be prepared in a stoppered test

tube or centrifuge tube.

Waste container for halogenated organic wastes.

#### Part D

Each student receives an unknown which contains 0.24 g of a neutral compound and 0.12 g of benzoic acid, the acid impurity. The neutral compound should be one of the following: fluorenone, fluorene, 1,2,4,5-tetrachlorobenzene, or triphenylmethanol.

1.0M NaOH	120 mL
6.0M HCl	12 mL
Saturated aqueous NaCl	60 mL
Diethyl ether	120 mL
Anhydrous sodium sulfate (granular)	10 g
Litmus paper	

Evaporation station in a hood (see “Equipping the Organic Chemistry Laboratory” earlier in this manual).

Waste containers for aqueous, non-halogenated and halogenated

#### Optional Exercise in Part D

Each student receives an unknown which contains 0.24 g of a neutral compound and 0.12 g of ethyl 4-aminobenzoate, the base impurity. The neutral compound should be one of the following: fluorenone, fluorene, 1,2,4,5-tetrachlorobenzene, or triphenylmethanol.

1.0M HCl	120 mL
6.0M NaOH	12 mL
Saturated aqueous NaCl	60 mL
Diethyl ether	120 mL
Anhydrous sodium sulfate (granular)	10 g

Litmus paper

Evaporation station in a hood (see “Equipping the Organic Chemistry Laboratory” earlier in this manual).

Waste containers for aqueous, non-halogenated and halogenated organic waste

### Part E

Methylene chloride 25 mL

Solution A: Mix 25 mg of 2,6-dichloroindophenol (sodium salt) with 50 mL of water and 1 mL of 1M NaOH. This solution should be prepared the same day it is used. 2 mL

1M HCl 2 mL

1M NaOH 4 mL

Waste container for halogenated organic wastes.

### **CAS Registry numbers:**

Caffeine	58-08-2
Methylene chloride	75-09-2
Diethyl ether	60-29-7
sodium sulfate	7757-82-6
Benzoic acid	65-85-0
Succinic acid	110-15-6
Sodium benzoate	532-32-1
Ethyl 4-aminobenzoate	94-09-7
Fluorenone	486-25-9
Fluorene	86-73-7
1,2,4,5-Tetrachlorobenzene	95-94-3
Triphenylmethanol	76-84-6
2,6-dichloroindophenol (sodium salt)	620-45-1

### **SPECIAL NOTE**

In Parts A and B, it is essential that students make all weighings very carefully on balances that weigh to the nearest 0.001 g. In Part B, it is still likely that results will vary a lot. However, definite trends will be seen when students average their results. In Part E, students may require some help in interpreting the results. It is helpful for them to read about acid/base indicators in their general chemistry book. This experiment is described in the reference given at the end of Experiment 3 in the Textbook.

## ANSWERS TO QUESTIONS

$$1. \quad \frac{52 - x / 2}{x / 2} = 4.6$$

$$52 - x = 4.6x$$

$$52 = 5.6x$$

$$x = 9.3 \text{ mg in the aqueous phase; } 42.7 \text{ mg in the organic phase}$$

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### Experiment 4

#### A SEPARATION AND PURIFICATION SCHEME

TIME ESTIMATE: 1-2 Periods

Students must be told the composition of their mixture well in advanced of the laboratory period so that they have sufficient time to devise a procedure. It is advisable to require that students turn in a copy of their procedure at the beginning of the lab period. It is also helpful if they draw a flow chart before they begin the experimental work. You may wish to allow enough time so that students can repeat the experiment if their procedure doesn't work the first time or if they want to improve on their percentage recovery and purity. We have found that many students benefit from doing this experiment a second time, even if their first attempt is somewhat successful.

We have used the following mixtures in this experiment (percent by mass):

- (1) 50% phenanthrene, 40% *o*-toluic acid, 10% 1,4-dibromobenzene
- (2) 50% phenanthrene, 40% methyl 4-aminobenzoate, 10% 1,4-dibromobenzene
- (3) 50% phenanthrene, 40% 2-chlorobenzoic acid, 10% 1,4-dibromobenzene
- (4) 50% phenanthrene, 40% 4-aminoacetophenone, 10% 1,4-dibromobenzene
- (5) 50% benzoin, 40% 4-aminoacetophenone, 10% 1,4-dibromobenzene
- (6) 50% 1,2,4,5-tetrachlorobenzene, 40% *o*-toluic acid, 10% 1,4-dibromobenzene

- (7) 50% 1,2,4,5-tetrachlorobenzene, 40% 2-chlorobenzoic acid, 10% 1,4-dibromobenzene
- (8) 50% 4-aminoacetophenone, 40% 1,2,4,5-tetrachlorobenzene, 10% 1,4-dibromobenzene
- (9) 50% methyl 4-aminobenzoate, 40% 1,2,4,5-tetrachlorobenzene, 10% 1,4-dibromobenzene
- (10) 50% methyl 4-aminobenzoate, 40% benzoin, 10% 1,4-dibromobenzene
- (11) 50% benzoic acid, 40% benzoin, 10% 1,4-dibromobenzene
- (12) 50% fluorene, 40% *O*-toluic acid, 10% 1,4-dibromobenzene
- (13) 50% benzoin, 40% benzil, 10% 1,4-dibromobenzene
- (14) 50% ethyl 4-aminobenzoate, 40% benzoin, 10% 1,4-dibromobenzene
- (15) 50% ethyl 4-aminobenzoate, 40% benzil, 10% 1,4-dibromobenzene

When you prepare these mixtures, it is important that the relative amounts be accurate, especially if you will be grading them on % recovery. One way to do this is to prepare each student mixture individually. For example, one sample of the first mixture would consist of 0.5 g phenanthrene, 0.4 g *o*-toluic acid, and 0.1 g 1,4-dibromobenzene. If you have a large class, however, this may require too much time. An alternative method is to weigh out a larger amount of the three compounds in a mixture according to the relative percentages given above. Make sure that each compound is a fine powder and then place them into a large enough bottle so that you can shake the mixture in the bottle thoroughly. Shake vigorously for several minutes. Another option is to place the powdered compounds in an Erlenmeyer flask and place the flask on a laboratory shaker for 1-2 hours. Individual samples of 1.0 g can then be weighed out either by the lab prep person or by the students.

**Additional comment about these mixtures:** In this experiment, students must find a solvent in which to crystallize the compounds that they isolate. Some of the compounds in the above mixtures are found in other experiments in this textbook, along with instructions on how to crystallize them. If students find these procedures, the task of crystallizing the compounds in this experiment becomes relatively easy. Depending on your goals in this experiment, you may or may not want to assign compounds that are found in other experiments in the book. The compounds above that are found in the book are: benzoin, benzil, 4-ethyl aminobenzoate, and fluorene.

## OTHER CHEMICALS AND SUPPLIES PER 10 STUDENTS

The actual amounts needed are difficult to estimate, since students will be developing their own procedures. The suggested amounts should be more than sufficient for 10 students.

1M NaOH	200 mL
1M HCl	200 mL
6M NaOH	50 mL
6M HCl	50 mL
1M NaHCO <sub>3</sub>	100 mL
Saturated aqueous sodium chloride	200 mL
Diethyl ether	200 mL
95% Ethanol	100 mL
Methanol	50 mL
Isopropyl alcohol	50 mL
Acetone	50 mL
Hexane	50 mL
Toluene	50 mL
Methylene chloride	100 mL
Anhydrous sodium sulfate (granular)	25 g
Other solvents may be needed for crystallization	
Melting point capillary tubes	
Filter paper for Büchner or Hirsch funnels	
Chemicals and supplies for infrared and NMR spectroscopy	

Waste containers for aqueous, nonhalogenated, and halogenated organics

**CAS Registry Numbers:**

phenanthrene	85-01-8
<i>o</i> -toluic acid	118-90-1
1,4-dibromobenzene	106-37-6
methyl 4-aminobenzoate	619-45-4
2-chlorobenzoic acid	118-91-2
4-aminoacetophenone	99-92-3
Benzoin	119-53-9
1,2,4,5-tetrachlorobenzene	95-94-3
benzoic acid	65-85-0
fluorene	86-73-7
benzil	134-81-6

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**Experiment 5**

**CHROMATOGRAPHY**

TIME ESTIMATE: 1 period for parts A and B working in pairs to save on TLC plates, and 1 period for Part D working in pairs. Part C can be done as an optional experiment during the first period.

**CHEMICALS AND SUPPLIES**

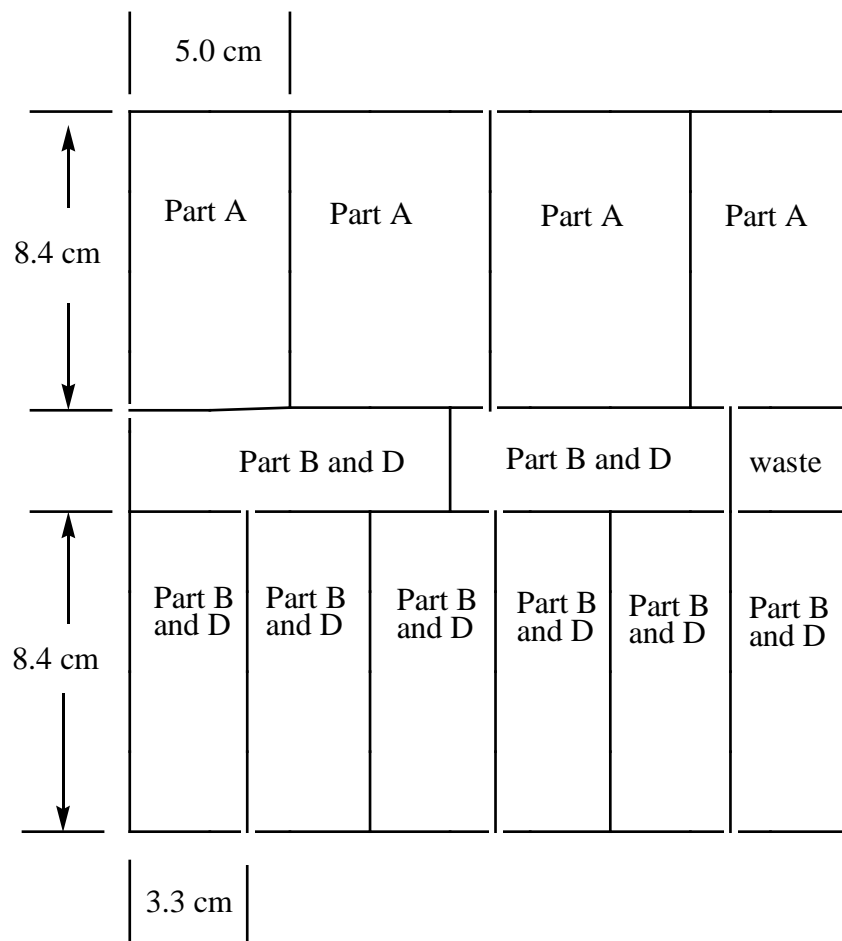
**Part A It is advised to set up at least two stations in the lab in order to speed up the experiment. Discard the solutions after the lab experiment is completed. Some of the samples are air-sensitive. We have observed that the commercial samples often contain some impurities: some fluorene in the fluorenone, for example.**

The presence of impurities is more of a problem when a UV lamp is used to visualize the spots than when iodine is used. This is because the UV lamp is more sensitive. Fluorene can be purchased in a very pure form. If necessary, commercial fluorene can be crystallized from toluene, but it will likely be necessary to filter the hot solution. Fluorenone can be crystallized from hexane.

Whatman Silica Gel Plates # 4410 222 (polyester backed). These plates are expensive (over \$7 for each 20 x 20 cm plate). Less expensive plates are available from Sorbent Technologies at about \$5/plate; #1634128 (Al backed



plates). The aluminum backed plates are easier to cut on a paper cutter. You can get more individual plates from a 20 x 20 cm plate by cutting it as shown in the figure. Note the sizes are different from those indicated in the Text, but they work fine! If you used the plate sizes suggested here rather than the sizes mentioned in the Textbook, you will need to tell students that the spotting instructions given in the first complete paragraph on page 44 will need to be changed slightly.



Once cut, the plates must be stored in a container over drying agent. If the plates have not been purchased recently, they should be placed in an oven at 100 °C for 30 minutes and stored in a desiccator until used.

Small bottles containing 2% solutions of each of the following compounds dissolved in acetone:

Fluorene  
 Fluorenol  
 Fluorenone

Reference mixture containing all three  
Unknowns containing one, two, or all three of these compounds.

Chromatography development jars, larger size (1 liter, screw capped)

Filter paper, squares to prepare liners

Methylene chloride (5-10 mL per jar)

Iodine chambers (small amount of iodine in jars with caps; keep for reuse)

Rulers and pencils

Thin wall open end capillary tubing (1 mm) for micro-pipets

Matches

Waste container for halogenated organic wastes.

**Part B It is advised to set up at least two stations in the lab in order to speed up the experiment. Discard the solutions after the lab experiment is completed. Some of the samples are air-sensitive.**

Whatman Silica Gel Plates No. 4410 222

8.4 cm x 3.3 cm plates; three plates for each pair of students. Once cut, the plates must be stored in a container over drying agent. If the plates have not been purchased recently, they should be placed in an oven at 100 °C for 30 minutes and stored in a desiccator until used. These sized plates fit nicely in smaller 4 oz development jars.

Each student should be assigned a pair of compounds. Possible pairs are given in the following list. The two compounds to be resolved are given first, followed by the three developing solvents to try: (1) benzoin and benzil; acetone, methylene chloride, hexane; (2) vanillin and vanillyl alcohol; ethyl acetate, 50% toluene-50% ethyl acetate, toluene; (3) diphenylmethanol and benzophenone; acetone, 70% hexane-30% acetone, hexane. Each compound in a pair should be prepared individually and as a mixture of the two compounds. Prepare all of them as 1% solutions in acetone.

Rulers and pencils

Thin wall open end capillary tubing (1 mm) for micro-pipets

Hand-held UV lamp

We prefer: Mineralight lamp UVP shortwave and long wavelength, 4 Watt, UV

light available from Fisher Scientific and other chemical supply houses.

Waste containers for non-halogenated and halogenated organic wastes.

Part C This part of Experiment 5 can be omitted if time is not available. Parts A, B and D are recommended for a two lab period experiment.

**SPECIAL NOTE:** It is best to use iodine to visualize the spots in Part C. A UV lamp is more sensitive and students will likely be unable to see the gradual change in the amounts of fluorenone and fluorenol..

Whatman Silica Gel Plates No. 4410 222

Each pair needs two plates: (1) 8.4 cm x 5.0 cm, (2) 8.4 cm x 3.3 cm. Once cut, the plates must be stored in a container over drying agent. If the plates have not been purchased recently, they should be placed in an oven at 100 °C for 30 minutes and stored in a desiccator until used.

Development chamber: Use the same development chamber as in Part A

Iodine chambers (small amounts of iodine in jars with caps; keep for reuse)

Rulers and pencils

Thin wall open end capillary tubing (1 mm) for micro-pipets

#### CHEMICALS PER 10 PAIRS OF STUDENTS (Part C)

Fluorenone	2.5 g
Methyl alcohol	50 mL
Sodium borohydride	0.25 g

Waste container for non-halogenated wastes

If performing Isolation of Fluorenol (Optional Exercise): 80% Methyl alcohol - 20% Water (by volume)	38 mL
---	-------

#### Part D

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS

Hexane	113 mL
Acetone	25 mL

70% Hexane - 30% acetone (by volume) 25 mL

Fluorene/Fluorenone solution: Dissolve 0.3 g of fluorene and 0.3 g of fluorenone in 9 mL of a mixture of 5% methylene chloride- 95% hexane. Store this solution in a closed container to prevent evaporation of solvent. This will provide enough solution for 20 students, assuming little waste.  
Cotton

Pasteur pipet (5 3/4-inch) for columns 10

Whatman Silica Gel Plates No. 4410 222  
8.4 cm x 3.3 cm plates; one plate per pair of students. Once cut, the plates must be stored in a container over drying agent. If the plates have not been purchased recently, they should be placed in an oven at 100 °C for 30 minutes and stored in a desiccator until used.

Development chambers: Use the same development chamber as in Part B.

Hand-held UV lamp  
We prefer: Mineralight lamp UVP shortwave and long wavelength, 4 Watt, UV light available from Fisher Scientific and other chemical supply houses.

Rulers and pencils

Thin wall open end capillary tubing (1 mm) for micro-pipets

Alumina 16 g  
Use EM Science No. AX0612-1 alumina. The particle size are 80-200 mesh and material is Type F-20. The alumina must be dried in an oven at 110 °C overnight and stored in a tightly sealed bottle.

Waste disposal container for non-halogenated organic waste

Evaporation station in a hood

**CAS Registry Numbers:**

Fluorene	86-73-7
Fluoreneol	1689-64-1
Fluorenone	486-25-9
Iodine	7553-56-2
Benzoin	119-53-9
Benzil	134-81-6
Vanillin	121-33-5
Vanillyl alcohol	498-00-0

Diphenylmethanol 91-01-0  
Benzophenone 119-61-9  
Sodium borohydride 16940-66-2

## ANSWERS TO QUESTIONS

1. a) Methylene chloride or hexane or mixtures of the two might be good choices because the compounds are somewhat polar. b) Hexane should work well because both compounds are relatively non-polar. c) Acetone should work well because the mixture is highly polar. An acetone-hexane mixture might work well, too. There are a number of possible answers to these questions.
2. a) Fluorene, an aromatic hydrocarbon compound, elutes first from the column because it is less polar than the ketone, fluorenone. b) Hexane was polar enough to remove the aromatic hydrocarbon, fluorene, but it is not polar enough to remove fluorenone. The 30% acetone and 70% hexane is more polar and will remove fluorenone from the column..
3. a) The initial choice of solvent was too polar. Since both compounds in the mixture are hydrocarbons, one should try hexane as the solvent. b) Carboxylic acids are very polar, especially the di- and tri-compounds. One should change to a much more polar solvent so that the compounds will move on the plate. Acetone or mixtures of acetone and hexane would be good choices. c) One can not determine the  $R_f$  value when this happens. Rerun the experiment.

---

## Experiment 6

### SIMPLE AND FRACTIONAL DISTILLATION

TIME ESTIMATE: 1 Period

#### CHEMICALS AND SUPPLIES PER 24 STUDENTS:

The quantities given here are based on the assumption that each pair selects one unknown mixture, with one person doing the simple distillation and the other doing the fractional distillation. It is also assumed that the unknowns are distributed evenly among the entire class. If one or more of the mixtures are omitted, then the amounts will need to be increased. *It is very important that someone check to see if the heptane-ethylbenzene mixture will distil using your equipment (see Results and Special Notes, below).*

Unknown mixtures. For each mixture, use an equal volume of both liquids.

Hexane-heptane 210 mL

Hexane-toluene 210 mL

Cyclohexane-toluene 210 mL

Heptane-ethylbenzene 210 mL

Stainless steel cleaning pad material for fractionating columns 54 g

Boiling Stones

GC-MS vials for storing distillates (see Results and Special Notes, below)

Cotton pad and aluminum foil for insulating the fractionating column and distilling head.

Waste container for non-halogenated organic wastes.

#### OTHER EQUIPMENT REQUIRED

Gas Chromatograph

Prepare as follows: column temperature, 140 °C; injection temperature, 150 °C; detector temperature, 135 °C; carrier gas flow rate, 100 mL/min. The recommended column is 8 feet long with a stationary phase such as Carbowax 20M.

On some columns, the order in which the compounds pass through the column will not correlate exactly with the boiling points. You must check the retention times on the instrument you use.

You should determine response factors for the five compounds given as unknowns. Because the data in this experiment are expressed as volume, the response factors should also be based on volume. Inject a mixture containing equal volumes of all five compounds and determine the relative peak areas. Choose one compound as the standard and define its response factor to be equal to 1.00. Calculate the other response factors based on this reference. Since response factors are instrument specific, you will be given the response factors for your instrument. Typical response factors obtained on a GowMac 69-350 gas chromatograph are: hexane (1.50), cyclohexane (1.80), heptane (1.63), toluene (1.41), and ethylbenzene (1.00).

10 µL Gas chromatograph syringe

Vernier LabPro interface (if available) with temperature probe and laptop computer. (See Results and Special notes, below for more information about this equipment.)

## RESULTS AND SPECIAL NOTES

If it is necessary to store the distillates before analyzing them by GC, it is very important that they be stored in leak-proof vials. Otherwise, more of the more volatile component will evaporate and the % composition will change. We use GC-MS vials from Agilent Technologies: vials (5182-0715) and caps (5182-0717). Samples may be stored in these vials at room temperature with very little loss.

Distillation of these four mixtures should provide a good contrast between the two distillation methods. *However, you should try out the heptane-ethyl benzene mixture before assigning it to your class.* Because ethyl benzene has a relatively high boiling point (136°C), your students may or may not be able to distill it with their distillation apparatus. This is most likely to be a problem with the fractional distillation procedure. The following factors will determine whether this is possible: how high a temperature the heating mantle can reach, how effectively the fractionating column and distilling head is insulated, the temperature of the laboratory, and the amount of air flow around the apparatus. It may also help to insulate the distillation head, although this is not described in the textbook.

The temperature recorded during the distillation will be most accurate if a partial immersion mercury thermometer is used (see Section 13.4 in the textbook for a discussion of this topic). Even with this type of thermometer, it may not be possible to obtain accurate boiling points for the unknown from the distillation curve. Therefore, it is often easier to identify the two liquids in the mixture from the gas chromatography results.

Another very good method to record the temperature is to use a Vernier LabPro interface with a temperature probe and a laptop computer. (See Technique 13, Section 13.5 in the textbook.) This method is quite accurate and it gives students a visual record of the temperature vs. time curve as the distillation is carried out. We have used Vernier LabPro interface (code LABPRO). It is important to make sure that the temperature probe works in the temperature range required by the experiment. We have used a 304 SS K type thermocouple from Omega.com (cat. #KMTSS-M 300-150). The Wide-Range Temperature Probe from Vernier (WRT\_BTA) should also work well.

### **CAS Registry Numbers:**

Hexanes        73513-42-5

Heptane	142-82-5
Toluene	108-88-3
Cyclohexane	110-82-7
Ethylbenzene	100-41-4

---

## Experiment 7

### **INFRARED SPECTROSCOPY AND BOILING-POINT DETERMINATION**

TIME ESTIMATE: 1 period

You should read carefully the Notes to the Instructor on page 50 of the textbook. This experiment can be performed in 2 ways:

(1) The experiment is performed individually with each student working on one unknown from the list on pages 52 - 53 of the textbook.

(2) Students work in groups of three and each group is assigned three different unknowns from the list on pages 52 - 53 of the textbook. The three unknowns should differ both in structure and functional group, with at least one aromatic compound in each set. Each student obtains an infrared spectrum and performs a boiling-point determination on one of the unknowns. This information is shared with the other two students in the group and each student analyzes the collective results for the 3 unknowns. We prefer to do the experiment this way because the opportunity to learn is greater.

The NMR portion of the experiment is optional. We suggest that access to the NMR be granted only after a plausible solution has been tendered.

#### **CHEMICALS AND SUPPLIES**

Unknowns from the list on pages 52 - 53 of the text book: 1-3 mL/sample, depending on the method used for the boiling-point determination

Apparatus for boiling-point determination, if necessary

Boiling stones

Salt plates for infrared spectroscopy

Optional: NMR tubes



Optional:  $\text{CDCl}_3$  (for NMR spectroscopy)

Waste disposal containers for nonhalogenated organic and halogenated organic wastes.

Vernier LabPro interface (if available) with temperature probe and laptop computer. (See Experiment 6 in this manual for more information about this equipment.)

## SPECIAL NOTES

A simple and reliable method of determining boiling points is the macroscale method using 13-mm x 100-mm test tubes described in Section 13.2 of the textbook. If an aluminum block and hot plate is used to heat the sample, a hole that is slightly larger than the test tube should be drilled all the way through the aluminum block. The aluminum block works well with small hot plates like those used in microscale work. However, if the aluminum block is used with larger hot plates, such as Corning, it can sometimes be difficult to avoid overheating, even at the lowest setting. This is a problem mainly with low boiling liquids ( $<100\text{ }^\circ\text{C}$ ). If these liquids are heated too strongly, all the liquid may evaporate before a temperature plateau is observed. If all the liquid evaporates, the temperature may actually go above the boiling point.

A sand bath, as described in Section 13.2, can also be used to heat the sample. However, a sand bath heated with a small hot plate may not provide enough heat to obtain an accurate boiling point with higher boiling liquids ( $>200\text{ }^\circ\text{C}$ ). When using a sand bath the larger hot plates, which generate more heat, work effectively with both low and high boiling liquids.

The method described in Section 13.2 works best with a partial immersion mercury thermometer. Even if the reflux ring does not reach the immersion line on the thermometer, the boiling point will usually be quite accurate. This is because the coefficient of expansion of mercury is small. Non-mercury partial immersion thermometers can also work well, but then it is more important that the reflux ring be close to the immersion line. With a total immersion thermometer, it will be necessary to perform a stem correction in order to obtain accurate results.

Another very good option is to use a Vernier LabPro interface with a laptop computer and temperature probe. See RESULTS AND SPECIAL NOTES in Experiment 6 in this manual for a discussion about this method.

Whatever method is used in your lab, we recommend that you try it with a low boiling liquid such as methanol and a high boiling liquid such as ethyl benzoate.

The most common mistake that students make is to report a boiling point below the actual boiling point. This usually happens because they have not heated the sample strongly enough and the actual boiling point plateau has not yet been reached. This is most likely to happen with high boiling liquids, but it can also occur with low boiling liquids.

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## **Experiment 8**

### **ACETYLSALICYLIC ACID**

TIME ESTIMATE: 1 period

The instructor or assistant should place the appropriate liquid measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Salicylic acid	25 g
Acetic anhydride	63 mL
1% (by weight) Aqueous ferric chloride solution 1 g/100 mL water (in a dropper bottle)	1 mL
Iodine solution (in a dropper bottle) 0.25 g iodine, 0.5 g potassium iodide, and 100 mL of water are mixed. The solution should be straw-colored in appearance.	1 mL
Concentrated sulfuric acid (in a dropper bottle)	5 mL
Ethyl acetate	40 mL
Aspirin tablets (must have starch binder!)	
Melting point tubes	
Filter paper for Büchner funnels	
Waste disposal containers for aqueous and non halogenated wastes	

#### **CAS Registry Numbers:**

Salicylic acid	69-72-7
Acetic anhydride	108-24-7

Ferric chloride	7705-08-0
Iodine	7553-56-2
Potassium iodide	7681-11-0
Phosphoric acid	7664-38-2

#### ANSWERS TO QUESTIONS:

1. The sulfuric acid acts as a catalyst in the acetylation reaction. Acetic anhydride reacts with salicylic acid too slowly for a practical reaction. However, protonating the carbonyl group oxygen of the acetic anhydride increases the electron-deficient nature of the carbonyl group. Salicylic acid's hydroxyl group, acting as a nucleophile, can attack this protonated group more easily.
2. The reaction occurs so slowly without the catalyst that very little acetyl salicylic acid would be formed. The final product would contain mainly salicylic acid.
3. The yield of acetylsalicylic acid, starting with 5.0 g of salicylic acid and an excess of acetic anhydride, would be:

Molecular weights: salicylic acid = 138.1  
acetylsalicylic acid = 180.2

$$5.0 \text{ g salicylic acid} = \frac{5.0}{138.1} = 0.036 \text{ mole salicylic acid}$$

$$\text{Theoretical yield of acetylsalicylic acid} = (0.036)(180.2) = 6.5 \text{ g}$$

4. When heated in boiling water, aspirin decomposes to give salicylic acid and acetic acid.
5. 1 grain = 0.0648 g  
  
5 grain aspirin = (5)(0.0648) = 0.324 g = 324 mg
6. The depressed melting point indicates that the product was impure. Since the ferric chloride test was negative, the impurity was not salicylic acid which has a phenolic hydroxyl group. Evidently a side reaction occurred at the elevated temperature (90°C) which produced an impurity that crystallized with aspirin. Although it is not discussed in this experiment, the carboxyl group of salicylic acid can react with the phenolic hydroxyl

group of another salicylic acid molecule to form a polymeric by-product.

7. The aspirin would "sweat" as the water was released. A student might interpret this as a depressed melting point indicating the aspirin was impure.

---

## Experiment 9

### ACETAMINOPHEN

TIME ESTIMATE: 1 to 1.5 periods

The instructor or assistant should place the appropriate measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

<i>p</i> -Aminophenol	20 g
This compound acquires a black color upon standing. You should purchase fresh material for this experiment. Even this chemical may possess a gray color. We strongly recommend that you decolorize <i>p</i> -aminophenol by heating it in a 10% aqueous solution of sodium dithionite (sodium hydrosulfite) prior to starting the experiment, otherwise it will be difficult for students to obtain a nearly colorless product.	
Acetic anhydride	25 mL
Sodium dithionite (sodium hydrosulfite)	25 g
Water-methanol (1:1 by volume)	150 mL
Melting point tubes	
Filter paper for Büchner funnels	
Waste disposal containers for aqueous and non halogenated wastes	

#### **CAS Registry Numbers:**

*p*-Aminophenol (4-aminophenol) 123-30-8  
Sodium dithionite (sodium hydrosulfite) 7775-14-6  
Acetic anhydride 108-24-7

## ANSWERS TO QUESTIONS:

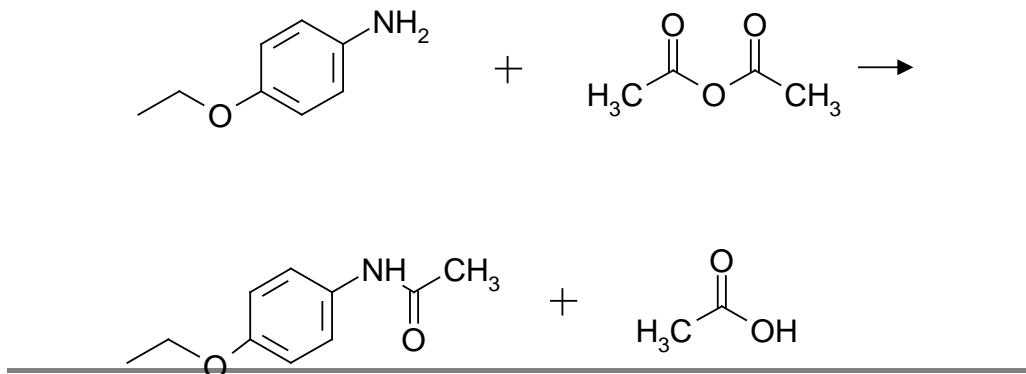
1. Since the solubility of *p*-aminophenol in water decreases as the temperature is lowered, cooling the mixture in an ice bath increases the amount of crystals recovered.
2. Water is a solvent which dissolves *p*-aminophenol and decomposes acetic anhydride to acetic acid. Acetic acid is soluble in water. Water removes the starting reactants from the product.
3. Acetaminophen is somewhat soluble in water. If an excess of water is used to help transfer the product, a decreased yield results, even if the water is cold.
4. The theoretical yield of acetaminophen, starting with 1.30 g of *p*-aminophenol and an excess of acetic anhydride would be:

Molecular weights: *p*-aminophenol = 109.1  
acetaminophen = 151.2

$$1.30 \text{ g } p\text{-aminophenol} = \frac{1.30}{109.1} = 0.0119 \text{ mole}$$

$$\text{Theoretical yield of acetaminophen} = (0.0119)(151.2) = 1.80 \text{ g}$$

5. Reactants which do not react completely would be present, along with small amounts of the catalyst (if used) and other products formed in the main reaction. In addition, side reactions may occur which would form products other than the desired product.
6. A proposed preparation of phenacetin



## Experiment 10

### TLC ANALYSIS OF ANALGESIC DRUGS

TIME ESTIMATE: One period, or less

Students may work individually or, alternatively, the experiment may be performed by students working in pairs, one student preparing the tlc slide of the reference substances, and one student preparing the tlc slide of the unknowns.

A common student error in this experiment occurs when the capillary micropipets are prepared. The pulled section of the capillary tubing should be only about 5 cm in length. If the student pulls a longer constriction, the pipets will have too fine a diameter and will not deliver enough sample to the slides. When this happens, the expected spots will either be absent or very, very light.

It is also important that the slide be aligned exactly perpendicular to the bottom of the jar when it is placed into the development solvent. If the slide is tilted when it enters the development solvent, the solvent front will not advance as a horizontal line and the compounds separated will not advance straight up the plate; their traces will be at an angle to the edge of the plate causing them to merge at the top corner of the plate.

A common prepping error is to misread the 0.5% acetic acid in the ethyl acetate solvent as 5%. Yes, 0.5% is correct; if the larger percentage is used, the entire experiment will fail. The 0.5% acetic acid is just enough acid to keep the RCOOH and RCOONa compounds protonated.

#### CHEMICALS AND SUPPLIES:

The following analgesics (at a minimum) should be made available in convenient size bottles sufficient for the class (each student requires 1/2 tablet):

- Advil (ibuprofen)
- Anacin (aspirin and caffeine)
- Excedrin, Extra Strength (aspirin, acetaminophen and caffeine)
- Tylenol (acetaminophen)
- Bufferin (buffered aspirin)
- B.C. Tablets or powder (aspirin, caffeine and salicylamide)
- Generic Aspirin
- Generic Acetaminophen
- Generic Ibuprofen

**We suggest the following set of drugs for complete coverage: Advil or generic, Anacin or generic, Excedrin or generic, Tylenol or generic, and B.C.**

## tablets.

Since the compositions of analgesic drugs are continuously being changed, you should look at the label to be sure of the composition. Generics are widely available, even for Anacin and Excedrin. Salicylamide containing drugs may be difficult to obtain, but B.C. tablets and powder still has it as one of the components. **Pharmacies in your area of the country may not stock B. C. tablets or powder. If B.C products are not stocked at all at your pharmacy, you can buy BC Powder on line: [www.bcpowder.com](http://www.bcpowder.com).** It is advised to include a salicylamide containing drug because it is the only one of the drugs that strongly fluoresces in UV light. Alternatively, you can supply students with a "synthetic mixture" that contains salicylamide.

Where possible, you should avoid analgesic preparations where the tablet has a hard coating or shell. In some brands of ibuprofen and ketoprofen the active ingredient is encapsulated in a hard, colored shell. These colored materials from the shell will show up as additional spots on the developed TLC plates.

Small bottles containing solutions of each of the following chemicals dissolved in 50/50 CH<sub>2</sub>Cl<sub>2</sub>/EtOH (1 g per 20 mL of mixed solvent except aspirin, for which 0.5 g is recommended) will be required:

4-Acetamidophenol (acetaminophen)	Aldrich A730-2 (100 g)
Acetylsalicylic acid (aspirin)	Aldrich 13,292-6 (500 g)
Caffeine	Aldrich C5-3 (100 g)
Salicylamide	Aldrich 86,041-7 (100 g)
Ibuprofen (4-isobutyl- $\alpha$ -methylphenylacetic acid)	
crystalline, free acid:	Aldrich 28,474-2 (5 g) Sigma I4883 (5 g)
sodium salt:	Sigma I1892 (100 g)
Naproxen	
(6-methoxy- $\alpha$ -methyl-2-naphthalene acetic acid)	
crystalline, free acid:	Sigma M4015 (5 g)
sodium salt:	Sigma M1275 (5 g)

In addition, 20 mL of a combined standard reference mixture of the first four compounds at the same concentrations is required. Use a steam bath for gentle heating where necessary. These solutions should be made up immediately prior to the laboratory period since they are not stable over long periods. Aspirin, for instance, will decompose to salicylic acid and acetic acid relatively quickly. The solutions are adequate for any size class.

The following additional supplies are required:

Silica Gel 60 F-254 Chromatogram Sheets (EM Science 5554-7)

Each sheet is cut into six 10 cm x 6.6 cm slides. Thus one large sheet will suffice for 3 students working individually, or for 6 students working in pairs. **Once cut, the plates must be stored in a container over drying agent.**

Hand-held UV lamp

We prefer: Mineralight lamp UVP shortwave and long wavelength, 4 Watt, UV light available from Fisher Scientific and other chemical supply houses.

Thin wall open end capillary tubing (1 mm) for micro-pipets

Filter paper, squares to prepare liners

32 oz. wide mouth, screw cap jars (Mason jars will work)

Iodine (small amounts in several 32 oz. developing jars, keep for reuse)

Development solvent: Ethyl acetate with 0.5% glacial acetic acid added is recommended (see also alternates mentioned in experiment). Since it is difficult to make this solvent in small portions, we recommend that a stock solution be prepared for the entire class to use (0.5 mL glacial acetic acid per 100 mL ethyl acetate).

Rulers and pencils

50: 50 Mixture of methylene chloride and ethanol used for dissolving tablets

Waste disposal bottle for non-halogenated waste (ethyl acetate)

Waste disposal bottle for halogenated waste (used to dissolve pills)

#### INSTRUCTIONS FOR SPECIAL EQUIPMENT OR REAGENT HANDLING:

We prefer to set aside one area in the laboratory (two areas in a large lab section) for spotting the tlc slides. A large piece of butcher paper is spread out on the desk and the bottles of standards, the analgesics, the tlc slides, and the development jars are all placed in this clean, organized area.

To visualize the plates, we place the uv lamp in a box on its side, with the opened end towards the student. When the box is placed in a semi-darkened room, it is easy to observe the spots on the plates.

Be sure to instruct the students to work in a hood if your laboratory does not have good air circulation. The ethyl acetate can cause a good degree of light-



headedness and eye irritation. Be sure to keep all containers covered or stoppered at all times to reduce solvent vapors.

#### SPECIAL NOTES:

The decreasing order of  $R_f$  values is:

Ibuprofen . Salicylamide > Aspirin > Acetaminophen > Caffeine

In a recent laboratory, we obtained the following  $R_f$  values:

Salicylamide, Ibuprofen	~0.58
Naproxen Sodium, Aspirin	~0.45
Acetaminophen	0.40
Caffeine	0.14

Fortunately, the analgesics which overlap (have approximately the same  $R_f$  values) never occur in the same preparation, and they have different behavior under the visualization techniques.

Visualization with UV light: Salicylamide fluoresces a strong bluish white color, while Naproxen Sodium fluoresces dimly white. The others do not fluoresce. Acetaminophen produces a dark spot, while the others are light.

Visualization with iodine: Salicylamide and acetaminophen produce dark brown spots. Naproxen Sodium produces a medium brown spot. Aspirin gives a light yellow spot. Caffeine and ibuprofen do not produce colored spots.

Ibuprofen has an  $R_f$  similar to that of salicylamide, but these two compounds never appear in combination; ibuprofen looks quite different from salicylamide when using the visualization techniques. Similarly, naproxen and aspirin have similar  $R_f$  values, but they never appear together and look quite different from one another under the visualization techniques.

#### CAS Registry Numbers:

4-Acetamidophenol (acetaminophen)	103-90-2
Acetylsalicylic acid (Aspirin)	50-78-2
Caffeine	58-08-2
Salicylamide	65-45-2

Ibuprofen (4-isobutyl- $\alpha$ -methylphenylacetic acid) 15687-27-1

Also known as 2-(4-Isobutylphenyl)propionic acid

Naproxen (6-methoxy- $\alpha$ -methyl-2-naphthalene acetic acid), also known as 2-(6-Methoxy-2-naphthyl)propionic acid

free acid	22204-53-1
sodium salt	26159-34-2

## ANSWERS TO QUESTIONS:

1. If the spots are made too large they may saturate the slides, show tailing, diffuse radially outward, or run into one another.
2. If the initial spots are made too small there may be even less material in the separated spots making them difficult or impossible to see after development.
3. If the spots are placed below the level of the solvent they will dissolve off the plate and into the solvent.
4. Ballpoint pen ink consists of organic compounds that will move with the development solvent and cause additional spots to appear on the plate. These additional spots could interfere with the analysis of the developed plate. Pencil lead is graphite-based and will not dissolve in any of the development solvents.
5. Yes. Spots with the same  $R_f$  value can be distinguished either: 1) by using several different development solvents or 2) by using several different visualization methods.
6. Acetaminophen is gentler on the lining of the stomach (less acidic) and has less tendency to cause bleeding. Acetaminophen also avoids the threat of Reyes Syndrome in children, a disease strongly linked to aspirin use.

---

## Experiment 11

### ISOLATION OF CAFFEINE

TIME ESTIMATE: 1 period

The instructor or assistant should place the appropriate measuring device by each reagent or solvent. In addition to the supplies for Exp. 11A and 11B, it is recommended that the sublimation be performed with a microscale apparatus such as that shown in Figure 17.2A. This apparatus is exceedingly efficient and it is worth purchasing a few (5 for a class of about 20 students) which can be shared among the students for performing this step.

CHEMICALS AND SUPPLIES FOR 10 STUDENTS:

**Experiment 11A** (Isolation of Caffeine from Tea Leaves)

Tea leaves	60 g
Calcium carbonate (powder)	25 g
Filter paper (E&D #617 or S&S #595) to fit a Büchner funnel	
Methylene chloride	400 mL
Anhydrous magnesium sulfate	50 g
Acetone	30 mL
Petroleum ether (bp 30-60°C)	30 mL
Sublimation equipment (see Fig. 17.2)	
Microburners	
Salicylic acid (optional -- for derivative formation)	225 g
Toluene (optional -- for derivative formation)	30 mL
Petroleum ether (bp 60-90°C) (optional -- for derivative formation)	6 mL
Melting point tubes	
Waste container for methylene chloride	

**Experiment 11B** (Isolation of Caffeine from a Tea Bag)

Tea bags	10
We find that the weight of tea in each bag varies somewhat from bag to bag. However, the weight of an empty bag, plus any string or tag or staple that may be present is a constant. The instructor should empty several bags in order to obtain the weight of an empty bag, string, tag and staple. Students can subtract this number from the weight of each individual tea bag to obtain the weight of the tea.	
Sodium carbonate, powder	7 g

Methylene chloride 80 mL

Anhydrous sodium sulfate (granular) 5 g

Vortex mixer for extraction (optional)

Sublimation equipment (see Fig. 17.2)

Microburners

Melting point tubes

Waste container for methylene chloride

**CAS Registry Numbers:**

Sodium carbonate 497-19-8

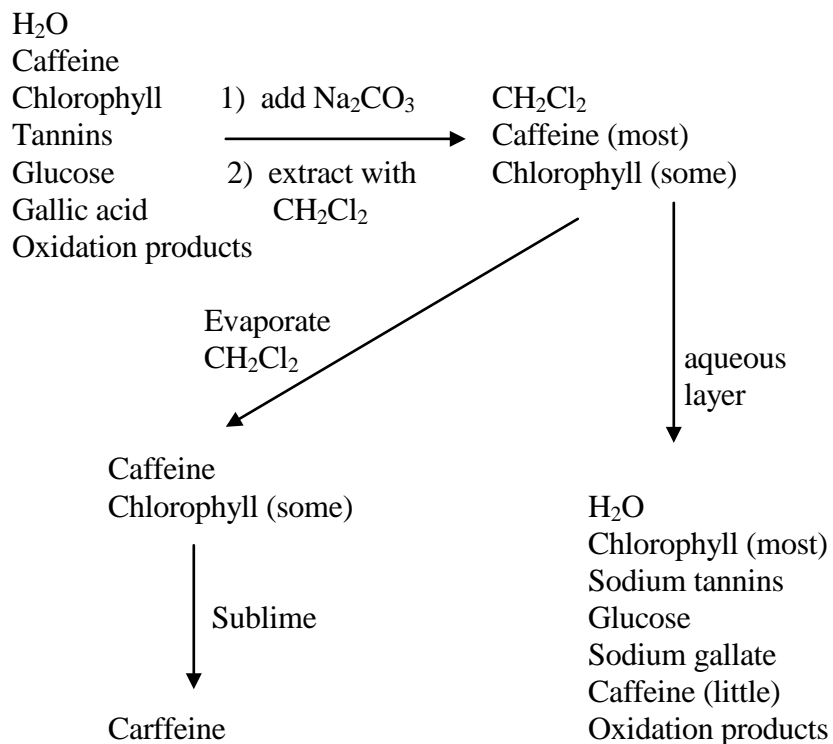
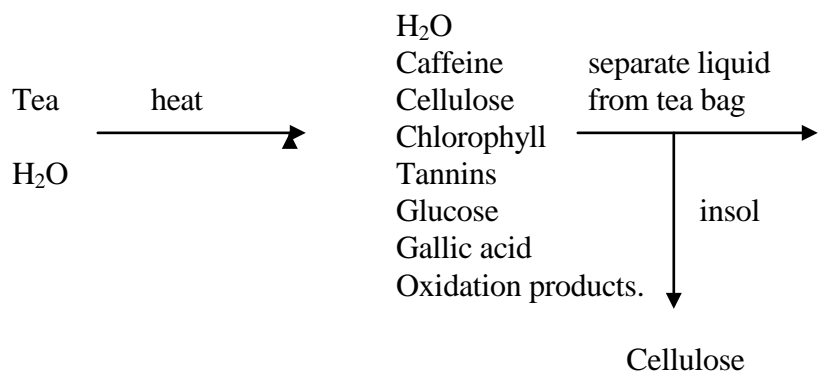
Methylene Chloride (dichloromethane) 75-09-2

Ethyl acetate 141-78-6

Sodium sulfate (anhydrous, granular) 7757-82-6

ANSWERS TO QUESTIONS:

1.



2. Sodium carbonate converts the tannins and gallic acid, which are acidic, into their sodium salts which are highly soluble in water. If sodium carbonate were not added, the tannins and gallic acid would dissolve in the methylene chloride layer along with caffeine in the extraction step.

The calcium carbonate has the opposite effect; it converts the tannins into insoluble products, which precipitate from the mixture and are removed by filtration.

3. A small amount of chlorophyll is present in the isolated caffeine giving it a greenish tinge.
4. The caffeine is impure. Possible impurities include decomposition products formed during the sublimation of caffeine and compounds such as theobromine and theophylline which are also found in tea and have structures similar to caffeine. A small amount of water may be present. Caffeine appears to have a very large freezing point depression constant ( $K_m$ ) with the result that small amounts of impurities lower the melting point a large amount.
5. Much of the caffeine would undergo decomposition since a higher temperature would be required for sublimation.

---

## **Experiment 12**

### **ISOPENTYL ACETATE (BANANA OIL)**

TIME ESTIMATE: 2 periods, including spectroscopy

The instructor or assistant should place the appropriate liquid measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Isopentyl alcohol (3-methyl-1-butanol)	65 mL (53 g)
Conc. acetic acid (glacial)	90 mL (96 g)
Conc. $H_2SO_4$ in a dropper bottle	15 mL

Corrundum boiling stones

5% Aqueous NaHCO<sub>3</sub> 75 mL

Saturated aqueous NaCl solution 75 mL  
Use to break emulsions. Dissolve 31.7 g salt per 100 mL water and store in polyethylene bottle.

Anhydrous sodium sulfate (granular) 25 g

Waste disposal containers for aqueous and non halogenated wastes

Optional: micro boiling point capillaries (Tech 6, Section 6.11)

Optional: salt plates for infrared spectroscopy

Optional: NMR tubes for proton and carbon spectroscopy

**SPECIAL INSTRUCTIONS:**

This experiment may be stopped just before the distillation. The ester should be left stored over anhydrous sodium sulfate in a tightly stoppered container (no rubber stoppers!). A longer reflux period may give a better yield, but is not necessary.

**CAS Registry Numbers:**

Isoamyl alcohol (isopentyl alcohol or 3-methyl-1-butanol) 123-51-3

Acetic acid 64-19-7

**ANSWERS TO QUESTIONS:**

- Remove water as it is formed.
  - Remove product as it is formed.
- Sodium bicarbonate assures neutralization and removal of excess acetic and sulfuric acids by converting them to ionic salts which are very water soluble:



(Recall that H<sub>2</sub>CO<sub>3</sub> is unstable, yielding H<sub>2</sub>O and CO<sub>2</sub>.)

- As indicated in the answer to Question 2, H<sub>2</sub>CO<sub>3</sub> is unstable yielding CO<sub>2</sub>, which leaves the solution as gas bubbles.

4. Isopentyl alcohol (i-PnOH) is the limiting reagent. Acetic acid (HOAc) is used in 2.7-fold excess.

$$\frac{(5.0 \text{ mL i-PnOH}) (0.813 \text{ g i-PnOH}) (1 \text{ mole i-PnOH})}{(1 \text{ mL i-PnOH}) (88.2 \text{ g i-PnOH})} = 0.046 \text{ mole}$$

$$\frac{(7.0 \text{ mL HOAc}) (1.06 \text{ g HOAc}) (1 \text{ mole HOAc})}{(1 \text{ mL HOAc}) (60.1 \text{ g HOAc})} = 0.123 \text{ mole}$$

5. See page 566 of the Textbook.
6. C-H stretch at 2800-2900  $\text{cm}^{-1}$   
C=O 1735  $\text{cm}^{-1}$   
CH<sub>2</sub> bending at 1440  $\text{cm}^{-1}$   
C(CH<sub>3</sub>)<sub>2</sub> CH<sub>3</sub> bending for *geminal* dimethyl groups shows split peaks at 1350  $\text{cm}^{-1}$   
C-O 1210 and 1030  $\text{cm}^{-1}$
7. This is a standard acid-catalyzed Fischer esterification mechanism.
8. The melting point of pure acetic acid is 16.7 °C (62 °F). It is a solid (glacial) on a chilly day.

---

### **Experiment 13**

#### **ISOLATION OF EUGENOL FROM CLOVES**

TIME ESTIMATE: 1 period, with additional time required to obtain spectra.

The instructor or assistant should place the appropriate measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:



Ground cloves or clove buds (NOTE: We prefer to use clove buds)	15 g
Methylene chloride	40 mL
Anhydrous sodium sulfate (granular)	4 g
Evaporation station in the hood	
Waste container for methylene chloride	
Salt plates for infrared spectroscopy	
Carbon tetrachloride, small bottle with dropper for spectroscopy	

**CAS Registry Numbers:**

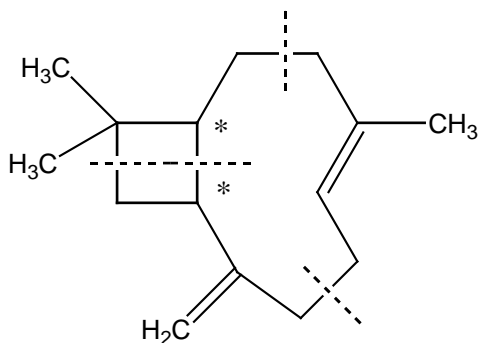
Methylene Chloride (dichloromethane)	75-09-2
Sodium sulfate (anhydrous, granular)	7757-82-6

**ANSWERS TO QUESTIONS:**

- m.p =  $-9^{\circ}$       density = 1.0664  
 b.p. =  $255^{\circ}$       index of refraction = 1.5410  
 solubility: H<sub>2</sub>O, insoluble; ethanol, miscible; chloroform, miscible;  
 ether; miscible

- Used medicinally for relief of toothache pain.

3.



- b.p. at 14 mm = 129-130; b.p. at 760 mm = about  $250^{\circ}$  using Fig 13.2  
 on page 710.
- Specific rotation =  $-5.2^{\circ}$ . Stereocenters are indicated with asterisks on  
 the structure shown in the answer to problem 3. Eugenol is not chiral.

6. The boiling point of eugenol is rather high, and distillation at high temperature would increase the risk that it would decompose. Furthermore, simple distillation in the presence of other materials present after the extractions increases the risk of decomposition.
7. Water is present in the steam distillate. It mixes in the distilling vapors, but separates (insoluble) when the vapors cool to a liquid, making the distillate cloudy.
8. a) No obvious drops of water on sides of flask  
b) Solution is clear (not cloudy).  
c) The drying agent does not clump, but flows freely.
9. a)  $P^{\circ}_{\text{substance}} = 760 - 733 = 27 \text{ mm at } 99^{\circ}\text{C}$

$$\frac{\text{moles substance}}{\text{moles water}} = \frac{P^{\circ}_{\text{substance}}}{P^{\circ}_{\text{water}}} = \frac{27}{733} = 0.037$$

$$1 \text{ g water} = \frac{1}{18} = 0.056 \text{ moles}$$

$$\text{moles substance} = (0.037)(0.056) = 0.0021$$

$$\text{g substance} = (\text{moles})(\text{M.W}) = (0.0021)(150) = 0.31 \text{ grams}$$

b)  $(0.10)(0.5) = 0.05 \text{ g of substance}$

$$\frac{0.05}{x} = \frac{0.31}{1} ; 0.31x = 0.05$$

$$x = 0.16 \text{ g of water}$$

The assumption that the substance is totally insoluble in water may not be strictly correct. In most cases the substance has some solubility in water. The amount of water which is required to steam distill the substance totally then becomes the amount calculated plus an additional amount required to distill the substance dissolved in water. Often one continues the steam distillation for several minutes after the distillate has become clear, in order to ensure that the distillation is complete.

---

## Experiment 14

### **SPEARMINT AND CARAWAY OILS: (+)- AND (-)-CARVONES**

TIME ESTIMATE: 1 period

It is suggested that students work in pairs or groups, especially if they are isolating carvones by preparative gas chromatography. A single student will not have enough material to perform all of the procedures which are given.

This experiment may be scheduled along with another experiment. Appointment schedules should be arranged for using both the polarimeter and the gas chromatograph so that students are able to make efficient use of their time.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Spearmint oil (contains R-(-)-carvone ) 2 mL

Caraway oil (contains S-(+)-carvone) 2 mL

Caraway oil (C1094) and Spearmint Oil (SP306) are available from Spectrum Chemical Mfg. Corp., 14422 South San Pedro Street, Gardena, CA., 90248-9985 (1-800-342-6615). You may also obtain spearmint oil from Rainbow Gardens, 2500 Whitefish Stage, Kalispell, MT 59901. Website: <http://rainbowgardens.net>

R-(-)-Carvone (Aldrich 12,493-1) 10 mL

S-(+)-Carvone (Aldrich 11,269-0) 10 mL

R-(+)-Limonene (Aldrich 18,316-4)  
reference standard for GC

Disposal container for non-halogenated wastes

#### **CAS Registry Numbers:**

R-(-)-Carvone 6485-40-1

S-(+)-Carvone 2244-16-8

R-(+)-Limonene 5989-27-5

## SPECIAL EQUIPMENT:

Gas chromatograph: Gow-Mac 69-350 or other suitable unit. If sample collection (Part B) is performed, the microscale collection attachments are required, and students must have the appropriate glassware. The gas chromatograph should be heated and equilibrated well in advance of the laboratory. Column temperature, 200 °C; injection and detector temperature, 210 °C; carrier gas flow rate, 20 mL/min. The recommended column is 8 feet long with a stationary phase such as Carbowax 20M. If you have a different gas chromatograph or column, you will need to check the experiment out in advance since conditions may vary.

1 or 10  $\mu$ L syringe (for analytical work)

50 or 100  $\mu$ L syringe (if sample collection is performed)

Polarimeter

The manual Zeiss and the automatic digital polarimeters are described in Technique 23.

Polarimeter cells (0.5 dm, two needed)

Refractometer (see Technique 24)

Salt plates (for infrared spectroscopy)

NMR tubes

$\text{CDCl}_3$  (for NMR spectroscopy)

## SPECIAL NOTES:

### **Odor Testing.**

For olfactory odor testing, samples of spearmint oil, caraway oil, R-(-)-carvone, and S-(+)-carvone should each be made available. Place 1 mL of each sample in separate 1 dram, screw-capped vials. Students can uncap these vials to sample the individual odors. **Save this material for future use.**

### **Gas Chromatography.**

Details and conditions are given above.

The instructor or lab assistant should prepare gas chromatograms using both carvone isomers and (+)-limonene as reference standards. Appropriate reference standards include a mixture of (+)-carvone and limonene and a second mixture of (-)-carvone and limonene. The chromatograms should be posted with retention

times so that students will know when to collect samples and how to identify their peaks.

When putting an O-ring on the gas chromatography collection tube, students should hold the tube as close to the ground glass tube as possible. To hold the collection tube more securely, it is tempting to push on the other end of the tube with the palm of one's hand. However, this additional pressure can easily break the tube and could result in an injury.

### **Polarimetry.**

The two polarimeter cells should be filled by the instructor. Students can use these prefilled cells to determine the optical rotations of the two enantiomers. Fill one cell with (+)-carvone, and the other cell with (-)-carvone. Stopper and label the cells. The rotations will not be exactly equal and opposite, but they will be close. Small amounts of limonene and other impurities affect the results.

Preparative gas chromatography will not yield enough material to perform the polarimetric analysis. The polarimeter cells should be filled with commercially available material as described above. **Save this material for future use.**

### **Spectroscopy.**

Preparative gas chromatography should yield enough material to determine an infrared spectrum of each of the enantiomers. For NMR, it will probably be necessary to have several students combine their samples. Alternatively, pure samples of the (+)- and (-) carvone can be made available for determination of the NMR spectra.

Analytical gas chromatography will only give a chromatogram trace and no sample. In this case, samples of (+)- and (-)-carvone will have to be provided for spectroscopy.

### **Boiling Points.**

Preparative gas chromatography will not yield enough material to perform microscale boiling point determinations unless several students combine their samples. Alternatively, pure samples of (+)- and (-)-carvone can be made available.

### **Refractometry.**

Once again, because of limited material, it may be best to provide pure samples of the two carvones for the students to use.

ANSWERS TO QUESTIONS:

1. Infrared spectra:

Carvone: vinyl C-H at  $3070\text{ cm}^{-1}$   
 aliphatic C-H centered on  $2900\text{ cm}^{-1}$   
 C=O (conjugated) at  $1660\text{ cm}^{-1}$   
 C=C at  $1635\text{ cm}^{-1}$

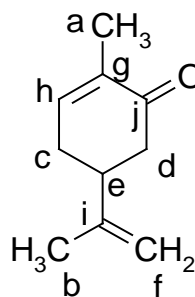
Limonene: vinyl C-H at  $3070\text{ cm}^{-1}$   
 aliphatic C-H centered on  $2900\text{ cm}^{-1}$   
 C=C at  $1635\text{ cm}^{-1}$

NMR spectrum of carvone:

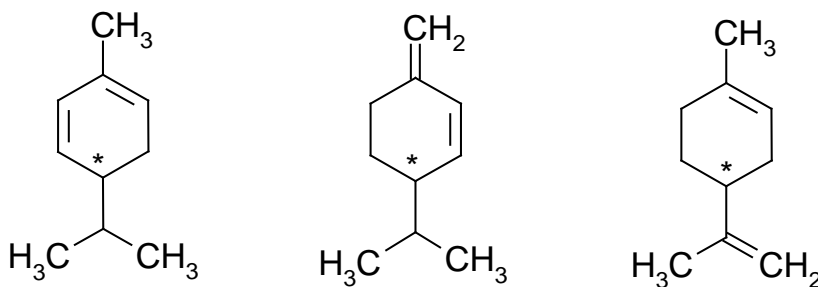
6.8 ppm C-H vinyl (1 proton)  
 4.8 ppm C=CH<sub>2</sub> vinyl (2 protons)  
 2.6 ppm methylene and methine (5 protons)  
 1.9 ppm CH<sub>3</sub> (6 protons)

carbon-13 NMR spectrum of carvone:

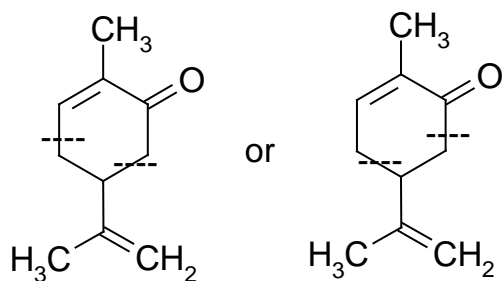
a = 15.6 q  
 b = 20.4 q  
 c = 31.2 t  
 d = 42.5 t  
 e = 43.1 d  
 f = 110.4 t  
 g = 135.3 s  
 h = 144.2 d  
 i = 146.6 s  
 j = 198.6 s



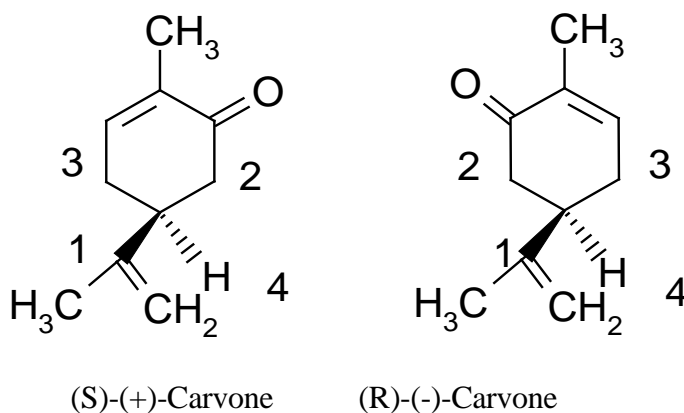
2.



3.



4.



5. Limonene is less polar and has a lower boiling point (176 °C) than the carvones (bp 230 °C).
6. Since the carvone isomers have the same boiling point and polarity, they have the same retention times. Enantiomers have the same physical properties.
7. The receptor sites which render carvone toxic are protein-based and are chiral. It is not surprising one enantiomer is more effective at binding than the other. This process, where one enantiomer is selected over the other, is called *chiral recognition*
-

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## Experiment 15

### ISOLATION OF CHLOROPHYLL AND CAROTENOID PIGMENTS FROM SPINACH

TIME ESTIMATE: 1 to 1.5 periods

The instructor should place the appropriate liquid measuring device by each reagent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Fresh spinach	8 g
or	
Frozen spinach	4 g
Fresh spinach is preferable to frozen spinach. Frozen spinach contains additional pigments which are difficult to identify.	
Mortar and pestle	1 per 5 students
Acetone	120 mL
Hexane	160 mL
Pasteur pipets (5 3/4-inch) for columns	2 per student
Anhydrous sodium sulfate (powdered or granular)	6.5 g
70% Hexane-30% acetone (by volume) Mix thoroughly until homogenous.	90 mL
80% Acetone-20% methanol (by volume) Mix thoroughly until homogenous.	90 mL
Alumina	16 g
Use EM Science No. AX0612-1 alumina. The particle sizes are 80-200 mesh and material is Type F-20. The Alumina must be dried in an oven at 110 °C overnight and stored in a tightly sealed bottle (see Notes to the Instructor on p 126 of Textbook)	
Whatman Silica gel plates with fluorescent indicator, No. 4410 222 (10-cm x 3.3-cm) Use a paper cutter to cut the plates to size, being careful not to touch the surface. If the plates have not been purchased recently, heat them at 100 °C for 30 minutes and store the plates in a desiccator.	1 per student



Wide-mouth screw cap jars with filter paper liner  
or 400 mL beaker (for use as developing tanks)

1 per student

Aluminum foil, if beakers are used as developing tanks

Cotton

Thin wall open end capillary tubing (1 mm) for micropipets  
Rulers with centimeter scale and pencils

Evaporation station in a hood

Waste disposal container for non-halogenated solvents

Container for disposal of Pasteur pipets filled with wet alumina

#### SPECIAL INSTRUCTIONS:

The alumina and silica gel plates specified above must be used to obtain the results described in this experiment. We have used different alumina and different prepared silica gel plates and have not obtained consistent results.

It is desirable to complete this experiment in one period, because the pigments are light sensitive and can undergo air oxidation.

#### ANSWERS TO QUESTIONS:

1. Chlorophyll is less mobile than  $\alpha$ -carotene in both column and thin-layer chromatographies because chlorophyll is a more polar molecule than  $\alpha$ -carotene. Chlorophyll has a greater number of double bonds, and it possesses a far greater number of electronegative elements. These structural differences mean that chlorophyll, because of its greater polarity, will be more strongly adsorbed onto the alumina than  $\beta$ -carotene would.
2. Refer to the structure of chlorophyll on p 116 of the Textbook. In both pheophytin **a** and pheophytin **b**, the  $Mg^{2+}$  ion is replaced by two hydrogen ions,  $2 H^+$ . One hydrogen is bonded to the nitrogen in the upper right position and the other hydrogen is bonded to the nitrogen in the lower left position.
3. Because acetone is more polar than hexane, increasing the concentration of acetone would cause the pigments to move up the plate more rapidly and the  $R_f$  values of the pigments would be greater.

4. Since the yellow band produces only one spot when analyzed by thin-layer chromatography, it can be considered to be pure (actually it consists of  $\alpha$ - and  $\beta$ -carotene which have similar  $R_f$  values). The green band separates into several spots when analyzed by TLC indicating that the green band is impure.

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## Experiment 16

### ETHANOL FROM SUCROSE

TIME ESTIMATE: 30 min. to set up fermentation (1st period) and 1 period for distillation (2nd period).

CHEMICALS PER 10 STUDENTS:

Sucrose	250 g
Dried baker's yeast	25 g
Pasteur's salts 2.0 g potassium dihydrogen phosphate, 0.20 g calcium phosphate (monobasic), 0.20 g magnesium sulfate, and 10.0 g ammonium tartrate (diammonium salt) dissolved in 860 mL water.	500 mL
Barium hydroxide solution (dissolve 15 g of solid barium Hydroxide in 150 mL of water)	150 mL
Filter Aid (Johns-Manville Celite)	125 g
Potassium carbonate (anhydrous)	400 g

OTHER APPARATUS REQUIRED:

250-mL Erlenmeyer flasks (if not included in locker equipment)	10
--	----

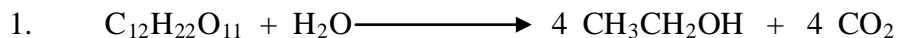
Stainless steel cleaning pad material for fractionating columns

Automatic pipet and tips for determining density of alcohol

Vernier Lab Pro (if available) with temperature probe and laptop computer. (See Experiment 6 in this manual for more information about this equipment).

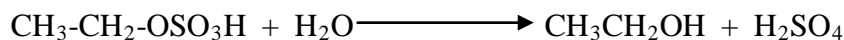
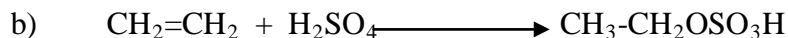
**CAS Registry Number:**

Potassium dihydrogen phosphate (monobasic)	7778-77-0
Calcium phosphate	10103-46-5
Magnesium sulfate	7487-88-9
Ammonium tartrate (diammonium salt)	3164-29-2

**ANSWERS TO QUESTIONS:**

2. Two possible methods:

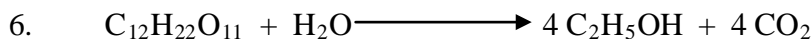
a) Obtain 95% ethanol from fermentation by distillation. Then add enough benzene to remove the water by means of the benzene-water-ethanol azeotrope and redistill.



3. The air trap is necessary to prevent air from reaching the fermentation mixture. In the presence of air, and with the aid of certain bacteria, the ethanol may be oxidized to acetic acid.

4. The acetaldehyde impurity results from the slow air oxidation of ethanol.

5. Diethylacetal arise from the reaction of 2 molecules of ethanol with the trace amount of acetaldehyde impurity formed from oxidation (see Question 4 above) resulting in the formation of 1,1-diethoxyethane.



Molecular weight:  $C_{12}H_{22}O_{11} = 342 \text{ g/mole}$

$$20.0 \text{ g sucrose} = \frac{20.0 \text{ g}}{342 \text{ g/mole}} = 0.058 \text{ mole sucrose}$$

$$0.058 \text{ mole sucrose} = (4)(0.058) = 0.23 \text{ mole } CO_2$$

$$\frac{0.23}{1} = \frac{x}{22400} ; x = \text{mL } CO_2 \text{ at STP} = 5150 \text{ mL}$$

$$\frac{5150}{273} = \frac{V}{298} \quad ; \quad V = \text{mL CO}_2 \text{ at 25 EC} = 5620 \text{ mL}$$

---

### **Experiment 17**

#### **AN INTRODUCTION TO MOLECULAR MODELING**

TIME ESTIMATE: 2 periods (this experiment can also be scheduled as an outside-of-class exercise)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

This experiment does not require any chemicals or special equipment. It does, however, require that the laboratory have available computers and the appropriate software. The exercises contained in this experiment were developed using PC Spartan Plus software. It should, however, be possible to use a number of other molecular modeling software packages, including Alchemy 2000, Spartan, PC Spartan, MacSpartan, HyperChem, CAChe, Personal CAChe, PCModel, Insight II, Nemesis, and Sybyl. It is important to use a software package that has the ability to perform calculations with minimization of the strain energy (not all programs contain a minimizer!).

Whatever program is used, it will be necessary for the instructor to provide an introduction to that particular implementation and to provide instructions in its use. The introduction should show students how to build a molecule, how to minimize its energy, how to measure bond lengths and bond angles, and how to load and save files.

---

### **Experiment 18**

#### **COMPUTATIONAL CHEMISTRY- *ab initio* and SEMIEMPIRICAL METHODS**

TIME ESTIMATE: 2 periods (this experiment can also be scheduled as an outside-of-class exercise)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

This experiment does not require any chemicals or special equipment. It does, however, require that the laboratory have available computers and the appropriate software. The exercises in this experiment were developed using PC Spartan Plus and MacSpartan Plus software (Wavefunction, Inc., 18401 von Karman, Suite 370, Irvine, CA, 714-660-6101, <http://www.wavefun.com>). It should also be possible to use other software packages such as CAChe Workstation, HyperChem Release 5 and others. Many software releases that feature the MOPAC package of programs are also capable. The software must be able to perform a current version of MNDO-type semiempirical calculations such as AM-1, MINDO (part of the MOPAC package), or ZINDO. As written, many of the exercises require a 3-D color display of isodensity surfaces upon which a property (such as elpot) has been mapped - not all programs do this equally well. The program should also be capable of plotting orbitals such as the HOMO and LUMO on the molecular skeleton.

Whatever program is used, it will be necessary for the instructor to provide an introduction to that particular implementation and to provide instructions in its use. The introduction should show students how to build a molecule, how to load and save files, and how to set up a calculation and request surfaces. Many of the options which must be chosen are discussed in the essay *Computational Chemistry* which precedes experiment 18.

The various sections 18A-18E can be assigned independently, perhaps with a related experiment. For instance, section 18B ( $S_N1$  rates) and 18D (carbocation stability) could be assigned with a related  $S_N1$  experiment such as Experiment 19 or Experiment 20. Section 18E (carbonyl reactivity) could be assigned with Experiments 31, 32A, 37 and 39. It is not necessary to assign all of the subparts at the same time. The full set of procedures in Experiment 18 was selected to show a cross section of the various applications of molecular modeling, but was not intended to be complete.

---

## **Experiment 19**

### **REACTIVITIES OF SOME ALKYL HALIDES**

TIME ESTIMATE: 1 period

This experiment requires very little time. We usually have students work in pairs on this experiment and co-schedule it with Experiment 20. Confusion often arises when students try to make conclusions before the solutions are adequately mixed. Since contamination is a potential problem, you should try each of the halides to test for purity. The expected results are given below.

See page 159 in the textbook, under Notes to the Instructor, for an alternative way of conducting this experiment using a guided-inquiry experience.

CHEMICALS PER 10 STUDENTS:

2-Chlorobutane	10 mL
2-Bromobutane	10 mL
1-Chlorobutane	10 mL
1-Bromobutane	10 mL
2-Chloro-2-methylpropane ( <i>tert</i> -butyl chloride)	10 mL
Crotyl chloride (1-chloro-2-butene)-- Lachrymator	10 mL
Benzyl chloride ( $\alpha$ -chlorotoluene)--Lachrymator	10 mL
Bromobenzene	10 mL
Bromocyclohexane	10 mL
Bromocyclopentane	10 mL

NOTE: It is helpful if each of the above reagents is contained in a dropper bottle. Dispensing of these chemicals is made easier thereby. Some of the materials are lachrymators. They should be stored in a hood.

15% (by weight) Sodium iodide in acetone solution (15 g/85 g acetone)	250 mL
--	--------

1% (by weight) Silver nitrate in ethanol solution (1 g/100 g absolute ethanol)	250 mL
---	--------

Disposal container for halides and acetone washings (halogenated waste).

Disposal container for silver nitrate wastes

RESULTS:

**NaI/Acetone Test ( $S_N2$ )**

2-chlorobutane: no precipitate cold or hot: secondary substrate, but poor leaving group

2-bromobutane: no precipitate cold, precipitates hot; better leaving group

1-bromobutane: precipitate cold; primary substrate, good leaving group

1-chlorobutane: no precipitate cold, cloudy when heated; primary but poor leaving group

*tert*-butyl chloride: no precipitate, cold or hot: tertiary substrate; however, **watch for false tests because of contamination!**

crotyl chloride: precipitate cold; primary and allylic substrate

benzyl chloride: precipitate cold; primary and benzylic substrate

bromobenzene: no precipitate cold or hot; phenyl halides are unreactive

bromocyclohexane: no precipitate cold or hot; even though it is a secondary substrate like 2-bromobutane, there is increased ring and torsional (eclipsing) strain in the transition state. Bromocyclohexane is the ideal unstrained molecule. Students should be told to ignore any color changes that may occur.

bromocyclopentane: no precipitate cold, precipitate hot; this secondary substrate reacts because of relief of ring strain in the transition state. Bromocyclopentane is relatively planar and has torsional (eclipsing) strain. In the transition state some of this torsional strain is relieved, leading to increased reactivity over bromocyclohexane.

### **AgNO<sub>3</sub>/Ethanol Test (S<sub>N</sub>1)**

2-chlorobutane: no precipitate cold, cloudy hot; secondary substrate but poor leaving group

2-bromobutane: heavy precipitate cold; secondary substrate, better leaving group

1-chlorobutane: no precipitate cold, slight cloudiness hot; primary substrate and poor leaving group

1-bromobutane: cloudy cold; primary substrate and better leaving group

*tert*-butyl chloride: heavy precipitate cold; tertiary substrate

crotyl chloride: heavy precipitate cold; allylic substrate

benzyl chloride: heavy precipitate cold, but forms more slowly than tertiary substrate; benzylic substrate

bromobenzene: no precipitate cold or hot; phenyl halides are unreactive

bromocyclohexane: medium cloudiness cold; even though it is a secondary substrate like 2-bromobutane there is increased ring strain and eclipsing in the planar carbocation intermediate when compared to starting material which has no ring strain or eclipsing (torsional) strain. This retards the reaction.

bromocyclopentane: heavy precipitate cold; this secondary substrate reacts rapidly in order to relieve eclipsing (torsional) strain present in the nearly planar starting material to give the less strained secondary carbocation intermediate. This increases the rate of reaction.

**CAS Registry Numbers:**

Sodium iodide	7681-82-5
Silver nitrate	7761-88-8
2-Chlorobutane	78-86-4
2-Bromobutane	78-76-2
1-Chlorobutane	109-69-3
1-Bromobutane	109-65-9
2-Chloro-2-methylpropane ( <i>tert</i> -butyl chloride)	507-20-0
Crotlyl chloride (1-chloro-2-butene)	591-97-9
Benzyl chloride ( $\alpha$ -chlorotoluene)	100-44-7
Bromobenzene	108-86-1
Bromocyclohexane	108-85-0
Bromocyclopentane	137-43-9

**ANSWERS TO QUESTIONS:**

1. 2-Bromobutane is more reactive than 2-chlorobutane because the bromo group is a better leaving group than the chloro group. The bromo group, being larger, is held to carbon by a weaker bond than the chloro group. Bromide ion is a more stable anion than chloride ion.
2. Benzyl chloride has its reactive carbon adjacent to a benzene ring. Electron delocalization involving this ring stabilizes the transition state in a  $S_N2$  reaction to some extent, thus leading to an accelerated reaction. In the  $S_N1$  reaction, benzyl chloride yields the carbocation that is stabilized by resonance with the benzene ring. Thus, benzyl chloride reacts quickly in both types of reactions. Bromobenzene is unreactive because the C-Cl bond is very strong. In addition, a phenyl cation is very unstable ( $S_N1$ ) and the benzene ring has a high electron density that makes attack by



negative nucleophiles unfavorable ( $S_N2$ ).

3. See answer in Question 2. The 1-chlorobutane, a saturated primary halide, is relatively unreactive because there is no benzene ring to help stabilize the  $S_N2$  transition state.
4. 2-Chlorobutane is a secondary halide that forms a secondary carbocation in the silver nitrate test ( $S_N1$ ). This cation is less stable than the tertiary cation formed from 2-chloro-2-methylpropane.
5. The reactivity differences for these  $S_N2$  reactions are discussed above under Results.
6. In the sodium iodide/acetone test ( $S_N2$ ) and the silver nitrate/ethanol test ( $S_N1$ ), the orders of reactivity would be the same:

1 > 3 > 2 (allylic halide > primary halide > vinyl halide)

---

## **Experiment 20**

### **NUCLEOPHILIC SUBSTITUTION REACTIONS: COMPETING NUCLEOPHILES**

**TIME ESTIMATE:** 1 period, with some additional time to analyze the products. Students may choose either 1-butanol or 2-butanol as substrates, or the instructor can divide the class into two groups. Everyone does 2-methyl-2-propanol (*tert*-butyl alcohol) as a substrate.

**CHEMICALS AND SUPPLIES PER 10 STUDENTS:**

Solvent-nucleophile medium (see below)

Screw-cap centrifuge tubes

1-Butanol 10 mL

2-Butanol 10 mL

*tert*-Butyl alcohol (2-methyl-2-propanol) 12 mL

During cold weather, it may be necessary to heat the *tert*-butyl alcohol before the class period in order to melt it.

Inert boiling stones

Saturated aqueous sodium bicarbonate	20 mL
Pentane	13 mL
Sodium bicarbonate (solid)	1 g
Anhydrous granular sodium sulfate	4 g

GC-MS vials for storing products overnight  
See Results and Special Notes, below

Disposal container for aqueous wastes

Disposal container for halogenated wastes

#### PREPARATION OF SOLVENT-NUCLEOPHILE MEDIUM

We have found that it is much more convenient and safer to have the solvent-nucleophile medium prepared in advance and dispensed to each student by a laboratory assistant. The following instructions are sufficient to prepare 500 mL of the solution. This quantity should be sufficient for about 30 students; 10 mL for 20A and 6 mL for 20B.

**NOTE WELL:** This solution should be prepared fresh each day. If the solution is allowed to stand over an extended period, it will change composition, as hydrogen chloride is more volatile than hydrogen bromide. HCl will preferentially evaporate from the solution on standing, resulting in a solution that is rich in bromide ion.

The solvent-nucleophile medium must be prepared in advance for entire class. The temperature of this mixture must be carefully maintained at 45°C to prevent the ammonium halides from precipitating (selectively) from the solution.

- Add 250 g of ice to a two-liter beaker
- Place the beaker in a large ice bath (we use a plastic tub filled with an ice-water mixture)
- Add 187 mL of concentrated sulfuric acid, *slowly*.
- Weigh 46.9 g of ammonium chloride and 86.5 g of ammonium bromide into a 600-mL beaker. Crush all lumps that may be present.
- Transfer the solid to a two-liter Erlenmeyer flask.
- Slowly add the sulfuric acid mixture to the solid, a little at a time. Swirl the flask during the addition to dissolve the solids.
- When all of the sulfuric acid has been added, it will be necessary to heat the mixture and stir it, using a magnetic stirring bar, to get the salts to dissolve.

- Keep the solvent-nucleophile medium in the two-liter Erlenmeyer flask, in a dispensing hood. Place the flask on a large hot plate. Keep a thermometer in the flask, and cover the opening with Parafilm. Maintain the mixture at 45°C (do not heat above this temperature) with stirring.
- The instructor or assistant should dispense the solvent-nucleophile mixture. Attach a Brinkman pipette helper to a 10-mL graduated pipette (one that dispenses its entire contents).
- Experiment 20A: Dispense 10 mL to each student directly into their 25 mL round bottom flask.
- Experiment 20B: Dispense 6 mL to each student directly into their centrifuge tube.
- Some halide salts may precipitate from the mixture, but students can reheat the solution to get the solids to redissolve.
- The results of the experiment are highly dependent on the care with which this solution is prepared and on the time that has passed between the when the solution was prepared and when the students actually use it.

#### OTHER EQUIPMENT REQUIRED:

##### Gas Chromatograph

Prepared as follows: column temperature, 100 °C; injection and detector temperature, 130 °C; carrier gas flow rate 50 mL/min. The recommended column is 8 feet long with a stationary phase such as Carbowax 20M. The gas chromatograph must be heated and equilibrated in advance.

It is recommended that the class store their samples in GC-MS tubes (see Results and Special Notes, below). **It possible, you should try to analyze the halide mixtures on the day of their preparation.**

It may be helpful to obtain small samples of each of the halide products (1-chlorobutane, 1-bromobutane, 2-chlorobutane, 2-bromobutane, 2-chloro-2-methylpropane, and 2-bromo-2-methyl propane) to check elution order and gas chromatographic retention times. It may also be instructive to prepare 50/50 mixtures of the 1-butyl, 2-butyl and *tert*-butyl halides to ascertain whether the gas chromatographic response factor is actually unity for each and every product. This is particularly important for the *tert*-butyl halides.

In addition, it should be noted that small amounts of starting alcohols and elimination products (1-butene, 2-butene, and 2-methylpropene) may be observed in the chromatograms. Elimination products are most likely to occur when analyzing the *tert*-butyl halides.

10 µL Gas chromatograph syringe

Refractometer

NMR tubes

Deuteriochloroform for NMR

#### RESULTS AND SPECIAL NOTES:

If it is necessary to store the distillates before analyzing them by GC, it is very important that they be stored in leak-proof vials. Otherwise, more of the more volatile component will evaporate and the % composition will change. We use GC-MS vials from Agilent Technologies: vials (5182-0715) and caps (5182-0717). Samples may be stored in these vials at room temperature with very little loss.

For the reaction with *tert*-butyl alcohol, typical percentages are 50% for both the alkyl chloride and the alkyl bromide. For the reaction with 1-butanol, typical percentages are 85% for the alkyl bromide and 15% for the alkyl chloride. The percentages for 2-butanol are 75% for the alkyl bromide and 25% for the alkyl chloride.

#### CAS Registry Numbers:

1-Butanol 71-36-3

2-Butanol 78-92-2

*tert*-Butyl alcohol (2-methyl-2-propanol) 75-65-0

Ammonium chloride 12125-02-9

Ammonium Bromide 12124-97-9

#### ANSWERS TO QUESTIONS:

1. *tert*-Butyl Alcohol: This is an S<sub>N</sub>1 reaction. According to the mechanism, the formation of the carbocation is rate-determining. Therefore, the cation should not be selective with respect to possible nucleophiles, and the product distribution should be approximately statistical (i.e., 50-50).

1-Butanol: This is an S<sub>N</sub>2 reaction. According to the mechanism, the nucleophile is present in the rate equation. Therefore, the more reactive nucleophile should lead to faster formation of products. As a result, the percentage of alkyl bromide in the products should be much higher than the percentage of alkyl chloride.

2. Bromide ion is the better nucleophile. Two explanations are commonly given: (a) bromide ion is more "polarizable", and (b) chloride ion has a higher charge to surface area ratio (size argument) and solvates more

strongly in aqueous media. As a result of this solvation, chloride ion is effectively larger and, in order to react, it must "escape" from this solvent cage. Both factors cause it to be a poor nucleophile.

3. The alkenes formed by elimination are the principal by-products: 1-butene from 1-butanol, and 2-methylpropene from 2-methyl-2-propanol.
4. The more volatile (lower b.p.) compound would diminish due to preferential evaporation. This would give more bromide as the chlorides have lower b.p.'s.
5. Unless all the solids are dissolved, one cannot be sure the reaction mixture contains a 50/50 mixture of the two nucleophiles -- an excess of one of the nucleophiles would give a larger than expected yield of the product resulting from that nucleophile.
6. In the  $S_N2$  reaction (1-butanol), more alkyl chloride than alkyl bromide would have been the result, just the opposite of the result in water. In aprotic solvents, chloride is a better nucleophile (less solvated) than bromide.
7. The elution order is according to boiling point. The lowest boiling point compound elutes first. In general, since molecules with lower molecular weights also have lower boiling points, the retention times follow an order of increasing molecular weight.
8. It is a mole percentage.
9.
  - a) 2-Methylbutene
  - b) In order for this elimination reaction to occur, molecules of the reactant (*tert*-butyl bromide) must have enough energy to get over the energy of activation barrier. When the temperature is increased, a greater proportion of *tert*-butyl bromide molecules have this necessary energy and the amount of alkene increases.
  - c) Because bromide is a better leaving group than chloride.

---

## Experiment 21

### **SYNTHESIS OF *n*-BUTYL BROMIDE AND *tert*-PENTYL CHLORIDE**

TIME ESTIMATE: 1-2 periods for *n*-butyl bromide and 1 period for *tert*-pentyl chloride

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### *n*-BUTYL BROMIDE

Sodium bromide	215 g
<i>n</i> -Butyl alcohol (1-butanol)	125 mL (102g)
Conc. sulfuric acid	175 mL
9M sulfuric acid	175 mL
Saturated Sodium bicarbonate solution	175 mL
Anhydrous calcium chloride (granular)	13 g
Microporous boiling stones	
Glass tubing	
Salt plates for infrared spectroscopy	
Micro boiling point tubes (optional)	
Disposal container for aqueous waste	

#### *tert*-PENTYL CHLORIDE

<i>tert</i> -Pentyl alcohol ( <i>t</i> -amyl alcohol, 2-methyl-2-butanol)	125 mL (101g)
Conc. hydrochloric acid	315 mL
5% Sodium bicarbonate solution	125 mL

Anhydrous calcium chloride (granular) 13 g

Microporous boiling stones

Salt plates for infrared spectroscopy

Micro boiling point tubes (optional)

Disposal container for aqueous waste

**CAS Registry Numbers:**

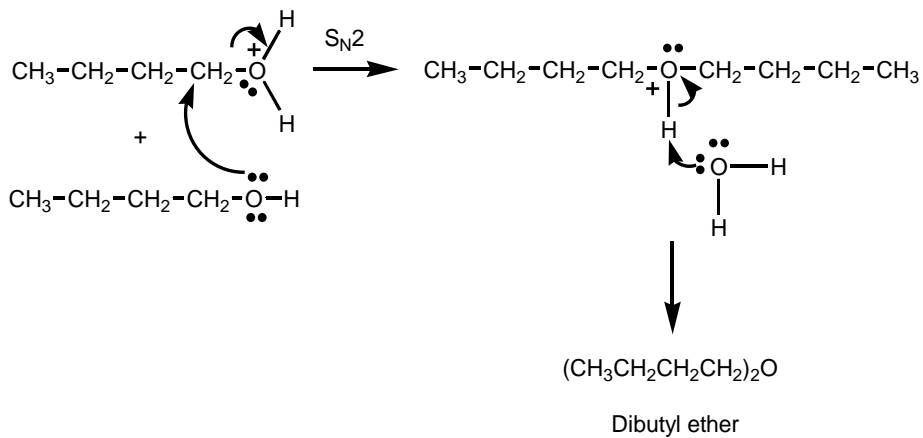
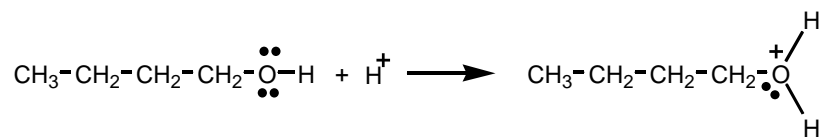
1-butanol 71-36-3

2-methyl-2-butanol (*t*-amyl alcohol) 75-85-4

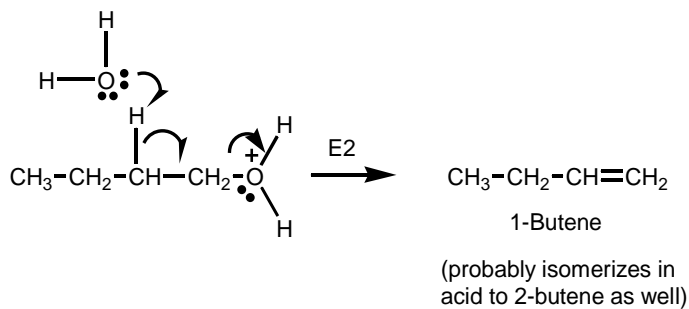
**ANSWERS TO QUESTIONS (*n*-BUTYL BROMIDE):**

1. NaBr, NaHSO<sub>4</sub>, Na<sub>2</sub>SO<sub>4</sub>
2. The density of *n*-butyl bromide is 1.269 g/mL. It is more dense than water, but less dense than the reaction mixture which contains a high concentration of dissolved salts, (H<sub>2</sub>O + NaBr + H<sub>2</sub>SO<sub>4</sub> + Na<sub>2</sub>SO<sub>4</sub> + NaHSO<sub>4</sub> + HBr, etc.)

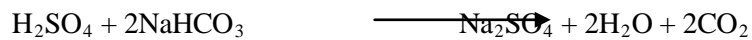
3. (a)



(b)

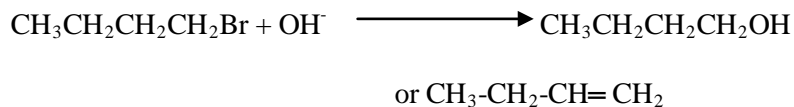


4. (a) Aqueous  $\text{NaHCO}_3$  was used to neutralize the acids:





- (b) Hydroxide is both a strong nucleophile and a strong base, both S<sub>N</sub>2 (by OH<sup>-</sup>) and E2 reactions could occur:



5. Since the density of *n*-butyl chloride is 0.88 g/mL, it will appear as the upper phase at each stage of the isolation. The other phases would all be more dense.
6. Many organic compounds will co-distill (azeotrope) with water. One may observe an incorrect boiling point in addition to obtaining an impure (cloudy) product.

ANSWERS TO QUESTIONS (*tert*-PENTYL CHLORIDE):

1. a) Aqueous NaHCO<sub>3</sub> was used to remove excess (unreacted) HCl:
- $$\text{HCl} + \text{NaHCO}_3 \longrightarrow \text{NaCl} + \text{H}_2\text{O} + \text{CO}_2$$
- b) Since *tert*-pentyl chloride is a tertiary alkyl halide, it can react readily with strong bases such as aqueous sodium hydroxide to form an alkene. The use of sodium bicarbonate avoids this problem.
2. Although some of the 2-methyl-2-butene can be produced *via* the carbocation (E1 reaction), most of it is likely to be produced by E2 reaction in the presence of base (sodium bicarbonate).
3. The unreacted *tert*-pentyl alcohol is removed by extraction with water. It is soluble in water while the *tert*-pentyl chloride product is only slightly soluble.
4. See the answer given above in question 6, above.
5. The density of 2-chloro-2-methylbutane is 0.8653 g/mL. It would float on water since it is less dense.
-

## Experiment 22

### 4-METHYLCYCLOHEXENE

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

4-Methylcyclohexanol 95 mL

85% Phosphoric acid (14.7 M) 25 mL

Concentrated sulfuric acid, with dropper 5 mL

Aqueous saturated sodium chloride 25 mL  
Dissolve 31.7 g salt in 100 mL water and store in a polyethylene bottle.

Centrifuge tubes

Anhydrous sodium sulfate (granular) 20 g

Boiling stones

Micro boiling point capillaries (optional)

Salt plates for infrared spectroscopy (optional)

For the unsaturation tests:

4-methylcyclohexanol in a dropper bottle 10 mL

Br<sub>2</sub>/CH<sub>2</sub>Cl<sub>2</sub> test solution in a dropper bottle 10 mL  
(2% bromine by volume)

Aqueous KMnO<sub>4</sub> solution in a dropper bottle 10 mL  
(1% weight/volume)

1,2-Dimethoxyethane in a dropper bottle 10 mL

Disposal container for aqueous wastes

Disposal container for potassium permanganate wastes

Disposal containers for halogenated and non-halogenated wastes

### SPECIAL NOTE:

We have had some problems with this experiment when using sulfuric acid and phosphoric acid stored in student-use bottles that had been around for some time. It may be advisable to use bottles of these reagents of known purity.

### CAS Registry Numbers:

4-Methylcyclohexanol 589-91-3

1,2-Dimethoxyethane 110-71-4

### ANSWERS TO QUESTIONS:

- This is just the usual E1 mechanism, wherein a hydrogen ion is removed from the carbocation to form 4-methylcyclohexene.
  - |                        |                            |
|------------------------|----------------------------|
| a) cyclohexene         | d) 1,2-dimethylcyclohexene |
| b) 1-methylcyclohexene | e) cyclohexanone           |
| c) 1-methylcyclohexene |                            |
  - |   |   |
|---|---|
| <u>4-Methylcyclohexene</u>                          | <u>4-Methylcyclohexanol</u>                         |
| C-H vinyl 3040 $\text{cm}^{-1}$                     | No C-H vinyl ( $>3000 \text{ cm}^{-1}$ )            |
| Methyl and ring C-H<br>2950 - 2850 $\text{cm}^{-1}$ | Methyl and ring C-H<br>2950 - 2850 $\text{cm}^{-1}$ |
| C=C 1660 $\text{cm}^{-1}$ (weak)                    | No C=C  |
| No OH   | OH 3100-3600 (broad)                                |
| Ring CH <sub>2</sub> groups 1450 $\text{cm}^{-1}$   | Ring CH <sub>2</sub> groups 1450 $\text{cm}^{-1}$   |
| Methyl bending 1375 $\text{cm}^{-1}$                | Methyl bending 1375 $\text{cm}^{-1}$                |
  - The C-H out-of-plane bending vibrations are seen as the strong peak at around 650  $\text{cm}^{-1}$ . The presence of a single strong peak in the neighborhood of 700  $\text{cm}^{-1}$  indicates a *cis*-1,2-disubstituted double bond.
  - Salt is added to force a better separation of the organic layer from the water.
-

## Experiment 23

### METHYL STEARATE FROM METHYL OLEATE

TIME ESTIMATE: 1 period

There is a potential danger of a fire or flash in this experiment. A particularly active batch of Pd/C may flash when the catalyst comes into contact with air, methanol and hydrogen. See page 192 of the Textbook.

A potentially less pyrophoric form of the palladium catalyst is available from GFS Chemical Company. The authors of this textbook haven't class tested the material for safety, but it seems to be a reasonable choice. See page 191 of the Textbook for the address and phone number for this company.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Mossy zinc	40 g
6M Sulfuric acid	200 mL
Methyl oleate (Aldrich Chemical Co., No. 31,111-1)	32 mL
Methanol	200 mL
10% Pd on carbon It facilitates this lab if the students are supplied with a vial or a glassine envelope containing the 0.050 g (50 mg) of Pd/C catalyst required.	0.7 g
6-inch lengths of rubber tubing (relatively new with no gas leakage)	2/student
Pasteur pipette for bubbler	
Glass tubing	
Rubber stoppers, solid and one-hole	
Mineral oil	
Centrifuge tubes	
Filter paper for Büchner funnel	

Melting point tubes

Unsaturation tests (optional)

5% Bromine in  $\text{CH}_2\text{Cl}_2$  20 mL

5 mL  $\text{Br}_2$ :95 mL  $\text{CH}_2\text{Cl}_2$ ; It should be freshly prepared every 2-3 days.

Methylene chloride 20 mL

Methyl oleate in dropper bottle 10 mL

Container for used mineral oil (can be reused)

Container for palladium catalyst

Waste container for mossy zinc (larger pieces can be reused)

Waste container for sulfuric acid from hydrogen generator

Waste containers for aqueous and halogenated solvents

**CAS Registry Numbers:**

Zinc (mossy) 7440-66-6

Sulfuric acid 7664-93-9

Methyl oleate 112-62-9

Methanol 67-56-1

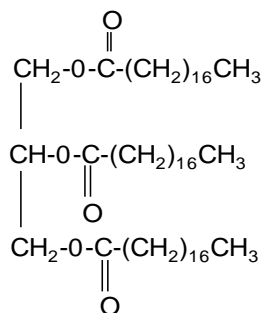
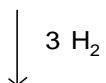
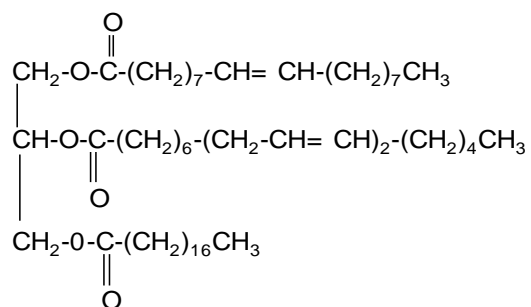
Palladium on carbon 7440-05-3

Bromine 7726-95-6

Methylene chloride (dichloromethane) 75-09-2

ANSWERS TO QUESTIONS:

1.



2. First calculate the number of moles of hydrogen absorbed. Then 0.15 g of the sample represents this same number of moles if the compound has only one double bond.

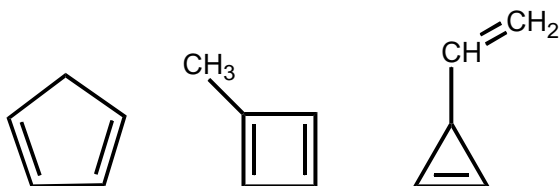
$$PV = nRT$$

or

$$n = \frac{PV}{RT} = \frac{(1 \text{ atm})(0.025 \text{ L})}{(0.082 \frac{\text{L-atm}}{\text{mol-K}})(298\text{K})} = 0.001 \text{ moles H}_2 = \text{mole sample}$$

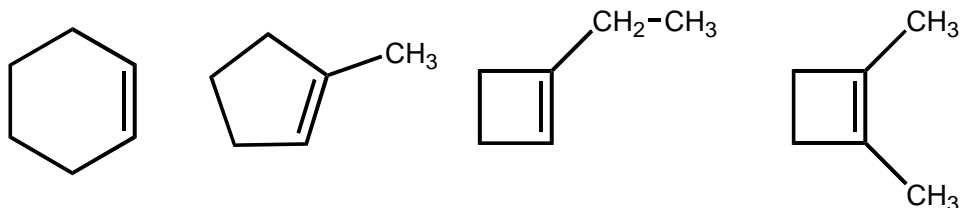
$$\text{Molecular weight} = \frac{0.15 \text{ gram}}{0.001 \text{ mole}} = 150 \text{ grams/mole}$$

3. The formula  $C_5H_6$  indicates 3 units of unsaturation when it is compared to  $C_5H_{12}$  ( $C_nH_{2n+2}$ ). Since it only absorbs two moles of hydrogen, one of those must be a ring. Possible structures include:



assuming the cyclopropane ring would not be reduced under these conditions of hydrogenation.

4. The formula  $C_6H_{10}$  indicates 2 units of unsaturation when it is compared to  $C_6H_{14}$  ( $C_nH_{2n+2}$ ). Since only one mole of hydrogen is absorbed, one of these units must be a ring. Possible structures include (many more possible):



5. A commercial oil, such as corn oil, would be composed of triglycerides rather than a pure fatty acid. The triglycerides in a typical sample of corn oil would have about 45% oleic, about 38% linoleic acid, and about 17% saturated fatty acids attached. When hydrogenated, this oil would yield a semi-solid product similar to Crisco, a cooking fat or "shortening."

---

### Experiment 24

#### GAS CHROMATOGRAPHIC ANALYSIS OF GASOLINES

TIME ESTIMATE: Less than 1/2 period

This experiment requires very little time, and it may be co-scheduled with another experiment. An appointment schedule should be arranged for use of the gas chromatograph.

#### CHEMICALS PER 10 STUDENTS:

Pentane	1 mL
Hexane	1 mL
Benzene	1 mL
Heptane	1 mL
Toluene	1 mL
Xylenes (mixture of ortho, <i>meta</i> and <i>para</i> )	1 mL
Mixture of 6 compounds, above	1 mL
Ethanol	1 mL
Mixture of 6 compounds, plus ethanol	1 mL
Methyl <i>tert</i> -butyl ether	1 mL



Mixture of 6 compounds, plus methyl *tert*-butyl ether 1 mL

Gasoline samples (select several different brands, including independents, from each of the following grades). These samples are provided by the instructor or collected by students.

Regular unleaded  
Premium unleaded  
Regular leaded (if available)  
Oxygenated gasolines

Waste container for gasoline samples

#### OTHER EQUIPMENT REQUIRED:

Gas chromatograph

Conditions for the Gow-Mac 69-350: 8-foot column with 20% DC-710; column temperature, 110 °C; injector and detector temperature, 130 °C; carrier gas flow rate, 50 mL/min.

It is recommended that you use a gas chromatograph with a capillary column, such as the Hewlett Packard 5890 gas chromatograph, equipped with FID detector and a 30-meter or longer, DB 5 capillary column (0.32 mm, with 0.25 micron film, available from J and W Scientific). Separations of gasoline samples are superb. Conditions are as follows: temperature programmed 5 to 45 °C at 10 °C/min, 45 to 55 °C at 30 °C/min, 55 to 150 at 50 °C/min, and then maintained at 150 °C for 3 min.; temperatures below ambient are achieved with a flow of gaseous carbon dioxide. Helium pressure at head: 13 psi; flow rate through column: 1.5 to 2 mL/min.; split flow: 100 mL/min.; injector temperature, 110 °C; detector temperature, 120 °C.

Syringe (10 microliter or smaller)

Sample jars or metal containers (if students are to collect gasoline samples).

#### CAS Registry Number:

Pentane	109-66-0]
Hexanes	110-54-3
Benzene	71-43-2
Heptane	142-82-5
Toluene	108-88-3
Xylenes (mixture of ortho, <i>meta</i> and <i>para</i> )	1330-20-7
Methyl <i>tert</i> -butyl ether	1634-04-4

## ANSWERS TO QUESTIONS:

1. Benzene has a higher vapor pressure than toluene; toluene has a higher vapor pressure than m-xylene. Gas chromatographic separations depend not only on polarity but also on volatility. The more volatile components have shorter retention times, provided that their polarities are similar. Such is the case with these aromatic hydrocarbons.
  2. The composition of a given grade of gasoline may vary slightly from one brand to another. These differences may be difficult to detect, however, and a great deal of experience would be required to make a precise identification. A high-quality capillary column would probably be required.
  3. The OH functional group can be seen in the infrared spectrum as a broad absorption at 3700 - 3300  $\text{cm}^{-1}$  (hydrogen-bonded) and a sharp peak near 3600  $\text{cm}^{-1}$  (free OH).
- 

## Experiment 25

### **BIODIESEL**

TIME ESTIMATE: 1 period for Experiment 25A (or 25B) and Experiment 25C plus time to run spectra.

We use this experiment to introduce IR and NMR spectroscopy and gas chromatography-mass spectrometry. Coconut oil gives great results on GC-MS since all of the major components of this biodiesel separate completely. All oils we've tried give good NMR and IR spectra that can be used to determine whether the biodiesel is contaminated with methanol, glycerol or unreacted vegetable oil.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### **Experiment 25A**

Coconut oil 125 mL

The coconut oil must be heated slightly to keep it in a liquid form that can be measured in a graduated cylinder.

Sodium hydroxide dissolved in methanol 25 mL

Dry sodium hydroxide pellets over night in an oven at 100°C. After grinding the dried sodium hydroxide with a mortar and pestle, add 0.875 g of this to an Erlenmeyer flask containing 50 mL of highly pure methanol. Place a magnetic stir bar in the flask and stir until all of the sodium hydroxide has dissolved. The mixture will be slightly cloudy and should be swirled before students take a 2-mL portion.

Waste containers for leftover biodiesel and glycerol

### **Experiment 25B**

Any vegetable oil from the bottom of Table 2 on page 185 in the textbook is suitable 125 mL

Sodium hydroxide dissolved in methanol (see above in Experiment 25A) 25 mL

Waste containers for leftover biodiesel and glycerol

### **Experiment 25C**

NMR tubes

Deuteriochloroform for NMR

Salts plates for IR spectroscopy

Solvent for GC-MS samples

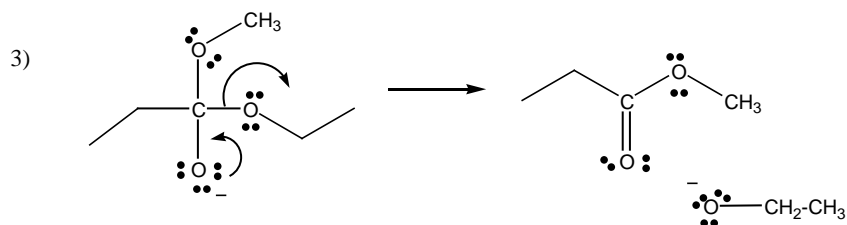
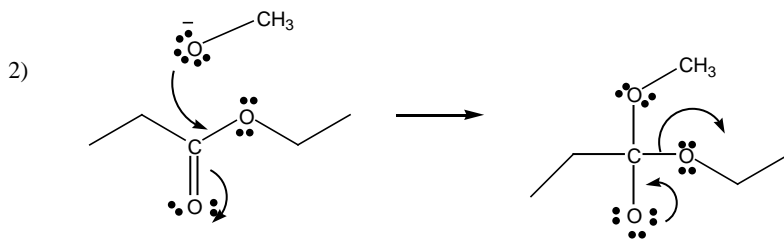
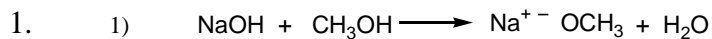
GC-MS vials

Bomb calorimeter (optional demonstration)

### **CAS Registry Numbers:**

Methyl alcohol	67-56-1
Sodium hydroxide	1310-73-2

ANSWERS TO QUESTIONS:



2. a. The heat of combustion of biodiesel should be about 41 kJ/g. This is lower than heptane (45 kJ/g) because biodiesel is already partially oxidized. (Note: this is not an easy question for students to answer.)
2. b. Because of the long hydrocarbon chains in biodiesel, ethanol is more highly oxidized than biodiesel and has a lower heat of combustion. The heat of combustion of ethanol is about 30 kJ/g.
3. Biodiesel is produced from vegetable oils that are extracted from living plant material. As the plant grows it takes in carbon dioxide from the atmosphere to make carbohydrates. This balances out the carbon dioxide that is released as biodiesel is burned.
4. Biodiesel layer: some methanol  
Glycerol layer: all of them including some methanol

## Experiment 26

### ETHANOL FROM CORN

TIME ESTIMATE: 60 min. to set up fermentation (1st period) and 1 period for distillation (2nd period).

#### CHEMICALS PER 10 STUDENTS:

Frozen corn kernels	1875 g
Amylase solution Mix 3 mL of stock solution (Bacterial amylase from Carolina Biological) with 97 mL water	188 mL
Calcium acetate solution Dissolve 0.5 g of calcium acetate in 100 mL water.	188 mL
Buffer solution 3.75 g glacial acetic acid and 3.125 g sodium acetate in 250 mL water.	694 mL
Amyloglucosidase solution Mix 3 mL of stock solution (amyloglucosidase from Carolina Biological) with 97 mL water.	188 mL
Dried baker's yeast	13 g
Anti-foam emulsion Make a 1/10 dilution of Antifoam B silicon emulsion (from JT Baker) in water	38 mL
Saran wrap to cover flask during fermentation	
Stainless steel cleaning pad material for fractionating column	
Cotton and aluminum foil to insulate distilling head	

#### OTHER EQUIPMENT REQUIRED:

500-mL Erlenmeyer flasks (if not included in locker equipment)	10
Three-neck 500-mL round-bottom flask	

Automatic pipet and tips for determining density of alcohol

Lamp if necessary to keep the temperature of the fermentation mixture at 30-35°C

Vernier LabPro interface (if available) with temperature probe and laptop computer. (See RESULTS AND SPECIAL NOTES in Experiment 6 in this manual for a discussion about this method.)

Bomb calorimeter (optional)

### SPECIAL NOTES

We have also done the fermentation step at room temperature (20-25°C) and this seems to work OK.

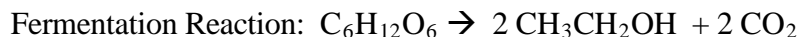
Getting good separation and a good recovery with the fractional distillation can be challenging for students. A lot of heat is required to bring the mixture to a boil and then the heat must be controlled much more carefully to get good separation. If students carefully follow the instructions for the distillation in the procedure, they should get good results. The typical recovery of distillate is 2- 4 grams.

### CAS Registry Number:

Amylase	9014-71-5
Calcium acetate	62-54-4
Glacial acetic acid	64-19-7
Sodium acetate	127-09-3
Amyloglucosidase	9032-08-0

### ANSWERS TO QUESTIONS:

1. Assumptions: 10.0 g of CO<sub>2</sub> produced  
4.0 g of distillate collected  
Percentage ethanol in distillate = 90%



$$10.0 \text{ g CO}_2 \left( \frac{1 \text{ mol CO}_2}{44.0 \text{ g}} \right) \left( \frac{2 \text{ mol EtOH}}{2 \text{ mol CO}_2} \right) \left( \frac{46.0 \text{ g EtOH}}{1 \text{ mol EtOH}} \right) = 10.5 \text{ g EtOH}$$

Actual weight of ethanol =  $0.9 \times 4.0 \text{ g} = 3.6 \text{ g}$

$$\% \text{ recovery} = \left( \frac{3.6 \text{ g}}{10.5 \text{ g}} \right) (100) = 34.3 \%$$

- The heat of combustion of biodiesel is about 41 kJ/g and about 30 kJ/g for ethanol. Because of the long hydrocarbon chains in biodiesel, ethanol is more highly oxidized than biodiesel and has a lower heat of combustion.

## Experiment 27

### CHIRAL REDUCTION OF ETHYL ACETOACETATE; OPTICAL PURITY DETERMINATION

TIME ESTIMATE FOR EXP 27A: 2 laboratory periods. The first laboratory period is used to start the yeast reduction. Another experiment can be conducted concurrently. The reduction requires at least two days. The second period is used to isolate the chiral product.

Be sure to read the “Notes to the Instructor” section on page 228 of the Textbook. Since a large amount of methylene chloride is involved, rotary evaporators will make the experiment more “green.”

**Important note:** *It is best to discard the mixture and start the reaction again if it appears that the yeast is not growing. Solutions where the yeast is growing rapidly will be very thick and will be difficult to stir magnetically. Try to store the fermenting mixtures in a place where the temperature is near 25°.*

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### Experiment 27A (Chiral Reduction of Ethyl Acetoacetate)

Sucrose	75 g
Fleischmann’s Rapid Rise dry bakers yeast (7 g/package)	10 packages

500-mL Erlenmeyer flasks	10
Magnetic stir bar, 1.5 or 2-inch sizes	10
Stirrer/ hot plates	10
Ethyl acetoacetate	35 g
Water (deionized)	
Hexanes	85 mL
Aluminum foil to cover the top of the Erlenmeyer flasks	
Cheese cloth (see note to the instructor for instructions on how to cut it, 3 ply; 4 x 8 inches; page 228 of the Text)	10
Filter Aid (Johns-Manville Celite)	60 g
Büchner funnels (10 cm)	10
Filter paper for Büchner funnels	10
Sodium chloride	250 g
500-mL Filter flasks	10
500-mL Separatory funnels	10
Methylene chloride	1 L
Granular Sodium sulfate (anhydrous)	20 g
Rotary evaporators (optional, but recommended!)	
Salt plates for infrared spectroscopy	
Chiral gas chromatography column (conditions listed on p. 229 of the Textbook)	
Polarimeter (optional)	
0.5-dm Polarimeter tubes (optional)	2 per class
Waste disposal container for nonhalogenated organic waste	



Waste disposal container for methylene chloride

Experiment 27B (Optional NMR Determination of the Optical Purity of (S)-(+)-Ethyl 3-Hydroxybutanoate)

TIME ESTIMATE: 1 period or less. This NMR experiment can be done as a class demonstration, with the instructor giving a photocopy of the resulting spectra to each student, in order that they might determine the percentages of each enantiomer.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

NMR tubes

Chloroform-d, 99.8 atom-%, 0.03% v/v TMS

Tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) derivative: [Eu(hfc)<sub>3</sub>] 8-11 mg/student

The resolved ethyl 3-hydroxybutanoate from Experiment 27A should be used. In addition, about 0.5 g of racemic ethyl 3-hydroxybutanoate may be made available for reference samples.

Waste disposal container for deuterated chloroform solutions

**CAS Registry Numbers:**

Sucrose (table sugar) 57-50-1

Ethyl acetoacetate 141-97-9

Tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III)  
also known as:

Europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]

Abbreviated as [Eu(hfc)<sub>3</sub>] 34788-82-4

ANSWERS TO QUESTIONS:

1. The gas chromatographs described in Technique 22 are not chiral. Since this is the case, each enantiomer will have the same retention time.
2. NADH (nicotinamide adenine dinucleotide) is the biological reducing agent. In effect, it is a source of hydride that reduces the carbonyl group.
3. Both H<sub>c</sub> and H<sub>d</sub> are each doublets of doublets because the geminal (<sup>2</sup>J) protons in the methylene group are non-equivalent, and split each other. Each leg is split again by the adjacent vicinal proton (<sup>3</sup>J). Geminal

couplings ( $^2J$ ) are large, in this case 16.5 Hz. The vicinal couplings ( $^3J$ ) values are smaller than the geminal couplings and are depended on the dihedral angle (Karplus relationship) making their values different.

---

## Experiment 28

### **NITRATION OF AROMATIC COMPOUNDS USING A RECYCLABLE CATALYST**

TIME ESTIMATE: 2 laboratory periods. The first laboratory period is used to isolate the product(s) from the electrophilic aromatic substitution reactions. The second period is used to analyze the product(s) by GC-MS and identifying compounds using the NIST mass spectral library. Since it is likely that schools will not have multiple licenses for the NIST database, it is best to have students work in pairs.

Be sure to read the “Notes to the Instructor” section on page 238 of the Textbook. The class would benefit from the use of rotary evaporators in the laboratory. In this way, 1,2-dichloroethane can be collected making the experiment more “green.”

If a GC-MS instrument is not available, the products can be analyzed on a gas chromatograph. If this is the case, it is recommended that the class use simple monosubstituted hydrocarbon substrates such as toluene, ethylbenzene, isopropylbenzene, etc. The nitro compounds emerge in the following order: *ortho*, *meta* and *para*. Integration will give the percentages.

#### CHEMICALS AND SUPPLIES PER PAIR OF STUDENTS:

The list of compounds given on page 238 of the Textbook should be made available for the class. Highly deactivated compounds, such as compounds with *meta*-directing groups, will not nitrate using this catalyst.

Ytterbium (III) trifluoromethanesulfonate hydrate (ytterbium triflate) 0.4 g  
This catalyst should be recovered and reused. However, if the recovered solid isn't colorless, it should probably be discarded.

1,2-Dichloroethane 10 mL

Automatic pipet

Conc. nitric acid 0.4 mL

Boiling stones

Anhydrous magnesium sulfate

Rotary evaporators (optional, but recommended!)

National Institutes of Standards and Technology (NIST) library of mass spectra data (see page 238 of the Textbook)

Gas chromatograph as described on page 238 of the Textbook, attached to a mass spectrometer.

Waste disposal container for aqueous waste containing ytterbium triflate, unless it is being recovered and reused. It is recommended that the catalyst be recovered to show students that instructor's are interested in saving the environment!

Waste disposal container for 1,2-dichloroethane, unless the solvent is recovered on a rotary evaporator.

**CAS Registry Numbers:**

Ytterbium (III) trifluoromethanesulfonate hydrate	54761-04-5
1,2-Dichloroethane	1300-21-6

**ANSWERS TO QUESTIONS:**

1. See Technique 28
2. The answer to this question will depend on the substrate used. All of the reactions involve electrophilic aromatic substitution.

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**Experiment 29**

**REDUCTION OF KETONES USING CARROTS AS BIOLOGICAL REDUCING AGENTS**

**TIME ESTIMATE:** 60 minutes to start the chiral reduction of a ketone with grated carrots (1<sup>st</sup> period) and part of 1 period to isolate the reduced product. Can be co-scheduled with another experiment.

The instructor or assistant should place the appropriate liquid measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY

LABORATORY”)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Fresh carrots	300 g
Benzofuran-2-yl methyl ketone	600 mg
Cheesecloth	
Diethyl ether	400 mL
Anhydrous magnesium sulfate	25 g

**CAS Registry Numbers:**

Benzofuran-2-yl methyl ketone (2-Acetylbenzofuran) 1646-26-0

Diethyl ether 60-29-7

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### Experiment 30

#### **RESOLUTION OF $\alpha$ -PHENYLETHYLAMINE AND DETERMINATION OF OPTICAL PURITY**

TIME ESTIMATE: 1 period. Experiment 30A should be started at least two laboratory periods in advance. When the reaction is begun in advance, the solutions can be reheated to yield prismatic crystals if the initial crystallization yields too many needles. See the "Crystallization" paragraph on page 246 of the Textbook.

Students should combine their **liquid** products with three other students for polarimetry. The amine has a strong tendency to form a white solid when exposed to carbon dioxide in air (see Special Instructions on page 246). This solid must be avoided. See "Workup" procedure on page 247 of the Textbook.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### **Experiment 30A: Resolution of $\alpha$ -Phenylethylamine**

L-(+)-Tartaric acid	90 g
Methanol	1700 mL
$\alpha$ -Phenylethylamine ( $\alpha$ -methylbenzylamine or 1-phenylethylamine)	80 g

Filter paper for Büchner funnels

50% Sodium hydroxide solution 50 mL  
Prepared by dissolving 50 g of sodium hydroxide in 50 mL of water. This gives about 70 mL of 50% NaOH.

Methylene chloride 375 mL

Anhydrous sodium sulfate 15 g

Melting point tubes

10-mL volumetric flask 1 for each group of 4 students

Polarimeter

The polarimeter is described in Technique 23. If students have enough material, it is best to run the samples neat (see "Polarimetry" on page 247 in the Textbook).

0.5-dm Polarimeter cells

Waste containers for aqueous, nonhalogenated and halogenated wastes

### **Experiment 30B: Determination of Optical Purity Using NMR**

Deuteriochloroform

NMR tubes

*S*-(+)-*O*-acetylmandelic acid 0.012 g for each group of 4 students

#### **CAS Registry Numbers:**

L-(+)-Tartaric acid 87-69-4

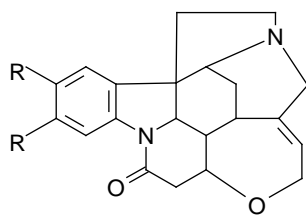
Methanol 67-56-1

**Racemic**  $\alpha$ -methylbenzylamine ( $\alpha$ -phenylethylamine) 618-36-0

*S*-(+)-*O*-Acetylmandelic acid 7322-88-5

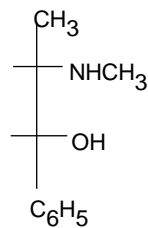
ANSWERS TO QUESTIONS:

1. Reagents used to resolve acidic compounds:

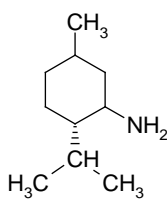


R= H (-) Strychnine

R= OCH<sub>3</sub> (-) Brucine

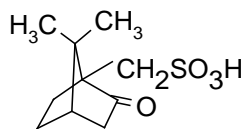


(-) Ephedrine

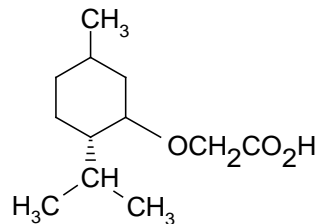


Menthylamine

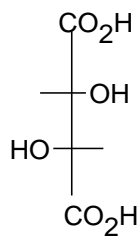
Reagents used to resolve basic compounds:



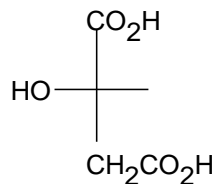
(+) Camphor-10-sulfonic acid



(-) Menthoxyacetic acid

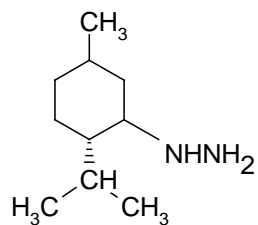


(+) Tartaric acid

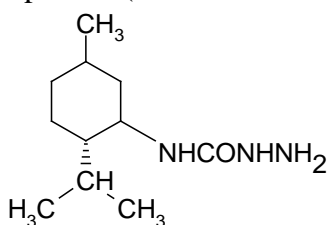


(-) Malic acid

Reagents used to resolve neutral compounds (ketones and aldehydes):

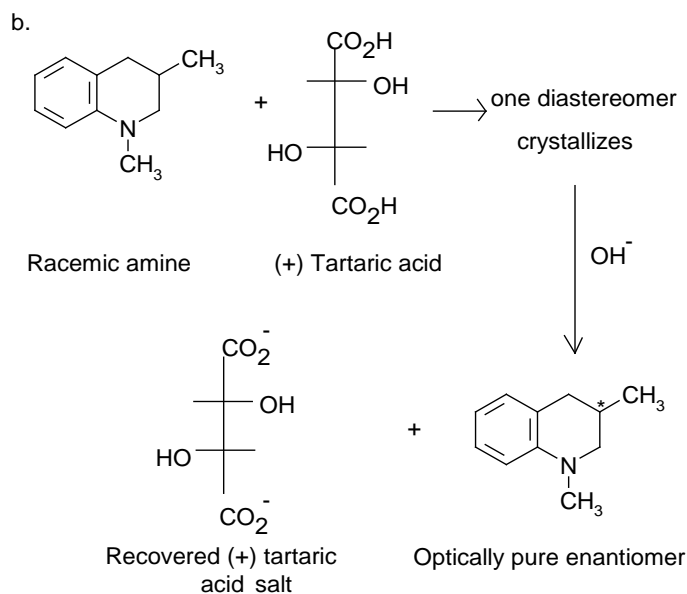
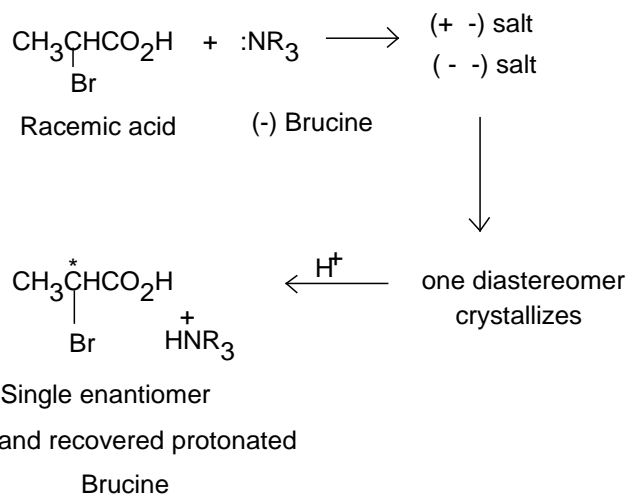


Menthylhydrazine



Menthylsemicarbazide

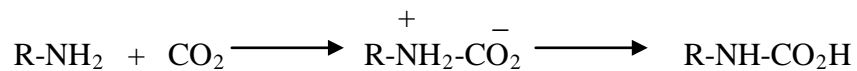
2. a.



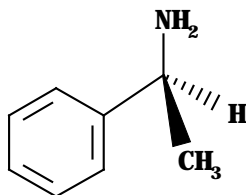
3. You could evaporate the mother liquor solution to dryness in order to obtain the diastereomeric salt crystals containing the R-(+)-amine. The

crystals could then be decomposed to give R-(+)-□-phenylethylamine by using the same workup procedure that you used for S-(-)-□-phenylethylamine. This includes treatment with NaOH to generate the free amine, which is then extracted with methylene chloride (see p. 247).

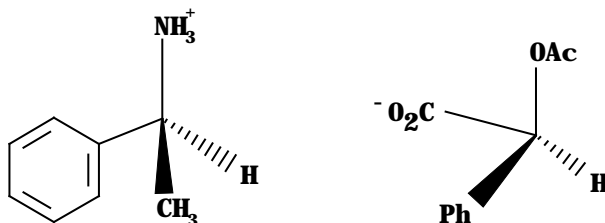
4. The white solid is an amine carbonate salt that results when the α-phenylethylamine reacts with carbon dioxide.



5. NMR spectroscopy should give more accurate results. The NMR method allows you to measure the amounts of the two enantiomers even in the presence of impurities. The amine carbonate and/or other impurities can make the amine solution cloudy. The cloudiness affects the polarimetry since it requires light to be transmitted through the solution, but cloudiness does not affect the NMR result.
6. S-(-)- α-phenylethylamine priorities:  $\text{NH}_2 > \text{Ph} > \text{CH}_3 > \text{H}$



7. S-(+)-O-acetylmandelic acid priorities:  $\text{OAc} > \text{CO}_2\text{H} > \text{Ph} > \text{H}$





## Experiment 31

### **AN OXIDATION-REDUCTION SCHEME BORNEOL, CAMPHOR, ISOBORNEOL**

TIME ESTIMATE: 2 periods

The instructor should read the “Notes to the Instructor” on page 255 of the Textbook. You may wish to determine the NMR spectra of the borohydride reduction mixtures for only a few students and post these spectra in the laboratory rather than determining them for all of the students. The instructor may also wish to determine the ratio of reduction products by gas chromatography. The conditions for the gas chromatograph are listed on page 255 of the Textbook.

In this edition, we replaced the sodium dichromate reagent with sodium hypochlorite in order to make the laboratory more “green.” However, we continue to find that some students do not obtain full oxidation of borneol to camphor with bleach. The commercial bleach from the grocery does not give consistent results. The revised procedure given in the Textbook makes use of 6% sodium hypochlorite obtained from a chemical supply house (VWR). The procedure should give success to most students. There is nothing like chromium compounds when it comes to full oxidation! Green chemistry does have its limitations!

**CHEMICALS AND SUPPLIES PER 10 STUDENTS:**

6% Sodium hypochlorite solution, VWR Scientific Products, # VW3248-1	200 mL
Borneol (racemic)	12 g
Acetone	50 mL
Acetic acid	10 mL
Methylene chloride	300 mL
Saturated aqueous sodium bicarbonate solution	75 mL
5% aqueous sodium bisulfite solution	75 mL
Anhydrous sodium sulfate (granular)	25 g

Sublimating apparatus (optional, microscale apparatus recommended. See Figure 17.2A on page 767 of the Textbook). Students can share the apparatus.

Camphor (if students obtain low yields, or the borneol wasn't completely

oxidized)

Methanol 30 mL

Sodium borohydride (**fresh!**) 3 g

It is essential that it be of high quality. Check the purity by placing a small amount of powdered material in some methanol and heating it gently. The solution should bubble vigorously if the hydride is active.

Methylene chloride 100 mL

Granular anhydrous sodium sulfate 5 g

Filter paper for Hirsch funnels

Salt plates for infrared spectroscopy

Methylene chloride in a dropper bottle for determining spectra using the dry film method

NMR tubes (optional)

Deuteriochloroform (optional)

Gas chromatograph (see p. 255 and 258 of the Textbook for conditions)

Melting point tubes

Disposal container for aqueous wastes

Disposal container for halogenated wastes

### **Monitoring the reaction by thin layer chromatography**

Centrifuge tubes, if not part of drawer stock 10

Methylene chloride 150 mL

Silica gel plates, Whatman #4420-222, with aluminum backing, and fluorescence indicator or similar plates with plastic backing.  
Cut them to 30 x 70 mm size

2 % borneol solution (2 g borneol dissolved in 100 mL methylene chloride)

2 % camphor solution (2 g camphor dissolved in 100 mL mL methylene chloride)

Wide-mouth jars (for developing tanks)	10
Open end capillary tubing	1 vial
Rulers with centimeter scale	
Iodine chambers for visualizing the spots on the TLC plates	10

**CAS Registry Numbers:**

Sodium hypochlorite solution	7681-52-9
Borneol	507-70-0
Camphor	76-22-2
Acetic acid	64-19-7
Methylene chloride (dichloromethane)	75-09-2
Sodium bisulfite	7631-90-5
Sodium sulfate (anhydrous and granular)	7757-82-6
Sodium borohydride	16940-66-2

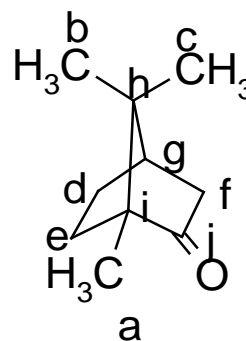
**ANSWERS TO QUESTIONS:**

1. Camphor:  
C=O band at  $1755\text{ cm}^{-1}$   
C-H bands at  $3000\text{ cm}^{-1}$   
  
Borneol and Isoborneol  
O-H band (free) at  $3625\text{ cm}^{-1}$   
O-H band (H bonded) at  $3400\text{ cm}^{-1}$   
C-H bands centered at  $2950\text{ cm}^{-1}$
2. The *gem*-dimethyl groups are nearly equivalent in borneol and have approximately equal chemical shift values because the electronegative oxygen atom is pointing away from the methyl groups. However, in isoborneol, the *gem*-dimethyl groups are not magnetically equivalent. One methyl group has a different chemical shift value, and they appear as separate peaks.
3. The camphor has not been reduced completely. This fact is determined because of the presence of a band at  $1750\text{ cm}^{-1}$ , a typical region for carbonyl absorption. If the reduction has been complete, this band would not have been present in the product.

4.  $K(\text{camphor}) = 39.7\text{ }^{\circ}\text{C}/\text{m}$
- m.p. (pure camphor) =  $179\text{ }^{\circ}\text{C}$
- $\Delta T = Km = (39.7)(0.5) = 19.9\text{ }^{\circ}\text{C} = \text{freezing point depression}$
- m.p. of impure camphor =  $159\text{ }^{\circ}\text{C}$
5. The sodium bicarbonate converts any remaining acetic acid into water soluble sodium salts which dissolves in the aqueous layer.
6. Sodium bisulfite removes chlorine from the sample.
7. The carbon-13 peaks are assigned as follows:

Camphor

a = 9.1 ppm q  
 b = 19.0 q  
 c = 19.6 q  
 d = 26.9 t  
 e = 29.8 t  
 f = 43.1 t  
 g = 43.1 d  
 h = 46.6 s  
 i = 57.4 s  
 j = 218.4 (not shown)

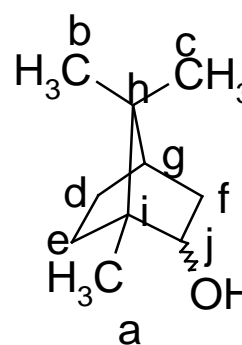


Borneol

a = 13.2 q  
 b,c = 18.5 q and 20.0 q  
 d,e = 25.9 t and 28.1 t  
 f = 38.8 t  
 g = 45.0 d  
 h,i = 47.8 s and 49.3 s  
 j = 77.0 d

Isoborneol

11.2  
 20.1, 20.4  
 27.2, 33.9  
 40.4  
 45.0  
 46.2, 48.9  
 79.7



## Experiment 32

### MULTISTEP REACTION SEQUENCES: THE CONVERSION OF BENZALDEHYDE TO BENZILIC ACID

#### Experiment 32A: Preparation of benzoin by thiamine catalysis

TIME ESTIMATE: 1 period

This experiment must be started 2 days in advance of the period where benzoin is being isolated. **Warning to the instructor: It is critical that the benzaldehyde is pure! See the information under "Notes to the Instructor" on page 269 of the Textbook. Try this experiment in advance of your laboratory period! Don't ever assume that the benzaldehyde will work without trying it in advance!**

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Benzaldehyde 60 mL

**It is essential that the benzaldehyde used in this experiment is pure. Use a newly opened bottle that has been purchased recently.** It must be free of benzoic acid impurity. If the benzaldehyde is old, it must be purified by the method given on page 270 of the Textbook. This purification procedure does not usually produce as good a material as that found in a fresh bottle of benzaldehyde. We have found that even benzaldehyde that has an excellent infrared spectrum may not necessarily work well! **Before the laboratory period, have someone try the procedure with your benzaldehyde and thiamine as indicated in the first three paragraphs, under "Procedure" on page 270 of the Textbook.** The product should appear as a solid mass, with little visible liquid after 2 days, or less (possibly with scratching). If this result isn't obtained, it is likely that your benzaldehyde is unsuitable. Good benzaldehyde gives excellent results!

Thiamine hydrochloride (Vitamin B<sub>1</sub>) 20 g

It is a good policy to use a relatively fresh bottle of thiamine for this experiment. The chemical seems to degrade somewhat with age. All thiamine should be stored in the dark or in a refrigerator when not in use. The purity of the thiamine does not appear to be nearly as critical as the purity of benzaldehyde.

95% Ethanol for running reaction 190 mL

Aqueous sodium hydroxide 60 mL  
Dissolve 40 g of NaOH in 500 mL water

Filter paper for Büchner funnels

Melting point tubes

95% Ethanol for recrystallization

400 mL

KBr pellet press for infrared spectroscopy (optional)

Salt plates for infrared spectroscopy

Methylene chloride (small dropper bottle) for spectroscopy

Waste container for nonhalogenated filtrates

**CAS Registry Numbers:**

Benzaldehyde 100-52-7

Thiamine hydrochloride (Vitamin B<sub>1</sub>) 67-03-8

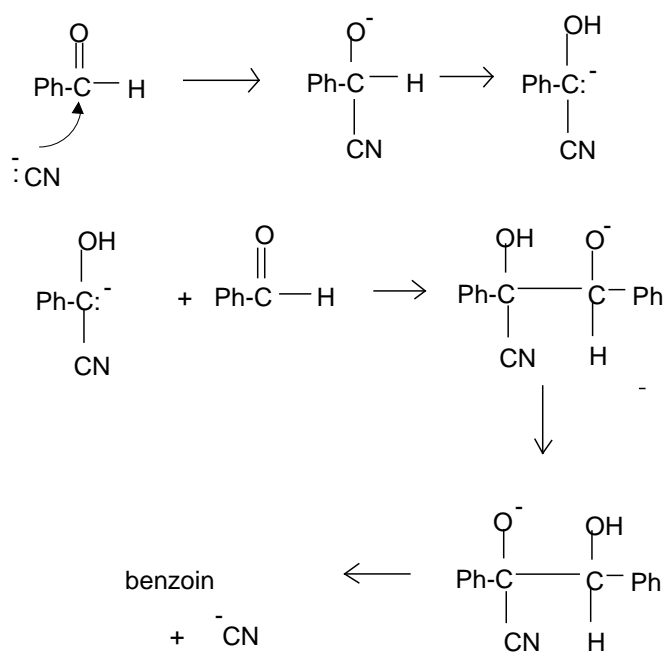
Benzoin 119-53-9

Benzil 134-81-6

**ANSWERS TO QUESTIONS:**

- |    |   |   |
|----|---|---|
| 1. | <u>Benzoin</u>  | <u>Benzaldehyde</u>   |
|    | -OH 3200-3500 cm <sup>-1</sup>                            | -CH aromatic 3030 cm <sup>-1</sup>                              |
|    | -CH aromatic 3050 cm <sup>-1</sup>                        | -CH aldehyde 2720 cm <sup>-1</sup><br>and 2800 cm <sup>-1</sup> |
|    | -CH aliphatic 2900 cm <sup>-1</sup>                       |   |
|    | C=O 1660 cm <sup>-1</sup>                                 | C=O 1705 cm <sup>-1</sup>                                       |
|    | C=C aromatic peaks<br>near 1450 and 1580 cm <sup>-1</sup> | C=C aromatic peaks<br>near 1450 and 1600 cm <sup>-1</sup>       |
|    | C-O 1250 cm <sup>-1</sup>                                 |   |
2. It should have increased the yield, controlled the stereochemistry (benzoin is chiral), and allowed the reaction to occur under milder conditions. Additionally, less of the thiamine should have been required.
3. Both temperature and pH would have to be controlled to avoid denaturation or destruction of the enzyme.

4.



### Experiment 32B: Preparation of Benzil

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Benzoin	32 g
Normally prepared by the student in Experiment 32A	
Conc. nitric acid	150 mL
Magnetic stir bar, if not present in drawer stock	
95% Ethanol	230 mL
Filter paper for Büchner funnels	
Melting point tubes	

KBr pellet press for infrared spectroscopy (optional)  
Salt plates for infrared spectroscopy  
Methylene chloride (small dropper bottle) for spectroscopy  
Waste container for nonhalogenated filtrates

---

### **Experiment 32C: Preparation of benzilic acid**

TIME ESTIMATE: 1 period

#### **CHEMICALS AND SUPPLIES PER 10 STUDENTS:**

Benzil (usually prepared by the student in Exp 32B)	25 g
Aqueous potassium hydroxide solution Dissolve 55 g of potassium hydroxide in 120 mL of water (enough for 20 students assuming little wastage).	65 mL
95% Ethanol	150 mL
Boiling stones	
Stopcock grease	
Filter paper for gravity filtration	
Conc. Hydrochloric acid	20 mL
pH paper	
Filter paper for Büchner funnel	
Melting point tubes	
KBr pellet press for infrared spectroscopy	
Disposal container for aqueous wastes	

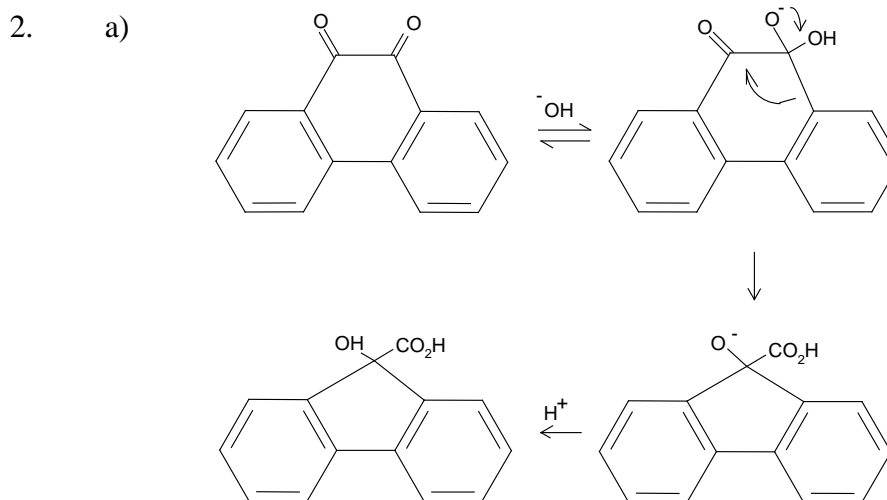


## SPECIAL NOTES:

Depending on the purity of the benzil, a light tan precipitate may form during the reaction period. Although this will not interfere with the isolation of potassium benzilate, it is important that students not mistake this precipitate for potassium benzilate which crystallizes after the reaction mixture is transferred to a beaker and the mixture is allowed to cool. Crystallization of the potassium benzilate is not complete until virtually the entire mixture has solidified.

## ANSWERS TO QUESTIONS:

- 4-methoxybenzaldehyde (*p*-anisaldehyde) is converted first to the benzoin derivative with thiamine hydrochloride (Exp. 32A). This intermediate is then oxidized to the benzil derivative with nitric acid (Exp. 32B). When the benzil derivative is reacted with potassium hydroxide, followed by acidification, the "benzilic acid" product is formed (Exp. 32C).
  - This scheme involves the same steps, but furfural is used instead of 4-methoxy benzaldehyde.





## Experiment 33

### 33A TRIPHENYLMETHANOL 33B BENZOIC ACID

TIME ESTIMATE: 2 periods for either experiment

Students should wash their glassware and store it in their lockers for at least two or three days in advance of starting the Grignard reaction. This should allow enough time for the glassware to dry thoroughly. If necessary, they can rinse their glassware with acetone and dry the glassware in an oven for at least 30 minutes, but this should not be necessary if the glassware has been dried in their drawers for several days. Students should be reminded to not put plasticware (plastic connectors) into the oven. We find that students will not need iodine to start the reaction if they have been careful in drying the apparatus completely.

In the first period, the Grignard Reagent (phenylmagnesium bromide) should be prepared and added to the substrate. In the case of triphenylmethanol (Experiment 33A) the procedure should be carried forward to the point where the addition product has formed (end of "Addition of Benzophenone" paragraph, page 284) or at the end of the "Separation and Drying" section on page 285 where the solution is dried over anhydrous sodium sulfate.

In the case of benzoic acid (Experiment 33B), the procedure may be stopped after the "Hydrolysis" step on page 286.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### **Experiment 33A (Triphenylmethanol)**

Bromobenzene (d = 1.5 g/ mL)	41 g (27 ml)
Magnesium turnings (fresh and untarnished)	7.5 g
Anhydrous ether ( <b>freshly opened can!</b> )	400 mL
Acetone to dry equipment	100 mL
Iodine (optional)	
Benzophenone	35 g
6 M Hydrochloric acid	125 mL

Anhydrous granular sodium sulfate	15 g
Petroleum ether (30-60°)	125 mL
Isopropyl alcohol (2-propanol)	1 L
Filter paper for Büchner funnels	
Melting point tubes	
Calcium chloride (drying tubes)	200 g
Cotton for drying tube	
Waste containers for aqueous and nonhalogenated wastes	
Waste container for ether and halogenated wastes	
Drying oven (optional)	
Anhydrous potassium bromide powder for infrared spectroscopy	
KBr pellet press for infrared spectroscopy	
<b>Experiment 33B (Benzoic Acid)</b>	
Bromobenzene (d = 1.5 g/mL)	41 g (27 mL)
Magnesium turnings (fresh and untarnished)	7.5 g
Anhydrous ether ( <b>freshly opened can!</b> )	400 mL
Acetone to dry equipment	100 mL
Iodine (optional)	
Dry ice	150 g
5% Aqueous NaOH	200 mL
6M Hydrochloric acid	350 mL
Calcium chloride (drying tubes)	200 g

Cotton for drying tube

Waste containers for aqueous and nonhalogenated wastes

Waste container for ether and halogenated wastes

Filter paper for Büchner funnels

Melting point tubes

Drying oven (optional)

Anhydrous potassium bromide powder for infrared spectroscopy

KBr pellet press for infrared spectroscopy

**CAS Registry Numbers:**

Bromobenzene	108-86-1
Magnesium	7439-95-4
Diethyl ether	60-29-7
benzophenone	119-61-9

**REACTIONS OF TRIPHENYLMETHANOL**

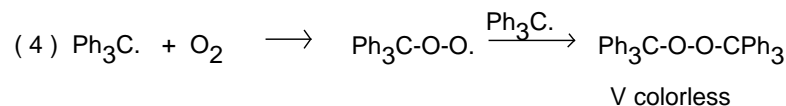
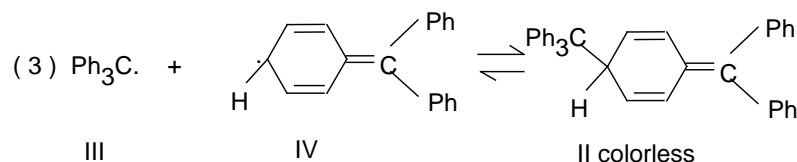
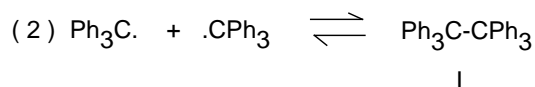
1. Triphenylcarbocation Formation

Place a small amount of purified triphenylmethanol in a small test tube and add dropwise concentrated sulfuric acid until the solid dissolves. Record the color of the solution. Pour the sulfuric acid mixture into about 10 mL of water and record the result.

2. Preparation of Bromotriphenylmethane

Dissolve 0.5 g of purified triphenylmethanol in 10 mL of glacial acetic acid in a 125 mL Erlenmeyer flask, with the aid of slight warming on a steam bath. Add 1.0 mL of 47-49% aqueous hydrobromic acid and heat the mixture on a steam bath. Cool the mixture in an ice bath and collect the bromotriphenylmethane by vacuum filtration on a small Buchner funnel. Wash the solid thoroughly with 3 mL of cold ligroin (65-90 °C) so that the odor of acetic acid is removed, and dry the product quickly in an oven at 80° for 5 minutes. Weigh the bromotriphenylmethane, calculate the percentage yield, and obtain the melting point (literature m.p. 152°C). Store the product in a tightly stoppered vial.

### 3. Triphenylmethyl Radical Formation



The colored triphenylmethyl radical, first discovered in 1900 by Gomberg, is obtained by reduction of bromotriphenylmethane with zinc metal as shown in equation (1). For years it was thought that the dimer formed by equation (2) was hexaphenylethane (I), and that this head-to-head dimer was in equilibrium with the radical. In 1968 it was reported (see references) that the actual dimer was the head-to-tail isomer (II) formed in essence by the reaction of radical (III) with its "resonance" structure (IV) by equation (3). Therefore, the colorless dimer (II) is in equilibrium with the colored triphenylmethyl radical as given in equation (3). When oxygen is present, the radical reacts quickly with oxygen (a diradical) to give the colorless peroxide (V) as shown in equation (4). Within a short time most of the dimer (II) is converted to the peroxide (V) via the radical (III).

**Procedure:** Dissolve a small amount (about 0.5 cm on the end of a spatula) of the bromotriphenylmethane prepared above in about 3 mL of toluene in a test tube. Add about the same amount of zinc powder (see note below), stopper the tube and observe the color of the solution. Do not shake the tube. After one minute, quickly decant the colored solution away from the solid into another test tube. Stopper the tube and shake it vigorously for several minutes, but remove the cork periodically to admit air. Observe the changes which occur, and allow the unstoppered test tube to stand in an ice bath for 30 minutes. Record the results and comment on the structure of any product which forms.

**NOTE:** If the solution is quickly degassed with nitrogen to remove oxygen following the addition of zinc and stoppered, the triphenylmethyl radical will have a much longer life-time. Peroxide formation (cloudiness) will be retarded. The instructor should check to see if the zinc metal is active.

## References:

H. Lankamp, W. Th. Nauta, and C. MacLean, *Tetrahedron Letters*, 249 (1968).

J. M. McBride, "The Hexaphenylethane Riddle," *Tetrahedron*, 30, 2009 (1974).

### 4. Triphenylmethyl Anion Formation (Demonstration by Instructor)

The preparation of the sodium amalgam and triphenylmethyl sodium is best conducted by the instructor as a demonstration. Place 34 g of mercury in a 50 mL standard tapered round bottom flask and add 0.43 g of sodium in small pieces. **CAUTION: The reaction is violent. Each piece of sodium should react before the next piece is added.** Cool the amalgam to room temperature and add about 30 mL of dry ether (dried over sodium wire, if possible) to the flask. Add 0.35 g of the bromotriphenylmethane prepared above, insert the glass stopper securely into the flask, and shake vigorously for about 5 minutes. Since the reaction is exothermic, release the pressure periodically during that time. A color change should be observed within a few minutes. Allow the solution to stand until the sediment settles somewhat. The solution should be used as soon as possible. Observe and record the color of the carbanion. With a clean and dry pipet or dropper draw a sample from the flask and place it in a test tube containing some water. Describe what happens and give a balanced equation for the reaction with water. Check the pH of the aqueous layer to see if the result is consistent with the prediction from the equation.

## **REACTIONS OF BENZOIC ACID**

### 1. Acidity of Aqueous Solutions

Place a small amount of the purified benzoic acid into a test tube and add about 2 mL of water. Heat the tube slightly to dissolve, or nearly dissolve, the solid. With blue litmus paper, check the acidity of the solution and record the result. Repeat the test with a sample of phenol.

### 2. Solubility Tests

Into each of three test tubes add about 2 mL of 5% aqueous sodium bicarbonate. Label the tubes and place a few crystals or pieces of one of the following compounds into each test tube: benzoic acid, 2-naphthol, and 2,4-dinitrophenol. Gently tap the test tube with a finger to assure mixing. The disappearance of the solid, or the appearance of mixing lines, indicates that the substance is dissolving. If the solid dissolves slowly, allow the mixture to stand for a while and then check it again. For the compounds that dissolve quickly, check for evolution of carbon dioxide gas. Add more solid if necessary to observe

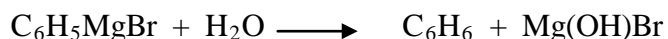
the gas. Record the solubility behavior of the three compounds. Repeat the solubility test on the three compounds using 5% aqueous sodium hydroxide, and record the results. Discuss the structural differences that give rise to the observed solubility behavior. Also comment on the change in color which one observes with the 2,4-dinitrophenol in basic solution.

### 3. Preparation of Ethyl Benzoate

Place 0.3 g of *dry* benzoic acid (the crude material is satisfactory), 3 mL of absolute ethanol, and 10 drops of concentrated sulfuric acid into a test tube. Heat the contents of the tube in a boiling water bath for about 30 minutes (with careful heating no boiling stone is needed). During that time, the volume will decrease somewhat. Cool the contents of the test tube to room temperature add 10 mL of diethyl ether and transfer the mixture to a separatory funnel. Add 10 mL of 5% aqueous sodium bicarbonate, and shake the funnel vigorously, but be sure to vent the funnel *frequently* to release the pressure. When the "whoosh" is no longer audible, drain and discard the lower aqueous layer, and reextract the remaining ether layer with another 10 mL portion of 5% sodium bicarbonate. Again separate and discard the lower aqueous phase, and pour the ether layer into a small Erlenmeyer flask. Dry the ether layer with a small amount of anhydrous magnesium sulfate, gravity filter the solution to remove the drying agent, and evaporate the ether on a steam bath or hot plate in a hood. Note the characteristic odor of the product. The infrared spectrum and/or the nmr spectrum of the product may be determined.

#### ANSWERS TO QUESTIONS:

- Most likely, benzene is formed by reaction of phenylmagnesium bromide with traces of water in the ether or from the air.



- $\text{C}_6\text{H}_5\text{COOH} + \text{OH}^- \longrightarrow \text{C}_6\text{H}_5\text{COO}^- + \text{H}_2\text{O}$

The extraction of the ether layer with base removes the benzoic acid, extracting it into the aqueous layer as its salt. The biphenyl is left behind in the ether layer.

### 3. Triphenylmethanol

OH    3450  $\text{cm}^{-1}$

### Benzoic Acid

acid OH    2400-3400  $\text{cm}^{-1}$   
 very broad due to dimerization  
 (Hydrogen bonding)



CH	aromatic 3050 cm <sup>-1</sup>	Overlaps OH region
C=C	aromatic 1400-1600 cm <sup>-1</sup>	C=C aromatic 1420 and 1600 cm <sup>-1</sup>
C-O	tertiary alcohol one of bands 1000- 1320 cm <sup>-1</sup>	C-O doublet 1300 cm <sup>-1</sup> C=O 1680 cm <sup>-1</sup>

4. In the benzoic acid preparation, the inorganic substances (magnesium chloride/bromide) and hydrochloric acid are soluble in water. The ether layer contains biphenyl, benzene and benzoic acid. Sodium hydroxide removes benzoic acid as its sodium salt from the ether layer and transfers it to the aqueous layer. Biphenyl and benzene remain in the ether layer. After heating the aqueous layer to remove dissolved ether, the aqueous layer is acidified to precipitate benzoic acid which is collected on the filter. The filtrate contains hydrochloric acid and sodium chloride, plus a very small amount of benzoic acid. In the triphenylmethanol preparation, the by-products, biphenyl and benzene are removed with petroleum ether.
5. a) React ethylmagnesium bromide with propanal.
- b) React methylmagnesium bromide with 3-pentanone or ethylmagnesium bromide with 2-butanone.
- c) React pentylmagnesium bromide with carbon dioxide.
- d) React ethylmagnesium bromide with benzaldehyde or phenylmagnesium bromide with propanal.
- 

### Experiment 34

#### AQUEOUS-BASED ORGANOZINC REACTIONS

TIME ESTIMATE: 2 periods

The instructor or assistant should place the appropriate liquid measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

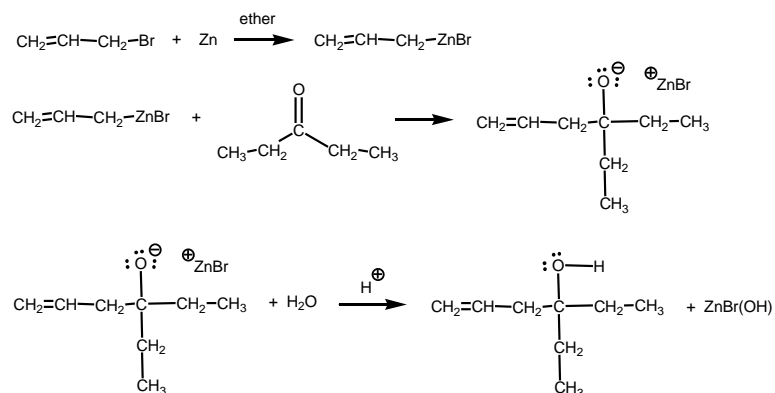
Zinc powder	15 g
5% aqueous hydrochloric acid solution	15 mL
Ethanol	15 mL
Diethyl ether	100 mL
Saturated ammonium chloride solution	125 mL
3-Pentanone	10 g
Tetrahydrofuran	20 mL
3-Bromopropene (allyl bromide)	30 g
Anhydrous sodium sulfate (granular)	
Evaporation station in a hood (optional)	
Salt plates for infrared spectroscopy	
Deuterated acetone or deuterated chloroform for spectroscopy (optional)	

**CAS Registry Numbers:**

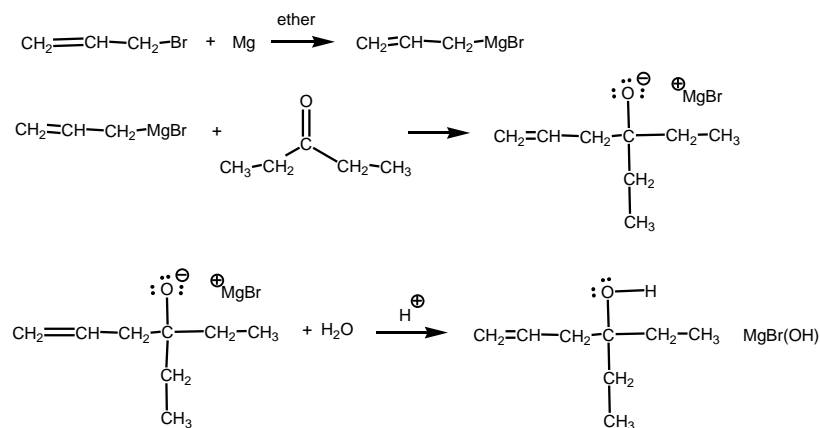
Zinc	7440-66-6	
Ethanol	64-17-5	
Diethyl ether	60-29-7	
Ammonium chloride	12125-02-9	
3-Pentanone	96-22-0	
Tetrahydrofuran	109-99-9	
3-Bromopropene (allyl bromide)	106-95-6	

## ANSWERS TO QUESTIONS:

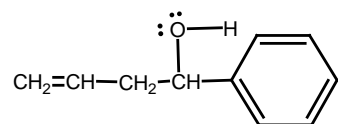
1.



2.



3.



4. The substance shown in #3 (above) has a stereogenic carbon. The two hydrogens of the CH<sub>2</sub> group are no longer equivalent, since they each bear a different relationship with respect to the stereocenter. The two hydrogens are thus *diastereotopic*.

## Experiment 35

### SONOGASHIRA COUPLING OF IODOAROMATIC COMPOUNDS WITH ALKYNES USING A PALLADIUM CATALYST

TIME ESTIMATE: 2 periods, including spectroscopy. It is suggested that students work in pairs for this experiment.

CHEMICALS AND SUPPLIES PER 10 STUDENTS, WORKING IN PAIRS:

1-Iodo-4-nitrobenzene	0.3 g
2-Iodo-5-nitrotoluene	0.3 g
4'-Iodoacetophenone	0.3 g
Ethyl 4-iodobenzoate	0.3 g
4-Iodoanisole (optional, if using microwave technique)	0.3 g
Piperazine	0.3 g
95% Ethanol	8 mL
Palladium(II) acetate	0.1 g
Copper(I) iodide	0.1 g
1-Pentyne	0.5 mL
1-Hexyne	0.5 mL
1-Heptyne	0.5 mL
Silica gel Fisher Chromatographic Silica Gel is recommended, see footnote 5 on page 296 of the Textbook for catalog number.	15 g
Methylene chloride (dichloromethane)	110 mL
Hexanes	60 mL

Rotary evaporator, suggested but not required. A stream of air can be substituted (see footnote 4 on page 296 of the Textbook).

Vacuum pump is advised to remove the remainder of the solvents and the dimer formed in the reaction from the 1-alkynes.

Alternatively, a good quality house vacuum system or aspirator may suffice. Be careful to allow enough time to remove volatile materials from the sample. Ethanol and hexanes remaining in the samples make it difficult to interpret the NMR spectrum! (See footnote 6 and 7 on page 296 of the Textbook).

10 mL Pyrex disposable cleanup/drying column (Corning #214210 available from Fisher #05-722-13). The column is about 30 cm long and 1 cm diameter. These can be cleaned and reused.

100 mL round-bottomed flasks, if not part of drawer stock

Cotton

Deuteriochloroform ( $\text{CDCl}_3$ ) for NMR

NMR tubes

Salt plates for IR spectroscopy

Waste container for solvents collected on the rotary evaporator

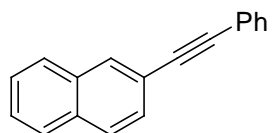
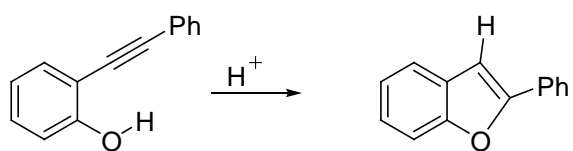
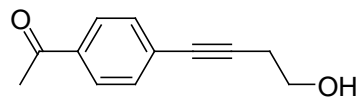
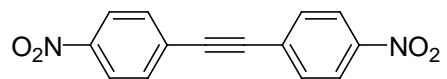
Microwave apparatus (optional). See page 300, footnote 8 for a suggestion on available equipment.

**CAS Registry Numbers:**

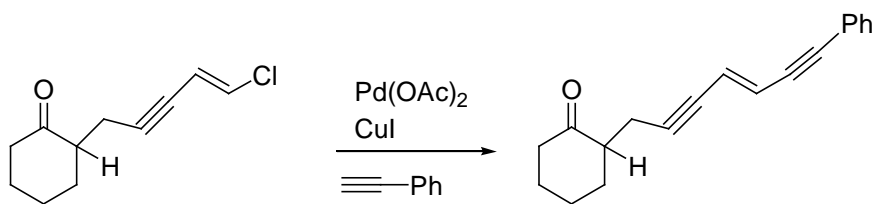
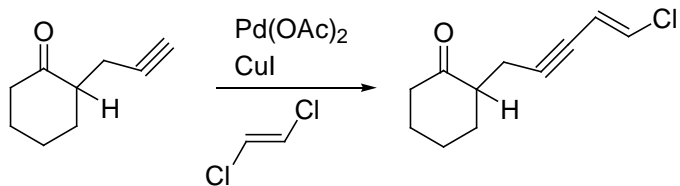
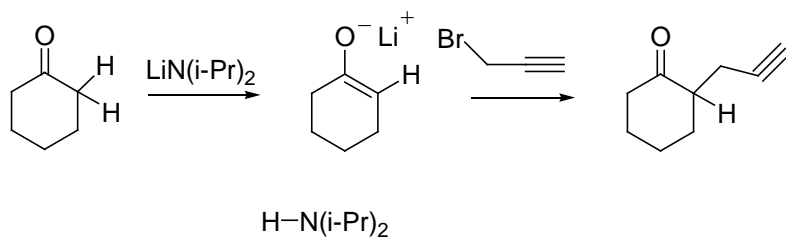
1-Iodo-4-nitrobenzene	636-98-6	
2-Iodo-5-nitrotoluene	5326-38-5	
4'-Iodoacetophenone	13329-40-3	
Ethyl 4-iodobenzoate	51934-41-9	
4-Iodoanisole (optional, if using microwave technique)		696-62-8
Piperazine	110-85-0	
Palladium(II) acetate	3375-31-3	
Copper(I) iodide	7681-65-4	
1-Pentyne	627-19-0	
1-Hexyne	693-02-7	
1-Heptyne	628-71-7	

## ANSWERS TO QUESTIONS

1.



2.



3. The dimer likely forms in the step involving the cuprate (step 3).
4. The mechanism for the formation of the product follows the scheme shown on pages 293-295.

---

### Experiment 36

#### **GRUBBS-CATALYZED METATHESIS OF EUGENOL WITH 1,4-BUTENEDIOL TO PREPARE A NATURAL PRODUCT**

TIME ESTIMATE: 1.5 periods. The reaction is started during part of one class period. After stirring the reaction mixture for one hour, then set the flask in the student locker until the next laboratory period. The next laboratory period is used for the workup and isolation of the product. It is suggested that students work in pairs.

You may desire to follow the elution of the product from the column using TLC so that more precise results are obtained (see page 306 of the Textbook). It is often difficult to follow the elution of the product on the column by observing colors.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS, WORKING IN PAIRS:

Eugenol	1.0 g
<i>cis</i> -2-butene-1,4-diol	2.5 g
Grubbs catalyst, 2 <sup>nd</sup> generation	0.15 g
Methylene chloride (dichloromethane)	200 mL

Plastic caps to fit the 19/22 round bottom flasks

Parafilm to cover plastic caps

Rotary evaporator, suggested but not required. A stream of air can be substituted for removing the solvent.

Silica gel	15 g
------------	------

Fisher Chromatographic Silica Gel is recommended, see footnote 2 on page 306 of the Textbook for catalog number.

10 mL Pyrex disposable cleanup/drying column (Corning #214210 available from Fisher #05-722-13). The column is about 30 cm long and 1 cm diameter. These can be cleaned and reused.

Cotton



Petroleum ether (30 to 60 °C grade) 60 mL

Hexanes 35 mL

Diethyl ether 10 mL

TLC plates to follow the elution of the product from the column (optional)

Filter paper for the Hirsch funnels

Deuteriochloroform (CDCl<sub>3</sub>) for NMR

NMR tubes

Waste container for solvents collected on the rotary evaporator

### CAS Registry Numbers:

Eugenol 97-53-0

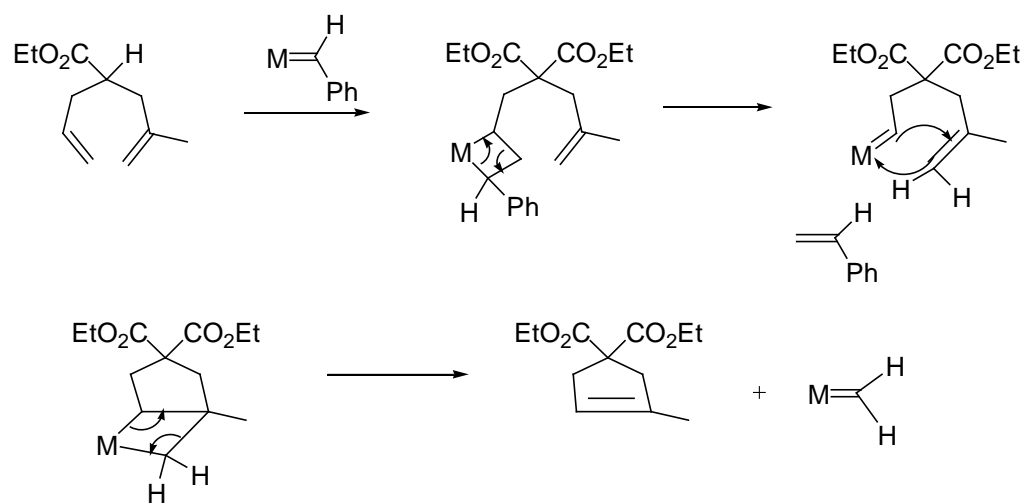
*cis*-2-Butene-1,4-diol 6117-80-2

Grubbs catalyst, 2<sup>nd</sup> generation 246047-72-3

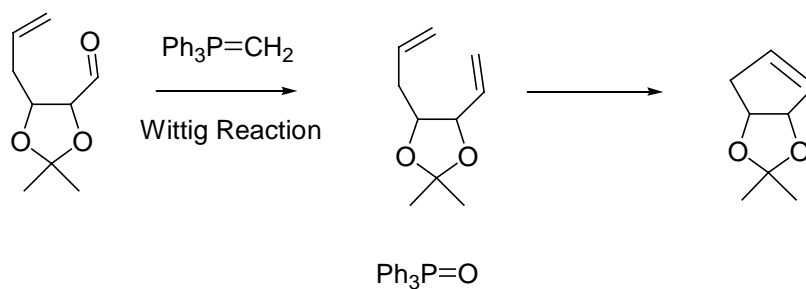
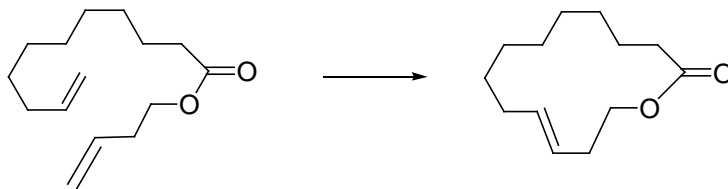
### ANSWERS TO QUESTIONS

- (1) Unreacted eugenol
  - (2) Your metathesized product
  - (3) Unreacted 1,4-butenediol (**does not elute and stays on column**)
  - (4) Ruthenium metal by-products (**stays at the top of the column**)

2.



3.



---

### Experiment 37

#### **THE ALDOL CONDENSATION REACTION: PREPARATION OF BENZALACETOPHENONES (CHALCONES)**

TIME ESTIMATE: 2 hours

The benzalacetophenone preparations may be completed during one period. Students may select one of the three substituted benzaldehydes or one may be assigned to them. This experiment would be a good place to use carbon NMR spectroscopy, since the proton spectra are rather uninteresting.

The aldol condensation reaction has been extensively reviewed: *Organic Reactions*, Vol 16, John Wiley, 1968, pp 1-444. It may be of interest to introduce other choices into the laboratory.

CHEMICALS AND SUPPLIES PER STUDENT:

This experiment involves choices, and amounts of substituted benzaldehydes will need to be adjusted to fit the demand.

Piperonaldehyde (3,4-methylenedioxybenzaldehyde)	0.75 g/student
Anisaldehyde (4-methoxybenzaldehyde)	0.65 mL/student
3-nitrobenzaldehyde	0.75 g/student
Acetophenone	0.60 mL/student
Sodium hydroxide solution Dissolve 6 g of sodium hydroxide in 10 mL water	0.5 mL/student
Filter paper for Büchner funnels	
Melting point tubes	
95% Ethanol	15 mL/student for piperonalchalcone  6 mL/student for 4-methoxychalcone
Methanol	20 mL/student for nitrochalcone
Waste disposal container for nonhalogenated organic waste	
Spectroscopy (optional)	
NMR tubes	
Deuteriochloroform for NMR	
<b>CAS Registry Numbers:</b>	
Piperonal (3,4-methylenedioxybenzaldehyde)	120-57-0
<i>p</i> -Anisaldehyde (4-methoxybenzaldehyde)	123-11-5
3-nitrobenzaldehyde	99-61-6
Acetophenone	98-86-2

## ANSWERS TO QUESTIONS:

1. These reactions proceed by the standard base-catalyzed aldol condensation mechanism, followed by base promoted elimination of water to form the conjugated ketone.
  2. The *trans* isomer is thermodynamically more stable than the *cis* one.
  3. The coupling constants for a *trans* vicinal interaction is about twice as large as a *cis* interaction. One can experimentally determine which isomer you have by use of the coupling constants.
  4. Acid and/or base catalyzed aldol condensation reactions are needed for each of the following reactions.
    - a) Dimerization of 2 molecules of propanal
    - b) Dimerization of 2 molecules of acetone
    - c) Dimerization of 2 molecules of acetophenone
    - d) Trimerization of 2 molecules of 4-methoxybenzaldehyde (*p*-anisaldehyde) and 1 molecule of acetone.
    - e) Dimerization of 4-nitrobenzaldehyde and 4-bromoacetophenone
    - f) Dimerization of 4-chlorobenzaldehyde and 3-nitroacetophenone
  5. Acylate ethylbenzene with acetyl chloride using a Friedel-Crafts reaction to give 4-ethylacetophenone, then react this with benzaldehyde (aldol).  
  
Acylate *m*-xylene with propanoyl chloride using a Friedel-Crafts reaction, then react this intermediate with benzaldehyde to give the aldol condensation product.
- 

### **Experiment 38**

#### **A GREEN ENANTIOSELECTIVE ALDOL CONDENSATION REACTION**

TIME ESTIMATE: 60 minutes to set up the reaction, then at least one week of reaction time followed by one period to isolate the product and to conduct polarimetry and spectroscopy.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Acetone, reagent grade 250 mL

Isobutyraldehyde 15 mL

Pivalaldehyde (trimethylacetaldehyde) optional

Acetophenone (optional)

*L*-Proline 2.5 g

Diethyl ether 75 mL

Saturated aqueous sodium chloride solution 600 mL

Filter paper, fluted

Automatic pipet, 1000  $\mu$ L

Volumetric flask, 5 mL

Chloroform for polarimetry 60 mL

Rotary evaporator, suggested but not required. A stream of air can be substituted

Vacuum pump is advised to remove the remainder of the diethyl ether and acetone. Alternatively, a good quality house vacuum system or aspirator may suffice. Be careful to allow enough time to remove volatile materials from the sample. Diethyl ether and acetone remaining in the samples make it difficult to interpret the NMR spectrum!

Deuteriochloroform ( $\text{CDCl}_3$ ) for NMR

NMR tubes

Salt plates for IR spectroscopy

Waste container for solvents collected on the rotary evaporator

**CAS Registry Numbers:**

Acetone, reagent grade 67-64-1

Isobutyraldehyde	78-84-2
Pivalaldehyde (trimethylacetaldehyde)	630-19-3
Acetophenone	98-86-2
<i>L</i> -Proline	147-85-3
Chloroform	67-66-3

---

### Experiment 39

#### **PREPARATION OF AN $\alpha,\beta$ -UNSATURATED KETONE *via* MICHAEL AND ALDOL CONDENSATION REACTIONS**

TIME ESTIMATE: 2 periods

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

<i>trans</i> -Chalcone (finely ground)	15 g
Ethyl acetoacetate	10 g
95 % Ethanol	500 mL
Boiling stones	
Sodium hydroxide pellets	1.5 g
Filter paper for Büchner funnel	
Oven (optional)	
Acetone (reagent grade)	175 mL
Centrifuge tubes	
Melting point tubes	
Salt plates for infrared spectroscopy	
Methylene chloride for dry film method	
NMR tubes and deuteriochloroform for NMR (optional)	

**CAS Registry Numbers:**

<i>trans</i> -Chalcone	614-47-1
Ethyl acetoacetate	141-97-9

## ANSWERS TO QUESTIONS:

1. The inorganic substance, sodium hydroxide, is nearly insoluble in acetone while the organic product is very soluble.
2. Sodium hydroxide reacts with atmospheric carbon dioxide to form sodium carbonate.



3. Ethyl acetoacetate forms the sodium salt in the presence of the base, sodium hydroxide. This nucleophile attacks the double bond in chalcone (conjugate addition, Michael reaction). The adduct picks up a proton from the solvent, ethanol, to form the first intermediate. This intermediate undergoes an aldol condensation reaction to form a six-membered ring (thermodynamically stable) as the second intermediate. The last step is a base-catalyzed elimination of water to give the final product which has a double bond in conjugation with a carbonyl group.
4. React benzaldehyde with acetophenone in the presence of base.

---

## Experiment 40

### PREPARATION OF TRIPHENYLPYRIDINE

TIME ESTIMATE: 2 periods

The instructor or assistant should place the appropriate liquid measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY LABORATORY")

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Sodium hydroxide pellets (1.25 g)	15 pellets
Acetophenone	4 g
Benzaldehyde	2 g

Ammonium acetate	2.5 g
Glacial acetic acid	200 mL
5% Sodium bicarbonate solution (aqueous)	200 mL
Ethyl acetate	200 mL
Mortars and pestles	10
Waste disposal containers for aqueous and non halogenated organic wastes	
NMR tubes for proton and carbon spectroscopy	

**SPECIAL INSTRUCTIONS:**

This experiment works best if the sodium hydroxide pellets are fresh. We recommend that students work in pairs for this procedure, in order to share the workload of the lengthy period of gringing.

**CAS Registry Numbers:**

Acetic acid	64-19-7
Acetophenone	98-86-2
Ammonium acetate	631-61-8
Benzaldehyde	100-52-7
Ethyl acetate	141-78-6

**Experiment 41**

**1,4-DIPHENYL-1,3-BUTADIENE**

TIME ESTIMATE: 2 periods (1 period if Part A is omitted)

The preparation of benzyltriphenylphosphonium chloride (Wittig salt) requires a 1.5 hr reflux. Because of the lengthy reflux period required, you may choose to purchase the Wittig salt and perform Part B, only. This experiment provides an excellent opportunity to demonstrate the use of UV spectroscopy.

**Experiment 41A Benzyltriphenylphosphonium Chloride**

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Waste container for xylenes



Benzyl chloride (□chlorotoluene). Keep in a hood. Dispense Dispense with a carefully calibrated pipet or automatic pipet.	18 mL
Triphenylphosphine	28 g
Xylenes	100 mL
Petroleum ether (bp 60-90°C)	50 mL

**CAS Registry Numbers:**

Benzyl chloride ( □chlorotoluene)	100-44-7
Triphenylphosphine	603-35-0
Xylenes (mixture of isomers)	1330-20-7

**Experiment 41B Preparation of the diene using sodium ethoxide**

Benzyltriphenylphosphonium chloride (if part A is omitted)	24 g
Sodium ethoxide solution (made from 200 proof alcohol) Preparation given on page 345 of the Textbook (footnote). Make sure that the 200 proof alcohol comes from a freshly opened bottle!	40 mL

Cinnamaldehyde 8 g  
Use fresh material that is free of cinnamic acid. Determine the infrared spectrum to make sure that the material contains no carboxylic acid. Dispense with a carefully calibrated pipet or automatic pipet. See footnote 2 on page 346.

It is recommended that you try the experiment in advance with the sodium ethoxide and cinnamaldehyde to make sure that the diene will form as indicated at the end of paragraph 2 on page 363. That way one knows that the sodium ethoxide and cinnamaldehyde are pure.

Absolute (anhydrous) ethanol	225 mL
Filter paper for Büchner funnels	
Melting point tubes	
95% Ethanol to recrystallize product (optional)	25 mL
Silica gel plates with fluorescent indicator (Eastman No. EK 1224294). Cut the plates into 2 x 8 cm strips. Note: The manufacturer has changed the stock	10

number for their plates. The one listed in the Textbook is incorrect.

Petroleum ether for chromatography (bp 60-90°C) 50 mL

Acetone for chromatography 10 mL

UV lamp

Waste container for xylenes (filtrate from Part A)

Waste container for triphenylphosphine oxide wastes (filtrate from Part B)

SPECTROSCOPY (optional or can be done as a demonstration)

NMR tubes

Deuteriochloroform for NMR

UV cells

100 mL Volumetric flasks

10 mL Pipets

**CAS Registry Numbers:**

Benzyltriphenylphosphonium chloride 1100-88-5

Sodium 7440-23-4

*trans*-Cinnamaldehyde 14371-10-9

**Experiment 41C Preparation of the diene using potassium phosphate (Green Chemistry)**

Benzyltriphenylphosphonium chloride (if part A is omitted) 4.0 g

Potassium phosphate, tribasic ( $K_3PO_4$ ) 8.0

6-cm porcelain mortar with pour spout, and pestle 10

Automatic pipet, 100  $\mu$ L

*trans*-Cinnamaldehyde 3 g

Use fresh material that is free of cinnamic acid. Determine the infrared spectrum to make sure that the material contains no carboxylic acid. Dispense with a carefully calibrated pipet or

automatic pipet. See Special Instructions on page 361.

Absolute ethanol 5 mL  
Filter paper for Hirsch funnels

See Experiment 44B, above, for information about TLC plates and spectroscopy

**CAS Registry Numbers:**

Benzyltriphenylphosphonium chloride 1100-88-5

*trans*-Cinnamaldehyde 14371-10-9

**ANSWERS TO QUESTIONS:**

1. The *cis,cis* isomer could only be produced from *cis*-cinnamaldehyde by reacting it with the Wittig reagent from benzyl chloride. *trans*-cinnamaldehyde was used in the experiment.
2. The steric effects are minimized by having the phenyl groups in the *trans* positions.
3. The rate of the bimolecular reaction is increased in the higher boiling solvent because of the higher temperature. More product is obtained in a shorter period of time.
4. The 1,2-diphenylethenes can be prepared by reacting benzaldehyde with the Wittig reagent formed from benzyl chloride.
5. Muscalure can be prepared by reacting nonanal with the Wittig reagent formed from 1-bromododecane. Some *cis* will be produced, but a considerable amount of *trans* will also be formed.

---

**Experiment 42**

**RELATIVE REACTIVITIES OF SEVERAL AROMATIC COMPOUNDS**

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Acetanilide 6 g  
Aniline 4 mL

Anisole	5 mL
Glacial acetic acid	32 mL
1.0 M aqueous sodium bisulfite	32 mL
Saturated sodium bisulfite	32 mL
Bromine/hydrobromic acid Add 13.0 mL of bromine to 87.0 mL of 48% hydrobromic acid. This will provide enough reagent for about 20 students assuming no waste. Store in the hood. Dispense in a hood.	63 mL
Glass wool	
Short sections of heavy-walled rubber tubing	
Filter paper for Hirsch funnel	
Melting point tubes	
95% Ethanol	240 mL
Hexane	80 mL
Waste disposal container for halogenated organic waste	
Waste disposal container for bromine/HBr filtrate	
SPECIAL EQUIPMENT:	
Magnetic stirrers and magnetic stir bars (if not part of general equipment).	

SPECIAL NOTES:

The brominating mixture can cause severe irritation to the respiratory tract. It should be prepared and used only with adequate ventilation. It may take considerable work to induce crystallization of the brominated anisole product. Seeding with a small portion of another student's crystallized material is particularly helpful.

## RESULTS:

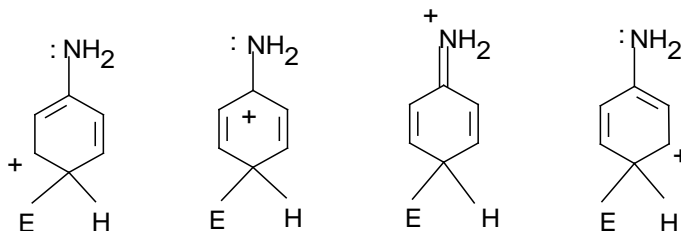
The three products are p-bromoacetanilide, 2,4-dibromoanisole, and 2,4,6-tribromoaniline.

### CAS Registry Number:

Acetanilide	103-84-4
Aniline	62-53-3
Anisole	100-66-3
Acetic acid (concentrated, glacial)	64-19-7
Sodium bisulfite	7631-90-5
Bromine	7726-95-6
hydrobromic acid	10035-10-6

### ANSWERS TO QUESTIONS:

1.



2. Steric hindrance by the acetamido group prevents electrophilic attack at the ortho positions in acetanilide.
3. Infrared, proton NMR, and carbon-13 NMR spectroscopies could be used to identify the products. Also mixed melting points and TLC with authentic compounds could be used.

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## Experiment 43

### NITRATION OF METHYL BENZOATE

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Methyl benzoate 38 g

Sulfuric acid/ nitric acid 50 mL

We recommend that the instructor prepare this reagent in advance for the class. Add one volume of conc. sulfuric acid to one volume of conc. Nitric acid. Students should add 4.0 mL of this acid mixture to methyl benzoate.

Sulfuric acid (concentrated) 75 mL

Crushed ice

Filter paper for Büchner funnels

Melting point tubes

Pasteur pipettes

Methanol 125 mL

Salt plates for infrared spectroscopy

Methylene chloride for the dry film method 5 mL

KBr for spectroscopy, if needed

**CAS Registry Numbers:**

Methyl benzoate 93-58-3

Sulfuric acid 7664-93-9

Nitric acid 7697-37-2

**ANSWERS TO QUESTIONS:**

1. Methyl *m*-nitrobenzoate is formed instead of the *ortho* or *para* isomer because the directive influence of the carbomethoxy group favors substitution at the *meta* position.
2. As the reaction temperature rises, the rate at which dinitration of methyl benzoate increases. An elevated temperature is required for dinitration since the first nitro group, together with the carbomethoxy group, deactivates the aromatic ring toward further substitution.
3. Adding the mixture slowly keeps the concentration of nitric acid low enough that the possibility of dinitration occurring is lessened.
4. 3100 cm<sup>-1</sup> Aromatic C-H stretch

2950  $\text{cm}^{-1}$  Aliphatic C-H stretch  
1710  $\text{cm}^{-1}$  C=O stretch of ester  
1610-1450  $\text{cm}^{-1}$  C=C stretch of aromatic ring  
1530 and 1350  $\text{cm}^{-1}$  N=O stretch of the nitro group

5. Nitration products (major products only):

Benzene:	nitrobenzene
Toluene:	<i>o</i> -nitrotoluene and <i>p</i> -nitrotoluene
Chlorobenzene:	<i>o</i> -chloronitrobenzene and <i>p</i> -chloronitrobenzene
Benzoic acid:	<i>m</i> -nitrobenzoic acid

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**Experiment 44**

**BENZOCAINE**

TIME ESTIMATE: 1 period

The procedures for testing the benzocaine on a frog's leg muscle are given below. This should be done as a demonstration. We don't want to kill all those frogs!

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

p-Aminobenzoic acid	15 g
Absolute (anhydrous) ethanol	150 mL
Conc. Sulfuric acid	15 mL
10% Sodium carbonate solution	200 mL
Methanol	200 mL
pH Paper	
Filter paper for Büchner funnel	
Melting point tubes	
Disposal container for aqueous waste	

Disposal container for nonhalogenated organic waste

Salt plates for infrared spectroscopy

Methylene chloride for dry film method

KBr for spectroscopy, if needed

NMR tubes

Deuteriochloroform for NMR spectroscopy. See footnote 1 on page 349 for information about the  $^1\text{H}$  NMR spectrum.

#### SPECIAL NOTE:

During the recrystallization from methanol/water, it is important not to melt the crude benzocaine before it is dissolved in hot methanol. Troublesome oils may form if the solid is melted rather than dissolved.

#### PROCEDURES FOR TESTING THE DRUGS ON A FROG'S LEG MUSCLE:

For added interest in the class, the student-prepared local anesthetics can be used to deaden a nerve. A frog's leg nerve-muscle segment can be used for the test since it is very sensitive to electrical stimulation and gives a strong response. The local anesthetic blocks the response of the muscle to electrical stimulation.

It is suggested that several leg muscle segments be prepared for a class demonstration. The muscles should be prepared immediately before they are to be used. If the instructors have had no experience in the biological techniques of a physiology laboratory, it is strongly recommended that a knowledgeable student be recruited to prepare the leg muscle segments. Special care and handling of the excised muscle will be necessary. The leg muscle, once excised, should be kept moist in an isotonic saline solution, or "Ringer's solution." If the muscle dries, its response will be deadened.

It is recommended that the purest samples available (as judged principally by melting point and melting range) be selected for use in the tests. The local anesthetics must be utilized in the form of their hydrochloride salts. For benzocaine, which was not converted to its hydrochloride salt, it will be necessary to dissolve the weighed sample in enough dilute hydrochloric acid to provide a stoichiometric amount of hydrogen chloride before proceeding with the experiment.



## PREPARATION OF THE LEG MUSCLE SEGMENT

The instructions given here will be adequate for a person trained in zoological techniques. A physiology laboratory manual should be consulted for those who are less experienced: W. S. Hoar and C. P. Hickman, Jr., Laboratory Companion for General and Comparative Physiology, Prentice-Hall, Englewood Cliffs, New Jersey (1967). This reference contains a series of pictorial drawings of the entire process.

Pithing the Frog. Prior to removing the leg muscle segment, the frog must be "double pithed." Hold the frog in the left hand with the mouth and nose between the first and second fingers and with the thumb on its back at the base of its neck. Using the dissecting needle, probe at the base of the skull until the depression there is located. Push the needle through this large opening, the foramen magnum, directly into the brain and rotate the needle to completely destroy the brain. Then, withdraw the needle partially and redirect its tip downward (caudally) through the vertebral canal to destroy the spinal cord. The hind legs of the frog should now be completely limp and flaccid and should also be unresponsive to any external stimulus like a prick with the needle.

Preparing the Leg Muscle Segment. During this procedure, care should be taken not to touch the exposed muscle or to allow it to dry. Care should also be exercised so as to not allow any of the frog's own blood to perfuse the exposed muscle or to allow any of the frog's outer skin or other injured tissue to touch the muscle. An isotonic physiological saline solution, or amphibian Ringer's solution, can be used to keep the muscle moist or to rinse it free from blood. Begin by cutting through the skin of the frog around the base of its abdomen and around the anus. Holding the frog by its head, peel the skin downward from the hind legs and remove it. Immediately rinse the exposed muscles in a tray containing an isotonic saline solution. Next, using a scissors, cut off the entire leg close to the pelvis. Cut away the thigh muscle and sciatic nerve, but leave a 1 cm length of the femur intact. Then, run the flat side of a scalpel blade under the Achilles tendon and cut it free at the base of the foot. Using a scissors, cut the tibio-fibula bone, which runs along behind the calf muscle, free near the knee joint. Store the leg muscle segment in a tray or beaker of fresh isotonic saline solution until it is needed.

## TESTING THE LOCAL ANESTHETIC

Attaching the Muscle to the Stimulator. Using muscle clamp electrodes, attach the muscle to two clamps fixed to a ring stand. Attach the short length of the femur bone, not the muscle itself, to the upper clamp, and then clamp the end of the Achilles tendon to the lower clamp. **DO NOT ATTACH THE CLAMPS TO THE MUSCLE ITSELF OR IT WILL BECOME INJURED.** Be sure to keep the muscle moistened with isotonic saline solution at all times. It may be applied by means of an eyedropper. Next, correctly attach the electrodes by means of wires

to the stimulator device. Use of a solid state electronic stimulator is recommended. A unit (Model No. 344), which includes complete instructions, is available from: Harvard Apparatus Co., 150 Dover Road, Millis, Mass. 02054. However, an induction coil attached by a key to a pair of dry cell batteries may also be used (Harvard Apparatus Model No. 308 Inductorium).

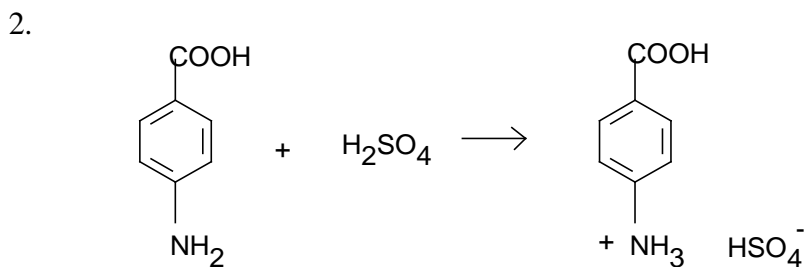
Testing the Local Anesthetic. Dissolve a small amount of the hydrochloride salt of the local anesthetic in the smallest possible amount of isotonic saline solution. Start the muscle contracting by the appropriate adjustment of the stimulating device. A rate of about 3 to 5 contractions per second should be established. Then, apply the solution of the local anesthetic dropwise using a capillary pipet or an eyedropper. If the drug is effective, the rate of contraction will decrease, and the muscle will actually cease to flex when a sufficient amount of the anesthetic has perfused the muscle. The muscle should not be flexed at too great a rate or for too long a period prior to testing or it will become fatigued and cease to function even before the local anesthetic is applied.

**CAS Registry Numbers:**

p-Aminobenzoic acid 150-13-0  
 Ethanol (anhydrous) 64-17-5  
 Sulfuric acid 7664-93-9  
 Sodium carbonate 497-19-8  
 Methanol 67-56-1

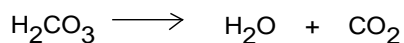
**ANSWERS TO QUESTIONS:**

1. <u>Infrared Spectrum</u>	<u>NMR Spectrum</u>
3410 and 3350 $\text{cm}^{-1}$ N-H	1.4 ppm (t) $\text{CH}_3$
3000 $\text{cm}^{-1}$ C-H	4.3 ppm (q) $\text{CH}_2$
1690 $\text{cm}^{-1}$ conjugated C=O	4.0 ppm (broad) $\text{NH}_2$
1620 to 1450 $\text{cm}^{-1}$ aromatic C=C	6.6, 7.8 ppm (d) ring H
1600 $\text{cm}^{-1}$ $\text{NH}_2$ bend	
1280 and 1170 $\text{cm}^{-1}$ C-O	

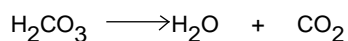
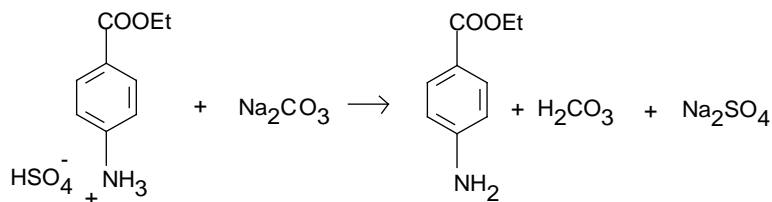


3. Carbon dioxide is evolved:

From excess sulfuric acid:

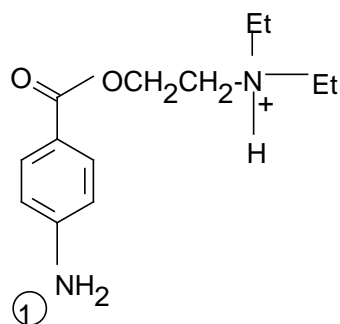


From benzocaine salt:



4. Before neutralization the solution is acidic and the protonated amino group on benzocaine makes it soluble in the aqueous solution. As sodium carbonate (a base) is added, the proton is pulled off the amino group, producing neutral benzocaine which has a low solubility in water.

5. The structure of procaine is shown on page 346 of the Textbook. It is prepared by the reaction of *p*-aminobenzoic acid and 2-diethylamino-ethanol in sulfuric acid. Procaine hydrochloride has the following structure:



The protonated amine shown formed from adding a proton to the more basic "normal" aliphatic amine position on procaine (a localized pair of electrons, no resonance). The electron pair on the amino group at position 1 is delocalized by resonance into the ring. This resonance effect decreases its basicity.

## Experiment 45

### ***N,N*-DIETHYL-*m*-TOLUAMIDE: THE INSECT REPELLENT "OFF"**

TIME ESTIMATE: 1 period. Most of this experiment must be run in a good fume hood! Thionyl chloride is very nasty stuff! This procedure is significantly revised from Small Scale 2.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

3-Methylbenzoic acid ( <i>m</i> -toluic acid)	20 g
Thionyl chloride (keep in hood) Provide with a one-piece plastic pipet	25 mL
Pyridine (put in small dropper bottle)	4 mL
Diethylamine (keep in hood!)	50 mL
10% Aqueous sodium hydroxide solution	200 mL
Saturated aqueous sodium chloride solution	250 mL
Anhydrous diethyl ether	450 mL
Anhydrous magnesium sulfate	15 g
Disposal container for aqueous wastes	
Salt plates for infrared spectroscopy	
Methylene chloride for dry film method	
NMR tubes	

Deuteriochloroform for NMR spectroscopy. See the analysis and spectrum on pages 361 and 362 for interpretation of the  $^1\text{H}$  NMR spectrum.

#### **CAS Registry Numbers:**

3-Methylbenzoic acid ( <i>m</i> -toluic acid)	99-0-07
Thionyl chloride	7719-09-07
Diethylamine	109-89-7
Pyridine	110-86-1

## ANSWERS TO QUESTIONS:

1.  $\text{SOCl}_2 + \text{H}_2\text{O} \longrightarrow 2 \text{HCl} + \text{SO}_2$
2. If the acid chloride of *m*-toluic acid were added to water, it would be converted to the parent acid and hydrochloric acid.
3. The mixture is extracted with base to remove any unreacted *m*-toluic acid by converting it to the water soluble sodium salt of the acid. The base also neutralizes HCl.
4. The first step follows a standard mechanism for the conversion of a carboxylic acid to its acid chloride with thionyl chloride. The second step is an example of a typical nucleophilic acyl substitution mechanism with diethylamine.
5. 

C-H stretch	2800-3100 $\text{cm}^{-1}$
C=O	1640 $\text{cm}^{-1}$
C=C aromatic	1400-1600 $\text{cm}^{-1}$

---

## Experiment 46

### SULFA DRUGS: PREPARATION OF SULFANILAMIDE

TIME ESTIMATE: 1 period for synthesis; some students may not have time to crystallize their product during the first period, and will need to do this and the melting point in a second period. If testing of the drug is desired, one additional period will be required.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Acetanilide	23 g
0.1 M Aqueous sodium hydroxide	32 mL
Chlorosulfonic acid	63 g

Place the reagent in a hood with rubber gloves.  
Supply with a graduated cylinder. Make sure that no water is present. **It reacts violently with water.**

Dilute ammonium hydroxide 138 mL  
Mix 70 mL of concentrated ammonium hydroxide  
with 70 mL water

Dilute hydrochloric acid 67 mL  
Mix 25 mL of concentrated hydrochloric acid with 49 mL water

Crushed ice

Sodium bicarbonate 63 g

Glass wool

Filter paper for Büchner funnels

Melting point tubes

pH paper

Methylene chloride for dry film method 5 mL

Anhydrous powdered potassium bromide for IR

KBr pellet press for infrared spectroscopy, if needed

Waste container for aqueous waste

Waste container for monhalogenated organic waste

**CAS Registry Numbers:**

Acetanilide 103-84-4

Chlorosulfonic acid 7790-94-5

TESTING OF SULFA DRUGS ON BACTERIA (OPTIONAL)

It is useful to test other sulfa drugs along with the student prepared sulfanilamide. Preparations for sulfapyridine and sulfathiazole are given in Pavia, Lampman, and Kriz, "Introduction to Organic Laboratory Techniques, 3rd Edition. The testing procedure given below assumes the availability of three sulfa drugs. The three drugs are tested on two kinds of bacteria. Although the testing part of the experiment can be omitted, it does add interest to the experiment.

## INSTRUCTIONS FOR STUDENTS

The prepared sulfa drug may be tested on two types of bacteria: Enterobacter aerogenes and Bacillus subtilis. A group of three students should team up for this experiment. A specific area in the laboratory should be equipped for this experiment. Dissolve 0.25 g of sulfanilamide or sulfathiazole in 70 mL of boiling distilled water. Dissolve 0.25 g of sulfapyridine in a boiling mixture of 50 mL of water and 20 mL of 95% ethanol.

While the drugs are dissolving, obtain agar plates which have been pre-inoculated with the bacteria (see below for preparation of plates). The name of the bacteria has been written on the top of the Petri dish. With a grease pencil divide the bottom of the Petri dish into quadrants. In each quadrant print one of the following symbols: SA (sulfanilamide), SP (sulfapyridine), ST (sulfathiazole), or C (control). Place the names or initials of the students in the group on the top of the Petri dish.

Dip a pair of tweezers in 95% ethanol and place them in a Bunsen burner flame to sterilize them. It is essential to maintain sterile conditions at all times. The attitude that contaminating bacteria are everywhere is a good one. The bacteria tend to drop into solutions from above, but never move up or sideways. After the tweezers have been sterilized, dip two tabs into one of the sulfa drug solutions while it is still boiling, and remove the tabs. Immediately place them under a watch glass on a piece of filter paper to dry for a few minutes. Again sterilize the tweezers and repeat the above steps in succession with the two remaining solutions of sulfa drugs. Finally, dip one tab in a beaker of boiling distilled water. This tab serves as a control, since it does not contain any sulfa drug. Lift the lid of a Petri dish containing one of the bacteria, straight up so that it is directly above the bottom. It should be lifted just high enough to allow room for the tweezers. Insert the tweezers with the control tab. Place this tab in the center of the quadrant that was previously marked. Sterilize the tweezers and transfer the tabs, in succession, to the center of the appropriate quadrants on the agar plate. Repeat this operation with another agar plate containing the second bacteria to be investigated. Again, care must be taken to avoid contamination of the bacteria. Once the tabs have been placed on the plates, store the agar plates in one general area where the temperature is maintained at 25 °C. The plates should be observed 24 and 48 hours after the introduction of the tabs. During the first 24 hours, the drugs may have the greatest growth-inhibiting effect. Thus, it is important to observe the results at that time or before.

Holding the plates approximately level, observe the plates from the bottom. The originally clear plates will be cloudy, in the area where bacteria has grown. Growth should be observed around the control tab, but the agar will be clear in the area where the sulfa drug has inhibited the growth of the bacteria. One usually observes a clear circular area where inhibition has occurred. The larger the circle,

the greater the effect of the sulfa drug in killing the bacteria. Inspect all of the plates, not just your own group's plates. Sometimes the bacteria will not grow at all. If this has happened, the plate will be totally clear, even around the control tab. Assess the relative effect of the three sulfa drugs on each of the bacteria. Report the results to the instructor.

### PREPARATION OF PLATES

The procedures given here are for the preparation of about 40 plates. There are enough plates to supply 60 students working in groups of three and testing 2 bacteria. These procedures can be followed by a laboratory assistant who has not completed a microbiology course, although it is preferred to have the plates prepared by a microbiology student. The chemicals and supplies are easily obtained from a biology stockroom or a microbiologist. The bacteria used in this experiment are relatively safe to use.

#### CHEMICALS AND SUPPLIES:

Peptone (Difco Labs #0118-01-8, available from suppliers)	15 g
Tryptone (Difco Labs #0123-01-1, available from Scientific Products, VWR, etc.)	18 g
Agar (Difco Labs #0140-01-0, available from suppliers)	15 g
Sodium chloride	16 g
Glucose	2 g
Inoculating loops	2
Bacteria slant ( <i>Bacillus subtilis</i> , var. <i>Niger</i> )	
Bacteria slant ( <i>Enterobacter aerogenes</i> )	
Cotton gauze for plugs	
Bunsen burner	
2 liter Erlenmeyer flasks	2
250 mL Erlenmeyer flasks	4
Disposable plastic petri dishes 150 mm x 15 mm size are the best, but	40



100 mm x 15 mm are satisfactory. These are available from Scientific Products and others (diSPo and Falcon #1058)

Filter paper discs (tabs)  
Schleicher and Schuell No. 740-E, 1/2 in. antibiotic discs; available from Scientific Products and others.

Disposable Serological pipet, 1 mL in 1/100 mL graduations, Kimble #56900 4

Glass "rake", described in Part IV 1

95% ethanol 500 mL

Shaker bath (30-35°C)

Autoclave

Equip an area in the lab for use by the students.

### PROCEDURE

The successful preparation of plates depends heavily on correctly timing the related parts and on careful adherence to sterile technique. A discussion of the proper timing is given below and a discussion on sterile technique is given in Part V.

An outline of the entire procedure follows:

- I Preparation of necessary solutions  
Nutrient broth  
Nutrient agar
- II Sterilization of solutions and plate preparation
- III Preparation of cell suspensions in nutrient broth
- IV Inoculation of the plates
- V Notes on sterile technique
- VI Results of testing

The plates should not be prepared until after the sulfa drugs have been synthesized and purified. A portion of a lab period is reserved for placing the drugs on the pre-inoculated plates.

The preparation scheme that has been successful with us is as follows: The morning of the day preceding the laboratory period, the solutions are made and sterilized. The plates are poured and stored in the refrigerator. The nutrient broths are inoculated and incubated until the next morning. The next morning the plates, which were prepared the preceding day, are inoculated with the nutrient broth containing the bacteria. These plates are then ready to use the day of the laboratory.

## I Preparation of necessary solutions

### Nutrient Broth

Peptone	15 g
Tryptone	8 g
NaCl	8 g
Glucose	1 g
Distilled water	
to make 1 liter	

### Nutrient Agar

Tryptone	10 g
NaCl	8 g
Glucose	1 g
Agar	15 g
Distilled water	
to make 1 liter	

Nutrient broth: This is a medium in which the bacteria are allowed to grow and form a cell suspension which is then used to inoculate the nutrient agar plates.

Nutrient agar: This is the support and nutrient for the bacteria while testing the effects of the drugs. One liter of solution makes about 40, 100 mm plates.

## II Sterilization of solutions and plate preparation

The nutrient agar is autoclaved as indicated below in a large Erlenmeyer flask which is fitted with a cotton gauze plug. The nutrient broth is made as indicated in Part I and 125 mL portions of this solution are transferred to each of four 250 mL Erlenmeyer flasks (two flasks for each bacteria). The flasks are then fitted with cotton gauze plugs. These flasks are then autoclaved as indicated below.

The solutions should be autoclaved for about 15 minutes at about 120 °C with pressurized steam (15 pounds pressure). The filter paper antibiotic discs (tabs) that will be used to carry the drugs must also be autoclaved in a glass petri dish. In addition, some disposable glass pipets with cotton plugs should be autoclaved after being wrapped in aluminum foil. Kimble disposable serological pipets may be used instead with-out being autoclaved.

The plates are then poured after the nutrient agar solution has been autoclaved

being careful to use sterile techniques (See Part V). The liquid agar is removed from the auto-clave and is allowed to cool before it is poured into the plastic petri dishes. The agar is cooled somewhat before pouring in order to prevent condensate from collecting on top of the petri dish. It is difficult to observe the zones on inhibition when the lid of the petri dish is fogged. The bottom of the dish is filled about one-half full with the agar. Do not allow the agar in the flask to solidify. Once the agar has been poured into the petri dish, the top is replaced, and the agar is allowed to cool and solidify. The poured plates can be stored for long periods as long as they are refrigerated in an air tight container. They can be prepared well in advance of the laboratory period.

### III Preparation of cell suspensions in nutrient broth

The four flasks containing the nutrient broth are cooled to room temperature. Slants of the desired bacteria (*Bacillus subtilis* and *Enterobacter aerogenes*) are obtained along with a small amount of 95% ethanol, a burner, and an inoculating loop. For each bacteria two flasks of nutrient broth are inoculated in case that one does not grow. To inoculate the broth, the loop is placed in the alcohol, removed, and flamed. Using sterile techniques (See Part V) the cap is removed and some of the bacteria are scrapped off of the slant onto the loop. The nutrient broth is then tilted at an angle and its cap removed. Some of the bacteria on the loop are smeared in the flask at a point where it will be under the level of the solution when it is tipped back after its cap has been replaced. The bacteria are burned off the loop and procedure is repeated with a new flask of nutrient broth.

In the case of *Bacillus subtilis* the flask should be swirled well so that there will be some cells on top of the solution. This is important because they are aerobic organisms while *Enterobacter aerogenes* are anaerobic.

The flasks are then put in a shaker bath which is controlled at 30 to 35°C. Within 12 hours the solutions should be cloudy. The *Enterobacter aerogenes* solutions will be white, while the *Bacillus subtilis* suspensions are orange. The cell suspensions have to be incubated (shaker bath) for 18 to 24 hours before they are used to inoculate the plates.

### IV Inoculation of the plates

If the plates have been in the refrigerator they should be allowed to warm to room temperature before they are inoculated. The following procedures are then followed:

1. A long piece of glass rod is cut and shaped over a flame into a "rake". It should have a shape similar to that shown in the diagram. The handle should be made



long enough so that the rake can be manipulated easily.  
The width should be about one-half the width of the petri dish.

2. A beaker is filled with 95% ethanol so that it extends 1 or 2 inches up the handle of the rake. 0.1 mL of the incubated nutrient broth containing the bacteria is pipeted onto the agar plates. The lid of the petri dish should be lifted only a few inches and straight up from the dish to prevent introduction of contaminants (See Part V). The top is replaced on the dish and the pipet is returned to the nutrient broth flask.

3. Next, the rake is removed from the ethanol and flamed until the alcohol has burned completely. The top of the petri dish is removed with one hand (1 or 2 inches) and the rake is used to evenly spread 0.1 mL of the nutrient broth over the agar surface. The top is replaced and the dish is turned 45°. Again, the top is removed and the surface is raked. The dish is turned and the surface raked in order to obtain an even bacterial growth. The plate is turned and raked in 45° increments until two or more complete 360° cycles have been completed. The rake is returned to the ethanol.

4. Steps two and three are repeated with another 0.1 mL sample of nutrient broth on another agar plate. When one-half of the agar plates have been inoculated with one bacteria, the remaining plates are inoculated with the second bacteria. The plates should be marked on top with initials (EA or BS) to indicate the bacteria contained in the petri dishes.

After the plates have been inoculated with the nutrient broth containing the bacteria, they should not sit out at room temperature for more than 3 hours without being used with the sulfa drugs. Procedures for testing the sulfa drugs are given above under "Instructions for Students." The plates can be stored after inoculation for up to 3 days at 15 °C, but the best results are obtained when they are used shortly after inoculation. Extra plates which have not been inoculated can be stored for long periods as long as they are refrigerated in an airtight container to prevent drying of the agar.

#### V Notes on sterile technique

The attitude that contamination bacteria are everywhere is a good one. They tend to drop into solutions from above, but never move up or sideways.

1. Whenever one transfers anything from one sterile solution to another, one must never let the solution be exposed in such a way that there is a direct vertical path from the atmosphere to the solution. It must therefore be tilted horizontally before removing the cap and should always be horizontal while the cap is off. After removing the cap, the mouth of the container should be lightly flamed. This should be done before replacing the cap. It should be flamed in such a way that it

will kill undesirable bacteria but not kill the bacteria in solution.

2. Whenever one opens a petri dish one must carefully lift it so that it is directly over the bottom. It should be lifted only the minimum distance and for the minimum time to prevent contamination.

## VI Results of testing

The results that the students obtain vary somewhat, but the usual expectations are the following:

### Enterobacter aerogenes

Sulfanilamide does not inhibit or only slightly inhibits the growth of the bacteria.

Sulfapyridine inhibits the growth for 24 to 48 hours, but begins to lose activity after that time. It is less active than sulfathiazole.

Sulfathiazole inhibits the growth of bacteria up to and after 48 hours. It exhibits the best zone of inhibition of the three drugs.

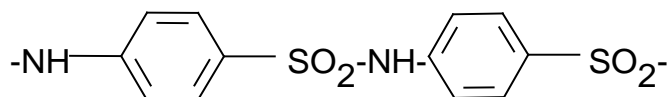
### Bacillus subtilis

All of the drugs show activity and inhibit the growth of the bacteria;  
sulfathiazole > sulfapyridine > sulfanilamide

After the experiment is over, the plates should be collected and autoclaved to kill the bacteria.

## ANSWERS TO QUESTIONS:

- $\text{HOSO}_2\text{Cl} + \text{H}_2\text{O} \longrightarrow \text{H}_2\text{SO}_4 + \text{HCl}$
- Since sodium hydroxide is a stronger base than sodium bicarbonate it can remove one of the sulfonamide hydrogens to produce a soluble ionic species. This would decrease the yield.
- 



polymer

*p*-Acetamidobenzenesulfonyl chloride has the amino group protected with an acetyl group. This group reduces the nucleophilicity of the amino group, and its reactivity towards the sulfonyl group is reduced.

---

### Experiment 47

#### **PREPARATION AND PROPERTIES OF POLYMERS: POLYESTER, NYLON, AND POLYSTYRENE**

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

#### EXPERIMENT 47A

The test tubes used by the students cannot be cleaned and will have to be discarded.

Phthalic anhydride	26 g
Sodium acetate	2 g
Ethylene glycol	5 mL
Glycerol	5 mL
Microburners	
Box to hold test tubes with polyester wastes	
Wooden applicator sticks	
Stopcock grease	

#### EXPERIMENT 47B

5% Aqueous 1,6-hexanediamine (hexamethylenediamine) Dissolve 5 g of diamine in 95 mL of water.	125 mL
5% Adipoyl chloride in cyclohexane Dissolve 5 g of adipoyl chloride in 95 mL of cyclohexane.	125 mL
20% Sodium hydroxide solution	3 mL

Dissolve 5 g of sodium hydroxide in 20 mL of water and place it in a plastic bottle.

6 inch lengths of copper wire 10 pieces

Waste container for nylon

Waste container for cyclohexane

### EXPERIMENT 47C

It is recommended that this experiment be performed as a demonstration since the glassware is difficult to clean. We prepare a large batch **in a hood** in a large flask, and reuse this flask each time the experiment is performed. The surface of the hood should be covered with butcher paper or newspaper.

Styrene (keep in hood; see caution on page 387) 175 mL

Benzoyl peroxide 4.4 g

Weigh this substance on a piece of glassine (glazed paper). Do not use ordinary paper. Wash the glassine paper with water before discarding it.

1 liter Erlenmeyer flask (reusable)

Hot plate

Newspaper or butcher paper

Stirring rod

Stopcock grease

Wooden applicator sticks

Solid waste container for polystyrene

#### **CAS Registry Numbers:**

Phthalic anhydride 85-44-9

Sodium acetate 127-09-3

Ethylene glycol 107-21-1

Glycerol 56-81-5

1,6-hexanediamine (hexamethylenediamine) 124-09-4

Adipoyl chloride	111-50-2
Cyclohexane	110-82-7
Styrene	100-42-5
Benzoyl peroxide	94-36-0

### EXPERIMENT 47D

You should have some polymer samples mounted on cardboard mounts that fit into your infrared spectrometer (see page 388 of the Textbook) in addition to samples supplied by your students. See the essay "Polymers and Plastics" for possible choices. Run the infrared spectrum in advance to make an identification, unless you like pleasant surprises! At a minimum, you should have the following polymer samples:

Scotch tape (cellulose acetate)  
 Sealing tape for packages (polypropylene/polyethylene copolymer)  
 Sandwich bag (polyethylene)  
 Packaging material such as clear florist wrap (polypropylene)  
 Candy wrapper (cellophane or polyester)  
 Packaging on light bulbs (plasticized polyvinyl chloride or polyester)  
 Window from envelope (polystyrene)  
 Top off a fresh pasta package (polyethylene terephthalate)  
 Food bags that can be boiled (polyamide)

In addition, you may be able to obtain samples from a polymer science or technology program on your campus:

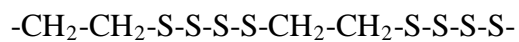
Polytetrafluoroethylene (Teflon)  
 Acrylonitrile/butadiene/styrene (ABS)  
 Polyurethane  
 Polycarbonate  
 Polyvinyl alcohol  
 Polyester

We find that the students enjoy searching a polymer library using the computer searching capabilities of modern infrared spectrometers. We created our own polymer library from common packaging materials and materials from the polymer engineering program. In many cases it is not possible to determine the exact chemical composition of the material you have (for example, is it nylon 6 or nylon 66?). It is helpful to provide students with a handout that includes generalized chemical structures along with their names.

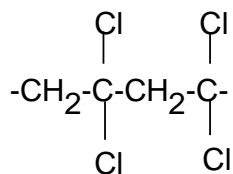


ANSWERS TO QUESTIONS:

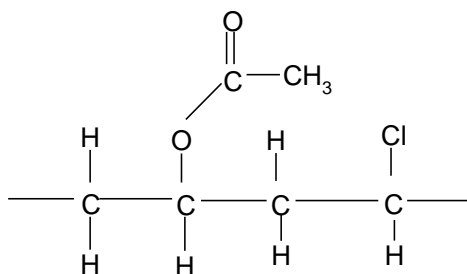
1.



2.



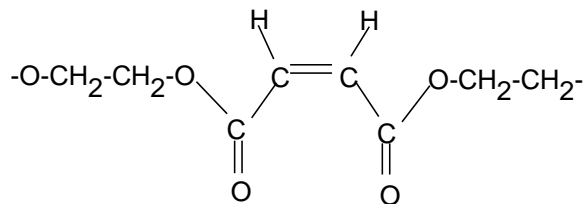
3.



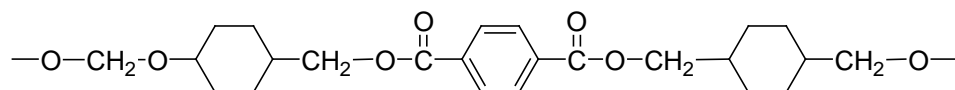
4. Replace chlorine atoms in Problem 2 with methyl groups

5. Polymerize chlorotrifluoroethylene.

6.



7.



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## Experiment 48

### **RING-OPENING METATHESIS POLYMERIZATION (ROMP) USING A GRUBBS CATALYST: A THREE-STEP SYNTHESIS OF A POLYMER**

TIME ESTIMATE: Page 393 in the Textbook suggests 4 laboratory periods for this experiment, but less time can be allocated, as well, if steps are combined. The following scheme provides suggestions for reducing the lab time to 3 periods.

A total of 3 laboratory periods will allow for completion of all parts of Experiment 48. Experiment 48A only requires a short period to set up the Diels-Alder reaction. Other work can be co-scheduled during this laboratory period. Allow the reaction mixture to stand until the next laboratory period. The workup from Experiment 48A and completing Experiment 48B can be completed during the second laboratory period. Experiment 48C must be started in the latter part of the second laboratory period. The third period is used to work up the ROMP polymer in Experiment 48C.

It is suggested that students do individual work for Experiment 48A, but work in pairs for Experiment 48B and 48C. One class period can be saved by purchasing the Diels-Alder product in Experiment 48A and starting with Experiment 48B, thus making this a 2 lab period experiment.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

##### EXPERIMENT 48A

Furan	10 mL
Maleic anhydride (“briquettes” need to be broken and ground with a mortar and pestle)	15 g
Anhydrous diethyl ether	125 mL
Automatic pipet, 1000 $\mu$ L	
Corks to stopper flask	
Parafilm to cover corks	
Filter paper to fit Büchner funnels	

Rotary evaporator, recommended to remove solvent, but evaporation in a hood also works

The Diels-Alder product can be recrystallized from ethyl acetate as described on page 394, **but this isn't really necessary**. Time can be saved by not allowing the product to dry until the next laboratory period, as suggested on line 6 on page 394, and proceeding on to Experiment 48B. The melting points of the Diels-Alder products are often low. Even commercial material doesn't give the literature melting point!

Deuterated DMSO (optional for NMR)

NMR tubes (optional)

#### EXPERIMENT 48B

Students need to filter the Diels-Alder product during the first part of the second lab period. Students should start the one-hour reflux as soon as possible in order to allow time to start Experiment 48C during the same laboratory period.

Diels-Alder adduct from Experiment 48A

Methanol 25 mL

Concentrated hydrochloric acid in with plastic Pasteur pipet attached for dispensing the acid 2 mL

Boiling stones

Filter paper for Hirsch funnel or Büchner funnel

Oven set at 90 °C

Deuterated chloroform (optional for NMR)

NMR tubes (optional)

#### EXPERIMENT 48C

Students must start Experiment 48C during the latter part of the same laboratory period following completion of Experiment 48B (2<sup>nd</sup> laboratory period). The reaction mixture is allowed to stand until the next laboratory period, at least 2 days, but one week is also fine.

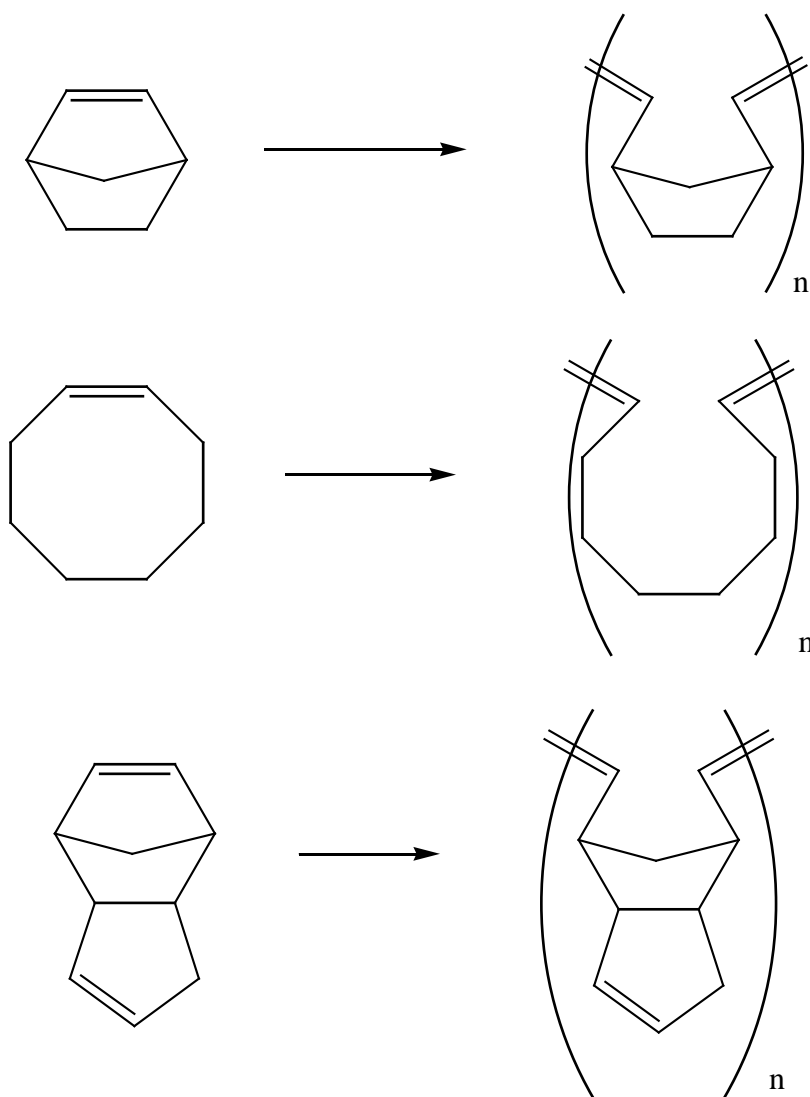
Diester from Experiment 48B

16 x 100 mm test tubes, if not part of drawer stock

Grubbs catalyst, 1 <sup>st</sup> generation	0.15 g
Dry dichloromethane (methylene chloride)	200 mL
Nitrogen or argon gas to deoxygenate mixture (do not use air!)	
Rubber septum caps to fit test tubes	
Parafilm to seal rubber septum	
Solution of 8 mL of methylene chloride, 1600 µL of butyl vinyl ether and 0.4 g of butylated hydroxyl toluene (BHT) as indicated in footnote 6 on page 396.	
Silica gel	5 g
Fisher Chromatographic Silica Gel is recommended. See footnote 2 on page 306 of the Textbook for catalog number.	
Cotton	
Dichloromethane (doesn't need to be dry)	25 mL
Rotary evaporator, suggested but not required, solvent can be evaporated with a stream of nitrogen or argon (not air!)	
Vacuum pump is advised to remove the remainder of the solvent from the polymer. Alternatively, a good quality house vacuum system or aspirator may suffice. Be careful to allow enough time to remove volatile materials from the sample.	
Methanol	125 mL
Tetrahydrofuran	125 mL
Glass-stoppered bottles to store polymer until analysis by HPLC	
Deuteriochloroform (CDCl <sub>3</sub> ) for NMR (optional)	
NMR tubes (optional)	
Waste container for solvents collected on the rotary evaporator	
<b>CAS Registry Numbers:</b>	
Furan	110-00-9
Maleic anhydride	108-31-6

Diethyl ether	60-29-7	
Methanol	67-56-1	
Grubbs catalyst, 1 <sup>st</sup> generation		172222-30-9
Dichloromethane (methylene chloride)		75-09-2
Butyl vinyl ether		111-34-2
2- <i>tert</i> -Butyl-4-methylphenol (butylated hydroxyl toluene)		2409-55-4
Tetrahydrofuran		109-99-9

### ANSWERS TO QUESTIONS



## Experiment 49

### **THE DIELS-ALDER REACTION OF CYCLOPENTADIENE WITH MALEIC ANHYDRIDE**

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Dicyclopentadiene	25 mL
Granular anhyd. sodium sulfate	2 g
Maleic anhydride	13 g
Ethyl acetate	50 mL
Ligroin (bp 60-90 °C)	50 mL

Apparatus to perform fractional distillation  
(cracking of dicyclopentadiene; see page 407 of Textbook)

Melting point tubes

Filter paper for Hirsch or small Büchner funnels

Waste disposal container for nonhalogenated organic waste

Methylene chloride for dry film method	5 mL
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Anhydrous powdered potassium bromide for infrared spectroscopy (optional)

KBr pellet press for spectroscopy (optional)

**SPECIAL NOTE:**

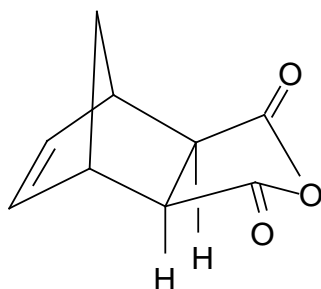
The cracking of dicyclopentadiene must be done in advance by the instructor or assistant. Instructions are given on page 406 in the Textbook. It can be stored in a freezer overnight, if necessary.

**CAS Registry Numbers:**

Maleic anhydride	108-31-6
Ethyl acetate	141-78-6
Ligroin (bp 60-90 °C)	8032-32-4

## ANSWERS TO QUESTIONS:

1.



2. This is an example of competing reactions in which the product is determined by kinetic rather than thermodynamic factors. Since the energy of activation for the reaction leading to the *endo* product is lower than the energy of activation for the formation of the *exo* product, the *endo* product is formed more rapidly. Since the formation of the *endo* product is irreversible under the reaction conditions, the *exo* product cannot be produced by a shift in the equilibrium towards the more stable product.

3. The main side reactions which could occur are:

- (a) maleic anhydride reacts with cyclopentadiene to form *cis*-norbornene-5,6-*exo*-dicarboxylic anhydride
- (b) two cyclopentadiene molecules dimerize to form the *endo* form of dicyclopentadiene
- (c) anhydride can be converted to dicarboxylic acid if water is present

4. Vinyl C-H at  $3020\text{ cm}^{-1}$

Aliphatic C-H bands at  $2880$ ,  $2950$ , and  $3000\text{ cm}^{-1}$

C=O bands at  $1770$  and  $1850\text{ cm}^{-1}$

C-O band at  $1230\text{ cm}^{-1}$

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### Experiment 50

#### DIELS-ALDER REACTION WITH ANTHRACENE-9-METHANOL

TIME ESTIMATE: 1 period

The instructor or assistant should place the appropriate liquid measuring device by each reagent or solvent (see "EQUIPPING THE ORGANIC CHEMISTRY

LABORATORY”)

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Anthracene-9-methanol 1 g

*N*-Methylmaleimide 1 g

Waste disposal container for aqueous wastes

NMR tubes for proton and carbon spectroscopy

**CAS Registry Numbers:**

Anthracene-9-methanol 1468-95-7

*N*-Methylmaleimide 930-88-1

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## **Experiment 51**

### **1**

#### **PHOTOREDUCTION OF BENZOPHENONE AND REARRANGEMENT OF BENZPINACOL TO BENZOPINACOLONE**

Experiment 51A (Photoreduction of Benzophenone)

**TIME ESTIMATE:** We usually set up this experiment a week or more in advance of the collection of the product. Place the test tubes on a window sill in a sunny place in the laboratory and leave them for about one week. Sunlight definitely works better than normal flood lamps. Sunlamps are not as available as they once were. If normal flood lamps are used, it will take several days to get results (crystals appear in the tube without naphthalene). About 15 minutes is required in the first period to set up the test tubes and another 15 minutes is needed in a subsequent laboratory period to collect the product.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

13 x 100 mm test tubes 20

If not available as a regular part of the drawer stock, any test tube holding at least 5 mL can be used as a substitute

Rubber stoppers to fit test tubes



Test tube racks or beakers to hold samples while in sunlight

Filter paper for Hirsch or Büchner funnels

Melting point tubes

Benzophenone 6 g

Naphthalene 1 g

2-Propanol (isopropyl alcohol) 100 mL

Glacial acetic acid in a small dropper bottle

Anhydrous powdered potassium bromide for infrared spectroscopy (optional)

Pellet press for KBr spectra (optional)

Waste container for nonhalogenated solvents

275 W Sun lamp (optional) 1 for class

#### SPECIAL NOTES:

The amount of naphthalene used to quench the reaction represents a huge excess. In fact, a useful modification of this experiment could be used by having each student use a different amount of naphthalene (down to as low as, say  $10^{-6}$  M, by powers of 10) and then to have the class as a whole compare results. In fact, if a method of evaluating the total amount of product (benzopinacol) is available (gas chromatography, column chromatography, etc.), a Stern-Volmer quenching plot of the  $O_q/O_o$  type is possible without recourse to actinometry.

An experiment using actinometry is described by P. Natarajan (*J. Chem. Ed.*, **53**, 200, March 1956). A general method, not using direct actinometry, is described by T. R. Evans in A. A. Lamola and N. J. Turro, "Energy Transfer and Organic Photochemistry," Chapter IV, Interscience (1969).

Experiment 51B (Synthesis of □-Benzopinacolone)

**TIME ESTIMATE:** This experiment requires very little time and can be co-scheduled with another short experiment

**CHEMICALS AND SUPPLIES PER 10 STUDENTS:**

Iodine solution in glacial acetic acid (0.015 M)  
(dissolve 0.25 g of iodine crystals in 65 mL  
glacial acetic acid) 65 mL

Benzpinacol 15 g  
Normally prepared by the student in Experiment 50A

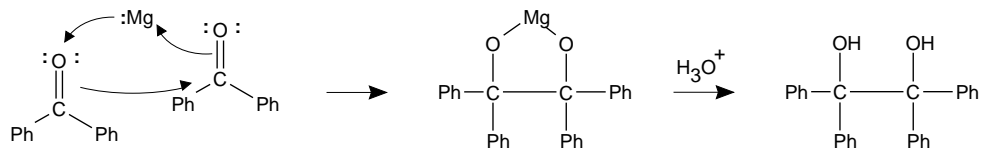
Glacial acetic acid 75 mL

**CAS Registry Numbers:**

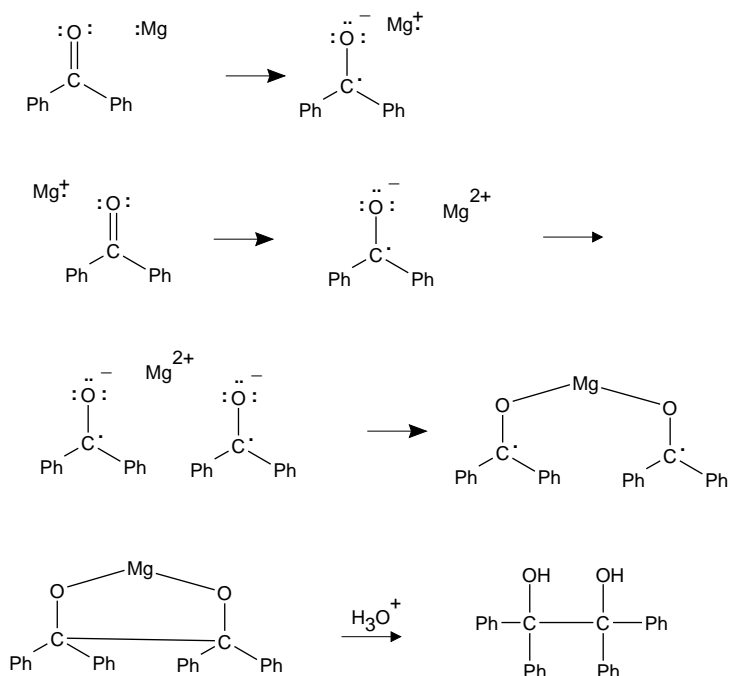
Naphthalene 91-20-3  
2-Propanol (isopropyl alcohol) 67-63-0  
Iodine 7553-56-2  
Benzpinacol 464-72-2

**ANSWERS TO QUESTIONS:**

1. The benzophenone triplet could also be produced by "sensitization." In this approach, it would be necessary to excite a sensitizer molecule with a triplet state of higher energy than that of benzophenone. The higher energy triplet could then transfer energy to benzophenone.
2. The pinacol reduction could be written as a concerted reaction,

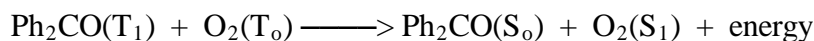


However, most references seem to feel it is a one-electron reduction of each carbonyl with a coupling of the radical anions.

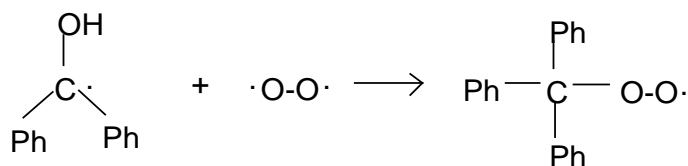


Thus, in this reaction, the coupling occurs between two benzophenone radical anions, stabilized by magnesium, rather than between two diphenylhydroxymethyl radicals as in the photochemical reaction.

3. The benzophenone triplet,  $T_1$ , has a triplet energy of 69 Kcal/mole. The quenchers must have triplet energies lower than this value. Therefore, toluene and benzene may be immediately excluded as possible quenchers. Oxygen is a special case. It is already a triplet molecule in its ground state. With oxygen a different type of quenching occurs, called "triplet-triplet annihilation." To conserve spin, two singlets are produced.



Oxygen may also interfere by radical addition reactions.



## Experiment 52

### LUMINOL

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

3-Nitrophthalic acid	7.5 g
Aqueous hydrazine (10% by weight) Dilute 15.6 g commercial 64% hydrazine solution to a volume of 100 mL using water.	10 mL
Triethylene glycol	20 mL
Boiling stones	
Filter paper for Hirsch funnels	
Sodium hydroxide (10% by weight) Dissolve 10 g sodium hydroxide pellets in 90 mL water.	35 mL
Sodium dithionite dihydrate (sodium hydrosulfite dihydrate)	20 g
Acetic acid (glacial)	13 mL
Waste container for nonhalogenated materials	
Potassium hydroxide pellets	10 g
Dimethyl sulfoxide	50 mL
Disposal container for aqueous wastes	
Disposal container for dimethyl sulfoxide wastes	
Fluorescent dye	0.5 g

Examples of dyes which may be used include:

9-Aminoacridine	Rhodamine B
Eosin	2,6-Dichloroindophenol
Fluorescein	Phenolphthalein
Dichlorofluorescein	9,10-diphenylanthracene

**CAS Registry Numbers:**

3-Nitrophthalic acid 603-11-2  
hydrazine (64% by weight) 302-01-2  
Triethylene glycol 112-27-6

**SPECIAL NOTES:**

To observe the chemiluminescence, a darkened room should be made available. An alternative is to darken a hood by taping heavy butcher paper across the glass window.

---

**Experiment 53****CARBOHYDRATES**

**TIME ESTIMATE:** 2 periods, including all tests and an unknown.

Galactose and lactose can be determined as an unknown without the mucic acid test by employing the remaining tests. If the mucic acid test is to be run, it should be started earlier in the laboratory period since it requires a 1 hour heating period. The carbohydrate solutions and reagents should be placed in several different locations in the laboratory depending on the number of students. Bottles should be supplied with calibrated Pasteur pipettes.

**CHEMICALS PER 10 STUDENTS:**

Xylose, arabinose, glucose, galactose, 1.7 g each  
fructose, lactose, sucrose, starch,  
glycogen (Glycogen from oysters, Sigma  
Chemical Co., No. G-8751)

The above amounts of carbohydrates include enough material to make all of the 1% and 10% solutions, provide solids for the mucic acid test, and provide unknowns.

**Carbohydrate solutions**

Place the following 1% carbohydrate solutions and test reagents in several locations in the laboratory depending upon the numbers of students. Equip each container with a calibrated Pasteur pipette.

1% Carbohydrate solutions (1g/100 mL 65 mL each

distilled water (xylose, arabinose,  
glucose, galactose, fructose, lactose,  
sucrose, starch, glycogen)

Place the following 10% carbohydrate solutions and phenylhydrazine reagent (osazone formation) in several places in the laboratory. Supply each solution with a calibrated Pasteur pipette.

10% Carbohydrate solutions (10g/100 mL distilled water (xylose, arabinose, glucose, galactose, fructose, lactose, sucrose, starch, glycogen)	7 mL each
---	-----------

Mucic acid test. Solids are needed.

Galactose	0.7 g
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Lactose	1.4 g
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### Reagents

Molisch Test Reagent Dissolve 2.5 g of $\alpha$ -naphthol in 50 mL of 95% ethanol. (enough reagent for 50 students).	15 mL
--	-------

Sulfuric acid	125 mL
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Bial's Test Reagent Dissolve 3 g of orcinol (Sigma Chemical Co., No. 0-1875) in 1 liter of conc. hydrochloric acid and add 3 mL of 10% aqueous ferric chloride (enough reagent for 80 students)	125 mL
--	--------

1-Pentanol ( <i>n</i> -amyl alcohol)	65 mL
--------------------------------------	-------

Seliwanoff's Test Reagent Dissolve 0.5 g of resorcinol in 1 liter of dilute hydrochloric acid (1 volume of conc. hydrochloric acid and 2 volumes of distilled water). (40 students)	250 mL
--	--------

Benedict's Test Reagent Dissolve 173 g of hydrated sodium citrate and 100 g of anhydrous sodium carbonate in 800 mL of distilled water, with heating. Filter the solution. Add to it a solution of 17.3 g of cupric sulfate ( $\text{CuSO}_4 \cdot 5 \text{H}_2\text{O}$ ) dissolved in 100 mL of distilled water. Dilute the combined solutions to 1 liter. (enough reagent for 40 students)	250 mL
---	--------

Barfoed's Test Reagent 250 mL  
Dissolve 66.6 g of cupric acetate in 1 liter of distilled water.  
Filter the solution, if necessary, and add 9 mL of glacial acetic acid. (enough reagent for 40 students)

Phenylhydrazine Reagent (osazone formation) 225 mL  
Dissolve 50 g of phenylhydrazine hydrochloride and 75 g of sodium acetate trihydrate in 500 mL of distilled water. The reagent is somewhat unstable.  
(enough reagent for about 20 students)

Starch-iodine Test Solution 3 mL  
Dissolve 1 g of potassium iodide in 25 mL of distilled water.  
Add 0.5 g of iodine and shake the solution until the iodine dissolves. Dilute the solution to 50 mL.  
(enough reagent for 150 students)

Sodium Thiosulfate Solution 10 mL  
Dissolve 1.25 g of sodium thiosulfate in 50 mL of water.  
(enough reagent for 50 students)

Conc. hydrochloric acid 2 mL

10% Sodium hydroxide solution 7 mL

Conc. nitric acid 40 mL

Waste container for copper residues

6M Hydrochloric acid (for decomposition of phenylhydrazine waste)

### Unknowns

About 0.26 g samples of unknown carbohydrates should be issued to the students. Starch is a poor unknown because it is insoluble in water, and it is easy to identify.

RESULTS:

Substance	Molisch	Bial's	Benedict's	Barfoed's
1 Control	no color	no color	no ppt.	no ppt.
2 Xylose	purple	blue-green	red ppt.	ppt.
3 Arabinose	purple	blue-green	red ppt.	ppt.
4 Glucose	faint purple	brown (amyl alc.)	red ppt.	ppt.
5 Galactose	faint purple	green (amyl alc.)	red ppt.	ppt.
6 Fructose	purple	red-brown	red ppt.	ppt.
7 Lactose	faint purple	brown (amyl alc.)	red ppt.	no ppt.
8 Sucrose	dark purple	red-brown	no ppt.	no ppt.
9 Starch	faint purple	brown (amyl alc.)	no ppt.	no ppt.
10 Glycogen	purple	brown (amyl alc.)	no ppt.	no ppt.



Seliwanoff's Test: NC = no color; VS = very slight; LT = light; DK = dark; \* VS pink after cooling 3 min

	1	2	3	4	5	6	7	8	9	10
1 min	NC	NC	NC	NC	NC	VS RED	NC	LT RED	NC	NC
2 min	NC	NC	NC	NC	NC	RED ORA N	NC	RED ORA N	NC	NC
3 min	NC	NC	NC	NC	NC	DK RED	NC	RED	NC	NC
4 min	NC	NC	NC	NC	NC	DK RED	NC	RED	NC	NC
5 min	NC	NC	NC	NC	NC	DK RED	NC	RED	NC	NC
6 min	NC	NC	*	*	VS PIN K	DK RED	VS PIN K	RED	*	VS PINK

### Osazone Formation (Part 53C)

	Time (min)	Observations
2 Xylose	13	turned from clear yellow to cloudy fine ppt. -- fine crystals
3 Arabinose	16	very fine yellow ppt. -- fine crystals
4 Glucose	9	fine needle-like yellow crystals
5 Galactose	21	fine needle-like yellow crystals
6 Fructose	3	yellow needle-like crystals
7 Lactose	30	remained clear yellow for 30 min.; precip. after 5 min. at room temp.
8 Sucrose	30	precipitates after cooling
9 Starch	30	solution turns clear; no ppt.
10 Glycogen	30	solution turns clear; no ppt.

Notes: fructose and glucose - easy to see when crystals start forming.

xylose and arabinose - hard to see when precipitation begins. Just becomes increasingly cloudy.

Iodine test for starch (Part D)

Purple color with starch, only. Decolorized with sodium thiosulfate solution

Hydrolysis of sucrose (Part E)

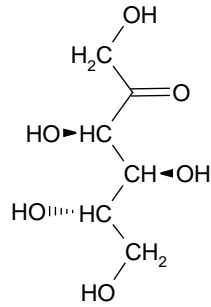
Red precipitate with Benedict's reagent.

Mucic acid test (Part F)

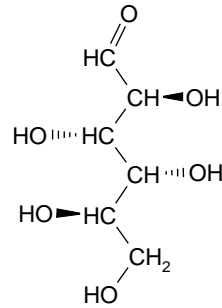
Precipitate forms with lactose and galactose, no precipitate with glucose

ANSWERS TO QUESTIONS:

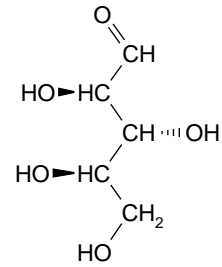
1.



Sorbose  
(reducing)

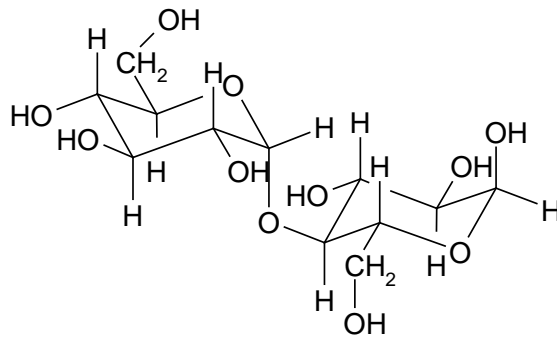


Mannose  
(reducing)



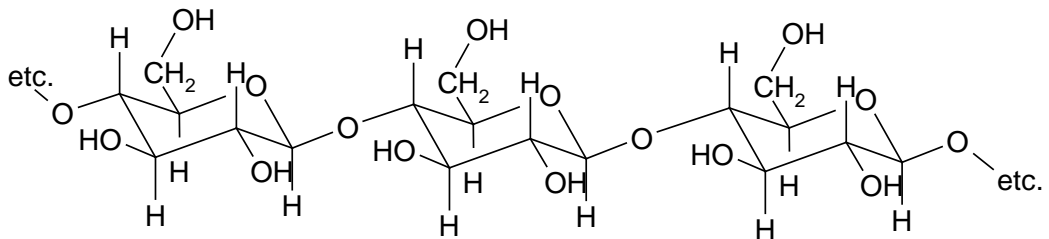
Ribose  
(reducing)

Maltose (reducing)

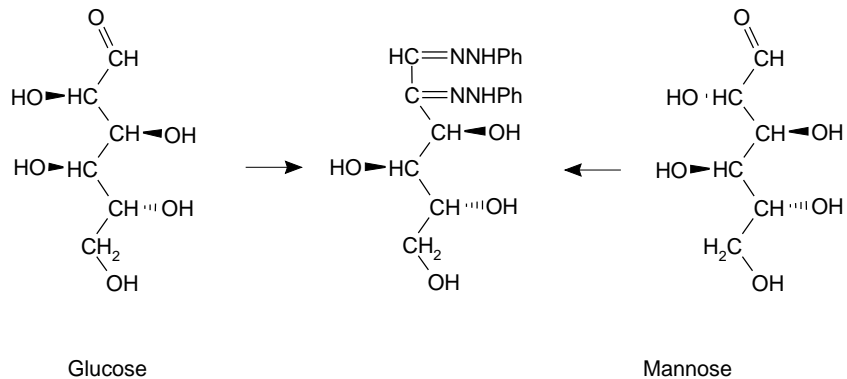


Raffinose: Trisaccharide made up of fructose, galactose, and glucose moieties. (non-reducing)

Cellulose (non-reducing):

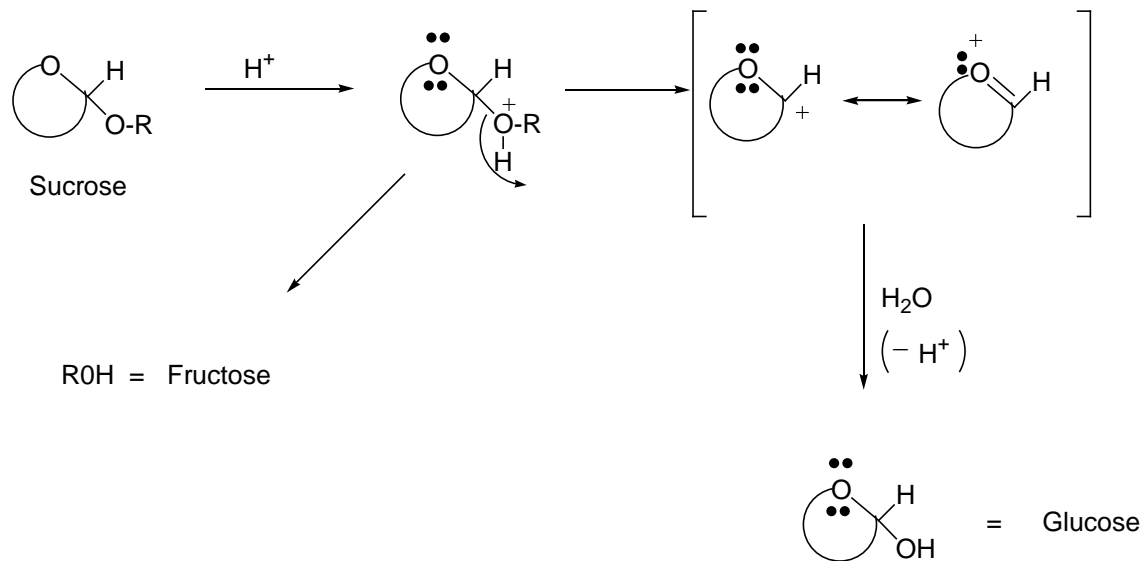


2. Mannose differs from glucose only at C-2. The chiral center is destroyed upon oxidation with phenylhydrazine. The dihydrazone (osazone) thus formed is identical, regardless of the sugar that was used as the starting material.

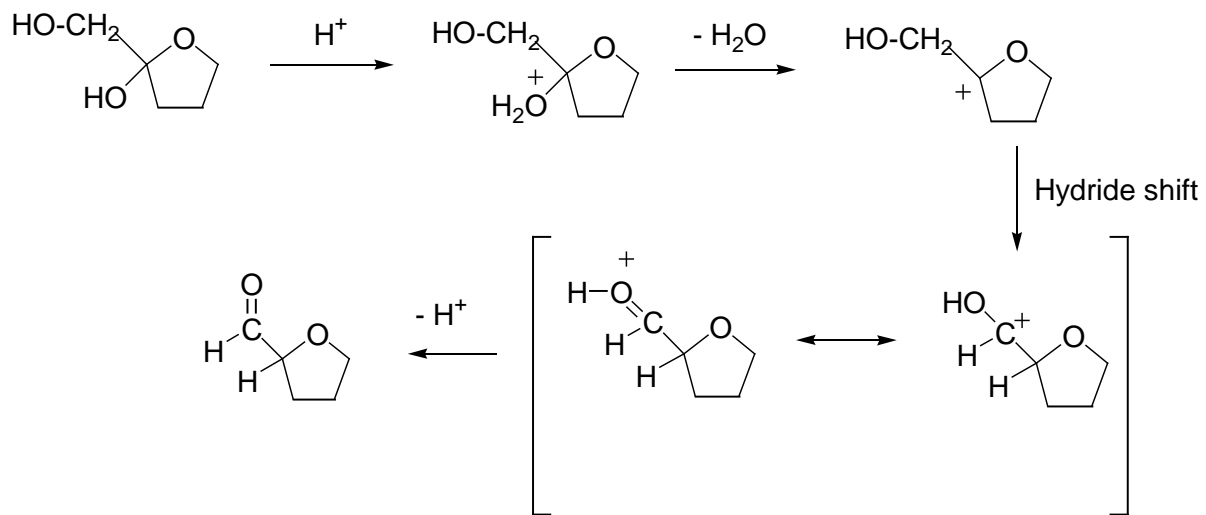


3. Molisch: All purple  
 Bial's: Ribose is blue-green; the rest are brown  
 Seliwanoff's:  
     Sorbose: dark red after 1 and 6 min.  
     Mannose: no color after 1 and slight red after 6 min.  
     Ribose: no color after 1 and 6 min.  
     Maltose: no color after 1 and slight red after 6 min.  
     Raffinose: light red after 1 and dark red after 6 min.  
     Cellulose: no color after 1 and slight red after 6 min.  
 Barfoed's: Sorbose, mannose, and ribose form precipitates; the others do not form precipitates.  
 Mucic acid test: Raffinose gives a precipitate; the others do not.

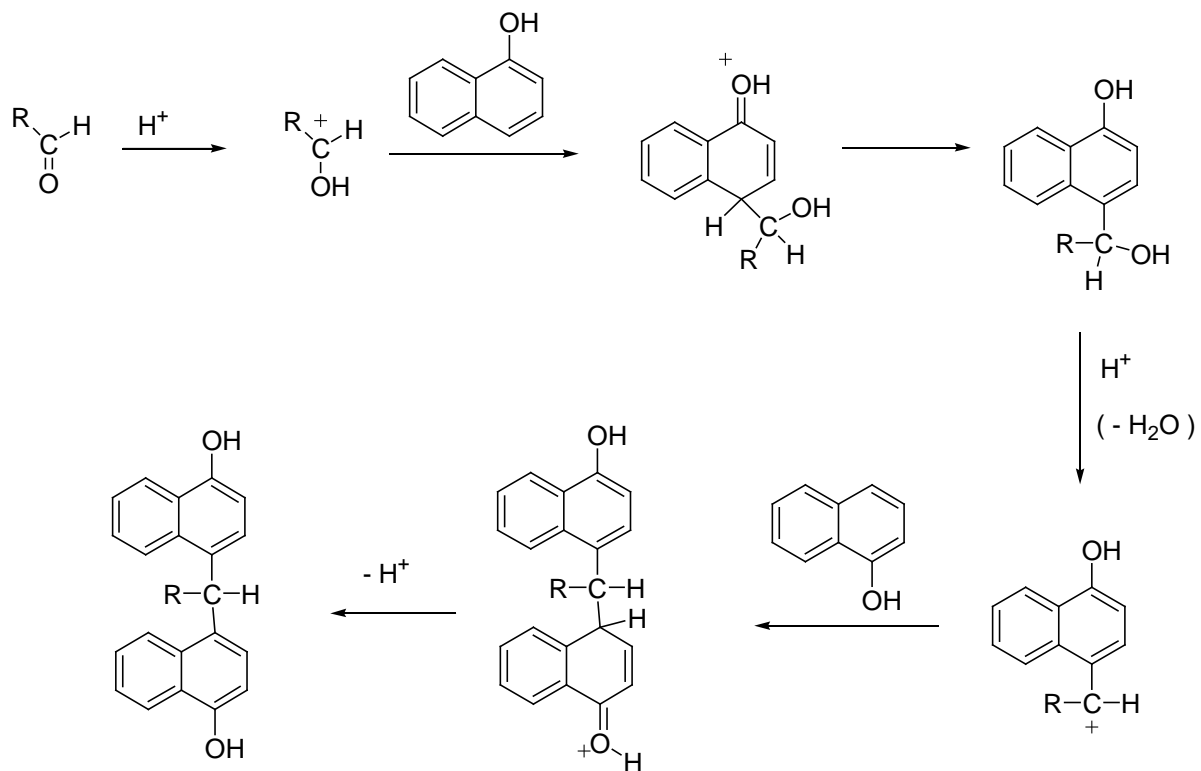
4.



5.



6.



7. The optical rotation would be expected to be *zero*. Mucic acid is a *meso* stereoisomer. Since it has a plane of symmetry, it cannot rotate polarized light.

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## Experiment 54

### **ANALYSIS OF A DIET SOFT DRINK BY HPLC**

**TIME ESTIMATE:** Less than one-half of a laboratory period. This experiment requires very little in-class time, and it may be co-scheduled with another experiment or it may be scheduled to be completed outside of the regularly-scheduled class period. An appointment schedule should be arranged for use of the HPLC instrument. We usually have students work in groups. The instrument must be operated by a knowledgeable person who will use careful filtration technique to prepare the solvents, samples and standard!

#### **CHEMICALS AND SUPPLIES FOR THE ENTIRE CLASS:**

Standard solution: 100 mL for class

Prepared by mixing 200 mg aspartame, 40 mg benzoic acid, 40 mg saccharine, and 20 mg caffeine in 100 mL of the mobile phase (see below). This procedure prepares a huge excess of standard solution, but it is difficult to prepare smaller amounts. Each group requires only a 10-20  $\mu$ L sample:

Soft drink samples: 1 can each for class

Examples include Diet Pepsi, Diet Coke, Diet 7-Up, Diet Sprite, Diet Mt. Dew, and TAB. It is a good idea to include TAB among the selections, since TAB contains saccharine; the other diet soft drinks do not. Allow each can to stand opened for several days. If the soft drinks are allowed to "go flat," most of the carbon dioxide is removed from the samples. The samples must still be filtered to remove all gas. We have also analyzed caffeinated and decaffeinated coffees.

Solvent for HPLC mobile phase:

Prepared by mixing 80% (volume) of 1M acetic acid (dilute 5.26 mL of conc. acetic acid to 100 mL to prepare 1M acetic acid) and 20% methanol, buffered to pH 4.2 by adding 50% sodium hydroxide. This solvent mixture must be prepared by someone that knows the HPLC instrument. The solvent needs to be subjected to careful filtration technique.

Filters (4  $\mu\text{m}$  and 0.2  $\mu\text{m}$ )

Waste container for methanol-acetic acid solvent

#### EQUIPMENT NEEDED AND SPECIAL NOTES:

We use a Waters HPLC that has a UV detector, set at 254 nm. We use a C-18 column, operated in an isocratic mode. For our instrument, the mobile phase has a 2500-3000 psi back pressure at 1 mL/min, and about 4500 psi for 1.5 mL/min. The HPLC is rated for a maximum of 6000 psi, but it is better to keep the pressure below 4000 psi. If the solvent is prepared carelessly, the system has too much back pressure.

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### **Experiment 55**

#### **IDENTIFICATION OF UNKNOWNNS**

**TIME ESTIMATE:** Variable, depending on how the experiment is utilized.

In our course, we schedule this experiment in the second quarter (or semester) of the laboratory and expect students to complete it on top of all other experiments during the quarter. Normally we assign three periods at the very beginning to this lab. During this period and subsequent ones, the students are expected to try all the functional group tests on the suggested known compounds and record the results. Once this has been completed, two unknowns (a solid and a liquid) are issued and students are expected to work on these in whatever free time they may have during the quarter (i.e., while waiting for a reflux period). Spectra are obtained (or issued) as soon as the student completes a probable identification of the unknown's functional groups based on boiling point/melting point, preliminary tests, solubility and chemical classification tests. Finally, we usually leave one or more unscheduled periods free at the end of the lab schedule to allow students to complete unfinished details of their unknowns. Extra credit unknowns may also be attempted.

Increasingly organic chemistry instructors have become concerned about the wastes generated in conducting organic qualitative analysis. In addition, instructors realize that in the "real world" spectroscopy plays a major role. A "green chemistry" (Option 2) approach is provided and is described starting on page 447 of the Textbook. In this approach, classification tests are essentially eliminated. Solubility tests are retained. Chemists realize that the classification tests may be somewhat old-fashioned. However, students learn organic chemistry reactions, and our students consider solving unknowns as "fun" and "interesting".



Certainly, there are sound pedagogical reasons to retain some of the classification tests in your course. Option One retains the standard approach to determining organic structures.

For safety reasons, we have made the chromic acid test an optional procedure for identifying alcohols and differentiating between aldehydes and ketones. Instead, we have added the cerium (IV) test for alcohols/phenols. We now advise students to differentiate between aldehydes and ketones with the Tollens test.

Under both Option 1 and 2, we require students to classify a series of five solubility unknowns (weak acid, strong acid, base, neutral-no functionality, neutral-with functionality) at the beginning of the term. Carefully determined solubility behavior is essential in both options, but especially so in Option 2. If students don't do a careful job there, then they can be located seriously out in "left-field"! We provide the standard sodium fusion tests, but rarely use them in our courses.

Some instructors may prefer to issue spectra at the same time as the unknowns are issued. We prefer that the student not bypass learning the chemical tests, and only permit students to use spectral data after they have achieved a preliminary chemical identification of the functional group. Either approach is possible. For institutions which have infrared and NMR spectrometers available for the students, instructors may ask students to obtain their own spectra. Otherwise, the experiment works equally well by simply issuing photocopies of library spectra to students. Most of the spectra for the unknowns listed in Appendix 1 are available from the Aldrich Library of C-13 and proton NMR Spectra or the Library of FT-IR Spectra. The availability of the spectra may be particularly important for those schools without spectrometers.

We prefer to issue general unknowns (functional group unknown). However, some instructors may wish to issue group or class unknowns (functional group known). We have tried to divide the experiment into sections in such a way that either approach is possible. Thus, for instance, it should also be possible to issue an unknown amine, an unknown aldehyde/ketone, etc.

Many more unknowns have been added to Appendix 1 in this edition of the Textbook in order to increase the challenge offered to our students. Because of this expansion, students may need an NMR spectrum to determine the structure of the unknown unless derivative formation is included in the class. To dissolve samples for NMR, the class should have available  $\text{CDCl}_3$  for routine spectra. For higher melting solids, a mixture of  $\text{CDCl}_3$  and  $\text{DMSO-d}_6$  works well. This mixture is prepared by mixing 75mL of  $\text{CDCl}_3$  containing TMS with 25 mL of  $\text{DMSO-d}_6$ .

To assist students in acquiring all available literature data, we supply in the lab a

copy of each of the following reference works and encourage their use:

1. Handbook of Chemistry and Physics
2. Tables for the Identification of Organic Compounds
3. The Merck Index
4. Shriner, Fuson, Curtin, and Morrill

These books are permanently mounted, either on a stand or a chained board, to prevent their removal from the lab. We encourage students to use these supplementary texts and references.

We maintain a special set of shelves in our laboratory where all the test reagents, test compounds, and special solvents are collected. This is convenient and saves a lot of confusion.

The collection of waste in this experiment can be a problem, especially since each unknown may or may not contain a halogen. Depending on how you segregate your wastes, you may want to use a different system for collecting waste than the one described here.

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### SPECIAL NOTES ON BOILING POINT DETERMINATION

A simple and reliable method of determining boiling points is the macroscale method using 13-mm x 100-mm test tubes described in Technique 13, Section 13.2 of the Textbook. If an aluminum block and hot plate is used to heat the sample, a hole that is slightly larger than the test tube should be drilled all the way through the aluminum block. The aluminum block works well with small hot plates like those used in microscale work. However, if the aluminum block is used with larger hot plates, such as Corning, it can sometimes be difficult to avoid overheating, even at the lowest setting. This is a problem mainly with low boiling liquids (<100 °C). If these liquids are heated too strongly, all the liquid may evaporate before a temperature plateau is observed. If all the liquid evaporates, the temperature may actually go above the boiling point.

The method described in Section 13.2 works best with a partial immersion mercury thermometer. Even if the reflux ring does not reach the immersion line on the thermometer, the boiling point will usually be quite accurate. This is because the coefficient of expansion of mercury is small. Non-mercury partial immersion thermometers can also work well, but then it is more important that the reflux ring be close to the immersion line. With a total immersion thermometer, it will be necessary to perform a stem correction in order to obtain accurate results.

Whatever method is used in your lab, we recommend that you try it with a low boiling liquid such as methanol and a high boiling liquid such as ethyl benzoate. The most common mistake that students make is to report a boiling point below the actual boiling point. This usually happens because they have not heated the sample strongly enough and the actual boiling point plateau has not yet been reached. This is most likely to happen with high boiling liquids, but it can also occur with low boiling liquids.

It is essential to obtain a reliable boiling point in either Option 1 or Option 2 in order to be able to find the unknown on the Tables in Appendix 1. Increasingly, we find that making use of a computer interface with a temperature probe has replaced thermometers in determining boiling points of liquids. To use this approach, we recommend Vernier LabPro interface, equipped with a stainless-steel probe and a laptop computer for determining an accurate and reliable boiling point. See Technique 13, Section 13.5 of the Textbook. Also see the Instructor's Manual, Experiment 6, Simple and Fractional Distillation for more specific information about selecting an appropriate temperature probe.

#### COMPUTER SUPPORT FOR THIS EXPERIMENT

"Simulated Qualitative Organic Analysis - SQUALOR AND MacSQUALOR," by D. Pavia is available from Trinity Software (MSDOS and Macintosh versions). It gives students an opportunity to solve many more unknowns than they could ever complete in the lab. We require students to solve a number of the unknowns in this program early in the term.

"Introduction to Spectroscopy" by Fred Clough (Trinity Software); available in MSDOS, covers infrared, proton and carbon NMR, and mass spectroscopy.

"Spectral Interpretation," by D. Pavia (Trinity Software); available in MSDOS, allows a user to display and plot spectra.

Trinity Software, Inc  
607 Tenney Mountain Hwy  
Suite 215  
Plymouth, NH 03264-3156

Phone: (603) 536-9661

## TEST SOLUTIONS AND REAGENTS

### **EXPERIMENT 55A** (Solubility Tests)

#### REAGENTS:

Concentrated H<sub>2</sub>SO<sub>4</sub>

5% aqueous HCl

5% aqueous NaHCO<sub>3</sub>

5% aqueous NaOH

#### UNKNOWN:

1. Dimethylaniline (strong base)
2. 2-Naphthol (weak acid)
3. Benzoic acid (strong acid)
4. Benzophenone (neutral - with functionality)
5. Biphenyl (neutral - no functionality)

Separate waste disposal containers for aqueous, nonhalogenated and halogenated wastes

### **EXPERIMENT 55B** (Tests for the Elements N, S, X)

Test Compounds: bromobenzene, benzoic acid, benzyl bromide (□-bromotoluene), 2-chloro-2-methylpropane (*tert*-butyl chloride), 2-nitrotoluene.

#### **Beilstein Test**

Copper wire

#### **Silver Nitrate Test**

2% Ethanolic AgNO<sub>3</sub>

2 g silver nitrate dissolved in 100 mL 95% ethanol)

5% Nitric acid

#### **Sodium Iodide in Acetone Test**

15% NaI in acetone

15 g sodium iodide dissolved in 100 mL acetone

#### **Ferrous Hydroxide Test**

2M Potassium hydroxide in methanol

5% Aqueous ferrous ammonium sulfate

5 g ferrous ammonium sulfate dissolved in 100 mL water. Make fresh.

2M Sulfuric acid

**SODIUM FUSION (optional):**

Sodium metal (stored under mineral oil). Place the sodium in a designated hood, along a balance, a knife, a shallow dish, and a waste container.

Methanol	10% Aqueous H <sub>2</sub> SO <sub>4</sub>
pH paper	Chlorine water or calcium hypochlorite (Clorox may also be used)
Sat'd ferrous ammonium sulfate (5 g/100 mL)	10% Aqueous NaOH
30% Aqueous KF (30 g/100 mL H <sub>2</sub> O)	Unknowns (if desired): Your choice - N, S, Cl, Br, I or combinations
Acetic acid (conc.)	
1% Aqueous lead acetate (1 g/100 mL)	
5% Aqueous AgNO <sub>3</sub> (5 g/100 mL)	
Methylene chloride	
Waste container for solutions containing silver	
Waste containers for halogenated and nonhalogenated waste	
Waste container for aqueous waste	

**EXPERIMENT 55C (Tests for Unsaturation)**

Test compounds: Cyclohexene, cyclohexane, toluene, acetone, ethyl benzoate and benzoin (**note:** we have omitted naphthalene in this edition).

**Bromine in Methylene Chloride Test**

2% Br<sub>2</sub>/CH<sub>2</sub>Cl<sub>2</sub>

Dissolve 2 mL bromine in 100 mL methylene chloride. **Caution:** Work in a good fume hood when preparing this reagent! See page 487 for a discussion of problems with using methylene chloride rather than carbon tetrachloride as the solvent. Replace this reagent every week.

Methylene chloride

### **Potassium Permanganate Test**

1,2-Dimethoxyethane

95% Ethanol

1% Aqueous  $\text{KMnO}_4$

Dissolve 1 g of potassium permanganate in 100 mL water

### **Ignition Test for Aromaticity**

Set up a station in a hood with a Bunsen burner

Waste containers for halogenated and nonhalogenated organic waste

Waste container for aqueous waste containing potassium permanganate

## **EXPERIMENT 55D (Aldehydes and Ketones)**

Test compounds: Cyclohexanone, benzaldehyde, benzophenone, butanal (butyraldehyde), acetone (reagent grade), 2-heptanone, 4-heptanone (dipropyl ketone), 2-pentanol.

### **2,4-Dinitrophenylhydrazine Test**

2,4-Dinitrophenylhydrazine reagent:

Dissolve 3.0 g of 2,4-dinitrophenylhydrazine in 15 mL conc.  $\text{H}_2\text{SO}_4$ . In a beaker, *slowly add*, with mixing, 23 mL of  $\text{H}_2\text{O}$  until the solid dissolves. Add 75 mL of 95% ethanol to the warm solution, with stirring. After thorough mixing, filter the solution if any solid remains. This reagent needs to be prepared fresh each term.

95% Ethanol

Bis(2-ethoxyethyl) ether also called di(ethylene glycol) diethyl ether

### **Tollens Test (recommended)**

**CAUTION!!!** Students need to be warned about the danger of this reagent. They need to make it fresh and dispose of it promptly and properly (see page 495 in the Textbook). Students need to acidify the waste with 5% HCl before placing it in the silver waste container.

Solution A: 3.0 g AgNO<sub>3</sub> in 30 mL H<sub>2</sub>O

Solution B: 10% aqueous NaOH  
10 g of sodium hydroxide dissolved in 100 mL water  
10% ammonia solution

40 mL conc. ammonium hydroxide dissolved in 60 mL water

Bis(2-ethoxyethyl) ether also called di(ethylene glycol) diethyl ether

### **Chromic Acid Test (optional, but not recommended for safety reasons)**

Chromic acid reagent:

Dissolve 20 g Chromium trioxide (CrO<sub>3</sub>) in 20 mL conc. H<sub>2</sub>SO<sub>4</sub>. *Slowly* add this solution to 60 mL cold H<sub>2</sub>O that is cooled in an ice bath. This reaction is very exothermic! This chromium trioxide reagent needs to be prepared fresh each term.

Reagent grade acetone

### **Iodoform Test**

Dissolve 20 g potassium iodide and 10 g iodine in 100 mL water

10% Aqueous sodium hydroxide solution  
10 g of sodium hydroxide dissolved in 100 mL water

1,2-Dimethoxyethane

Clean corks/ large test tubes if not available in drawer stock

### **Ferric Chloride Test**

2.5% Aqueous ferric chloride (2.5 g/100 mL)

### **DERIVATIVE PREPARATION (optional)**

2 M aqueous solution of semicarbazide hydrochloride (1.1 g for every 5 mL H<sub>2</sub>O)

Semicarbazide hydrochloride

Sodium acetate

Ethanol

2,4-Dinitrophenylhydrazine reagent (as prepared above)

Waste containers for halogenated and nonhalogenated organic waste

Waste container for chromium waste

Waste container for solutions containing silver (**CAUTION:** this container should already contain 5% hydrochloric acid just in case students fail to acidify their Tollens waste).

Waste container for aqueous waste.

Waste containers for 2,4-dinitrophenylhydrazone and semicarbazone wastes

### **EXPERIMENT 55E (Carboxylic Acids)**

Test Compounds: Benzoic acid.

#### **Solubility Test**

5% Aqueous sodium bicarbonate solution

#### **Silver Nitrate Test**

2% ethanolic AgNO<sub>3</sub>

2 g silver nitrate dissolved in 100 mL of 95% ethanol

#### **Neutralization Equivalent (optional)**

Phenolphthalein indicator

Standardized NaOH solution (approx. 0.1 M, but precisely standardized)

#### **DERIVATIVE PREPARATION (optional):**



Thionyl chloride	Anhydrous Na <sub>2</sub> SO <sub>4</sub>
Conc. NH <sub>4</sub> OH	5% Aqueous NaOH
Aniline	5% Aqueous HCl
p-Toluidine	
Toluene	

Waste containers for halogenated and nonhalogenated organic wastes

Waste container for aqueous waste

Waste container for silver waste

### **EXPERIMENT 55F (Phenols)**

Test Compounds: Phenol (solid), 1% aqueous phenol solution and 2-naphthol.

#### **Sodium Hydroxide Test**

10% aqueous sodium hydroxide solution

#### **Ferric Chloride Test**

2.5% Aqueous ferric chloride (2.5 g/100 mL)

#### **Cerium (IV) Test**

Prepare 2M nitric acid solution by diluting 12.8 mL of concentrated nitric acid to 100 mL with water. Dissolve 8 g of ceric ammonium nitrate [Ce(NH<sub>4</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>6</sub>] in 20 mL of the dilute nitric acid solution. Ceric ammonium nitrate is listed in catalogs as ammonium cerium (IV) nitrate; CAS registry number: 16774-21-3

1,2-dimethoxyethane

#### **Bromine in Water Test**

Saturated bromine water:

Add bromine to water until it no longer dissolves and forms a red pool in the bottom - use a glass stoppered bottle.

#### **DERIVATIVE PREPARATION (optional):**

□-Naphthylisocyanate                      Methanol

Brominating solution:  
0.5 g bromine and 0.75 g potassium bromide dissolved in 5 mL water

Waste containers for halogenated and nonhalogenated organic waste

Waste container for aqueous waste

### **EXPERIMENT 55G (Amines)**

Test Compounds: Aniline, *N*-methylaniline and butylamine.

#### **Nitrous Acid Test**

Concentrated sulfuric acid

10% Aqueous sodium nitrite ( $\text{NaNO}_2$ ) solution  
Dissolve 10 g of sodium nitrite in 100 mL of water

2-Naphthol (□-naphthol)

10% aqueous sodium hydroxide solution  
Dissolve 10 g of sodium hydroxide in 100 mL of water

#### **Acetyl Chloride Test**

Acetyl chloride

#### **DERIVATIVE PREPARATION (optional):**

Acetic anhydride                      Ethanol

5% Aqueous HCl                      5% Aqueous  $\text{Na}_2\text{CO}_3$

Pyridine                                  Toluene

5% Aqueous  $\text{H}_2\text{SO}_4$                       Saturated picric acid in EtOH

10% Aqueous NaOH                      Methyl iodide

Benzoyl chloride                      Ethyl acetate

Waste containers for halogenated and nonhalogenated organic waste

Waste container for nitrous acid test (put 6 M hydrochloric in the bottle)

Waste container for aqueous waste

### **EXPERIMENT 55H (Alcohols)**

Test Compounds: 1-Butanol, 2-pentanol, 2-methyl-2-butanol, phenol, butanal, cyclohexanone, ethyl acetate, 1-octanol, 2-naphthol, benzoic acid.

#### **Acetyl Chloride Test**

Acetyl chloride

#### **Lucas Test**

Lucas reagent: Cool 10 mL of conc. hydrochloric acid in a beaker using an ice bath. While still cooling, and, with stirring, add 16 g anhydrous zinc chloride to the acid.

#### **Cerium (IV) test**

Cerium (IV) reagent (see Experiment 55F Phenols, prepared in the same way).

#### **Chromic Acid Test (optional)**

Test compounds for the chromic acid test: 1-butanol, 2-butanol, 2-methyl-2-propanol

Chromic acid reagent (See Experiment 55D, prepared in the same way).

Reagent grade acetone

#### **DERIVATIVE PREPARATION (Optional):**

3,5-Dinitrobenzoyl chloride

Check the melting point of the material to determine purity (Appendix 2).

5% Aqueous  $\text{Na}_2\text{CO}_3$

Phenylisocyanate

Ethanol

Ligroin or hexane

Waste containers for halogenated and nonhalogenated organic wastes.

Waste container for solutions containing chromium

Waste container for solutions containing zinc

Waste container for aqueous waste

### **EXPERIMENT 55I (Esters)**

Test Compound: Ethyl butanoate (ethyl butyrate).

#### **Ferric Hydroxamate Test**

Hydroxylamine hydrochloride (0.5 *M* in ethanol)

5% Aqueous FeCl<sub>3</sub> (5 g/100 mL)

1*M* Aqueous hydrochloric acid

6*M* Aqueous sodium hydroxide

95% Ethanol

#### **Basic Hydrolysis (optional)**

25% aqueous sodium hydroxide solution

Dissolve 25 g of sodium hydroxide in 100 mL of water

Stopcock grease

Waste container for solutions containing hydroxylamine or derivatives (put 6 *M* hydrochloric acid in the bottle).

Waste containers for organic and aqueous wastes

#### **CAS Registry Numbers:**

<i>N,N</i> -dimethylaniline	121-69-7
2-naphthol	135-19-3
phenol	108-95-2
benzoic acid	65-85-0
benzophenone	119-61-9

biphenyl	92-52-4
bromobenzene,	108-86-1
benzyl bromide (□bromotoluene)	100-39-0
2-chloro-2-methylpropane	507-20-0
2-nitrotoluene	88-72-2
cyclohexene	110-83-8
cyclohexane	110-82-7
toluene	108-88-3
acetone	67-64-1
ethyl benzoate	93-89-0
benzoin	119-53-9
ferrous ammonium sulfate	10045-89-3
cyclohexanone	108-94-1
benzaldehyde	100-52-7
butanal (butyraldehyde)	123-72-8
aniline	62-53-3
butylamine	109-73-9
2-heptanone (methyl n-amyl ketone)	110-43-0]
4-heptanone (dipropyl ketone)	123-19-3
1-butanol	71-36-3
2-butanol	78-92-2
2-methyl-2-propanol	75-65-0
2-pentanol (sec-amyl alcohol)	6032-29-7
2-methyl-2-butanol ( <i>t</i> -amyl alcohol)	75-85-4
1-octanol	111-87-5
2,4-Dinitrophenylhydrazine	119-26-6
bis(2-ethoxyethyl) ether (diethylene glycol diethyl ether)	112-36-7
1,2-dimethoxyethane	110-71-4
chromium trioxide (CrO <sub>3</sub> )	1333-82-0
cerric ammonium nitrate	16774-21-3
sodium nitrite (NaNO <sub>2</sub> )	7632-00-0
acetyl chloride	75-36-5
hydroxylamine hydrochloride	5470-11-1
ethyl acetate.	141-78-6
ethyl butanoate (ethyl butyrate)	105-54-4

## Experiment 56

### PREPARATION OF A C-4 or C-5 ACETATE ESTER

TIME ESTIMATE: 1-2 periods

CHEMICALS AND SUPPLIES PER STUDENT:

Students will choose or be assigned an alcohol from the following list:

1-butanol	1-pentanol
2-butanol	2-pentanol
2-methyl-1-propanol	3-pentanol
cyclopentanol	3-methyl-1-butanol

You will require 5 mL of alcohol for each student. We usually supply a bottle of each alcohol along with a sign-up sheet that has lines for only 2-3 names for each alcohol. In this way we get an even distribution of the alcohols among the students in the class.

Glacial acetic acid (d = 1.06 g/mL) 7 mL

Concentrated sulfuric acid 1 mL

Calcium chloride for drying tubes

5% Aqueous sodium bicarbonate 5 mL

Saturated aqueous sodium chloride (31.7g NaCl /100 mL water) 5 mL

Anhydrous granular sodium sulfate 1.5 g

Inert boiling stones (corrundum, black)

Waste disposal containers for aqueous and non-halogenated wastes

Salt plates for infrared spectroscopy

NMR tubes (optional)

Deuteriochloroform for NMR (optional)

#### **CAS Registry Numbers:**

1-butanol 71-36-3

1-pentanol	71-41-0
2-butanol	78-92-2
2-pentanol	6032-29-7
2-methyl-1-propanol	78-83-1
3-pentanol	584-02-1
Cyclopentanol	96-41-3
3-methyl-1-butanol	123-51-3

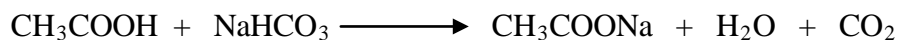
SPECIAL NOTES:

Secondary alcohols such as 2-butanol are prone to give a good deal of elimination unless the amount of sulfuric acid is reduced to 0.5 mL from the specified 1.0 mL. It is also helpful to reduce the heating time to something less than 60 minutes. With the other secondary alcohols, our students have actually isolated 2-pentene, 3-pentene and cyclopentene from 2-pentanol, 3-pentanol and cyclopentanol, respectively. With these alcohols, it may be interesting for students to have two containers available so that they can collect the alkene and ester in separate containers. The infrared spectra should be obtained on both fractions. Here is an excellent opportunity for students to discover and learn some interesting chemistry! Just to make life more interesting, a solid may appear in the reflux condenser when refluxing cyclopentanol with acetic acid and sulfuric acid. This solid is dicyclopentyl ether.

White, calcium carbonate-based boiling stones will dissolve in the strongly acidic solution. Use either a stir bar or the black, corundum-based boiling stones.

ANSWERS TO QUESTIONS:

- Remove water as it is formed.
  - Remove product as it is formed.
- Sodium bicarbonate assures neutralization and removal of excess acetic and sulfuric acids by converting them to ionic salts that are very water-soluble.



- The evolution of  $\text{CO}_2$  according to the equations in Question 2 causes the bubbles.
- The answer to this question will vary depending on which alcohol is chosen. However, in every case, the glacial acetic acid will be present in a three to four-fold excess. A sample calculation is given in the answer to

Question 4, Experiment 12 (Isopentyl acetate).

5. The separation schemes will be similar to the one shown in Technique 2, page 566.
6. The esters will all have similar infrared spectra (see answer to Question 6 in experiment 12).
7. The mechanisms will be a standard acid-catalyzed Fischer esterification differing only in which alcohol is used.
8. The alcohol 2-methyl-2-propanol will give an E1 elimination reaction in the acid solution, yielding 2-methylpropene.
9. It is called *glacial* acetic acid because its melting point is 16.7 °C (62 °F). On a cold winter day, it will solidify (freeze) if the room is cool.

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### **Experiment 57**

#### **ISOLATION OF ESSENTIAL OILS FROM ALLSPICE, CLOVES, CUMIN, CARAWAY, CINNAMON, FENNEL OR STAR ANISE**

TIME ESTIMATE: 1 period

CHEMICALS AND SUPPLIES PER 10 STUDENTS (Exp. 57A)

Students will choose or be assigned a spice from the following list:

allspice (whole)	caraway
cloves (whole buds)	cinnamon (sticks)
cumin	fennel
star anise	

You will require 3.0 g of spice for each student. We usually supply a container of each spice along with a sign-up sheet that has lines for only 2-3 names for each spice. In this way we get an even distribution of the spices among the students in the class.

Methylene chloride (dichloromethane)	120 mL
Saturated aqueous sodium chloride (31.7g NaCl /100 mL water)	120 mL
Anhydrous granular sodium sulfate	20 g



Boiling stones

Mortars and pestles

Scissors

Salt plates for infrared spectroscopy

Carbon tetrachloride for spectroscopy in small dropper bottle

NMR tubes (optional)

Deuteriochloroform for NMR (optional)

Disposal container for aqueous wastes

Disposal container for halogenated wastes

#### OPTIONAL HPLC EXPERIMENT

Methanol 10mL/group

4- $\mu$ m filter to fit a Büchner funnel 1/group

2- $\mu$ m filter to fit a Büchner funnel 1/group

4-dram snap-cap vials 1/group

85% methanol and 15% water solvent for HPLC

#### SPECIAL NOTES:

Foaming can be a severe problem in this experiment if ground spices are used. The problem is at its worst if ground cinnamon is used. Use cinnamon sticks, breaking them into pieces, to avoid the problem. It is also suggested that you use clove buds and whole allspice in place of the corresponding ground spices.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS (Exp. 57B)

Capillary tubing, open at both ends 1/sample

Essential oil sample (from Exp. 58A)

Methylene chloride (HPLC grade) 70 mL

Anhydrous sodium sulfate 10 g

Aluminum foil

0.45- $\mu$ m filter cartridge 1/sample

Gas chromatography-mass spectrometry instrument

**SPECIAL NOTE:** It may be advisable for the instructor to check the correct conditions for the GC/MS experiment by running a few test samples before the students are allowed to run their samples.

**CHEMICALS AND SUPPLIES PER 10 STUDENTS (Exp. 57C):**

The materials and equipment required for this experiment are identical to those used in Experiment 57B. The spices used are different from those used in Experiments 57A and 57B. This experiment is intended as a project-based experiment.

The instructor should provide a variety of spice or herb samples that can be run. We have had success with the following materials:

Rosemary  
Thyme  
Lavender leaf  
Sage  
Dill

We have obtained best results when the sample of spice or herb is fresh.

**ANSWERS TO QUESTIONS:**

1. The students' matrix chart should look something like the one shown below, but it should also show the expected infrared frequencies for each feature.

	<b>Aldehyde CHO arom</b>	<b>Phenolic OH</b>	<b>Ketone C=O conjugated</b>	<b>Phenyl ring, Double bond</b>
<b>Cmpd A</b>	yes +++	No	no	yes +++, yes +++
<b>Cmpd B</b>	yes +++	No	no	yes +++

<b>Cmpd C</b>	No	yes +++	no	yes +++, yes +++
<b>Cmpd D</b>	No	No	no	yes +++, yes +++
<b>Cmpd E</b>	No	No	yes +++	no, yes +++

- The newly condensed steam distillate appears cloudy because the oil that has codistilled is insoluble and begins to separate as fine droplets of oil suspended in the water.
- If the solution is "dry" there will be no drops of water visible either in the solution or clinging to the side of the vial. In addition, dry solutions will be completely clear, and not cloudy. If drying agent is present, it should flow freely like sand; if it clumps, the solution is still wet.

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### Experiment 58

#### **COMPETING NUCLEOPHILES IN S<sub>N</sub>1 AND S<sub>N</sub>2 REACTIONS: INVESTIGATIONS USING 2-PENTANOL AND 3-PENTANOL**

TIME ESTIMATE AND NOTES: 1 period, with some additional time to analyze the products outside of class. Students may choose either 2-pentanol or 3-pentanol as substrates in order to use the experiment as written.

However, at Western Washington University we run this experiment with 1-pentanol, 2-pentanol, 3-pentanol and 2-methyl-2-butanol (*tert*-amyl alcohol). Students choose 1-pentanol or 2-pentanol or 3-pentanol and run the experiment as described on page 506 in the Text (see also Experiment 21A where the only change required is to have the students substitute alcohols). Once the students have the reflux going, then everyone runs the reaction as described on pages 177-178 with *tert*-amyl alcohol as the substrate (Experiment 21B). The students have the opportunity to compare the results from a primary, secondary and tertiary alcohol. The results of these experiments are described below.

#### **CHEMICALS AND SUPPLIES PER 10 STUDENTS:**

Preparation of solvent-nucleophile medium.

See the Instructors Manual description for Experiment 21. The same medium is used for this experiment. Also see the Notes to the Instructor on page 505 of the textbook.

Remainder of chemicals and supplies per 10 students

1-Pentanol (optional)	8 mL
2-Pentanol	8 mL
3-Pentanol	8 mL
2-methyl-2-butanol (optional)	8 mL
Inert boiling stones	
Saturated aqueous sodium bicarbonate	
Pentane	10 mL
Anhydrous sodium sulfate (granular)	5 g
Crushed ice	

Parafilm if the samples are to be stored (not recommended!)

#### OTHER EQUIPMENT NEEDED:

See the Instructors Manual for Experiment 21. Analysis by gas chromatography on a capillary column is required because the compounds will not separate adequately on a packed column. See page 511 for ideal conditions for setting up the gas chromatograph. Suitable NMR results can be obtained on a high-field NMR spectrometer (at least 300 MHz).

#### RESULTS:

The interesting part of this experiment is that 2-pentanol gives both 2-chloro/3-chloropentanes and 2-bromo/3-bromopentanes. Likewise, 3-pentanol gives 2-chloro/3-chloropentanes and 2-bromo/3-bromopentanes. The ratio of the products is not exactly the same as the table shows. For example, 2-pentanol gives more 2-chloropentane than 3-chloropentane and the reverse occurs for the 3-pentanol. The results for a typical class are shown in the table.

Alcohol	percent 2-chloro- pentane	percent 3-chloro- pentane	percent 2-bromo- pentane	percent 3-bromo- pentane
2-pentanol	20.8	11.2	47.0	21.0
3-pentanol	13.0	19.6	23.5	43.9

Notice, however, that the overall percentages of the chloropentanes (about 32%) and bromopentanes (about 68%) are about the same for the two alcohols. In some preliminary research, it appears the “rearrangement” results can be partially explained by an initial formation of the secondary carbocation followed by an elimination reaction (E1) to yield mainly 2-pentene. When H-X adds to the alkene, one would expect to obtain a mixture of 2-halides and 3-halides. We have shown that when the reaction is run in D<sub>2</sub>SO<sub>4</sub>, there is evidence of some deuterium being incorporated into the isolated products which supports the mechanism suggested. It is also possible that the two secondary carbocations are interconverted by some sort of equilibrium, perhaps by a hydride shift. Unfortunately, the equilibration is not quite complete as one sees in the table of results. Since the overall percentages of bromides are larger than the chlorides, we suggest that the S<sub>N</sub>2 predominates in the reaction. However, a significant S<sub>N</sub>1 reaction competes.

Retention times for the halides under the conditions provided on page 507.

2-chloropentane	4.03 min
3-chloropentane	4.10 min
2-bromopentane	4.74 min
3-bromopentane	4.82 min

As mentioned at the beginning, our classes at Western Washington University include 1-pentanol and 2-methyl-2-butanol (*tert*-amyl alcohol) in the experiment. Inclusion of these compounds nicely completes the picture! 1-Pentanol reacts by an S<sub>N</sub>2 reaction to give 13.4% of 1-chloropentane and 86.6% of 1-bromopentane. You can expect that the class average will not deviate from this amount by more than ± 2%. The results support the notion that the bromide ion is more nucleophilic than chloride. The secondary alcohols give a smaller amount of bromides because the S<sub>N</sub>1 reaction competes with the S<sub>N</sub>2 reaction.

For the tertiary alcohol, 2-methyl-2-butanol, we expect an S<sub>N</sub>1 reaction will be involved exclusively. On a good day we obtain values that are close to 50-50 (see table). The halides react indiscriminately with the tertiary carbocation, and nucleophilicity is not involved so one should expect 50% of each halide. On a not so nice day, you might get results such as 45/55. Students should realize that

the tertiary halides are very volatile, and this can affect the product ratios. Because of the volatility problem we recommend that you run the gas chromatograms on the same day! It is critical to control the temperature of the solvent/nucleophile mixture so that the temperature does not become too high. If the temperature isn't controlled, it is likely that some of the H-X will distill from the mixture and that would influence the halide composition in the solvent/nucleophile mixture. We compare the results from gas chromatography with NMR results. You should expect similar ratios.

Alcohol	% chloro	Retention time (min)	% bromo	Retention time (min)
1-pentanol	13.4	4.46	86.6	5.23
2-methyl-2-pentanol	49.0	3.74	51.0	4.39

---

## Experiment 59

### FRIEDEL-CRAFTS ACYLATION

TIME ESTIMATE: 2 periods

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Dichloromethane (methylene chloride)	1 L
Anhydrous aluminum chloride (fresh)	150 g
Acetyl chloride	100 g
Hydrochloric acid, concentrated	350 mL
Saturated sodium bicarbonate solution 6.9 g/100 mL water	1 L
Anhydrous sodium sulfate (granular)	40 g
Calcium chloride (drying tubes)	100 g
Cotton for drying tubes	
Rubber tubing and stoppers	

The following chemicals will be needed in an amount of approximately 8 g

(10mL) per student. Each student will use (or be assigned) one of the compounds from this list:

Toluene  
Ethyl benzene  
*o*-Xylene (1,2-dimethylbenzene)  
*m*-Xylene (1,3-dimethylbenzene)  
*p*-Xylene (1,4-dimethylbenzene)  
Pseudocumene (1,2,4-trimethylbenzene)  
Anisole (methoxybenzene)  
1,2-Dimethoxybenzene  
1,3-Dimethoxybenzene  
1,4-Dimethoxybenzene  
Mesitylene (1,3,5-trimethylbenzene)  
Hemellitotol (1,2,3-trimethylbenzene, **gives two products**)

Disposal bottles for halogenated and nonhalogenated wastes

Disposal bottle for aqueous wastes

Manometers (optional)

Carbon tetrachloride in dropper bottle for infrared spectroscopy

Deuteriochloroform for NMR spectroscopy

NMR tubes

Salt plates for infrared spectroscopy

**CAS Registry Numbers:**

Toluene	108-88-3
Ethylbenzene	100-41-4
<i>o</i> -Xylene (1,2-dimethylbenzene)	95-47-6
<i>m</i> -Xylene (1,3-dimethylbenzene)	108-38-3
<i>p</i> -Xylene (1,4-dimethylbenzene)	106-42-3
1,2,4-trimethylbenzene	95-63-6
Anisole (methoxybenzene)	100-66-3
1,2-Dimethoxybenzene	91-16-7
1,3-Dimethoxybenzene	151-10-0
1,4-Dimethoxybenzene	150-78-7
Mesitylene (1,3,5-trimethylbenzene)	108-67-8
1,2,3-Trimethylbenzene	526-73-8

## SPECIAL NOTES:

It is recommended that the anhydrous aluminum chloride be placed in a hood along with a balance. All weighing can then be conducted in the hood to minimize noxious vapors.

If vacuum resources are limited, students may combine with another student and work in pairs for the vacuum distillation. Alternatively, you may omit the distillation part of the experiment. In most cases, a single product is obtained, and the vacuum distillation does not materially improve the quality of the product. See the notes to the instructor on page 511 of the Textbook which suggests using GC/MS and the NIST database to analyze the product of the Friedel-Crafts reaction. You may observe some starting material in the NMR spectra and gas chromatograms.

A four-step synthesis may be considered by linking together the Friedel-Crafts reaction with the synthesis of a chalcone (Experiment 63). Cyclopropanation and epoxidation of the chalcone can extend the multistep synthesis (Experiments 64 and 65). Suggestions of aromatic compounds that work well in these sequences are provided on page 512.

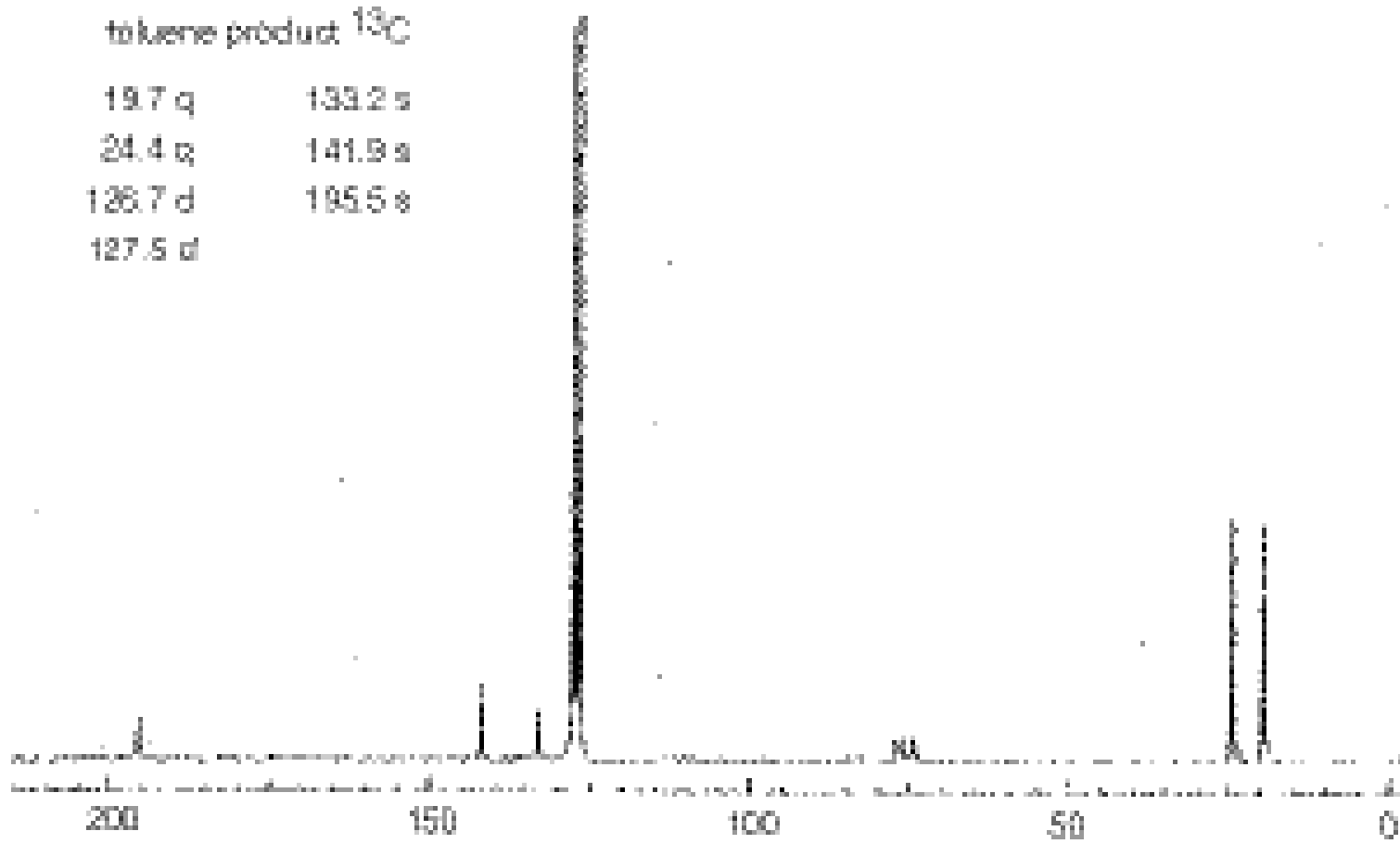
We prefer to keep the solvents for spectroscopy in small bottles, with a test tube attached to the side, which in turn contains a disposable pipette for dispensing the small quantities required. This bottle is stored in a hood where an area is set aside for preparation of spectroscopic samples. Salt plates are stored in a desiccator in this same area.

Decoupled carbon-13 NMR spectra are included for some of the products. They can be photocopied and handed out. The chemical shifts are given, along with the observed pattern when the carbon is coupled to protons: singlet (s), doublet (d), triplet (t) and quartet (q). The spectra were all obtained from actual student prepared samples.



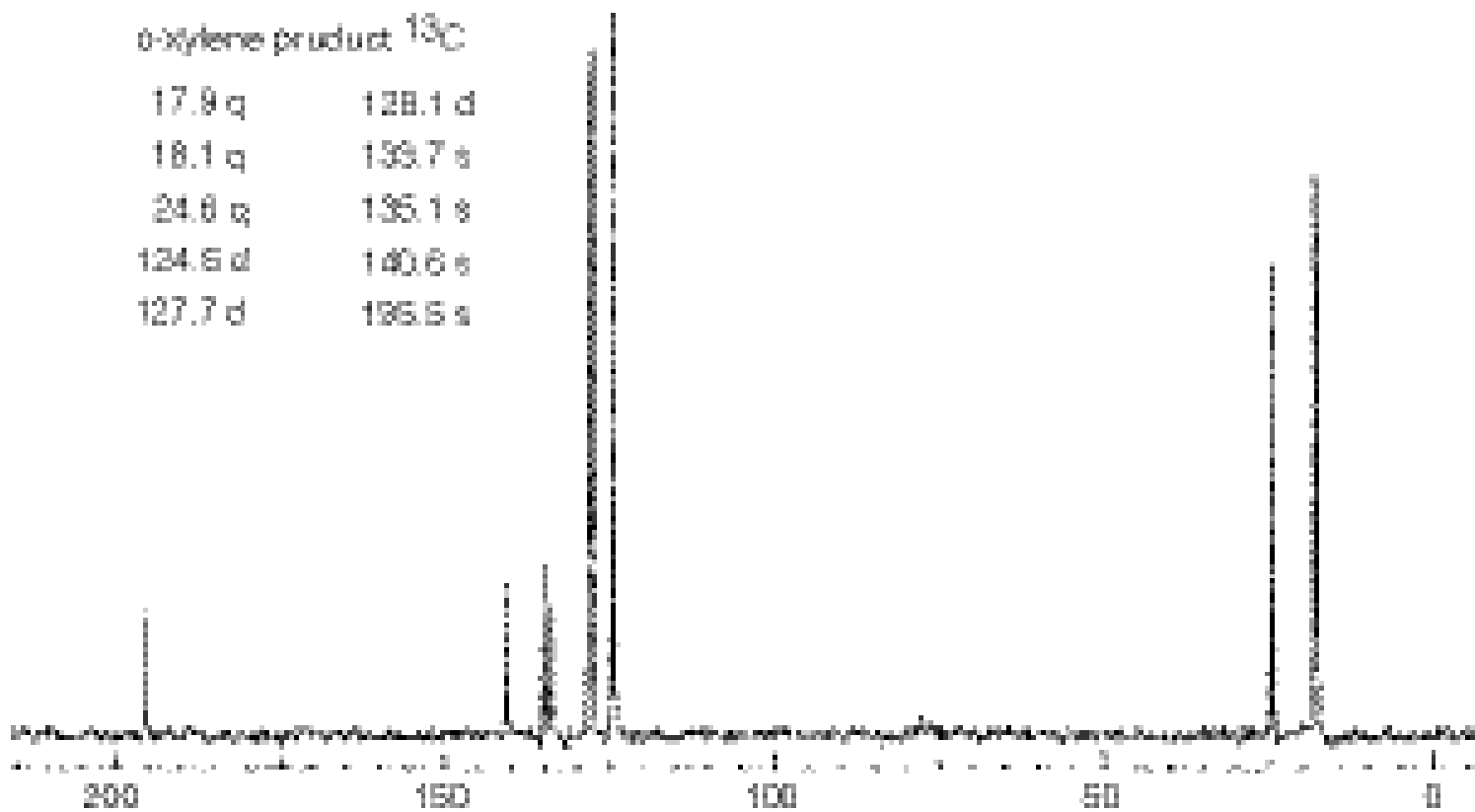
toluene product  $^{13}\text{C}$

19.7 q	133.2 s
24.4 q	141.9 s
126.7 d	195.5 s
127.5 d	



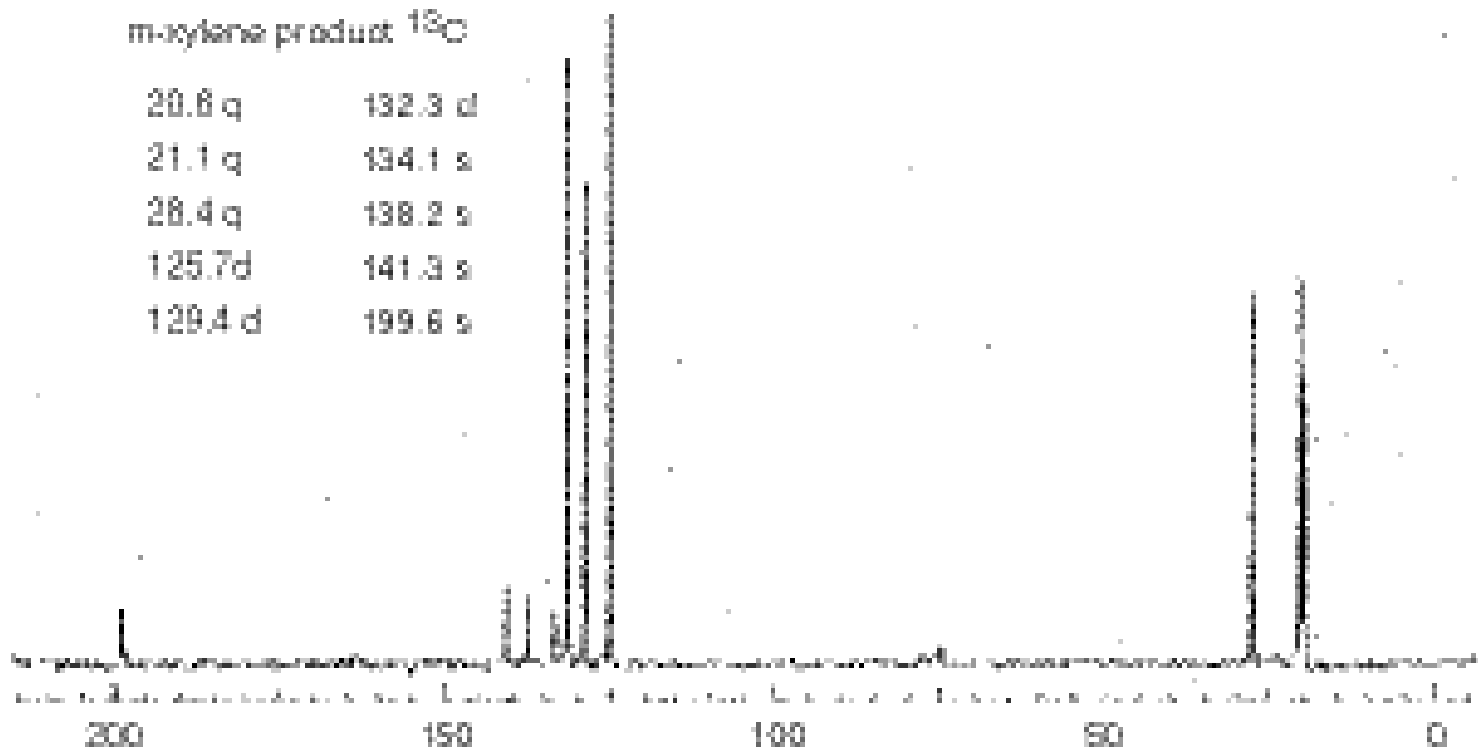
o-xylene product  $^{13}\text{C}$

17.9 q	128.1 d
18.1 q	133.7 s
24.8 q	135.1 s
124.6 d	140.6 s
127.7 d	155.5 s



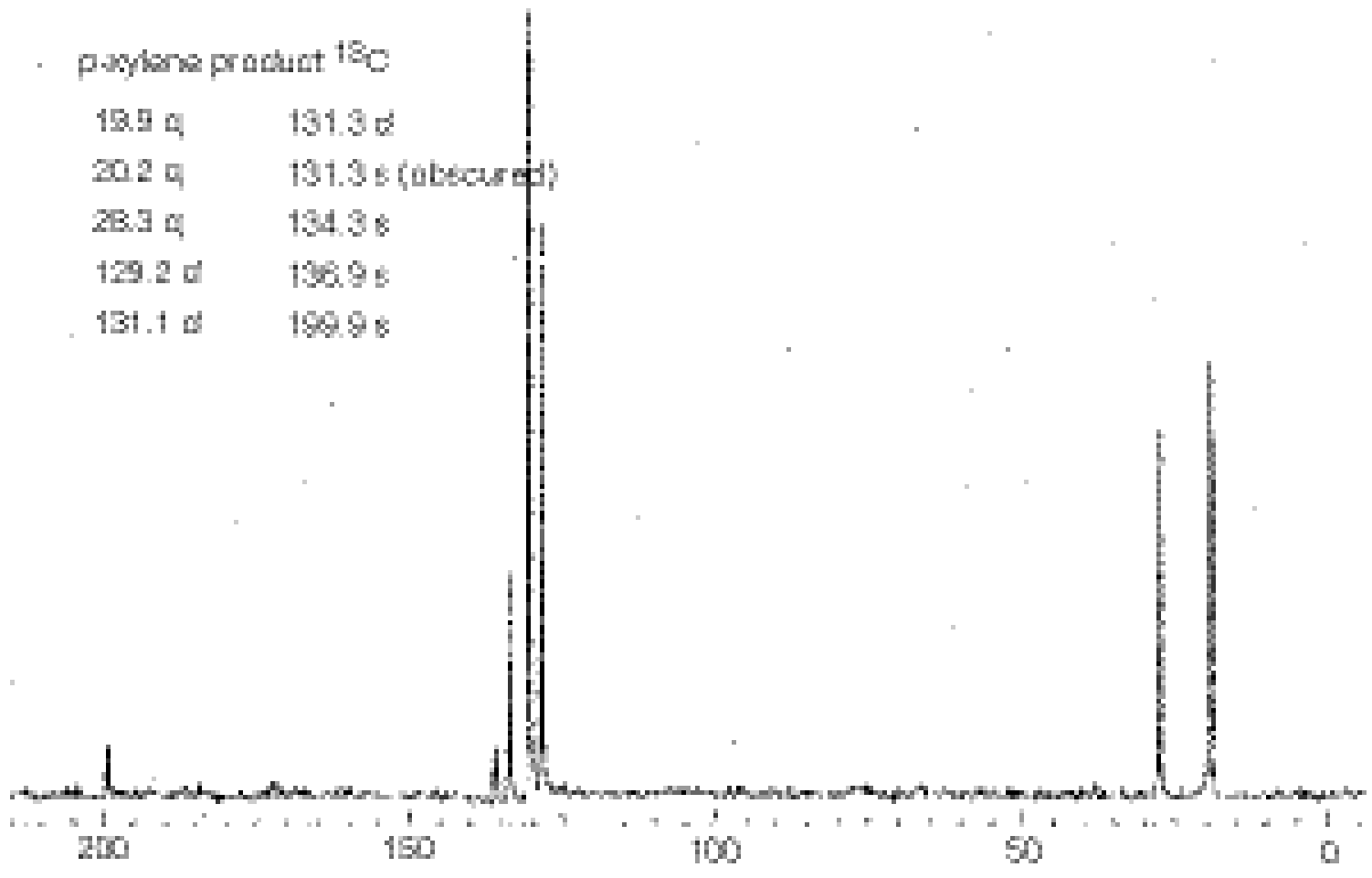
m-xylene product  $^{13}\text{C}$

20.6 q	132.3 d
21.1 q	134.1 s
28.4 q	138.2 s
125.7 d	141.3 s
129.4 d	199.6 s



p-xylene product  $^{13}\text{C}$

19.9 q	131.3 d
20.2 q	131.3 s (obscured)
28.3 q	134.3 s
129.2 d	136.9 s
131.1 d	199.9 s



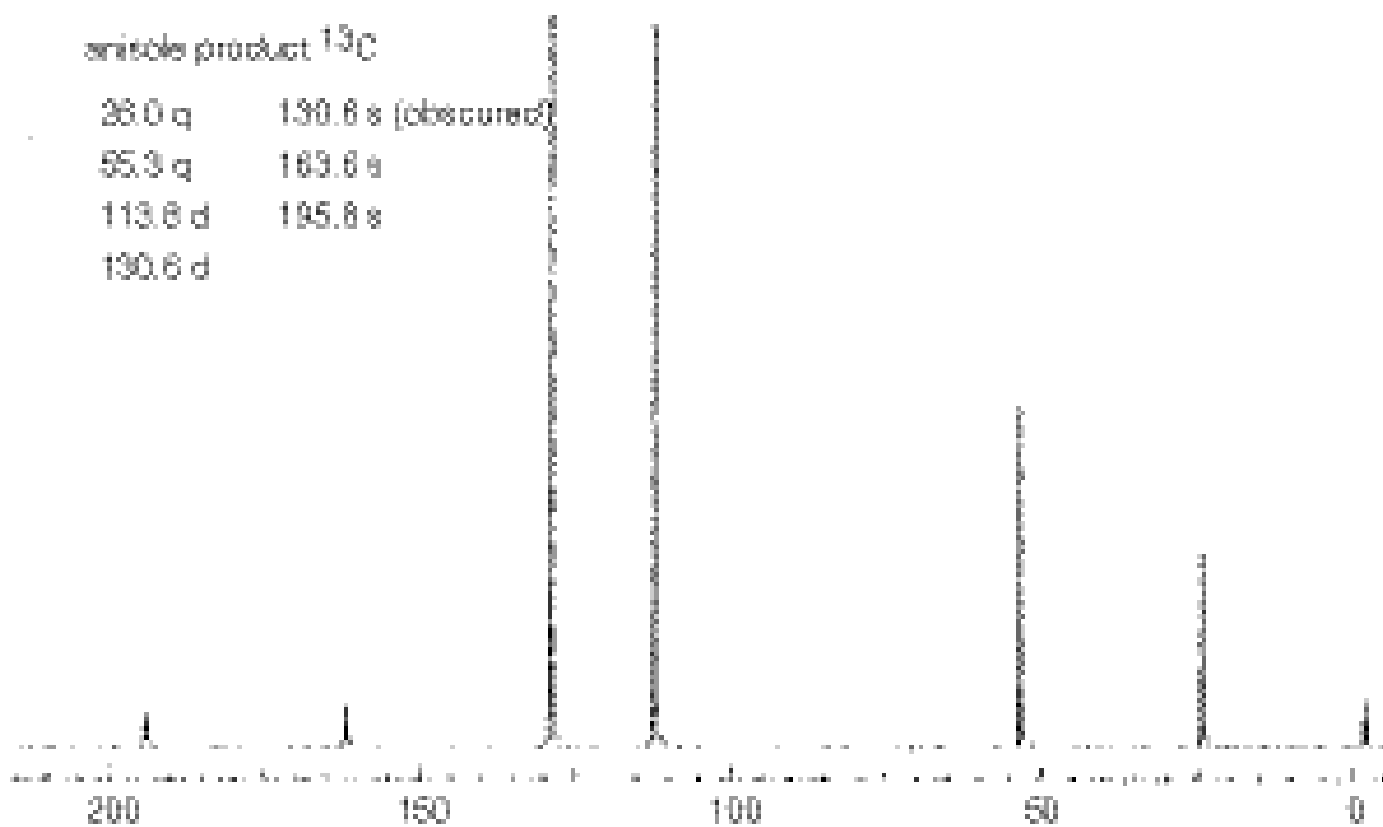
anisole product  $^{13}\text{C}$

26.0 q 130.6 s (observed)

55.3 q 163.6 s

113.6 d 195.6 s

130.6 d



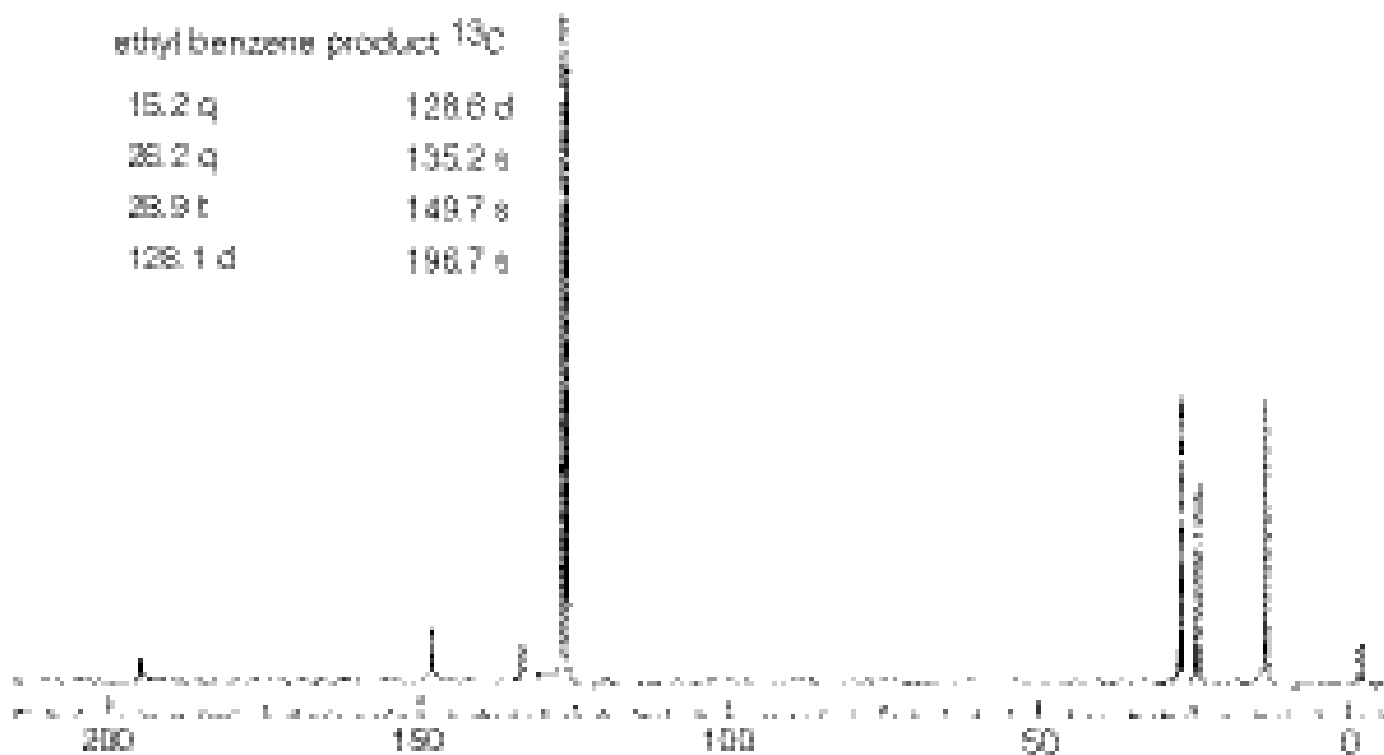
ethyl benzene product  $^{13}\text{C}$

15.2 q      128.6 d

28.2 q      135.2 s

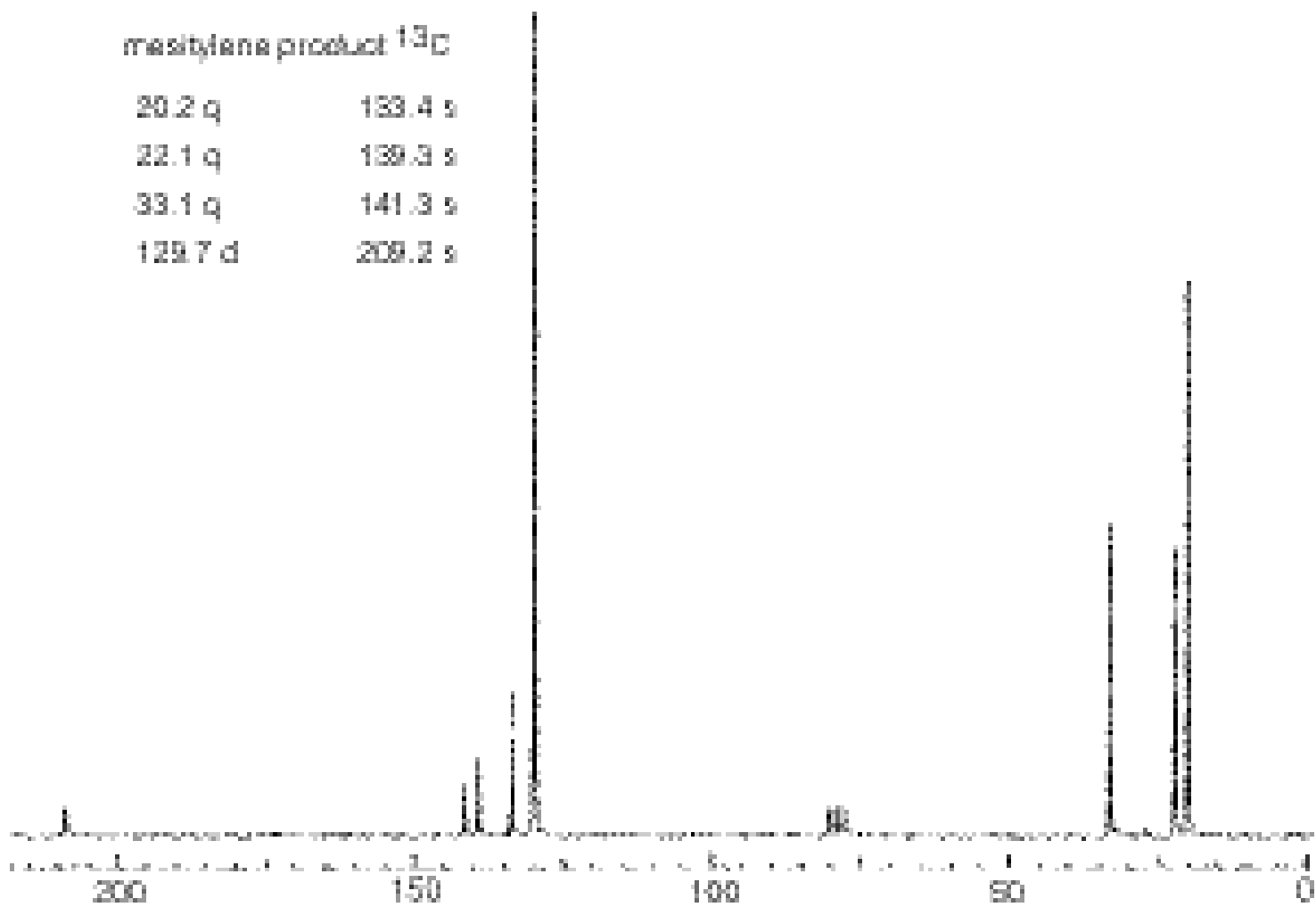
28.9 t      149.7 s

128.1 d      198.7 s



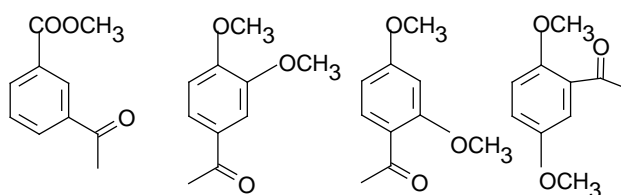
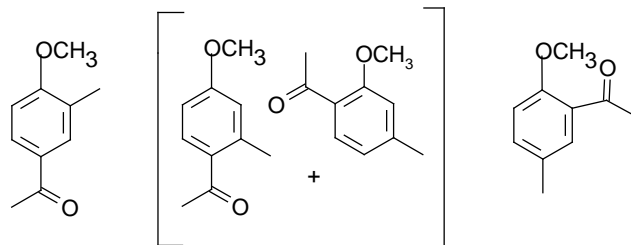
mesitylene product  $^{13}\text{C}$

20.2 q	133.4 s
22.1 q	139.3 s
33.1 q	141.3 s
129.7 d	209.2 s

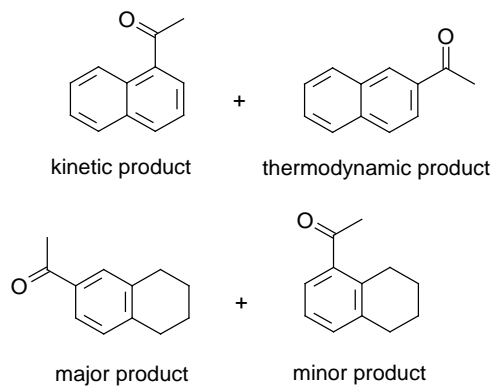
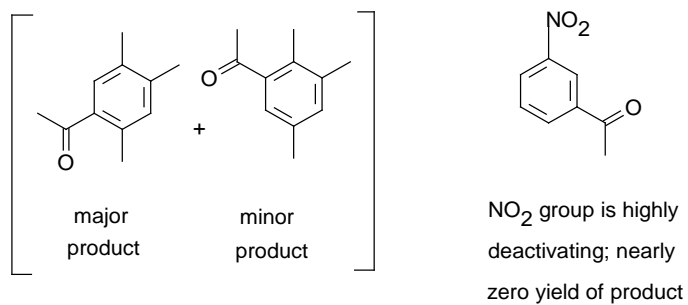


ANSWERS TO QUESTIONS:

1.



-COOCH<sub>3</sub> is  
deactivating;  
yield is nearly zero





2. It is difficult to acylate twice because the acyl group that is introduced the first time around deactivates the ring toward further substitution. In addition, *para* substitution usually dominates over *ortho* substitution due to the size of the acetyl group.
  3. The answer will vary according to the substrate used by the student. However, this is the standard Friedel-Crafts acylation mechanism.
  4. Meta directing groups deactivate the rings. In general, it is not possible to perform a Friedel-Crafts Reaction on a deactivated ring compound.
  5. The aluminum chloride causes a rearrangement of the propyl group to isopropyl. Mechanistically, the propyl group is removed from the ring as a primary carbocation (propyl). This primary cation rearranges to the more stable secondary carbocation (isopropyl) and then reattaches itself on the ring. Isopropylbenzene then undergoes a Friedel-Crafts acylation leading to the "abnormal" side-product.
  6. 
$$\text{AlCl}_3 + 3 \text{H}_2\text{O} \longrightarrow \text{Al}(\text{OH})_3 + 3 \text{HCl}$$
  

$$\text{CH}_3\text{COCl} + \text{H}_2\text{O} \longrightarrow \text{CH}_3\text{COOH} + \text{HCl}$$
  7. This is due to an anisotropic field originating from the pi electron cloud on the carbonyl group. See Technique 26, Section 26.8. This anisotropy effect deshields the *ortho* protons.
  8. In each case there will be *one* shielded ring proton next to the acetyl group, while the other proton should be more or less normal. However, in the first case the second ring proton is *para*, with a very small coupling constant (nearly 0 Hz). The second structure has the two hydrogens *meta* with respect to each other. These hydrogens have a larger coupling constant (about 2 Hz). See Technique 26, Table 26.4.
-

## Experiment 60

### THE ANALYSIS OF ANTIHISTAMINE DRUGS BY GAS CHROMATOGRAPHY-MASS SPECTROMETRY

TIME ESTIMATE: 1 or 2 periods

This is a “critical thinking” experiment. It involves an analysis of an over-the-counter antihistamine drug and a search of the chemical literature to determine the structure of the significant antihistamine substance present in the drug.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Antihistamine tablets or cold-remedy tablets; a variety should be supplied by the instructor or the student may bring in a tablet.

Snap-cap sample vials 1 /sample

Ethanol (chromatography or spectral grade) 125 mL

Mortar and pestle

Aluminum foil

0.45- $\mu\text{m}$  filter cartridge 1 /sample

Nonhalogenated waste container

Halogenated waste container for drugs that contain halogens

Gas chromatography-mass spectrometry instrument

**SPECIAL NOTE:** It may be advisable for the instructor to check the correct conditions for the GC-MS experiment by running a few test samples before the students are allowed to run their samples.

#### **CAS Registry Numbers:**

Ethanol 64-17-5

Aluminum foil 7429-90-5

## Experiment 61

### **CARBONATION OF AN UNKNOWN AROMATIC HALIDE**

TIME ESTIMATE: 3 periods

This experiment may require a good deal of individual help with each student. As a result it may be difficult to use this experiment with a large class. It is a good idea to have students to present their procedures (with stoichiometric calculations and amounts) for approval before they are allowed to begin the experimental work. Experiment 33B (benzoic acid) provides a guide for them to follow. The instructions call for the students to use 3 g of their halide. Experiment 33B is also scaled pretty close to this amount. Students could be required to do a bit more scaling of the procedure if they were to use 2.5 or 3.5 g of the halide, rather than the requested 3.0 g.

You will need 3 g of a halide for each student's unknown (unless you choose a different starting quantity). It is not necessary to have all of the halides listed in order for your class to perform this experiment. For instance, in a class of 16 students, you could distribute 8 or even 6 of the unknowns. If they are not told, the students will not necessarily realize that you do not have the entire list and that there are duplicate unknowns.

Be sure that the halides that you use have at least 90% purity. Avoid technical grade chemicals or it will be difficult for students to achieve a good melting point.

Some of the compounds in the list are named in a very strange fashion in the Aldrich catalog. In the lists below, excepting only the anisole and toluene compounds, the halides are all named so that the bromo group has the same priority as the carboxyl group that will replace it - this does not always yield a correct IUPAC name, but it is consistent. Where it is different, these names are followed by the name as given in the Aldrich catalog.

Compounds from List B can only be used if NMR is available. They cannot be distinguished from those in List A by melting point alone.

## CHEMICALS AND SUPPLIES PER STUDENT:

Unknown Aromatic Halide; 3.0 g for each student from the lists below:

### LIST A

2-bromoanisole	Aldrich	15,923-9	25g
3-bromoanisole	Aldrich	B5,649-8	5g
1-bromo-2,4-dimethylbenzene, 4-bromo-m-xylene	Aldrich	B8,382-7	25g
1-bromo-2,5-dimethylbenzene, 2-bromo-p-xylene	Aldrich	16,726-6	5g
1-bromo-4-propylbenzene	Aldrich	31,988-0	5g
1-bromo-2,4,6-trimethylbenzene, 2-bromo-mesitylene	Aldrich	B7,160-8	25g
1-bromo-4- <i>t</i> -butylbenzene	Aldrich	25,392-8	5g
1-bromo-3,5-dimethylbenzene, 5-bromo-m-xylene	Aldrich	27,631-6	5g
4-bromoanisole	Aldrich	B5,650-1	50g

### LIST B

1-bromo-4-butylbenzene	Aldrich	33,576-2	25g
2-bromotoluene	Aldrich	B8,200-6	25g
3-bromotoluene	Aldrich	16,721-5	5g
1-bromo-2,6-dimethylbenzene 2-bromo-m-xylene	Aldrich	11,585-1	5g
1-bromo-2,3-dimethylbenzene 3-bromo-o-xylene	Aldrich	B8,378-9	5g
4-bromotoluene	Aldrich	B8,220-0	5g

Magnesium turnings (fresh)	0.6 g
Anhydrous ether (freshly opened can)	30 mL
6M HCl	50 mL
5% NaOH	30 mL

Calcium chloride (2 drying tubes) 20 g

Cotton for drying tube

Filter paper for Büchner funnels

Melting point tubes

Iodine

Drying oven (optional)

Waste containers for aqueous and nonhalogenated wastes

Waste container for ether and halogenated wastes

Anhydrous powdered KBr for IR spectroscopy

Pellet press for KBr

NMR tubes (optional)

Deuteriochloroform for NMR (optional)

$\text{CDCl}_3$  and  $\text{DMSO-d}_6$  for NMR. Prepared by mixing 75mL of  $\text{CDCl}_3$  containing TMS with 25 mL of  $\text{DMSO-d}_6$  (optional).

---

## Experiment 62

### THE ALDEHYDE ENIGMA

TIME ESTIMATE: 2 Periods

This experiment is a project in which students must develop at least part of their own procedure. The reaction is an example of a Cannizzaro reaction. Since this reaction is often omitted or de-emphasized in many organic lecture texts, students are not likely to immediately know what is likely to happen when an aromatic aldehyde is heated in strong base. Students also must decide for themselves which solvents are suitable for crystallizing their two products.

CHEMICALS AND SUPPLIES PER 10 STUDENTS (If students work in pairs, the actual amounts required will be about 50% less):

4-Chlorobenzaldehyde	19 g
Methanol	150 mL
Aqueous potassium hydroxide Dissolve 61.7 g of potassium hydroxide in 100 mL of water.	50 mL
Methylene chloride	250 mL
5% aqueous sodium bicarbonate	250 mL
Saturated aqueous sodium chloride	50 mL
Anhydrous sodium sulfate (granular)	10 g
95% ethanol	200 mL
Xylene (mixed isomers)	100 mL
6M HCl	100 mL

Drying oven, set at 110 °C to dry the carboxylic acid (optional);  
students should not dry 4-chlorobenzyl alcohol as it has a low melting point

Filter paper for Hirsch or small Buchner funnel

Melting point capillary tubes

Anhydrous powdered potassium bromide for infrared spectroscopy

KBr pellet press for spectroscopy

Deuteriochloroform with TMS added for NMR spectroscopy

$\text{CDCl}_3$  and  $\text{DMSO-d}_6$  for NMR. Prepared by mixing 75mL of  $\text{CDCl}_3$  containing TMS with 25 mL of  $\text{DMSO-d}_6$  (optional).

**CAS Registry Numbers:**

4-Chlorobenzaldehyde      104-88-1

Waste disposal containers for aqueous and nonhalogenated organic wastes

Container for recovered methylene chloride if students distill off the solvent from the organic layer.

---

**RESULTS**

Compound 1 is 4-chlorobenzyl alcohol and Compound 2 is 4-chlorobenzoic acid. This is the Cannizzaro reaction in which some of the aldehyde is oxidized to carboxylic acid and some of the aldehyde is reduced to alcohol.

---

**Experiment 63**

**SYNTHESIS OF SUBSTITUTED CHALCONES: A GUIDED-INQUIRY EXPERIENCE**

TIME ESTIMATE:      1 session using SciFinder Scholar  
                                 1 laboratory period

If the instructor chooses to link this experiment with the Friedel-Crafts reaction, Experiment 59, it is suggested to inspect the list on page 512 of the Textbook for suggestions on more suitable chalcones to prepare. On page 525 of the Textbook, there are shown schemes for linking together the synthesis of a chalcone and Experiment 64 (Epoxidation of Chalcones) and/or Experiment 65 (Cyclopropanation of Chalcones).

**CHEMICALS AND SUPPLIES PER STUDENT:**

NOTE: When we do this experiment, we assign each student a different combination of benzaldehyde and acetophenone. This assignment may be made by asking students to select each reactant in a random manner, or the aldehyde-ketone combinations may be assigned by the instructor.

The following substituted benzaldehydes should be on hand (0.005 moles per student):

benzaldehyde	4-chlorobenzaldehyde
3-nitrobenzaldehyde	4-fluorobenzaldehyde
4-bromobenzaldehyde	4-methoxybenzaldehyde
2-chlorobenzaldehyde	( <i>p</i> -anisaldehyde)
2,4-dichlorobenzaldehyde	4-methylbenzaldehyde
piperonal	( <i>p</i> -tolualdehyde)

The following substituted acetophenones should be on hand (0.005 moles per student):

acetophenone	4-chloroacetophenone
4-fluoroacetophenone	4-bromoacetophenone
4-methoxyacetophenone	4-methylacetophenone

We have also tried assigning benzaldehyde to each student and allowing them to choose their own substituted acetophenone or assigning acetophenone to each student and allowing them to choose their own substituted benzaldehyde. Both systems worked well.

#### OTHER CHEMICALS AND SUPPLIES PER 10 STUDENTS:

95% Ethanol 100 mL

Sodium hydroxide solution 60 mL  
(prepared in advance – add 6.0 grams of solid sodium hydroxide to 10 mL of water)

Supplies and solvents for infrared and NMR spectroscopy

#### CAS Registry Numbers:

Benzaldehyde	100-52-7
4-chlorobenzaldehyde	104-88-1
3-nitrobenzaldehyde	99-61-6
4-fluorobenzaldehyde	459-57-4
4-bromobenzaldehyde	1122-91-4
4-methoxybenzaldehyde ( <i>p</i> -anisaldehyde)	123-11-5
2-chlorobenzaldehyde	89-98-5



2,4-dichlorobenzaldehyde	874-42-0	
4-methylbenzaldehyde (p-tolualdehyde)		104-87-0
Piperonal	120-57-0	
acetophenone	98-86-2	
4-chloroacetophenone	99-91-2	
4-fluoroacetophenone	403-42-9	
4-bromoacetophenone	99-90-1	
4-methoxyacetophenone	100-06-1	
4-methylacetophenone	122-00-9	

#### SPECIAL NOTES:

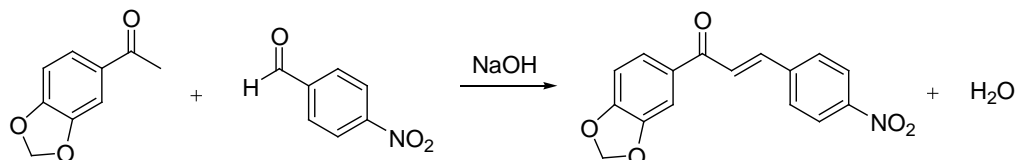
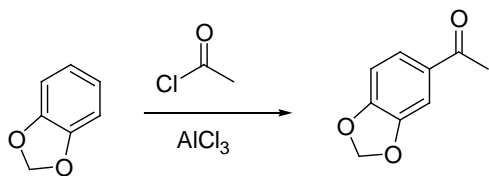
In order to do the literature search using SciFinder Scholar with your class, you should introduce this project two or three weeks before the date of the actual synthesis to allow time for searching the literature. Our students are given a handout that explains how to do a literature search using *Chemical Abstracts*. The handout guides students through the process of finding the registry number for the target compound and for finding pertinent references, with particular attention to references that describe the physical properties or preparation of the desired compound.

This project also provides an opportunity to introduce students to the preparation of a formal research-style laboratory report. If you add that dimension to this experiment, a guide to students that outlines what is to be expected in a formal report should be provided.

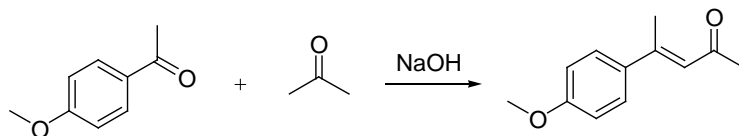
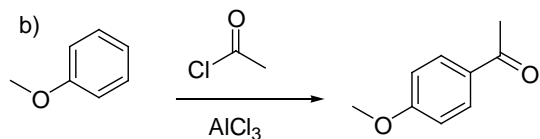
Some of the chalcone products may not crystallize immediately. We have found that an extended period of highly vigorous stirring often induces the products to crystallize. Some of the aldehyde-ketone combinations yield a condensation product that does not spontaneously dehydrate completely. In such cases, the product appears as a gummy mass that does not crystallize. We explain to students that such an outcome is part of doing original research, and that not every attempted laboratory synthesis will be successful.

## ANSWERS TO QUESTIONS

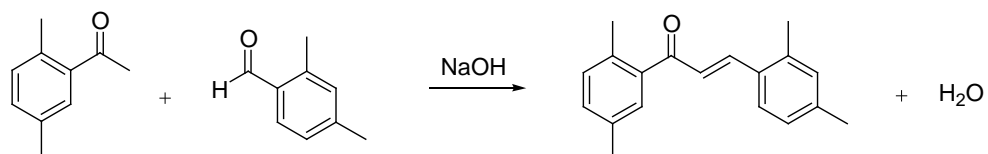
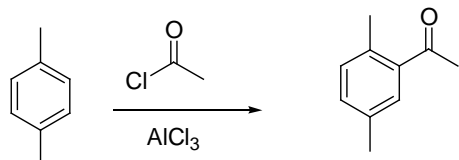
a)



b)



c)



## Experiment 64

### GREEN EPOXIDATION OF CHALCONES

TIME ESTIMATE: One period

This experiment should be linked to the chalcone preparation, Experiment 63, to provide a multistep synthesis, as suggested on page 525 of the Textbook.

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Chalcone from Experiment 63

Methanol 40 mL

Dimethylsulfoxide 20 mL

2M Aqueous sodium hydroxide solution 4 mL

30% Aqueous hydrogen peroxide 2 mL

100  $\mu$ L automatic pipet

Diethyl ether 250 mL

Anhydrous magnesium sulfate 5 g

Filter paper to prepare fluted filters

Rotary evaporator, suggested but not required. Alternatively, the solvent can be removed with the apparatus shown in Technique 7, Figure 7.17C

Vacuum pump to remove the last traces of solvent, otherwise diethyl ether peaks may appear in the NMR spectrum.

Deuteriochloroform ( $\text{CDCl}_3$ ) for NMR

NMR tubes

Disposal bottles for nonhalogenated wastes

Disposal bottle for aqueous wastes

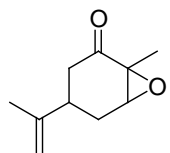
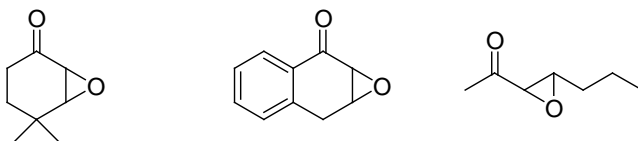
**CAS Registry Numbers:**

Methanol	67-56-1
Dimethylsulfoxide	67-68-5
30% Aqueous hydrogen peroxide	7722-84-1
Diethyl ether	60-29-7
Anhydrous magnesium sulfate	7487-88-9

**ANSWERS TO QUESTIONS:**

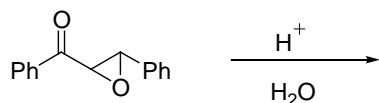
1) In the infrared spectrum, the starting conjugated ketone will show the C=O near  $1680\text{ cm}^{-1}$  while the epoxide will have a higher value. The NMR changes expected are discussed on page 530 of the Textbook (Spectroscopy).

2)



The carbonyl group is required to activate the C=C bond towards conjugate addition

3)



---

**Experiment 65****CYCLOPROPANATION OF CHALCONES**

TIME ESTIMATE: One period

This experiment should be linked to the chalcone preparation, Experiment 63, to provide a multistep synthesis, as suggested on page 525 of the Textbook.

CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Chalcone from Experiment 63

**Anhydrous** dimethylsulfoxide (see footnote 2 on page 533 for source) 25 mL

Dry powder of dimethylsulfoxonium iodide and potassium *tert*-butoxide ground and stored in a desiccator (see footnote 4 on page 533 for preparation). 3 g

Anhydrous calcium chloride for drying tube

Diethyl ether 350 mL

Saturated aqueous sodium chloride solution 600 mL

Anhydrous magnesium sulfate

Filter paper to prepare fluted filters

Rotary evaporator, suggested but not required. Alternatively, the solvent can be removed with the apparatus shown in Technique 7, Figure 7.17C

Vacuum pump to remove the last traces of solvent, otherwise diethyl ether peaks may appear in the NMR spectrum.

TLC plates (optional)

Deuteriochloroform ( $\text{CDCl}_3$ ) for NMR

NMR tubes

Disposal bottles for nonhalogenated wastes

Disposal bottle for aqueous wastes

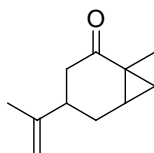
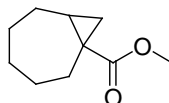
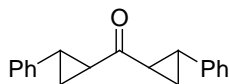
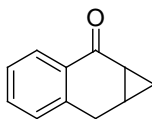
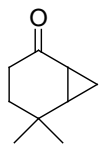
**CAS Registry Numbers:**

Dimethylsulfoxide	67-68-5
Diethyl ether	60-29-7
Anhydrous magnesium sulfate	7487-88-9
Dimethylsulfoxonium iodide	1774-47-6
Potassium <i>tert</i> -butoxide	865-47-4

## ANSWERS TO QUESTIONS:

1) In the infrared spectrum, the starting conjugated ketone will show the C=O near  $1680\text{ cm}^{-1}$  while the cyclopropanated product will have a higher value. The NMR changes expected are discussed on page 534 of the Textbook (Spectroscopy).

2)



The carbonyl group is required to activate the C=C bond towards conjugate addition

---

## Experiment 66

### MICHAEL AND ALDOL CONDENSATION REACTIONS

TIME ESTIMATE: 3 Periods

This experiment is a project in which students must develop their own procedure, using the procedures in Experiments 37 and 39 as a guide. Since some students may require individual help, this experiment may not work well with large classes. It is best to schedule enough lab time so that students can repeat parts of their procedure, if necessary. Students must pay attention to scale to make sure that they have enough chalcone to do the second part of the experiment (preparation of the Michael/Aldol product). Most likely, they will need to scale up the procedure in Experiment 37 by 2 - 4 times. It is a good idea to have students prepare and present their procedure for approval before they be allowed to begin the experimental work.

#### PREPARATION OF CHALCONE

CHEMICALS AND SUPPLIES PER STUDENT (These amounts are based on the assumption that the procedure in Experiment 37 is scaled up two times.)

4-Chlorobenzaldehyde	0.34 g
4-Methoxybenzaldehyde	0.33 g
4-Methylbenzaldehyde	0.29 g
4-Nitrobenzaldehyde	0.38 g
Piperonaldehyde	0.38 g

For other chemicals and supplies, see Experiment 37 in this manual. Multiply all the amounts given in Experiment 37 by two.

#### PREPARATION OF THE MICHAEL/ALDOL PRODUCT

See Experiment 39 in this manual. *trans*-Chalcone will be replaced by the chalcone which the students prepared. All other chemicals and supplies given in Experiment 39 are for 10 students.

Waste disposal containers for aqueous, nonhalogenated organic, and halogenated organic wastes.

#### Crystallization Solvents

In both Experiments 37 and 39, 95% ethanol is suggested as the solvent for crystallizing the products. In most cases, 95% ethanol will also work to crystallize the products made in this experiment. If this solvent does not work, students may use the procedure in Technique 11, Section 11.6 (page 675) to find an appropriate solvent. Other solvents to try include methanol or a mixture of ethanol and water.

#### SPECIAL NOTES:

Students must be very careful when they are removing the catalyst according to the procedure in Experiment 39 (See “Removal of Catalyst” section on page 322 of the Textbook). If they do not add enough acetone to dissolve most of the solid, it is likely that they will lose a significant amount of their product.

#### CAS Registry Numbers:

4-Chlorobenzaldehyde	104-88-1
4-Methoxybenzaldehyde ( <i>p</i> -anisaldehyde)	123-11-5
4-Methylbenzaldehyde ( <i>p</i> -tolualdehyde)	104-87-0

Piperonal (3,4-methylenedioxybenzaldehyde)	120-57-0
Acetophenone	98-86-2
Ethyl acetoacetate	141-97-9

---

### Experiment 67

#### **ESTERIFICATION REACTIONS OF VANILLIN: THE USE OF NMR TO SOLVE A STRUCTURE PROOF PROBLEM**

TIME ESTIMATE: 1 period. Note, however, that not all students will be able to use the NMR instrument at the same time. The product of the acid-catalyzed reaction is 4-acetoxy-3-methoxy-1,1-diacetoxytoluene (mp 90-91°). The mechanism for the reaction of acetic anhydride with the aldehyde group is given in Kochhar, *et. al*, *J. Org. Chem.*, **48**, 1765 (1983).

#### CHEMICALS AND SUPPLIES PER 10 STUDENTS:

Vanillin	38 g
Acetic anhydride	175 mL
10% aqueous sodium hydroxide	313 mL
95% Ethanol	250 mL
1.0 M Sulfuric acid (supply with dropper)	10 mL
Crushed ice	
Filter paper for Hirsch or Büchner funnels	
Melting point tubes	
Anhydrous powdered potassium bromide for infrared spectroscopy	
KBr pellet press for spectroscopy	
Deuteriochloroform with TMS added for NMR spectroscopy	
NMR tubes	
Waste disposal containers for nonhalogenated and halogenated organic waste	
Waste disposal container for aqueous waste	



**CAS Registry Numbers:**

Vanillin 121-33-5

Acetic anhydride 108-24-7

---

**Experiment 68****AN OXIDATION PUZZLE**

TIME ESTIMATE: 1 ½ periods

**CHEMICALS AND SUPPLIES PER 10 STUDENTS:**

2-Ethyl-1,3-hexanediol	10 mL
Glacial acetic acid	50 mL
6% Sodium hypochlorite solution Aldrich Chemical Co., #42-504-4 (11-13% available chlorine). Dilute this reagent with an equal volume of water for use in this experiment. <i>Store the diluted and undiluted reagent in a refrigerator! We do not recommend using bleach from the grocery store.</i>	50 mL
Potassium iodide starch test paper	
Diethyl ether	200 mL
Saturated aqueous sodium carbonate	75 mL
5% aqueous sodium hydroxide	75 mL
Magnesium sulfate, anhydrous	10 g
Salt plates for infrared spectroscopy	
Methylene chloride for the dry film method	5 mL

**CAS Registry Numbers:**

2-Ethyl-1,3-hexanediol 94-96-2

Sodium hypochlorite 7681-52-9

**Technique 1**

**LABORATORY SAFETY**

**No problems**

---

**Technique 2**

**THE LABORATORY NOTEBOOK, CALCULATIONS,  
AND LABORATORY RECORDS**

**No problems**

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**Technique 3**

**LABORATORY GLASSWARE: CARE AND CLEANING**

**No problems**

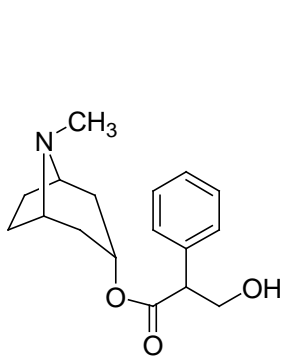
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## Technique 4

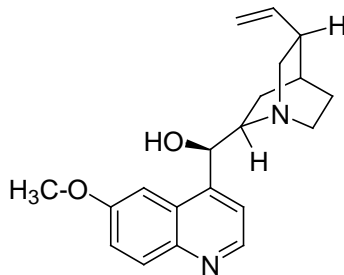
### HOW TO FIND DATA FOR COMPOUNDS: HANDBOOKS AND CATALOGS

#### Answers to Problems

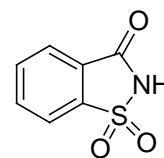
1.



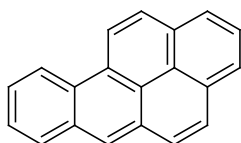
atropine



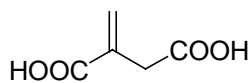
quinine



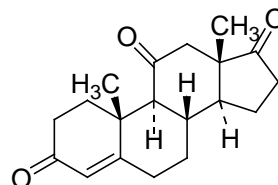
saccharin



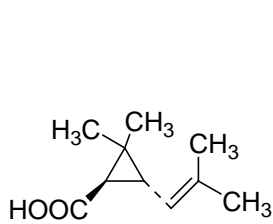
benzo[a]pyrene



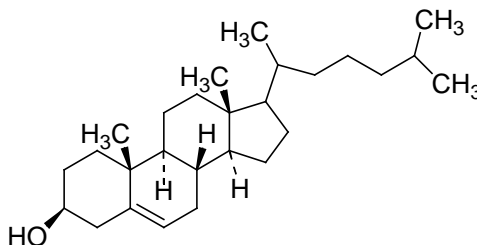
itaconic acid



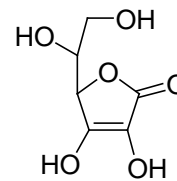
adrenosterone



crysanthemic acid



cholesterol



ascorbic acid

2. Biphenyl: mp 69-72 °C (Aldrich Handbook)  
4-Bromobenzoic acid: mp 252-254 °C (Aldrich Handbook)  
3-Nitrophenol: mp 96-98 °C (Aldrich Handbook)
  3. Octanoic acid: 110-111 °C at 4mm pressure (CRC Handbook)  
Acetophenone, 4-chloro: 273 °C at 760mm and 124-126 at 30mm (CRC)  
2-Heptanol, 2-methyl: 156 °C at 760mm (CRC Handbook)
  4. Octanoic acid: density 0.8615; index of refraction 1.4278  
Acetophenone, 4-chloro: density 1.1922; index of refraction 1.5550  
2-Heptanol, 2-methyl: density 0.8142; index of refraction 1.4238 (CRC)
  5. (*R*)-Camphor: +44.1°  
(*S*)-Camphor: -43°
  6. Poisoning may occur by inhalation, ingestion or skin absorption.  
High concentrations results in depression of the central nervous system.  
Inhalation may cause pulmonary edema.
- 

### Technique 5

#### MEASUREMENT OF VOLUME AND WEIGHT

##### Answers to Problems

1. (a) Graduated cylinder  
(b) 5.0 mL graduated pipet or dispensing pump  
(c) Automatic pipet  
(c) Graduated cylinder
2. You should preweigh the round-bottom flask and add the specified volume. The flask should then be reweighed. The difference gives the actual weight of the limiting reagent.
3. (a) Diethyl ether,  $d = 0.71 \text{ g/mL}$   
weight =  $(0.71 \text{ g/mL})(2.5 \text{ mL}) = 1.8 \text{ g}$   
(b) Methylene chloride,  $d = 1.32 \text{ g/mL}$   
weight =  $(1.32 \text{ g/mL})(2.5 \text{ mL}) = 3.3 \text{ g}$

(c) Acetone,  $d = 0.79 \text{ g/mL}$   
weight =  $(0.79 \text{ g/mL})(2.5 \text{ mL}) = 2.0 \text{ g}$

4. Acetic anhydride,  $d = 1.08 \text{ g/mL}$

$$\text{Volume} = \frac{5.46 \text{ g}}{1.08 \text{ g/mL}} = 5.05 \text{ mL}$$

5. a) A 100 mL graduated cylinder is too large for the small amount indicated. A dispensing pump or graduated pipet would be suitable.
- b) The one-piece pipet isn't accurate enough. Use an automatic pipet and weigh the liquid after the transfer to obtain an accurate weight.
- c) It would take you a long time to transfer 25 mL with this device. Use a 25 mL graduated cylinder.
- d) The graduations on a beaker are only approximate. Use a 10 mL graduated cylinder.
- e) Most automatic pipets only transfer 1 mL or less. Use a graduated cylinder.
- f) Graduated cylinders should not be used for such small volumes. Use an automatic pipet, instead.
- g) For small-scale reactions, liquid need to be transferred and then weighed. Densities can be used with large scale reactions.

---

## **Technique 6**

### **HEATING AND COOLING METHODS**

#### **Answers to Problems**

1. (a) Hot water bath or heating mantle (if temperature can be adjusted to the low temperature) or steam bath or hot plate
- (b) Heating mantle or aluminum block on a hot plate

- (c) Heating mantle or aluminum block on a hot plate
- 2.
- (a) Butyl benzoate, bp = 247 °C; heating mantle or aluminum block
  - (b) 1-Pentanol, bp = 138 °C; heating mantle or aluminum block
  - (c) 1-Chloropropane, bp = 47 °C; hot water bath or hot plate
3. Ice-salt bath
- 4.
- (a) Since benzene freezes at 5°C, an ice-salt bath would freeze the reaction mixture. A water bath with a small amount of ice would not freeze the mixture.
  - (b) A dry ice/isopropyl alcohol bath would keep ammonia (bp -33°C) in the liquid state. An ice-salt bath or ice bath would not be cold enough, and the ammonia would boil off.
- 5.
- a) Diethyl ether is extremely volatile and flammable. A Bunsen burner would be a bad choice because of the danger of a fire.
  - b) Toluene boils at 110 °C. A hot water bath would not reflux the mixture.
  - c) The unclamped thermometer can be easily broken. If it is a mercury thermometer, you have a big cleanup problem.
  - d) See 5c.
  - e) *tert*-Butyl alcohol has a melting point of about 25 °C. It would freeze if it were cooled to 0 °C.
- 

## Technique 7

### REACTION METHODS

#### Answers to Problems

- 1.
- a) Magnetic spin vane
  - b) A very small magnetic stir bar
  - c) A magnetic stir bar

2. Do not use a drying tube. Since water is produced in the reaction as a product, it makes no sense to protect the reaction from moisture.
3.
  - a) Sulfur dioxide and hydrogen chloride are both noxious gases. Use a gas trap.
  - b) Hydrogen chloride is a noxious gas. Use a gas trap.
  - c) Carbon dioxide is harmless. A gas trap is not needed.
  - d) Ammonia is a noxious gas. Use a gas trap.
4.
  - a) This is a very dangerous situation since the inclusion of a stopper makes for a closed system. Pressure will build up and an explosion may occur.
  - b) The water flow is very excessive. It is likely that a hose will come loose, and water will be splashed about.
  - c) It is likely that the solvent will be lost through the top of the condenser if the solvent has a low boiling point.
  - d) If the mixture is boiling rapidly, the addition of a boiling stone shouldn't cause any problems. However, if the solution is superheated, but not yet boiling, the addition of a boiling stone could cause the mixture to suddenly boil rapidly, and cause liquid to shoot out of the flask.
  - e) Used boiling stones may have their irregular surface filled with liquid. If this is the case, then they may not function correctly until the liquid is boiled out. There is also a possibility of contamination.
  - f) The liquid is being refluxed too rapidly and you may lose some solvent out the top of the condenser. Allow the mixture to cool slightly.
  - g) The joint may leak solvent if the O-ring is omitted.
  - h) If the funnel is completely submerged in the beaker, there is a possibility that water will be drawn into the apparatus when the apparatus is cooled.
  - i) Granular drying agent is easier to remove by decantation.

- j) If the apparatus has a gas trap, one could carefully conduct the reaction on the bench. If no gas trap is included in the apparatus, then the reaction must be conducted in a fume hood. Common practice, however, is that the reaction should be conducted in a hood with a gas trap.
- k) The apparatus is open to the atmosphere. Since it is open, air can enter the apparatus. A balloon assembly should be used to exclude air from the reaction.
- l) Air contains oxygen that can cause the material to decompose. Nitrogen should be used in the evaporation process.

---

### **Technique 8**

### **FILTRATION**

#### **Answers to Problems**

- 1.
  - (a) Gravity filtration using a fluted filter
  - (b) Craig tube
  - (c) Filter tip pipet
  - (d) Vacuum filtration with a Hirsch or Büchner funnel
  - (e) Dissolved materials cannot be removed by filtration; however, many students suggest that the impurities can be removed on a silica gel or alumina column. Also decolorizing carbon (palletized Norit) may be used (see Technique 11).
  - (f) Gravity filtration using a filtering pipet



## Technique 9

### PHYSICAL CONSTANTS OF SOLIDS: THE MELTING POINT

#### Answers to Problems

1. A mixed-melting-point could be used. Equal quantities of A and B are intimately mixed using a mortar and pestle. The mixture is placed in a melting point capillary tube, and the melting point determined. If the melting point is identical to that of pure A (and pure B) without depression or expansion, then A and B are identical.
2. Curve 2 would be an ideal heating rate.
3. The melting point tube should be sealed as shown in Figure 9.6.
4. Perform a mixture-melting-point with the unknown and each of the other substances independently. The mixture that gives no depression or expansion of the melting point reveals the identity of the compound.
5. The compound may have undergone a chemical change such as conversion of an acid to an anhydride. Alternatively, there may have been a change in the form of the crystal lattice or a loss of water (or another solvent) from the crystal.

---

## Technique 10

### SOLUBILITY

#### Answers to Problems

1.
  - a) Malic acid, soluble in water
  - b) Naphthalene, insoluble in water
  - c) Amphetamine, soluble in alcohol
  - d) Aspirin, slightly soluble in water; essentially insoluble
  - e) Succinic acid, insoluble in hexane
  - f) Ibuprofen, soluble in diethyl ether
  - g) 1-Decanol, insoluble in water
2.
  - a) water and methyl alcohol, miscible
  - b) hexane and benzene, miscible

- c) methylene chloride and benzene, miscible
  - d) water and toluene, immiscible
  - e) ethyl alcohol and isopropyl alcohol, miscible
3. Ibuprofen would be soluble in NaOH. The water soluble sodium salt would be formed.
  4. Thymol is a phenolic compound. It is a weak acid that will dissolve in NaOH. The sodium salt that is formed is soluble in the aqueous medium.
  5. Cannabinol has a large hydrocarbon-like and non-polar part of the molecule rendering it relatively non polar even though there is a hydroxyl group. Methanol is very polar.
  6.
    - a) Ether is an oxygen-containing compound, which has the formula:  $\text{CH}_3\text{-CH}_2\text{-O-CH}_2\text{-CH}_3$ . Petroleum ether is a mixture of hydrocarbons (alkanes), principally consisting of four- and five-carbon isomers. Petroleum ether does not include any oxygen-containing compounds.
    - b) Ether and diethyl ether are synonyms. They are the same solvent.
    - c) Ligroin and petroleum ether are similar, in that they are both mixtures of hydrocarbons (alkanes). While petroleum ether consists mostly of alkane isomers which boil in the range of 30 to 60 °C, ligroin consists of higher-molecular-weight alkane isomers, which boil in the range of 60 to 90 °C (or 60-75 °C).
- 

## Technique 11

### CRYSTALLIZATION: PURIFICATION OF SOLIDS

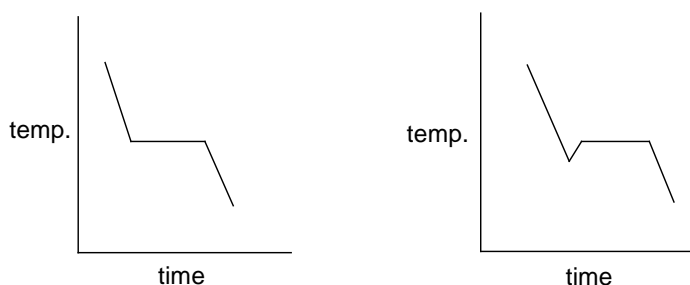
#### Answers to Problems

1.
  - (a) A plot similar to line A in Figure 11.1 on page 680 will be obtained. The line will be slightly curved.
  - (b) All of the substance A would dissolve at 80°C. A solubility of 17.0 g in 100 mL of water is equivalent to a solubility of 0.17 g in 1 mL of water. This is a greater solubility than is required.

- (c) Crystals of A should appear around 56°C.
- (d) The recovery of A would amount to 0.085 g. A solubility of 1.5 g in 100 mL of water at 0°C is equivalent to a solubility of 0.015 g in 1 mL of water. Therefore, 0.015 g of A would remain dissolved in the water, with the remainder being formed as crystals.

2. If a saturated hot solution was filtered by vacuum filtration, the cooling which occurred as the solvent was drawn through the filter paper would cause the solute to precipitate in the form of crystals. The result would be that the filter paper would become clogged with crystals, and impurities would not be removed successfully from the solution being filtered.
3. No. Since the product is pale yellow, the yellow color in the solution is likely due to the dissolved product. Using decolorizing charcoal when it is not needed can lead to unnecessary loss of product and time.
4. A filtration should not be performed because there are no solids to remove. Filtration is unnecessary and would result in the loss of some product.

5. (a) (b)



6. (a) Add 1.0 mL of boiling water to the mixture, remove the solution from insoluble B with a filter tip pipet while the solution is hot, and allow the liquid to cool to 25° or less. If the solution is cooled to 25°, 10 mg of A will remain in solution and 90 mg of A will crystallize. The crystals are collected with a Craig tube.
- (b) Add 1.0 mL of boiling water to the mixture in order to dissolve both A and B. Allow the mixture to cool to 25° or below and collect the crystals. Since the solvent is capable of holding as much as 10 mg of impurity B, and since the amount of B is much less than 10 mg, no B will crystallize at 25°. The crystals which form are those of pure A, which is collected with a Craig tube.

- (c) For the first crystallization, add 1.0 mL of boiling water. Allow the solution to cool to 25°. The solid which precipitates will contain 90 mg of A and 15 mg of B. The solution will contain 10 mg of A and 10 mg of B. For the second crystallization, 0.9 mL of hot water is required. When this solution is cooled to 25°, the solid which precipitates will contain 81 mg of A and 6 g of B. The remaining solution will contain 9 mg of A and 9 mg of B. For the third crystallization, 0.81 mL of hot water is required. When this solution is cooled, the mother liquor will be capable of holding 8.1 mg of A and 8.1 mg of B. Since the amount of B is greater than the amount of B left in the solid, no B will crystallize during this third crystallization. The crystals of A will weigh 72.9 mg. This purification sequence required three crystallizations. From the 100 mg of A which were taken initially, 72.9 mg were recovered. This corresponds to a percent recovery of 72.9%.
7. The student should have dissolved the solid in hot ethanol, rather than dissolving it at 25 °C and cooling it to 0 °C (a 25 degree difference). One would obtain a larger difference in solubility by using hot ethanol and cooling (a 80 degree difference). In this way, one would obtain a better yield of product. Also, it is likely that the student may have used too much ethanol to rinse the product.
-

## Technique 12

### EXTRACTIONS, SEPARATIONS, AND DRYING AGENTS

#### Answers to Problems

1. Following the method given in Section 12.2, we obtain:

First extraction:

$$K = 1.0 = \frac{C_2}{C_1} = \frac{\frac{(5.0-x \text{ g})}{(25 \text{ mL ether})}}{\frac{(x \text{ g})}{(100 \text{ mL H}_2\text{O})}}$$

$$1.0 = \frac{(5.0-x)(100)}{25x}$$

$$25x = 500 - 100x$$

$$125x = 500$$

$x = 4.0$  g remaining in aqueous phase

Second extraction:

$$K = 1.0 = \frac{\frac{(4.0-x \text{ g})}{(25 \text{ mL ether})}}{\frac{(x \text{ g})}{(100 \text{ mL H}_2\text{O})}}$$

$$1.0 = \frac{(4.0-x)(100)}{25x}$$

$$25x = 400 - 100x$$

$$125x = 400$$

$x = 3.2$  g remaining in aqueous phase

$5.0 - x = 1.8$  g extracted into ether phase

For one 50 mL extraction:

$$K = 1.0 = \frac{\frac{(5.0-x \text{ g})}{(50 \text{ mL ether})}}{\frac{(x \text{ g})}{(100 \text{ mL H}_2\text{O})}}$$

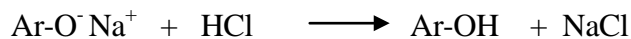
$$1.0 = \frac{(5.0-x)(100)}{50x}$$

$$50x = 500 - 100x$$

$$150x = 500$$

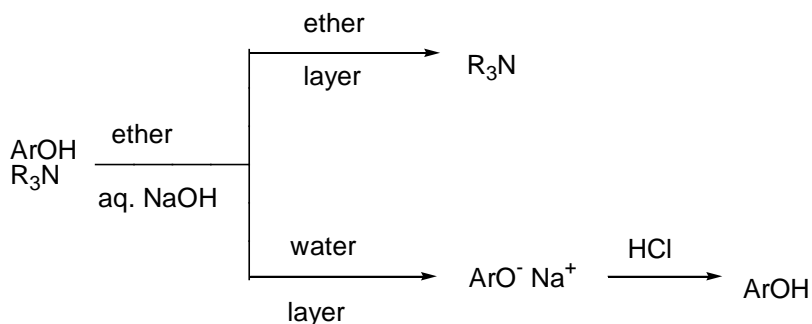
$x = 3.33$  g remaining in aqueous phase

$5.0 - x = 1.67$  g extracted into ether phase



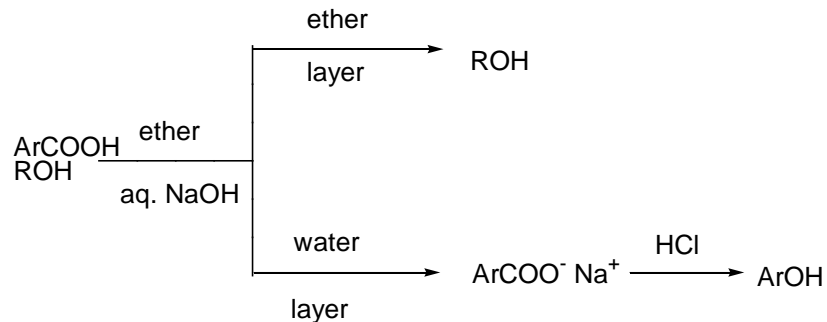
3. One could extract the mixture with hydrochloric acid at any point in the separation procedure. However the sodium bicarbonate extraction must be done before the sodium hydroxide extraction.

4. (a)



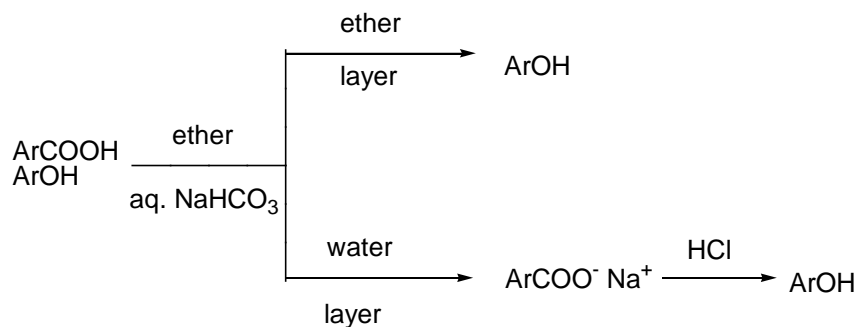
Or use HCl to give a water soluble  $\text{R}_3\text{NH}^+ \text{Cl}^-$

(b)



Or use NaHCO<sub>3</sub> to give a water soluble ArCOO<sup>-</sup> Na<sup>+</sup>

(c)



One must use NaHCO<sub>3</sub> to remove the carboxylic acid. If you use NaOH, both will be removed

5. (a) 1,1,1-Trichloroethane; density = 1.35 g/mL;  
lower layer
- (b) Hexane; density = 0.66 g/mL; upper layer
6. Ethanol and sulfuric acid are very soluble in water, so one would add water to the mixture to remove these substances. Benzoic acid would be removed as its water soluble sodium salt when sodium bicarbonate is added. Ethyl benzoate would be insoluble in both water and sodium bicarbonate.

7. 
$$\frac{50.0 \text{ mg}}{120.4 \text{ g/mole}} = 0.415 \text{ mmole MgSO}_4$$

0.415 mmole  $\text{MgSO}_4$  will remove  $(7)(0.415)$  mmole water  
 $(7)(0.415)(18.0) = 52 \text{ mg water}$

- 8a. The washing procedure involves adding 1 mL of aqueous sodium bicarbonate to an organic mixture and shaking the mixture vigorously. When this procedure is followed, any acidic substances are removed into the sodium bicarbonate as their sodium salts.
- 8b. Extracting an aqueous layer three times with methylene chloride involves adding a volume of methylene chloride to an aqueous layer, shaking it vigorously, allowing the layers to separate and removing the lower (methylene chloride) layer while leaving the aqueous layer behind. Save the methylene chloride layer in another container. Then add another portion of methylene chloride to the aqueous layer and repeat the above procedure. Each time save the methylene chloride layer and leave the aqueous layer in the original container. The procedure involves a total of three extractions with methylene chloride.
9. You should not add drying agent at this point. First, transfer the organic layer with a dry Pasteur pipet to a dry container and then add drying agent to the organic layer.
10. See Section 12.8.
11. (a) High-density organic compound dissolved in methylene chloride  
(b) Sodium chloride layer
- 

### **Technique 13**

#### **PHYSICAL CONSTANTS OF LIQUIDS: THE BOILING POINT AND DENSITY**

##### **Answers to Problems**

1. (a)  $290^\circ$   
(b)  $185^\circ$   
(c)  $155\text{-}165^\circ$



2.  $T = 205^\circ$   
 $t_1 = 0^\circ$   
 $t_2 = 35^\circ$
- $(0.000154)(205^\circ)(205-35^\circ) = 5.4^\circ$  correction
- Corrected b.p. =  $205+5 = 210^\circ$
3. No stem correction should be applied, the calibration curve already applies a better correction than the equation can provide- one determined empirically.
- 4.
- $$\text{Density} = \frac{(0.082 \text{ g})}{(100 \times 10^{-6} \text{ L})} \frac{(10^{-3} \text{ L})}{(1 \text{ mL})} = 0.82 \text{ g/mL}$$
5. The true boiling point of the liquid was  $161^\circ\text{C}$ . If you stop heating *at any point below the true boiling point* when using this method, the liquid will be forced into the capillary tube. This is what happened at  $154^\circ\text{C}$ . Heating to  $165^\circ\text{C}$  carried the temperature *above* the boiling point as should be done for this method.

### Technique 14

#### SIMPLE DISTILLATION

#### Answers to Problems

1. (a) Approximately 92% A, 8% B.  
 (b) Approximately 18% A, 82% B.
- 2.
- $$PV = \frac{gRT}{(MW)}; g = \frac{PV(MW)}{RT} = \frac{(1 \text{ atm})(0.112 \text{ L})(200 \text{ g/mole})}{(0.082)(273+100^\circ)}$$
- $$= 0.732 \text{ g}$$
- $$0.732 \text{ g} \frac{(1 \text{ mL})}{(0.9 \text{ g})} = 0.814 \text{ mL}$$

3. The line connects the compositions of the boiling liquid (lower curve) and its equilibrium vapor (upper curve) at the same temperature. Using line xy in Figure 14.4, if the boiling liquid has composition W, its vapor has composition Z.
4. It would boil at about 110°C.
5.
  - (a) The bulb of the thermometer should be placed in the lower stem of the Hickman head, just *below* the bottom of the well. See the inset in Figure 14.6.
  - (b) The bulb of the thermometer should be placed in the neck which has the sidearm leading to the condenser. It should be placed so that the bulb is below the lower bend of the arm. See the inset in Figure 14.5.
6. A good separation can be achieved in a simple distillation if there is a large (>100°C) difference in the boiling points of the liquids to be separated. Also a good separation may be achieved if the impurity is less than 10% or if one of the components is not volatile (i.e. a solid).

### Technique 15

#### FRACTIONAL DISTILLATION, AZEOTROPES

##### Answers to Problems

1. (a) 3.9 g = 0.05 mole benzene; 4.6 g = 0.05 mole toluene

$$N_{\text{benzene}} = \frac{0.05}{0.05 + 0.05} = 0.5; \quad N_{\text{toluene}} = 0.5$$

- (b) Partial vapor pressure of benzene = (270 mm)(0.5) = 135 mm

- (c) At 90°,  $P_{\text{total}} = (1010 \text{ mm})(0.5) + (405 \text{ mm})(0.5) = 707 \text{ mm}$

$$\text{at } 100^\circ, P_{\text{total}} = (1340 \text{ mm})(0.5) + (560 \text{ mm})(0.5) = 950 \text{ mm}$$

The boiling point is greater than 90°, but less than 100°. Assume a linear relationship between the vapor pressure of each substance and the temperature from 90 to 100°.

$$\text{For benzene; } \frac{2}{10} (1340-1010) = 66 \text{ mm change in vapor pressure for each } 2^\circ \text{ change in temperature}$$

$$\text{For toluene; } \frac{2}{10} (560-405) = 31 \text{ mm change in vapor pressure for each } 2^\circ \text{ change}$$

The following approximate vapor pressures are obtained at certain temperatures:

	<u>benzene</u>	<u>toluene</u>
90°	1010	405
92°	1076	436
94°	1142	467
96°	1208	498
98°	1274	529
100°	1340	560

$$\text{At } 92^\circ; P_{\text{total}} = (1076)(0.5) + (436)(0.5) = 756 \text{ mm}$$

Thus, the boiling point is approximately 92°.

(d) Partial vapor pressure of benzene at 92° = (1076)(0.5) = 538 mm

Partial vapor pressure of toluene at 92° = (436)(0.5) = 218 mm

$$\text{Vapor composition: } \frac{538}{760} = 0.71 \text{ benzene, } 0.29 \text{ toluene}$$

(e) 0.71 mole = 55.4 g benzene; 0.29 mole = 26.7 g toluene

$$\frac{55.4 \text{ g}}{55.4 + 26.7 \text{ g}} \times 100 = 67.5\% \text{ benzene; } 32.5\% \text{ toluene}$$

2. Three theoretical plates are needed.
3. (a)  $P_{\text{total}} = P^{\circ}_{\text{water}}N_{\text{water}} + P^{\circ}_{\text{sucrose}}N_{\text{sucrose}} = (760 \text{ mm})(0.8) = 608 \text{ mm}$   
 (b)  $100^{\circ}$   
 (c) Pure water  
 (d) The temperature would be above  $100^{\circ}$ , and would rise continuously during the distillation process.
4. See the explanation given in Section 14.2 in Technique 14.
5. The mole fractions and boiling point data are used to obtain the lower curve such as that shown in Figure 15.3. The upper curve (vapor composition) such as that shown in Figure 15.3 may be obtained by performing calculations similar to those given in Section 15.3 for each mixture.
6. The distillate will have the composition of the azeotrope (95.6% ethanol). As the distillation proceeds, the residue in the distillation flask will become richer in the higher boiling component (pure ethanol). When all of the water has been removed as the azeotrope, pure ethanol will distill.
7. This mixture will yield a minimum-boiling azeotrope similar to that shown in Figure 15.10. With an efficient column and a mixture that is initially rich in benzene, the azeotrope (39.5 % methanol and 65.5 % benzene) has the lowest boiling point, and it distills first. Benzene has a higher boiling point, and will distill second. You will not obtain pure methanol.  
  
 For mixture initially rich in methanol, the azeotrope distills first and methanol distills second. You will not obtain pure benzene.
8. This mixture will yield a maximum-boiling azeotrope similar to that shown in Figure 15.11. With an efficient column and a mixture that is initially rich in acetone, acetone distills first and the azeotrope (20 % acetone and 80 % chloroform) will distill second.  
  
 For a mixture initially rich in chloroform, chloroform will distill first and the azeotrope distills second.
9. From Table 15.2, ten plates would be required to separate the mixture.

10. 
$$\frac{(12 \text{ plates})(0.25 \text{ in})}{(1 \text{ plate})} = 3 \text{ inches long}$$

---

### **Technique 16**

#### **VACUUM DISTILLATION, MANOMETERS**

##### **Answers to Problems**

1. The boiling point may be too high to conveniently distill it at atmospheric pressure. Also, the compound may decompose at high temperature or it may be sensitive to oxygen when heated.
  2. No, the system should be vented before turning the aspirator off or water may back up into the evacuated system.
  3. About 180°C (using Figure 13.2, page 725 of the Textbook).
  4. A magnetic stirring bar (spin vane), a wooden applicator stick, or an ebulliator tube may be used in place of a boiling stone.
  5. The major purpose of the trap is to prevent the back up of water into the system when (or if) the pressure in the system fluctuates.
- 

### **Technique 17**

#### **SUBLIMATION**

##### **Answers to Problems**

1. Solid carbon dioxide passes directly from the solid state to the gaseous state. Since one does not observe a liquid, as with solid water, it is called "dry ice".
2. At a pressure above 5.1 atm and below -57°C, one can have liquid carbon dioxide.

3. As the temperature is raised, the vapor pressure of the solid increases. When this pressure equals the applied pressure (760 mm), it will sublime. One will not observe a solid to liquid transition (melting point).
4. The solid will show a normal solid to liquid transition at 100 °C.
5. When the applied pressure is reduced to a value equal to or below 50mm, it will sublime upon heating to about 100 °C.

### Technique 18

#### STEAM DISTILLATION

#### Answers to Problems

$$1. \quad \frac{\text{Wt. benzene}}{\text{Wt. water}} = \frac{(P^{\circ}_{\text{benzene}})(\text{M.W. benzene})}{(P^{\circ}_{\text{water}})(\text{M.W. water})} = \frac{(760-227.7)(78)}{(227.7)(18)} = \frac{10.1 \text{ g}}{1 \text{ g water}}$$

$$\frac{10.1 \text{ g}}{10.1 + 1.0 \text{ g}} \times 100 = 91.0 \text{ benzene, } 9.0 \text{ water}$$

Table 18.1 gives 8.9% water.

$$2. \quad \text{At } 95^{\circ}; P_{\text{total}} = 634 + 118 = 752 \text{ mm}$$

$$\text{At } 96^{\circ}; P_{\text{total}} = 657 + 122 = 779 \text{ mm}$$

The boiling point would be between 95 and 96°.

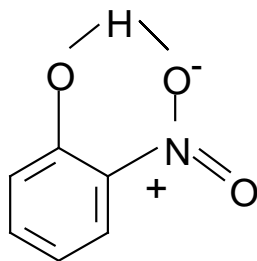
$$3. \quad P_{\text{total}} = 733 \text{ mm} + P_{\text{nitrobenzene}} = 760 \text{ mm}$$

$$\text{v.p. H}_2\text{O at } 99^\circ = 733 \text{ mm}$$

$$P_{\text{nitrobenzene}} = 760 - 733 = 27 \text{ mm}$$

$$\frac{\text{Wt C}_6\text{H}_5\text{NO}_2}{\text{Wt water}} = \frac{(27)(123)}{(733)(18)} = \frac{0.25 \text{ g C}_6\text{H}_5\text{NO}_2}{1 \text{ g water}}$$

4. The o-nitrophenol has an internal hydrogen bond. Since p-nitrophenol cannot bond internally, it will hydrogen bond to water and will not co-distill (its vapor pressure is much lower than the ortho isomer because it is strongly associated with water molecules).



## Technique 19

### COLUMN CHROMATOGRAPHY

#### Answers to Problems

1. If the components of the mixture all passed through the column, the solvent must have been too polar. In that case, repeat the chromatography using a less polar solvent, such as petroleum ether. If all of the mixture stayed on the column too long, the solvent was probably not polar enough. Switch to a more polar solvent, such as methanol or ethanol. Other parameters which might be adjusted include the length of the column and the column packing.
2. Naphthalene is an aromatic hydrocarbon, which means that it has a low-to-intermediate polarity. A non-polar solvent, such as petroleum ether or cyclohexane can be used.

3. Order of elution:  
Biphenyl (elutes first) > benzyl alcohol > benzoic acid (elutes last).
4. The person forgot to allow the column to drain until the surface of the liquid containing the orange compound had passed the upper surface of the adsorbent. Then a small amount of solvent should have been added, and that solvent should have been allowed to drain below the upper surface of the adsorbent. Only then would it be permissible to fill the solvent reservoir. The solvent reservoir should not be filled until the sample has been completely applied to the adsorbent.
5. Clearly, petroleum ether is not sufficiently polar to elute this sample. A more polar solvent, such as methanol or ethanol, should be selected.
6. About 15 grams of adsorbent should be used. A column of about 12 mm diameter and 100 mm height should be selected.
7. Gel chromatography should be used.
8. During the elution, gradually increase the polarity of the solvent. This is done by adding increasingly higher proportions of a polar solvent to the reservoir.
9. Method 1: A series of fractions of a pre-determined volume can be collected into pre-weighed test tubes. The contents of each test tube are evaporated, and the test tubes are weighed a second time. Fractions are observed by noting which test tubes have gained weight during the chromatography.

Method 2: Thin-layer chromatography can be used to analyze the contents of each fraction.

Method 3: An adsorbent containing an inorganic phosphor can be used. The presence of bands on the column can be detected using an ultraviolet lamp.



## Technique 20

### THIN-LAYER CHROMATOGRAPHY

#### Answers to Problems

1. The presence of only one, highly-mobile spot does not necessarily indicate that the unknown material contains one pure compound. It is possible that the material is a mixture, but that all of the components travel all the way up the TLC plate because the solvent is too polar. The experiment should be repeated with a less polar solvent, such as petroleum ether or cyclohexane. If only one spot appears in this experiment, it is safer to conclude that the unknown is a single, pure compound.
2. It is not safe to conclude that the two samples are identical. The experiment should be repeated with both samples applied to the same TLC plate. If they both have the same  $R_f$  value on the same plate, one may conclude that they are identical although other evidence, such as spectroscopy, should be employed.
3.
  - a) methylene chloride
  - b) hexane
  - c) acetone
4. Relative  $R_f$  values: biphenyl > benzyl alcohol > benzoic acid.
5.
  - a) The solvent is too polar. Repeat the experiment using a less polar solvent such as hexane.
  - b) The solvent is not polar enough. Repeat the experiment using a more polar solvent such as acetone.
  - c) You will not be able to calculate the  $R_f$  value. Repeat the experiment and remove the plate before the solvent reaches the top of the plate.
6.  $R_f = 5.7/13 = 0.44$
7. This is the reverse situation of that described in Problem 1. In this case, the solvent is not sufficiently polar to move the components up the plate. The experiment should be repeated in a more polar solvent. If only one spot is observed in this second experiment, one may conclude that the sample is pure.

8.
    - a) spray the plate with silver nitrate solution.
    - b) spray the plate with 2,4-dinitrophenylhydrazine solution.
    - c) spray the plate with ninhydrin solution.
    - d) spray the plate with sulfuric acid. This will char the sugar to yield a black spot. Alternatively, you can use Molisch reagent (see Experiment 52).
- 

### **Technique 21**

## **HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)**

### **Answers to Problems**

1. In a normal-phase HPLC experiment (hexane solvent), you should expect the relatively non-polar substance to elute first (biphenyl) leading to the following order:

Biphenyl (elutes first) > benzyl alcohol > benzoic acid (elutes last)

In a reversed-phase experiment, the order of elution should be reversed, and the most polar substance (benzoic acid) will elute first in THF-water. As the solvent mixture becomes less polar (percentage of THF increases), the less polar substances will begin to elute.

2. In a normal-phase chromatography, the gradient elution program would begin with a non-polar solvent and would increase the proportion of polar solvent as a function of time. In a reversed-phase chromatography, the elution program would start with a more polar solvent, and there would be an increase in the less-polar solvent as a function of time.
-

## Technique 22

### GAS CHROMATOGRAPHY

#### Answers to Problems

1. (a) 1-Chloropropane would have the shorter retention time (elutes first).  
The elution order is according to boiling point.

(b) The retention times would not be identical because it is impossible to duplicate exactly all the factors affecting retention times. However, the order of elution would be the same.

2. Area Peak A =  $66 \times 8 = 528 \text{ mm}^2$

Area Peak B =  $43 \times 8 = 344 \text{ mm}^2$

Total area =  $872 \text{ mm}^2$

$$\%A = \frac{528}{872} \times 100 = 60.6\%$$

$$\%B = \frac{344}{872} \times 100 = 39.4\%$$

3. Weight Peak A = 0.0447 g

Weight Peak B = 0.0260 g

total weight = 0.0707 g

$$\%A = \frac{0.0447 \text{ g}}{0.0707 \text{ g}} \times 100 = 63.2\%$$

$$\%B = \frac{0.0260 \text{ g}}{0.0707 \text{ g}} \times 100 = 36.8\%$$

The results obtained by this method are within about 2.5% of the results obtained by triangulation.

4. (a) Retention time would increase.  
 (b) Retention time would decrease.  
 (c) Retention time would increase.
- 

### Technique 23

### POLARIMETRY

#### Answers to Problems

1. 
$$[\alpha]_{\text{D}}^{25} = \frac{\alpha}{cl}$$

$\alpha = -10$   
 $c = 0.4 \text{ g/mL}$   
 $l = 0.5 \text{ dm}$

$$[\alpha]_{\text{D}}^{25} = \frac{-10^{\circ}}{(0.4)(0.5)} = -50^{\circ}$$

2. Observed specific rotation =

$$\frac{\text{optical purity} \times \text{specific rotation of pure substance}}{100} = \frac{(80)(+20)}{100} = +16^{\circ}$$

$$\begin{aligned} \alpha &= [\alpha]_{\text{D}}^{25} cl & c &= 2.0 \text{ g/mL} \\ &= (+16)(2.0)(2) & l &= 2 \text{ dm} \\ &= +64^{\circ} \end{aligned}$$

3.

$$\begin{aligned}\text{Optical purity} &= \frac{\text{observed } [\alpha]}{[\alpha] \text{ of pure substance}} \times 100 \\ &= \frac{-8^\circ}{-10^\circ} \times 100 = 80\%\end{aligned}$$

The product contains:

$$\begin{aligned}\% \text{ (-)-enantiomer} &= X + \frac{(100-X)}{2} \quad X = \text{optical purity} \\ &= 80 + \frac{20}{2} = 90\%\end{aligned}$$

$$\% \text{ (+)-enantiomer} = 100 - 90 = 10\%$$

---

### Technique 24

### REFRACTOMETRY

#### Answers to Problems

1. Let  $X$  = mole fraction of isobutyl bromide;

then  $1 - X$  = mole fraction of isobutyl chloride.

$$1.4368(X) + 1.3785(1 - X) = 1.3932$$

$$0.0538(X) = 0.0146; \quad X = 0.25 \text{ or } 25\% \text{ isobutyl bromide}$$

and 75% isobutyl chloride

$$2. \quad n_D^{20} = 1.3982 - 4(0.00045) = 1.3964$$

## Technique 25

### INFRARED SPECTROSCOPY

#### Answers to Problems

1.
    - (a) No change.
    - (b) The compound is too volatile. Use AgCl plates or solution cells.
    - (c) No change.
    - (d) A satisfactory KBr pellet may not be obtained. Run the compound in solution.
    - (e) Nujol is a mixture of saturated hydrocarbons. The spectrum of the aliphatic hydrocarbon compound would have bonds in the same region as Nujol. Run the spectrum in solution (CCl<sub>4</sub>).
    - (f) Aniline will react with silver chloride. Run the compound on salt plates (neat).
    - (g) Water dissolves salt plates. Use AgCl plates.
  
  2.
    - a) Butanal: C=O 1725; C-H 2750 and 2850 for aldehyde.  
2-Butanone: C=O 1715
    - b) 2-Cyclohexenone is conjugated: C=O 1685  
3-Cyclohexenone is unconjugated: C=O 1715
    - c) Diethylamine: singlet at about 3400  
Butylamine: doublet at about 3400
    - d) Ethyl propanoate: C=O 1735  
1-Methoxy-2-butanone: C=O 1715
    - e) Propanoic acid: broad peak centering on C-H stretch region  
Propanol: broad peak at about 3300 or 3400.
    - f) 1,4-dimethylbenzene: strong out-of-plane bending at about 850  
1,2-dimethylbenzene: strong out-of-plane bending at about 750
    - g) 1-Butene: C=C 1650  
2-Butene: no C=C peak at 1650
    - h) 1-Pentyne: terminal C-H 3300; C≡C 2150  
1-Pentene: C=C 1650, C-H 3050
    - i) *m*-Toluidine: out-of-plane bendings 700, 800, and 900  
*o*-Toluidine: out-of-plane bending 850  
Both have NH<sub>2</sub> doublets at 3400
    - j) Pentanoic acid: OH centers on C-H stretches; C=O 1710  
Methyl butanoate: C=O 1735
    - k) Pentane: C-H about 2950  
1-Hexene: C-H about 3050 and 2950; C=C 1650
    - l) 1-Hexyne: terminal C-H 3300; C≡C 2150  
2-Hexyne: no terminal C-H at 3300; C≡C 2150 very weak
-

## Technique 26

### NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

#### Answers to Problems

1. Prepare some sodium deuterioxide as described in Section 26.2 (Non routine Sample Preparation). The carboxylic acid will be converted to sodium salt, and dissolve in  $D_2O$ .
2. Use  $CDCl_3$  or some other deuterium containing solvent to run a carbon-13 NMR spectrum. Deuterium is needed to stabilize (lock) the field.
3.
  - (a) Glycerol (1,2,3-propanetriol) is very soluble in water. Use  $D_2O$  as the solvent.
  - (b) 1,4-Diethoxybenzene (hydroquinone, diethyl ether) is very soluble in organic solvents. Use  $CDCl_3$ .
  - (c) Propyl pentanoate (propyl valerate) is very soluble in organic solvents and insoluble in water. Run the spectrum in  $CDCl_3$ .
4. 2-Nitroaniline with amino group at C-1 position: 6.7 ppm (t) 4-H; 6.8 ppm (d) 6-H; 7.3 ppm (t) 5-H; 8.1 ppm (d) 3-H.  
3-Nitroaniline: 6.9 ppm (d) 6-H; 7.3 ppm (t) 5-H; 7.5 ppm (s) 2-H; 7.6 ppm (d) 4-H.  
4-Nitroaniline: 6.6 ppm (d) 2-H and 6-H; 7.9 ppm (d) 3-H and 5-H
5.
  - (a) Propyl acetate
  - (b) Isopropyl acetate
6. 1,3-Dibromopropane
7. 2,2-Dimethoxypropane
8.
  - (a) Isobutyl propanoate
  - (b) *tert*-Butyl propanoate
  - (c) Butyl propanoate
9.
  - (a) 3-Chloropropanoic acid
  - (b) 2-Chloropropanoic acid
10.
  - (a) 1-Phenyl-2-butanone
  - (b) 4-Phenyl-2-butanone

---

### Technique 27

## CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

### Answers to Problems

1. c) 7 peaks; d) 3 peaks; e) 5 peaks; f) 10 peaks; g) 10 peaks; h) 4 peaks; i) 5 peaks; j) 6 peaks; k) 8 peaks.
  2. a) *tert*-butyl bromide; b) 2-bromobutane; c) 1-bromobutane; d) isobutyl bromide.
  3. a) 4-heptanone; b) 2,4-dimethyl-3-pentanone; c) 4,4-dimethyl-2-pentanone
- 

### Technique 28

## MASS SPECTROMETRY

No problems

---

### Technique 29

## GUIDE TO THE CHEMICAL LITERATURE

### Answers to Problems

1. (a) 2,5-Hexanedione  
Main 1, 788 Syst. No. 95  
Suppl I 405 H 788  
II 841  
III 3128  
IV 3688



- (b) 3-Nitroacetophenone  
Main 7, 288 Syst. No. 639  
Suppl I 153 H 288  
    II 223  
    III 991  
    IV 656
  
- (c) 4-*tert*-Butylcyclohexanone  
Main --  
Suppl I (Vol 7) 29 Syst. No. 613  
    II -- H 33  
    III 144  
    IV 82
  
- (d) 4-Phenylbutanoic acid  
Main 9, 539 Syst. No. 943  
Suppl I 211 H 539  
    II 354  
    III 2451  
    IV 1811

- 2. Numerous references; see the Science Citation Index
- 3. Numerous possible answers; see Smith and March, Appendix B
- 4. (a) See Organic Syntheses, Collective Volume V, page 747  
(b) Collective Volume IV, page 890
- 5. Numerous possible answers

## CORRELATION OF EXPERIMENTS WITH LECTURE TOPICS

**NOTE:** Most of the major classes of reactions are covered in Experiment 55, Identification of Unknowns.

### Alkanes

Experiment 5	Chromatography
Experiment 6	Simple and Fractional Distillation
Experiment 17	An Introduction to Molecular Modeling
Experiment 24	Gas Chromatographic Analysis of Gasolines

### Stereochemistry

Experiment 14	Spearmint and Caraway Oil
Experiment 17	An Introduction to Molecular Modeling
Experiment 27	Chiral Reduction of Ethyl Acetoacetate
Experiment 29	Reduction of Ketones Using Carrot Extract
Experiment 30	Resolution of $\alpha$ -Phenylethylamine
Experiment 38	A Green Enantioselective Aldol Condensation

### Nucleophilic Substitution (Halides)

Experiment 19	Reactivities of Some Alkyl Halides
Experiment 20	Nucleophilic Substitution Reactions: Competing Nucleophiles
Experiment 21	Synthesis of <i>n</i> -Butyl Bromide and <i>t</i> -Pentyl Chloride
Experiment 58	Competing Nucleophiles using 2-pentanol and 3- pentanol

### Preparation and Reactions of Alkenes and Alkynes

Experiment 15	Carotenoid Pigments from Spinach
Experiment 22	4-Methylcyclohexene
Experiment 23	Methyl Stearate from Methyl Oleate (hydrogenation)
Experiment 35	Sonogashira Coupling of Iodoaromatic Compounds with Alkynes
Experiment 36	Grubbs-Catalyzed Metathesis of Eugenol with <i>cis</i> 1,4-butenediol
Experiment 47C	Polymers: Polystyrene
Experiment 48	Ring-Opening Metathesis Polymerization using Grubbs Catalyst

Experiment 64	Green Epoxidation of Chalcones
Experiment 65	Cyclopropanation of Chalcones

### Electrophilic Aromatic Substitution

Experiment 28	Nitration of Aromatic Compounds Using a Recyclable Catalyst
Experiment 42	Relative Reactivities of Several Aromatic Compounds
Experiment 43	Nitration of Methyl Benzoate
Experiment 59	Friedel-Crafts Acylation

### Green Chemistry

Experiment 16	Ethanol from Sucrose
Experiment 25	Biodiesels
Experiment 26	Ethanol from Corn
Experiment 27	Chiral Reduction of Ethyl Acetoacetate
Experiment 28	Nitration of Aromatic Compounds Using a Recyclable Catalyst
Experiment 29	Reduction of Ketones Using Carrot Extract
Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol
Experiment 32A	Coenzyme Synthesis of Benzoin
Experiment 34	Aqueous-Based Organozinc Reactions
Experiment 35	Sonogashira Coupling of Iodoaromatic Compounds with Alkynes
Experiment 36	Grubbs-Catalyzed Metathesis of Eugenol with <i>cis</i> 1,4-butanediol
Experiment 38	A Green Enantioselective Aldol Condensation
Experiment 40	Preparation of Triarylpyridines
Experiment 48	Ring-Opening Metathesis Polymerization using Grubbs Catalyst
Experiment 50	Diels-Alder Reaction with Anthracene-9-methanol
Experiment 64	Green Epoxidation of Chalcones
Experiment 65	Cyclopropanation of Chalcones

### Grignard and Organozinc Chemistry

Experiment 33	Triphenylmethanol and Benzoic Acid
Experiment 34	Aqueous-Based Organozinc Reactions
Experiment 61	Carbonation of an Unknown Aromatic Halide

## Oxidation/Reduction Chemistry (Carbonyl and Carboxyl)

Experiment 29	Reduction of Ketones Using Carrot Extract
Experiment 31	Chiral Reduction of Ethyl Acetoacetate
Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol
Experiment 32B	Benzil
Experiment 68	An Oxidation Puzzle

## Additions to Carbonyl Group

Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol
Experiment 32A	Coenzyme Synthesis of Benzoin
Experiment 33	Triphenylmethanol and Benzoic Acid
Experiment 41	1,4-Diphenyl-1,3-butadiene (Wittig)
Experiment 61	Carbonation of an Unknown Aromatic Halide
Experiment 62	The Aldehyde Enigma

## Preparations of Carboxylic Acids

Experiment 33B	Benzoic Acid (Grignard)
Experiment 61	Carbonation of an Unknown Aromatic Halide

## Carboxylic Acid Derivatives (also Sulfonyl Chlorides and Sulfonamides)

Experiment 8	Acetylsalicylic Acid (ester)
Experiment 12	Isopentyl Acetate (ester)
Experiment 25	Biodiesel (ester)
Experiment 44	Benzocaine (ester)
Experiment 56	Preparation of a C-4 or C-5 Acetate Ester
Experiment 9	Acetaminophen (amide)
Experiment 45	<i>N,N</i> -Diethyl- <i>m</i> -toluamide (amide)
Experiment 52	Luminol (hydrazide)
Experiment 47	Polymers: polyesters and polyamides
Experiment 46	Sulfa Drugs: Preparation of Sulfanilamide

## Reactions of $\alpha$ -Hydrogens on Carbonyl Compounds; Aldol, Claisen, and Conjugate Addition.

Experiment 37	The Aldol Condensation Reaction: Preparation of Benzalacetophenones
Experiment 38	A Green Enantioselective Aldol Condensation

Experiment 39	Preparation of an $\alpha,\beta$ -Unsaturated Ketone <i>via</i> Michael and Aldol Condensation Reactions
Experiment 63	Synthesis of Substituted Chalcones: A Guided- Inquiry Experience
Experiment 66	Michael and Aldol Condensation Reactions

#### Diels-Alder Reaction

Experiment 48	Ring-Opening Metathesis Polymerization using Grubbs Catalyst
Experiment 49	The Diels-Alder Reaction of cyclopentadiene with Maleic Anhydride
Experiment 50	Diels-Alder Reaction with Anthracene-9-methanol

#### Amines

Experiment 30	Resolution of $\alpha$ -Phenylethylamine
Experiment 52	Luminol (Reduction of $\text{NO}_2$ )

#### Rearrangements

Experiment 51	Photoreduction of Benzophenone and Rearrangement of Benzpinacol to Benzopinacolone
Experiment 32C	Benzilic Acid

#### Photochemistry

Experiment 51	Photoreduction of Benzophenone
Experiment 52	Luminol

#### Multistep syntheses

Experiment 32	
Experiment 48	
Experiment 51	
Experiment 59, 63, 64, 65	

#### Carbohydrates and Artificial Sweeteners

Experiment 53	Carbohydrates
Experiment 54	Analysis of Diet Soft Drink by HPLC

#### Natural Products (see also Carbohydrates)

Experiment 11	Isolation of Caffeine from Tea
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Experiment 13	Isolation of Eugenol from Cloves
Experiment 14	Spearmint and Caraway Oil: (-)- and (+)-Carvones
Experiment 15	Isolation of Chlorophyll and Carotenoid Pigments
Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol
Experiment 57	Isolation of Essential Oils from Alspice, Cloves, Cumen, Caraway, Cinnamon, or Fennel

#### Infrared Spectroscopy (partial listing, only)

There are many applications of infrared spectroscopy throughout the textbook. Special use of this technique is made in the following experiments:

Experiment 7	Infrared Spectroscopy
Experiment 12/56	Isopentyl Acetate (Banana Oil)
Experiment 13/57	Essential Oils from Spices
Experiment 14	Spearmint and Caraway Oil
Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol
Experiment 55	Identification of Unknowns
Experiment 59	Friedel-Crafts Acylation
Experiment 47D	Identification of Polymers

#### NMR Spectroscopy (partial listing, only)

Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol (proton and carbon)
Experiment 14	Spearmint and Caraway Oil: (-) and (+) Carvones (proton)
Experiment 59	Friedel-Crafts Acylation (proton and carbon)
Experiment 27	NMR Determination of Optical Purity of (S)-(+)-Ethyl 3-Hydroxybutanoate (proton)
Experiment 30	Determination of Optical Purity of □-Phenylethylamine (proton)
Experiment 55	Identification of Unknowns (proton and carbon)
Experiment 67	Esterification of Vanillin (proton)

#### Mass Spectrometry

Experiment 28	Nitration of Aromatic Compounds Using a Recyclable Catalyst
Experiment 60	The Analysis of Antihistamine Drugs by Gas Chromatography-Mass Spectrometry

## Molecular Modeling

Experiment 17	An Introduction to Molecular Modeling
Experiment 18	Computational Chemistry
Experiment 31	Modeling of the camphor reduction reaction
Experiment 37	The Aldol Condensation Reaction
Experiment 43	Nitration of methyl benzoate

## TABLE OF CONTENTS

Preface	4
Equipping the Organic Chemistry Laboratory	7
Waste Management Guidelines	12
Laboratory Equipment and Supplies	17
Organic Laboratory Techniques Practical Exams	
Organic lab practical exam advice for instructors	21
Organic lab practical exam instructions for students	22
Organic lab practical exam instructions and report sheet for crystallization	23
Organic lab practical exam instructions and report sheet for extraction	24

### Chemicals and Supplies for Each Experiment Answers to Questions

Experiment 1	Solubility	25
Experiment 2	Crystallization	30
Experiment 3	Extraction	32
Experiment 4	A Separation and Purification Scheme	36
Experiment 5	Chromatography	39
Experiment 6	Simple and Fractional Distillation	44
Experiment 7	Infrared Spectroscopy and Boiling-Point Determination	47
Experiment 8	Acetylsalicylic acid	49
Experiment 9	Acetaminophen	51
Experiment 10	TLC of Analgesic Drugs	53
Experiment 11	Isolation of Caffeine	57
Experiment 12	Isopentyl Acetate (Banana Oil)	61
Experiment 13	Isolation of Eugenol from Cloves	63
Experiment 14	Spearmint and Caraway Oil: (+)- and (-)-Carvones	66
Experiment 15	Isolation of Chlorophyll and Carotenoid Pigments from Spinach	71
Experiment 16	Ethanol from Sucrose	73
Experiment 17	An Introduction to Molecular Modeling	75
Experiment 18	Computation Chemistry	75
Experiment 19	Reactivity of Some Alkyl Halides	76
Experiment 20	Nucleophilic Substitution Reactions: Competing Nucleophiles	80
Experiment 21	Synthesis of <i>n</i> -Butyl Bromide and <i>t</i> -Pentyl Chloride	85
Experiment 22	4-Methylcyclohexene	89
Experiment 23	Methyl Stearate from Methyl Oleate	91
Experiment 24	Gas Chromatographic Analysis of Gasolines	95
Experiment 25	Biodiesel	97
Experiment 26	Ethanol from Corn	100
Experiment 27	Chiral Reduction of Ethyl Acetoacetate; Optical Purity Determination	102
Experiment 28	Nitration of Aromatic Compounds Using a Recyclable Catalyst	105
Experiment 29	Reduction of Ketones Using Carrot Extract	106
Experiment 30	Resolution of $\alpha$ -Phenylethylamine and Determination of Optical Purity	107
Experiment 31	An Oxidation-Reduction Scheme: Borneol, Camphor, Isoborneol	112



Experiment 32	Multistep Reaction Sequence: The Conversion of Benzaldehyde to Benzilic Acid	116
Experiment 33	Triphenylmethanol and Benzoic Acid	122
Experiment 34	Aqueous-Based Organozinc Reactions	128
Experiment 35	Sonogashira coupling of Iodoaromatic Compounds with Alkynes	131
Experiment 36	Grubbs-Catalyzed Metathesis of Eugenol with <i>cis</i> -1,4-Butenediol	135
Experiment 37	The Aldol Condensation: Preparation of Benzalacetophenones (Chalcones)	137
Experiment 38	A Green Enantioselective Aldol Condensation Reaction	139
Experiment 39	Preparation of an $\alpha,\beta$ -Unsaturated Ketone <i>via</i> Michael and Aldol Condensation Reactions	141
Experiment 40	Preparation of Triphenylpyridines	142
Experiment 41	1,4-Diphenyl-1,3-Butadiene	143
Experiment 42	Relative Reactivities of Several Aromatic Compounds	146
Experiment 43	Nitration of Methyl Benzoate	148
Experiment 44	Benzocaine	150
Experiment 45	<i>N,N</i> -Diethyl- <i>m</i> -Toluamide: The Insect Repellent "OFF"	155
Experiment 46	Sulfa Drugs: Preparation of Sulfanilamide	156
Experiment 47	Preparation and Properties of Polymers: Polyester, Nylon, and Polystyrene	165
Experiment 48	Ring-opening Metathesis Polymerization using a Grubbs Catalyst	169
Experiment 49	The Diels-Alder Reaction of Cyclopentadiene with Maleic Anhydride	173
Experiment 50	Diels-Alder Reaction with Anthracene-9-methanol	174
Experiment 51	Photoreduction of Benzophenone and Rearrangement of Benzpinacol to Benzopinacolone	175
Experiment 52	Luminol	179
Experiment 53	Carbohydrates	180
Experiment 54	Analysis of a Diet Soft Drink by HPLC	190
Experiment 55	Identification of Unknowns	191
Experiment 56	Preparation of a C-4 or C-5 Acetate Ester	205
Experiment 57	Isolation of Essential Oils from Allspice, Cloves, Cumin, Caraway, Cinnamon, Fennel or Star Anise	207
Experiment 58	Competing Nucleophiles in $S_N1$ and $S_N2$ Reactions: Investigations Using 2-Pentanol and 3-Pentanol	210
Experiment 59	Friedel-Crafts Acylation	213
Experiment 60	The Analysis of Antihistamine Drugs by Gas Chromatography-Mass Spectrometry	225
Experiment 61	Carbonation of an Unknown Aromatic Halide	226
Experiment 62	The Aldehyde Enigma	229
Experiment 63	Synthesis of Substituted Chalcones: A Guided-Inquiry Experience	230
Experiment 64	Green Epoxidation of Chalcones	234
Experiment 65	Cyclopropanation of Chalcones	235
Experiment 66	Michael and Aldol Condensation Reactions	237

Experiment 67	Esterification Reactions of Vanillin: The Use of NMR to Determine a Structure	239
Experiment 68	An Oxidation Puzzle	240

### Answers to Problems in the Techniques Section

Technique 1	Laboratory Safety	241
Technique 2	The Laboratory Notebook, Calculations, and Laboratory Records	241
Technique 3	Laboratory Glassware: Care and Cleaning	241
Technique 4	How to Find Data for Compounds: Handbooks And catalogs	242
Technique 5	Measurement of Volume and Weight	243
Technique 6	Heating and Cooling Methods	244
Technique 7	Reaction Methods	245
Technique 8	Filtration	247
Technique 9	Physical Constants of Solids: The Melting Point	248
Technique 10	Solubility	248
Technique 11	Crystallization: Purification of Solids	249
Technique 12	Extractions, Separations, and Drying Agents	252
Technique 13	Physical Constants of Liquids: The Boiling Point and Density	255
Technique 14	Simple Distillation	256
Technique 15	Fractional Distillation, Azeotropes	257
Technique 16	Vacuum Distillation, Manometers	260
Technique 17	Sublimation	260
Technique 18	Steam Distillation	261
Technique 19	Column Chromatography	262
Technique 20	Thin-Layer Chromatography	264
Technique 21	High-Performance Liquid Chromatography (HPLC)	265
Technique 22	Gas Chromatography	266
Technique 23	Polarimetry	267
Technique 24	Refractometry	268
Technique 25	Infrared Spectroscopy	269
Technique 26	Nuclear Magnetic Resonance Spectroscopy	270
Technique 27	Carbon-13 Nuclear Magnetic Resonance Spectroscopy	271
Technique 28	Mass Spectrometry	271
Technique 29	Guide to the Chemical Literature	271
Correlation of Experiments with Lecture Topics		273

## PREFACE

*Introduction to Organic Laboratory Techniques: A Small Scale Approach (Third Edition)* continues our dedication to the teaching of the organic chemistry laboratory. As we have gathered experience with microscale techniques in the organic laboratory through the development of experiments and methods for the microscale versions of our textbook, we have discovered that students *can* learn to do careful work in the organic laboratory on a small scale. They do not have to consume large quantities of chemicals, and they do not have to work with very large flasks to learn the standard laboratory techniques. Furthermore, we recognize that many instructors do not wish to abandon the traditional-scale approach to their courses, and many colleges and universities cannot afford to convert all of their glassware to microscale.

In the traditional approach to teaching this subject, the quantities of chemicals used were on the order of 5-100 grams. The approach used in this textbook differs from the traditional laboratory in that nearly all of the experiments use smaller amounts of chemicals (1-10 grams). However, the glassware and methods used in this approach are identical to the glassware and methods used in traditional-scale experiments. The advantages of the small-scale approach include improved safety in the laboratory, reduced risk of fire and explosion, and reduced exposure to hazardous vapors. This approach decreases the need for hazardous waste disposal, leading to reduced contamination of the environment.

In this edition we have devoted considerable effort toward improving the safety of all of the experiments. Technique Chapter 1, "Laboratory Safety," places strong emphasis on the safe use and disposal of hazardous chemicals. We have included information on Material Safety Data Sheets (MSDS) and Right-to-Know laws. We have continued to update and improve instructions for the handling of waste products that are produced in the experiments. We recommend that virtually all waste, including aqueous solutions, be placed into appropriate waste containers.

The new experiments are listed in the Preface of the Textbook. These include several "green" chemistry experiments and some project-based experiments. In the latter experiments, students must either solve a significant problem or they must generate all or part of the experimental procedure. A Green Chemistry essay has been added and some of the experiments have been modified to make them more "green." We have significantly increased the number of unknowns listed in Appendix 1. We also offer an alternative way of solving unknowns using mainly spectroscopy.

We hope that this instructor's manual will assist you in preparing solutions, chemical reagents, supplies, and equipment necessary for each experiment that you choose to do. The lists of chemicals and equipment required for each experiment are based on the amount required for ten students. For chemicals, the amounts indicated include at least a 25% excess. At the end of the manual we have included a section that correlates the experiments with topics presented in standard organic lecture courses.

The time required for each experiment is given in laboratory periods. It is assumed that a laboratory period is about three hours in length. For laboratory periods that are either shorter or longer, appropriate adjustments must be made.

The technique chapters of the textbook are designed to stand independently from the experiments. You may have a favorite experiment that you like to do in your course. If this is the case, you can freely add your experiment and still take advantage of the technique chapters in the textbook. Since both standard-scale and microscale techniques are described in the technique chapters, you may even add some microscale experiments and still be able to refer your students to the appropriate sections in these chapters for information on each technique.

The publishers have made available videos to accompany the Textbook. These videos can be studied by students in advance of the laboratory session. They show the various steps for assembling an apparatus and carrying out a technique. See the Preface to the Textbook for more information. Students may purchase access to the website: [www.cengagebrain.com](http://www.cengagebrain.com)

A new feature of the Instructor's Manual is the inclusion of some laboratory practical exams that test students on two basic organic laboratory techniques: crystallization and extraction. You may find these exams to be a useful way of evaluating student technique. The idea is to have students perform techniques without the textbook and without looking over another student's shoulder for help!

If you encounter problems with any of the experiments in the Textbook or if you need help in setting up your laboratory, please contact us. We would also like to hear from you if you have any suggestions for improvements in techniques or in any of the experiments.

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## EQUIPPING THE ORGANIC CHEMISTRY LABORATORY

This section includes some suggestions for equipping a macroscale laboratory using a reduced scale approach. In addition, this section provides information for all instructors on some of the laboratory requirements for doing the experiments found in the textbook.

Although some experiments involve microscale techniques, they do not require special equipment. These experiments can be conducted with flasks, beakers, test tubes and other simple equipment.

### Dispensing and Measuring Liquids

Where possible liquid reagents and solvents should be stored in a hood in small glass or plastic bottles. To avoid waste, the exact amount of liquid should be transferred to the student's container by one of the methods described below. Students should not pour an approximate amount of liquid into one container and then measure the required volume, leaving some excess liquid behind which must be discarded.

When accuracy is not important, one-piece polyethylene transfer pipets or calibrated Pasteur pipets shown in Technique 5, Figures 5.6B and 5.6C, provide an efficient method for delivering liquids, especially solvents to be used for extractions or crystallizations. We tape a test tube to the bottle containing the liquid in order to hold the pipet. It is easy for students to use one of these pipets to transfer liquid to a graduated cylinder for more careful measurement. If one of these techniques is used for measuring a limiting reagent, students need to be strongly encouraged to weigh the liquid following transfer.

Dispensing pumps (Technique 5, Figure 5.2) may be used to deliver larger amounts (more than 0.5 mL) of liquid. They are especially useful in dispensing solvents or non-limiting reagents. *Care must be taken to ensure that the tip is filled with liquid and that no air bubbles are observed in the tubing.* These units easily lose their "prime" especially with more volatile solvents. We have observed that some solvents swell the plastic plunger such that it can not be pulled up easily. If this happens to you, remove the solvent from the unit. After drying out thoroughly, the unit can be used again (with another solvent!). We have found that waste has been significantly reduced with dispensing pumps. They can be set individually for a particular solvent. Students simply raise the pump and dispense exactly the right amount of solvent thus eliminating waste.

If you plan to do some microscale experiments, it is useful to have available several adjustable 100-1000  $\mu\text{L}$  automatic pipets for dispensing very small amounts (less than 1 mL) of liquids used as limiting reagents. They are also useful for measuring densities of liquids. The automatic pipet is very accurate with

aqueous solutions, but it is not as accurate with organic liquids. With all limiting reagents, it will be necessary to obtain the weight in order to determine accurately the amount of substance used. Since most of the errors that occur in the laboratory may be attributed to "sloppy" transfers, you should give a thorough demonstration of how to use the automatic pipet. They should be cautioned about not allowing the plunger to snap back rapidly. The automatic pipet should be placed near the appropriate reagent and supported in a vertical holding device. Automatic pipets should never be used with corrosive or caustic liquids.

A graduated 1 or 2-mL one-piece polyethylene pipet should be used to dispense small amounts of corrosive or caustic liquids, such as sulfuric acid, hydrochloric acid, or sodium hydroxide. Alternatively, a graduated pipet and pipet pump can be used. When using graduated pipets, we prefer the pipet pump shown in Technique 5, Figure 5.3B in the Textbook. The top of the pipet fits more securely in a pipet pump of this style than in a pump similar to the one shown in Figure 5.3A. To avoid contamination of the stock reagent and to minimize waste, we provide a graduated pipet and pipet pump with the reagent for community use. A pint bottle is a convenient container for holding the pipet when it is not in use.

For most procedures one of the above methods will work well to deliver the volumes of liquid required in the experiments in the Textbook. Even when more than 2 mL of liquid is required, we prefer to use one of the pipet methods for transferring the liquid, rather than having the students pour an approximate amount of liquid from the original container into their own.

The instructor should place the appropriate measuring device with each reagent and solvent. In most cases, the device will be a one-piece polyethylene pipet, a graduated pipet with a pipet pump, or dispensing pump. *The person who prepares the laboratory for an experiment should read the procedure in order to determine which device is appropriate.*

### **Dispensing Solids and Weighing Reagents**

Four top-loading balances that read to 0.01 or 0.001 gram are required for a class of 20 students. The balances should be used with draft shields to improve accuracy. It is convenient to store solids in containers near the balances. To avoid the possibility of contamination, we provide a community spatula with the reagent.

### **Evaporating Solvents**

Ideally, students should remove solvent by heating at a low temperature and by directing a stream of nitrogen or air through a Pasteur pipet into a flask in order to evaporate a solvent. This procedure gives a student complete control of the evaporation process, but only works well in a laboratory with many individual hoods. In laboratories where there are only a few hoods it becomes necessary to

have a permanent community evaporation station assembled in the hood. A community station may consist of aluminum heating blocks on hot plates (see Ludwig, S.N. "The Use of Solid Aluminum Heat Transfer Devices in Organic Chemistry Laboratory Instruction and Research," *Journal of Chemical Education*, 66 (1989): 77). Hot plates with containers filled with small pebbles or sand may also be used to heat the samples. The station is equipped with multiple outlets using Y-connectors and screw clamps with flexible tubing. In this way, several students can evaporate solvents using one air or nitrogen source.

The N-EVAP evaporator is a commercially available unit which is useful for larger classes. Several commercial models are available from Organomation Associates, Inc., 266 River Road West, Berlin, MA 01503-1699. Phone: (888) 838-7300. These units consist of an electrically heated water-bath container and a gas manifold equipped with blunt-end, stainless-steel needles. The holders are made with 6, 12, 24, 36 or 45 positions and will accept a variety of containers including test tubes and Erlenmeyer flasks. The 12 position model provides an exceptionally efficient means of evaporating solvents in a lab with 20 students.

### **Rotary Evaporators**

It is becoming more common to equip the laboratory with rotary evaporators to avoid some environmental problems with evaporating solvents in the hood. We suggest systems that have coolers attached to the evaporators to improve solvent recovery thereby making the laboratory a greener environment for students and instructors. You may want to continue evaporating small amounts of solvents, approximate 10 mL or less, as indicated in the above section. Use a rotary evaporator for larger amounts, about 25 mL or more. The use of a rotary evaporator can create a large student backup unless reserved for evaporating large volumes of solvent.

A "rotacool" model rotary evaporator is available from Heidolph-Brinkmann for about \$10,000. It is equipped with vacuum pump, condensation cooler and rotacool circulating chiller. This is a very efficient system that does a great job of collecting even the most volatile solvents. If you can afford to buy a rotary evaporator with a cooler, you won't regret it!

### **Heating Mantles and Hot Plates**

For most applications involving reflux and distillation, we recommend that you use a heating mantle equipped with a temperature controller, such as the one shown on page 610 of the Textbook (Thermowell mantle with Powermite controller). These mantles employ a ceramic heating shell with electric heating coils embedded within the shell. The ceramic shell protects the mantle from damage caused by chemical spills. A 100-mL mantle will heat 25, 50, and 100 mL flasks, and should be sufficient for most experiments in this Textbook.



Hot plates are very useful for heating solvents required for crystallization. In some cases, reactions mixtures need to be stirred as well as heated. For this reason, we suggest purchasing combination stirrer/hot plate units. If the hot plate is used for refluxing a mixture in a round-bottom flask, it is best to use a hot plate with an aluminum top and an aluminum block as a heating source. *You should not use hot plates with ceramic tops unless you are certain that the tops will withstand high temperatures without cracking.* The holes that have been drilled in the aluminum block easily support and accommodate smaller round-bottom flasks and a thermometer. The aluminum block is especially useful when temperatures above 200 °C are required. The stirrer/hot plate units should provide a temperature range of about 60 to above 250 °C. Reaction mixtures which boil at less than about 100°C can usually be heated under reflux with only a hot plate without an aluminum block.

*If you wish to monitor the temperature of aluminum blocks, we recommend that you not employ mercury thermometers, especially those inserted in the aluminum blocks.* Glass thermometers break too easily. We suggest that you use metal dial thermometers rather than mercury thermometers. They are sufficiently accurate for monitoring the temperature of the aluminum blocks.

### **Melting Point Apparatus**

Four electrically-heated melting point apparatus should be provided for a class of 20 students (Mel-Temp or Electrothermal). A Thomas-Hoover Uni-Melt apparatus should be considered if the class is determining micro boiling points. This device has a rapid temperature response. The Mel-Temp or Electrothermal units are less expensive and more serviceable alternative, but the temperature response is not as rapid and micro boiling point determinations may be more difficult to perform. You should try several different melting point units before buying them to see which one is the best for you.

### **Gas Chromatographs**

At least two gas chromatographs should be provided for every 20 students, if students are expected to perform their own injections. Conditions for running samples on the Gow-Mac 69-350 or Hewlett Packard 5890 gas chromatographs are given in this Textbook. If students are expected to collect samples from a chromatograph, Gow-Mac models 69-350 or 580 can be equipped with a convenient sample collection device. Gow-Mac instruments should be equipped with an 8-foot column packed with Carbowax 20M and an 8-foot column containing 20% DC-710. Columns required for the Hewlett Packard chromatographs are given in the Textbook or in this manual.

### **Spectrometers/Polarimeters**

The laboratory should have at least one FT-infrared spectrometer for every 20 students. The FT-infrared instruments increase the through-put of students in the laboratory. If you can afford it, an FT instrument with ATR (attenuated total reflectance) accessory is highly recommended. Use of this accessory makes analysis of solids totally trivial! Otherwise, you will need to make do with determining a spectrum using the dry film method or with a KBr pellet. For conventional IR spectroscopy we have available two of the hand press units for solids. NMR spectroscopy is important in the modern organic chemistry laboratory and you should make this available to your students, if possible. The availability of both proton and carbon NMR increases student interest especially when solving unknowns. The laboratory should be equipped with one polarimeter for use by the class.

### **Centrifuges**

Several experiments or experimental techniques require the use of a centrifuge. They are very useful for breaking emulsions. One or two "clinical" centrifuges are adequate for 20 students. They should hold 15 mL centrifuge tubes.

### **Vortex Mixer**

Extractions can be carried out conveniently in a 15-mL centrifuge tube. Although the tube can be stoppered and shaken to mix the layers, mixing can be accomplished efficiently with a vortex mixer. This method eliminates the problems of pressure buildup and leakage. One mixer easily serves 20 students.

### **Syringes and Rubber Septa**

In some experiments a syringe is used to add reagents to a reaction mixture. A 1 or 2-mL glass or plastic syringe should be provided to allow use with organic solvents without contamination occurring. The plastic syringes are readily available and are much cheaper and durable than glass syringes. Disposable hypodermic needles may be used for most applications. We recommend 1 1/2- or 2-inch needles (21 or 22 gauge). When the experiment is completed, they should be saved for reuse.

### **Plastic Joint Clips ("Blue Clips")**

It is essential that the lab be supplied with plastic joint clips to secure the 19/22 ground glass equipment (Technique 7, Figure 7.3). Breakage is dramatically reduced when they are used to secure equipment. At least 3 should be included in each laboratory locker.

### **Monometers**

Several monometers should be available in the laboratory for use in vacuum distillations. A simple U-tube manometer is shown in Technique 16, Figure 16.9 of the Textbook.

### **Sublimation Equipment**

It is suggested that the laboratory be supplied with microscale sublimation equipment such as that shown in Technique 17, Figure 17.2 A or B. This apparatus is equipped with 14/10 joints and can be used to perform all sublimation procedures described in this Textbook. We suggest 5 complete units as part of the community equipment.

### **Washing Glassware and Equipment**

A plastic dishpan provides a convenient container in which to soak and wash dirty glassware. You may want to consider buying an ultrasound cleaner (sonicator) cleaner for the laboratory. Especially dirty glassware can often be effectively cleaned with one of these devices. There are some disadvantages: they are noisy and students often forget to retrieve their glassware.

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## **WASTE MANAGEMENT GUIDELINES**

These guidelines are intended for schools where the chemistry department is responsible for its own waste management. Although most of this information should apply to your situation, specific waste management practices will depend on the size of your program, other hazardous wastes generated on your campus, and state and local regulations. This information may not cover everything you need to know; however, it can help you get started or may provide some new ideas that will improve your existing waste management program.

To get started, you need to determine who regulates hazardous waste in your state. The U.S. Environmental Protection Agency (EPA) has ultimate responsibility for regulating hazardous waste in all 50 states plus the District of Columbia, Puerto Rico, and the Virgin Islands. Many states have been delegated the authority to regulate their own hazardous waste by the EPA. States which have the authority to regulate their own hazardous waste must have regulations that are as strict as the federal laws. If you operate in a state that has a hazardous waste regulating agency, then you must follow the regulations for your state rather than the federal regulations. The EPA has a home page (<http://www.epa.gov>) and ten regional offices that can help you find out if there is a state program in your area.

Region	States in the Region	Telephone Number
1	ME, NH, VT, MA, RI, CT	617-565-3423
2	NY,NJ,PR,VI	212-637-5000
3	PA,DE,DC,MD,VA,WV	800-438-2474
4	KY, TN,NC,SC,MS,AL,GA,FL	800-241-1754
5	MN,WI,IL,MI,IN,OH	800-621-8431
6	NM,TX,OK,AR,LA	214-665-2200
7	NE,KS,IA,MO	913-551-7000
8	MT,ND,WY,SD,UT,CO	800-227-8917
9	CA,NV,AZ,HI	415-744-1500
10	WA,OR,ID,AK	800-424-4372

You must obtain a Resource Conservation and Recovery Act (RCRA) site identification number if your campus does not already have one. This number identifies your site and all the waste generated there. This identification number is obtained through the agency that regulates hazardous waste in your state. You must supply this number to waste disposal firms when you ship waste off site, and it identifies your site on your annual hazardous waste report.

We collect all chemical waste generated in student laboratories, and we make a serious attempt to teach students that waste management is important. Therefore, students do not dispose of any chemical materials down the drain or in the trash. We find that labeling waste containers with the experiment name and a list of the chemicals that should be placed in the container greatly increases the chances that students will put wastes into the correct containers. We will use our "Isolation of Caffeine from Tea" experiment to give an example. The students generate an aqueous layer contaminated with methylene chloride. Unfortunately, the small amount of methylene chloride that dissolves in water renders the entire aqueous solution hazardous waste. The waste bottle would be labeled as follows:

Isolation of Caffeine from Tea  
Hazardous Waste  
Aqueous layer contaminated w/ methylene chloride  
Suspect Human Carcinogen

Note that "Hazardous Waste" must be included on the label, as required by law. Also, the primary hazard of the waste, the last entry on this label, is required by law. Refer to the material safety data sheet (MSDS) for the primary or most hazardous constituent of the waste to determine an appropriate warning.

Wastes collected from student labs are consolidated by waste type or treated, if it is safe and legal to do so. We find that all wastes we generate fit into one of the following categories:

**Nonhazardous Solids** such as paper, tea bags, and corks are disposed of with the ordinary trash.

**Broken Glassware** is disposed of in a container designated for this purpose. When the container is full, it is packaged securely and disposed of with the ordinary trash.

**Organic Solids** with halogens are consolidated with our halogenated organic solvents, and those without halogens are consolidated with our non-halogenated organic solvents.

**Inorganic Solids** such as alumina and drying agents are accumulated together and disposed of as hazardous waste.

**Non-Halogenated Organic Solvents** such as alcohols, toluene, hexane, and diethyl ether are disposed of as hazardous waste. Intentional evaporation or drain disposal of these materials is illegal. However, evaporation of these solvents as part of the workup in an experiment *is legal*, since the material is not yet waste and the evaporation is a legitimate part of the procedure.

**Halogenated Organic Solvents** such as dichloromethane (methylene chloride), chloroform, and carbon tetrachloride are disposed of as hazardous waste. Intentional evaporation or drain disposal of these materials is illegal. However, evaporation of these solvents as part of the workup in an experiment is legal, since the material is not yet waste and the evaporation is a legitimate part of the procedure.

**Inorganic Acids** without heavy metals or halogenated solvent contamination are neutralized and discharged to the sewer. A log of these treatment activities is maintained.

**Inorganic Bases** without heavy metals or halogenated solvent contamination are neutralized and discharged to the sewer. A log of these treatment activities is maintained.

**Aqueous Solutions Contaminated with Halogenated Solvents** are disposed of as hazardous waste. Intentional evaporation or drain disposal of these materials is illegal.

**Aqueous Solutions with Heavy Metals** may either be treated to remove the heavy metal or disposed of as hazardous waste. If you treat these wastes, you

must test the pH and metal levels before discharge of the treated waste to the sewer to confirm successful treatment. In most states, the water may be legally evaporated to reduce the waste volume, and the remaining metal sludge treated as hazardous waste. The original amount of waste including water must be reported on your annual hazardous waste report.

Most states allow some forms of treatment by the waste generator without the need for special permits. Before you treat a waste you must make sure that your regulators allow the treatment practice. Prior to waste treatment, all of the constituents of the waste, such as heavy metal, solvent content, and low or high pH must be determined. You also need to contact your local sewer district to find out if they have limits on what may be discharged to their system. In many cases a material may not be considered hazardous waste by the EPA or a State Environmental Regulatory Agency, but is restricted from disposal to the sanitary sewer. Treatment and discharge of waste is not recommended if you are on a septic system.

If you elect to treat waste, you are required to test the treated waste for each constituent that made the untreated waste hazardous before you discharge it to the sewer. For example, if you treated an aqueous waste that contained silver, barium, and chromium by precipitating the metals, you would have to check the barium, silver, and chromium levels of the treated waste before discharge to the sewer. Because of this burden, we limit our treatment to neutralization of non-heavy-metal-bearing aqueous wastes that have a low or high pH. Also, remember that intentional evaporation of solvents, and dilution and drain disposal of hazardous wastes not only violates EPA regulations but is also harmful to the environment.

Maintain a log of all wastes treated on site. At a minimum this log should include: a description of the waste, the amount of waste treated, the name of the person treating the waste, the treatment method, and the treatment date. Hazardous wastes that are treated on site must be "counted" and reported on your annual hazardous waste report.

Maintain a waste generation log, which includes the total amount of waste treated and generated. At a minimum this log should include: date, description of the waste, amount, and identity of generator. This log must be included in the annual hazardous waste report that is described below.

We recommend that you limit the amount of waste you accumulate not only to simplify your regulatory requirements, but also to minimize the risk of leaks and spills. In most states, by accumulating less than 55 gallons of each type of waste you simplify the storage and record keeping requirements associated with waste storage. Larger waste accumulation areas must be inspected weekly and equipped with emergency response supplies. Waste must be stored in a secure (locked) area, segregated by type, capped when not in use, and provided with

secondary containment (several bottles of the same type of waste can be placed in a tray or individual bottles may be stored in pails). We recommend hazardous waste shipments at intervals as dictated by your operation to limit the amount of waste stored.

At smaller schools you may find that annual waste shipments are a good management practice. At larger schools shipments each semester, quarterly, or even monthly may be required. At Western Washington University, the motor pool and the physical plant operations generate far more waste than the chemistry department. You may find it worthwhile to coordinate your waste disposal with other departments or operations within your school.

If you elect to ship your own waste, you must learn and follow all of the mandated procedures. As a simpler alternative, there are private contractors who will consolidate, treat, package, and ship your waste for you. However, this alternative does not keep you from having to keep good records.

Contact your local fire department to find out about requirements concerning hazardous material storage. Often these agencies require chemical inventory and storage information about your site so that they can respond appropriately in the event of an emergency.

Establish written hazardous waste management procedures for your campus and communicate these procedures to those involved with waste handling. Also, assure that the person on your campus who signs manifests has received Department of Transportation training on hazardous material shipping.

Retain copies of all manifests and land disposal restriction certifications, sometimes known as "land bans", of waste sent off site for disposal. Manifests can be thought of as the shipping papers for hazardous waste shipments. Land disposal restriction certifications accompany manifests and document disposal and treatment restrictions based on the characteristics of the waste being sent for disposal.

Complete an annual hazardous waste report for all hazardous waste activities on your campus. This report is required by law and must be submitted to the agency that regulates hazardous waste in your area. The report summarizes your hazardous waste activities for the previous calendar year. To complete this report you will need: your RCRA site identification number, copies of all manifests for the past year and your treatment and generation logs.

## LABORATORY EQUIPMENT AND SUPPLIES

- A. Individual student glassware and equipment contained in the locker
1. Organic Chemistry Kit (19/22 joints)  
  
500 mL 3-Neck round bottom flask  
250 mL Round-bottom flask with side tubulation  
25, 50, and 100 mL Round-bottom boiling flasks  
Stoppers (2)  
Thermometer adapter  
Rubber thermometer holder  
Bleed tube (ebulliator tube)  
Claisen head  
Distilling head  
Vacuum adapter  
Condenser  
Fractionating column (packed with steel wool)  
125 mL Separatory funnel, Teflon stopcock
  2. Other individual glassware  
  
Beakers; 50 mL (2), 100 mL (2), 250 mL (2), 400 mL (1)  
Graduated cylinders; 10 mL and 100 mL  
Drying tubes (2)  
Evaporating dish, size 00  
Erlenmeyer flasks; 25 mL (2), 50 mL (2), 125 mL (1), 250 mL (1),  
500 mL (1)  
Filter flask; 125 mL  
Aspirator trap bottle (part of community equipment)  
Conical funnel (stemless), 50 mm  
Powder funnel  
Büchner funnel; size 0  
Büchner funnel; size 2A (optional)  
Hirsch funnel, plastic preferred  
Test tubes or culture tubes; 10 x 75 mm (6);  
16 x 100 mm (5); 15 x 125 mm (3)  
Thermometer, non-mercury; 360°  
Watch glasses; 50 mm (2) and 100 mm (2)  
Small ground glass bottles for submitting liquid samples (2)  
Small vials for submitting solid samples to the instructor (2)  
4 oz. Screw cap bottles (2)  
Centrifuge tubes, glass, screw cap with Teflon liner; 15 mL (2)  
or Centrifuge tubes, polypropylene, screw cap, 15 mL (2), VWR  
20171-010



Centrifuge tubes, plastic (no screw cap), 15 mL (2)  
2 mL Glass or plastic syringe (Luer lock and Teflon plunger  
tip preferred)  
Needles to fit syringe

3. Individual equipment

Plastic joint clips to fit 19/22 joints (3)  
Condenser clamp, 3-prong with holder  
Utility clamps (2)  
Screw clamp  
Dropper bulbs, latex, 2 mL (4)  
Rubber policeman  
Stirring rod  
Neoprene adapters, nos. 2, 3, and 4  
Rubber serum bottle stopper to fit over 19/22 joint  
Brushes, small and large  
Microburner and chimney (optional)  
Wire gauze (optional)  
Test tube holder  
Spatula  
Stir bar  
Test tube block  
Rubber tubing  
Pressure tubing  
Scorer or file  
Safety glasses  
Aluminum blocks (optional)  
Metal thermometer to measure temperature when accuracy  
is not required (optional)

B. Community Equipment

The following equipment should be available in the laboratory or nearby.  
(Numbers in parentheses indicate requirements for 20 students)

Hot plate/stirrer (20)  
Ring stands (40)  
Iron rings to hold separatory funnels (20)  
Heating mantles with controllers, two sizes (20 each)  
Wooden blocks to support glassware  
Automatic pipets; 100 - 1000  $\mu$ L (optional)  
Dispensing pumps; 2 and 5 mL sizes (optional)  
Pipet pumps (optional)  
Sponges (10)  
Screw cap bottles for chromatography (40)

Ice buckets (5)  
Filter flasks; 500 mL (optional)  
Separatory funnels, 500 mL (optional)  
Microscale sublimation apparatus, with 14/10 joints (optional, 5)  
Melting point apparatus (4)  
Top-loading balances with draft shields, 0.001 g (4)  
Refractometer (1)  
Polarimeter (1)  
Centrifuges (2)  
Gas Chromatographs, Gow-Mac, model 69-350  
Equipment required for optional collection of liquids from Gow-Mac chromatographs: metal adapter for collection of samples (2), 1 mL conical reaction vials with 5/5 joint (2) and collection tubes with 5/5 joint (2)  
Vortex mixer (optional, 1)  
Infrared Spectrometer (2)  
Potassium bromide hand press (2)  
Salt plates for infrared spectroscopy (2 pairs)  
NMR spectrometer  
Ovens (2)  
Glass working bench with burners and supply of glass tubing  
Matches or gas lighters for burners  
Scissors (2)  
Handbook of Chemistry and Physics (mounted on board)  
Handbook of Tables for Organic Compound Identification  
Merck Index (mounted on board)  
Rotary Evaporators (recommended)

## C. Community Supplies

### 1. Chemicals and supplies

The following materials should be available at all times on the side shelves or desks.

Gloves, disposable  
Pasteur pipets; 5 3/4-inch and 9-inch sizes  
Graduated one-piece polyethylene transfer pipets  
Applicator sticks  
Decolorizing carbon, pelletized and powdered  
Sample vials for submitting products  
Filter paper to fit Büchner and Hirsch funnels  
Filter paper for gravity filtrations  
Stopcock grease  
Glycerol in dropper bottle  
Boiling stones, inert such as corundum

Corks, assorted  
pH paper  
Red and blue litmus paper  
Copper wire  
Capillary tubes, sealed on one end for melting points  
Capillary tubes, open on both ends for TLC chromatography  
Glass wool  
Cotton  
Labeling tape  
Soap  
Celite (Filter Aid)  
Rock salt  
Anhydrous magnesium sulfate (powdered)  
Anhydrous calcium chloride (4-20 mesh)  
Anhydrous sodium sulfate (granular)

2. Acids and bases

The solutions and reagents should be placed in one area of the laboratory on a chemically resistant surface.

Acids need to be separated from bases.

Sodium hydroxide solutions; 5%

Sodium bicarbonate solution, 5%

Hydrochloric acid solutions; concentrated and 5%

Sodium chloride solution, saturated

Nitric acid, concentrated

Ammonium hydroxide, concentrated

Sulfuric acid, concentrated

3. Common solvents

These solvents should be placed in a hood during use and stored in a special cabinet at other times (see below).

Hexane

Petroleum ether (various boiling ranges)

Acetone

Methanol

Toluene

Methylene chloride

95% Ethanol (5 % water)

Diethyl ether

Carbon tetrachloride and methylene chloride, kept in a hood near the infrared spectrometer, with a Pasteur pipet attached.

4. Test reagent shelves

We usually keep the reagents and known compounds for

Experiment 55 (qualitative analysis) in a designated area of the laboratory at all times. The noxious chemicals are kept in a hood.

D. Safety

Storage cabinet for flammable organic solvents  
Fire extinguishers  
Eye wash fountains  
Showers  
Fire blankets  
Solvent waste containers (see individual experiment)

E. Safety References and MSDS sheets (Technique 1)

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## ORGANIC LABORATORY TECHNIQUES PRACTICAL EXAMS

Some instructors may desire to test students on two very basic organic laboratory techniques: crystallization and extraction. We call this a laboratory practical exam. With the technique exam, you can determine who really has the best technique and who the leaders and followers are in your laboratory course. Students do their work without a textbook in front of them. They are prohibited from looking at what other students are doing.

### Organic lab practical exam advice for instructors

You may desire to give this test to students at the end of the first organic laboratory course. Each student will be required to purify a compound either by acid-base extraction or crystallization. These students have completed Experiment 2 (Crystallization) and Experiment 3 (Extraction). They have also completed Experiment 4 (A Separation and Purification Scheme).

Several days before the exam they are given the handout titled “Organic Lab Practical Exam Instructions for Students”. At this point they don’t know if they will be doing an extraction or crystallization. Therefore, they must prepare for both possibilities. On the test day, they are given either the sheet titled “Extraction” or “Crystallization” and a sample of an impure compound. They have three hour to complete this assignment, but most students are done after two hours.

We make up the samples for crystallization by mixing thoroughly 12 g of urea and 0.53 g of trans-cinnamic acid. Each student is given 1.0 g of the mixture. We don’t tell them the actual weight and they are told not to weigh it. For the extraction, dissolve 3.0 g of fluorene and 0.75 g of benzoic acid in 60

mL of methylene chloride. Each student is given 4.0 mL of this solution. Students should use a centrifuge tube to perform the extraction procedure.

Because of the way this test is designed, students do not know how much of the compound they start with or the melting point. Therefore, it is impossible for them to change their data to get a better grade.

### **Organic lab practical exam instructions for students**

For this lab practical exam you will be given an impure sample of a compound to be purified either by acid/base extraction or crystallization. You are to carry out this task without the aid of other students or any written or electronic resources.

When you arrive in lab, you will be given an impure sample and an instruction sheet that will inform you whether the compound is to be purified by acid/base extraction or crystallization. You will be told the structure of the compound, but not the melting point.

**Extraction.** On the instruction sheet for the acid/base extraction purification you will be told the structure of the neutral compound, the approximate weight of the compound, and what organic solvent it is dissolved in (the compound and impurity will already be dissolved in an appropriate solvent to do the extraction). The volume of this solution will be 4.0 mL. Therefore, you should use a centrifuge tube to perform the extraction. You will also be told whether the impurity is an organic acid or base (amine) and how much 1M NaOH or 1 M HCl you should use for the extraction step. You do not have to isolate the acid or base impurity. You must decide whether to use NaOH or HCl to extract the impurity.

Your goal will be to separate the neutral compound from the acid or base impurity, isolate it in a pure form, and determine the weight recovered and the melting point. You will **not** know exactly how much of the neutral compound is in the original sample or the melting point.

**Crystallization.** For the crystallization purification, you will be told the structure of the impure compound and the approximate weight of the sample. You will also be given three suggestions as to which solvent could be used for crystallization. One of these solvents will be suitable for crystallizing this compound. The compound will be too soluble in one of them and not soluble enough in the third solvent. Your goal will be to determine the best solvent, purify your sample by crystallization, and determine the weight recovered and melting point. You will **not** know the exact amount of the compound that you start with or the literature melting point of the compound

**General comments and grading procedures.** You may **not** use your textbook, handbooks, or any other resources (written or electronic) while completing this exercise. You may not talk to other students and you should refrain from looking at the set-ups used by other students. This exam will be worth 20 points and will be based on the weight recovered of the purified material and the purity based on melting point. You will also be graded on how your sample looks and whether or not the sample is dry. You may have a second sample, but it will cost you 2 points. If you take a third sample, this will cost you an additional 3 points.

### Organic lab practical exam instructions and report sheet for crystallization

\_\_\_\_\_ Name

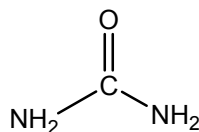
\_\_\_\_\_ Tube Number

You may **not** use your textbook, handbooks, or any other written material while completing this exercise. You may not use any electronic resources. However, you may take down notes on this sheet of paper. You may not talk to other students during this exercise and you should refrain from looking at the set-ups used by other students. If you have questions during the lab, **ask your instructor.**

There will be a 2-point subjective grade. The subjective grade will be determined by the instructor's assessment of such things as whether or not you talk to other students or if you obviously look at what other students are doing. You may have a second sample, but it will cost you 2 points.

**Instructions.** You will be given a sample of impure urea that has a weight between 0.8 – 1.2 g. **Do not weigh the sample.** You should crystallize the entire sample. **Write down the number of the tube and your name in the space above.**

The structure of urea is:



Urea can be crystallized from one of the three following solvents: 95% ethyl alcohol, water, or hexane. You may determine which solvent to use either by experimentation or by making an educated guess.

After crystallizing the sample of impure urea, determine the weight and melting point of the dry crystals. The melting point should be between 120 - 140° C. Turn in this sheet and your sample in a vial labeled as follows: your name, the name of the compound, weight of sample, and melting point. You

will be graded on the recovery and purity, as determined by appearance and melting point. Record the recovery and melting point below:

Recovered weight of sample \_\_\_\_\_

Melting point of sample \_\_\_\_\_

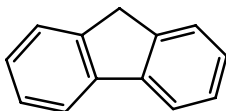
### Organic lab practical exam instructions and report sheet for extraction

\_\_\_\_\_ Name

You may **not** use your textbook, handbooks, or any other written material while completing this exercise. You may not use any electronic resources. However, you may take down notes on this sheet of paper. You may not talk to other students during this exercise and you should refrain from looking at the set-ups used by other students. If you have questions during the lab, **ask your instructor.**

There will be a 2-point subjective grade. The subjective grade will be determined by the instructor's assessment of such things as whether or not you talk to other students or if you obviously look at what other students are doing. You may have a second sample, but it will cost you 2 points.

**Instructions.** You will be given 4.0 mL of a methylene chloride solution containing fluorene (a neutral compound) and an **acid** impurity. The weight of fluorene will be between 0.15 - 0.25 g. Your goal is to isolate the neutral compound and determine its weight and melting point. To remove the impurity, you should extract the methylene chloride solution with two 2-mL portions of either 1.0M NaOH or 1.0M HCl. After drying the organic layer, evaporate off the methylene chloride. Weigh the solid and determine the melting point. The melting point should be between 105-125 °C.



Fluorene:

Turn in this sheet and your sample in a vial labeled as follows: your name, the name of the compound, weight of sample, and mp. You will be graded on the recovery and purity, as determined by appearance and melting point. Record the recovery and melting point below

Recovered weight of sample \_\_\_\_\_

Melting point of sample \_\_\_\_\_