MORAVIAN COLLEGE CHEMISTRY DEPARTMENT

Chemistry 212L

Organic Laboratory

LABORATORY MANUAL

Spring Semester 2012

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# Part I: Introduction

## Weekly Schedule

### Week 1

#### Laboratory Discussion
(Monday, January 16)

**Topic:** Regular Class Period

**Laboratory Periods**
(T-Th, January 17-19)

**Assignment:**
- **Lab Manual:** Read:
  - Experiment 1: How Can We Tell the Difference Between Stereoisomers and Why is it Important for NSAID Drugs?
    - **A. What are chiral compounds and how can we recognize them?**
      - (pp. Ex1-1 & Ex1-2)
    - **CGWW:** Stereogenic Centres: (pp. 384-385)
  - **Topic:** Configurational Isomers – Lab Manual Part V A pp. A3-A6

#### Week 2

#### Laboratory Discussion
(Monday, January 23)

**Assignment:**
- **Lab Manual:** Read:
  - Experiment 1: How Can We Tell the Difference Between Stereoisomers and Why is it Important for NSAID Drugs?
    - **B. How can we isolate the drugs?**
      - Part V A: Stereoisomers pp. A7 & A8
    - **Padías:** Extraction (pp. 116-127)
    - **Chem 211-10 Lab Manual Appendices A & B** (pp. A1-B2)
    - **CGWW:** Chiral Compounds, Enantiomers & Diastereomers: (pp. 386-392)
    - **Website:** Experiment 1: Part B Prelab.
  - **Topic:** Isolation of acidic compounds & Chirality and Optical Activity – Lab Manual Part V A pp. A7-A8

**Laboratory Periods**
(T-Th, January 24-26)

**Activity:**
- **Experiment 1:** How Can We Tell the Difference Between Stereoisomers and Why is it Important for NSAID Drugs? (See Website)
  - **B. How can we isolate the drugs?**
### Week 3

**Laboratory Discussion**  
(Monday, January 30)

| Assignment: | Lab Manual: | Experiment 1: How Can We Tell the Difference Between Stereoisomers and Why is it important for NSAID Drugs? (pp. 27-34)  
C. *How can we characterize their stereoisomers?*  
Part V A: Stereoisomers: Complete Out of Class Applications on pp. A9-A10  
Padías: | Optical Rotation (Polarimetry) (pp. 54-58)  
CGWW: | Optical Activity pp. 388-389  
Website: | Experiment 1: Part C Prelab.  
Topic: | Chirality and Optical Activity (continued) and Nomenclature of Chiral Compounds |

### Week 4

**Laboratory Discussion**  
(Monday, February 6)

| Assignment: | Lab Manual: | Experiment 2  
A. What experiments will allow us to determine the cause of different reaction outcomes for vanillin acetylation in acidic vs. basic reaction mixtures if they occur? (EX-2-1 & EX-2-2)  
Website: | Experiment 2: Part A Prelab.  
Topic: | Discussion of answers to the Question of the Week and How do we Determine Structures of Organic Compounds from Spectra? |

### Week 5

**Laboratory Discussion**  
(Monday, February 13)

Website: | Experiment 2: Part B Prelab.  
Topics: | Retrosynthetic Approach for Synthesis of Organic Compounds: Alcohol Synthesis  
Activity: | Experiment 2  
A. What experiments will allow us to determine the cause of different reaction outcomes for vanillin acetylation in acidic vs. basic reaction mixtures if they occur?  
B. *How can we determine the structures of the products?* |
### Week 6

**Laboratory Discussion**

(Monday, February 20)


**Website:** Experiment 2: Part C Prelab.

**Topics:** Retrosynthetic Approach for Synthesis of Organic Compounds: Alkene Synthesis

**Laboratory Periods**

(T-Th, February 21-23)

**Activity:** Experiment 2  How Can We Determine if Acid and Base Catalysis Work Equally Well in Acyl Substitution Reactions?

C. What do our results reveal about structures and reaction conditions that cause unexpected acetylation products to form and what new mechanisms are operating?

**Due:** Report on Experiment 1

### Week 7

**Laboratory Discussion**

(Monday, February 27)

**Assignment:** Lab Manual: Experiment 3: How can a Complex Alkene be Synthesized? *A multi-step synthesis of 2-methylheptenes.* (See Website)

A. How can we choose starting materials for the synthesis and get the synthesis started? (pp. EX-3-1 & EX-3-2)

Part V C sec. C. Alkene Synthesis by Dehydration of Alcohols: Out of class applications (p. C8)

**Website:** Experiment 3: Part A Prelab.

**Topics:** Discussion of Out of Class Applications from Lab Manual p. C 8 and Choice of Starting Materials for Synthesis of 2-Methylheptenes

**Laboratory Periods**

(T-Th, February 28 - March 1)

**Activity:** Experiment 3: How can a Complex Alkene be Synthesized? *A multi-step synthesis of 2-methylheptenes.* (See Website)

A. How can we choose starting materials for the synthesis and get the synthesis started?
Week 8
Laboratory Discussion
(Monday, March 12)

Assignment: Experiment 3: How can a Complex Alkene be Synthesized?
A multi-step synthesis of 2-methylheptenes. (See Website)
A. How can we choose starting materials for the synthesis and get the synthesis started?
Part V C sec. D. Oxidation of Alcohols to Ketones: Complete FGI Oxidation (p. C8)

Website: Experiment 3: Part A Prelab. 2

Topics:
Alcohol Oxidation
and
Multiple Disconnections in Organic Syntheses

Laboratory Periods
(T-Th March 13-15)

Activity: Experiment 3: How can a Complex Alkene be Synthesized?
A multi-step synthesis of 2-methylheptenes.
A. How can we choose starting materials for the synthesis and get the synthesis started?

Due: Report on Experiment 2

Week 9
Laboratory Discussion
(Monday, March 19)

Assignment: Lab Manual: Experiment 3: How can a Complex Alkene be Synthesized?
A multi-step synthesis of 2-methylheptenes. (See Website)
B. What is the outcome of the dehydration of an alcohol?
Part V C sec. D. Oxidation of Alcohols to Ketones: Out of class applications (p. C9)

Website: Experiment 3: Part B Prelab. 2
Alcohol Oxidation
and

Topics:
Multiple Disconnections in Organic Syntheses

Laboratory Periods
(T-Th March 20-22)

Activity: Experiment 3: How can a Complex Alkene be Synthesized?
A multi-step synthesis of 2-methylheptenes.
B. What is the outcome of the dehydration of an alcohol?

Week 10
Laboratory Discussion
(Monday, March 26)

Assignment: Regular class period

Laboratory Periods
(T-Th March 27-29)

Activity: Experiment 3: How can a Complex Alkene be Synthesized?
A multi-step synthesis of 2-methylheptenes. (See Website)
B. What is the outcome of the dehydration of an alcohol?
### Week 11

**Laboratory Discussion**  
(Monday, April 2)

**Assignment:**  
A. *What reactions should be studied and how might we analyze the products?* (See pp. EX-4-1 and the Expt 4 Part A page of the Website)

**Review Summaries of Class Activities on Elimination Reactions**  
CGWW: Eliminations: pp. 477-488

**Website:**  
**Experiment 4: Part A Prelab.**

**Topic:**  
Choices of reactions and analytical methods for Experiment 4 Part A

**Laboratory Periods**  
(T-Th April 3-5)

**Activity:**  
Experiment 4: What Can Identities of Products Tells Us About Mechanisms of Elimination Reactions of Alcohols and Alkyl halides?  
A. *What reactions should be studied and how might we analyze the products?* (See Website)

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### Week 12

**Laboratory Discussion**  
(Monday, April 9)

**Assignment:**  
Easter Break

**Laboratory Periods**  
(T-Th April 10-12)

**Activity:**  
Experiment 4: What Can Identities of Products Tells Us About Mechanisms of Elimination Reactions of Alcohols and Alkyl halides?  
B. *How do product identities help us determine the reaction mechanism?* (See Website)

**Due:**  
Report on Experiment 3
<table>
<thead>
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<tr>
<td><strong>Laboratory Discussion</strong></td>
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<td>(Tuesday, April 16)</td>
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<td><strong>Assignment:</strong> Lab Manual: Experiment 5: Do Aromatic Halides Behave Like Alkyl Halides? <em>Part A: What Structures Favor Reactions?</em> (pp. EX-5-1 &amp; Ex-5-2)</td>
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<tr>
<td>Review Summaries of Class Activities on Substitution Reactions at Saturated Carbon</td>
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<td>CGWW: Substitutions pp. 407-441</td>
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<td><strong>Website:</strong> Experiment 4: Part B Prelab.</td>
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<tr>
<td><strong>Topic:</strong> Experiment 5: Do Aromatic Halides Behave Like Alkyl Halides? <em>Part A: What Structures Favor Reactions?</em></td>
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<tr>
<td>(T-Th April 17-19)</td>
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<td><strong>Activity:</strong> Experiment 5: Do Aromatic Halides Behave Like Alkyl or Acyl Halides?</td>
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<td><strong>Due:</strong> Report on Experiment 4</td>
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<td>CGWW: Nucleophilic Substitution pp. 411-426</td>
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<td><strong>Website:</strong> Experiment 5:</td>
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<tr>
<td><strong>Topic:</strong> Prediction of outcomes expected for S_N1 and S_N2 reactions for compounds studied in Experiment 5.</td>
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<td><strong>Activity:</strong> Experiment 5: Do Aromatic Halides Behave Like Alkyl Halides?</td>
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<td>Discussion of all-class data for Experiment 5 &amp; Check Out</td>
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<td><strong>Due:</strong> Lab report for Experiment 5 - due by the end your last lab period.</td>
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The laboratory part of Chemistry 211-212 is designed as an exploratory introduction to several major standard techniques in the contexts they are used by organic chemists to solve problems in the laboratory. The Chemistry 212 laboratory will continue to introduce new techniques but will also employ those you discovered in Chemistry 211. This semester you will study organic isomerism, synthesize organic molecules and investigate both the outcomes and mechanisms of organic reactions.

This semester you will be exploring more complex problems than you did in CH 211, so again, IT IS ABSOLUTELY ESSENTIAL THAT YOU PREPARE FOR EACH EXPERIMENT AHEAD OF TIME. Without a general understanding of the overall goals of each Experiment, and a plan for carrying out the procedure, you will have great difficulty in successfully completing the work presented to you.

Administrative Details.

Required Materials; (Same as for CHEM 211L)

Lab Text:  

Lab Notebook: must have a hard cover and be permanently bound (not spiral), must also fit into the inside pocket of your data binder. (Can continue in CHEM 211 notebook)

Data Binder:  A 1.5-inch three-ring loose-leaf binder with a hard cover and at least 9 tab dividers and an inside pocket that will accommodate your lab notebook.

Grades: In general, satisfactory preparation for each lab period, completion of all work, laboratory notebook records and laboratory reports including answers to all prelab and postlab questions will earn a grade of B for the lab. Higher grades will be given for demonstration of excellent understanding of the concepts, preparation for the lab periods, performance in the lab, well organized and thorough lab records and well-written lab reports.

Your grade for the laboratory portion of the course will be calculated as indicated below:

- 30% The quality and completeness of the laboratory notebook and data binder
- 30% The quality and completeness of the laboratory reports
- 25% Performance in the laboratory
- 10% Preparation for each laboratory period (Includes completion of electronic pre-lab assignments, contributions to pre-lab discussions and initial awareness of experiment requirements.)
- 5% Attendance in the laboratory discussion (AM) and laboratory (PM) periods

Attendance

Students are required to attend all laboratory discussions (Mon. 8:55-9:45 AM) and all scheduled laboratory periods (See the Weekly Schedule on pp. 2-8) unless excused due to a valid medical excuse (verified by a physician, the Health Center or Dean of Students' office) or other accepted prior excuse. Make-ups or grade adjustments for excused absences will be arranged. Grades for work missed due to unexcused absences will be zero.

Note: Trips scheduled for other courses or travel schedules for weekends or breaks are NOT acceptable excuses for missing lab discussions or lab periods.
Lab Records

Notebook
As in CHEM 211L, all notebooks must be permanently bound hard cover record books not spiral bound books. Your records must be permanent; so all entries must be made in non-erasable ink. You may continue with the same notebook used in CHEM 211L, but you must be sure the laboratory section designation on the front is correct for this semester. Whether you use your CHEM 211L notebook or not, you should have the material from CHEM 211L available in the lab for information on lab techniques.

Data Binders
Again this semester, your data binder will provide you with a convenient place to keep the spectra, chromatographs and other sheets of data generated by your lab work. If it has sufficient space, you may continue to use the your binder from CHEM 211L. Just add additional tabs for this semester’s Experiments in front of last semesters tabs and be sure the laboratory section designation on the front is correct for this semester. Whether you use your CHEM 211L binder or not, you should have the material from CHEM 211L available in the lab for information on lab techniques.

Laboratory Reports
Once your laboratory work on each experiment is complete you will summarize and interpret your results in a formal group laboratory report as you did for experiment 7 last semester. As for last semester, all reports will be prepared using a word processing program. The Weekly Schedule (pp. 2-8) lists specific due dates for your laboratory reports. The format for lab reports is provided in Part II (pp. 18-19) and specific instructions for each report will be provided on the course website for each experiment.
Part II: Laboratory Rules and Regulations:

General Daily Routines
Because of the increased complexity of this semester’s experiments, it is more essential than it was last semester that you prepare for each experiment ahead of time. You have a limited amount of time in the laboratory each week to collect data, so you need to be ready to work when you arrive. The lab is designed to begin at 12:45 (T-R) or 1:15 PM (W) and end at 3:45 (T-R) or 4:15 PM (W). You are expected to be able to complete your assigned work in that time period. Only with a general understanding of the concepts and techniques to be applied to a given problem will you be able to reach the goals of each experiment in the time provided. Again to help you prepare, there will be assigned background reading to assist you in responding to the QOW for each experiment, an electronic pre-lab assignment and a laboratory discussion on Monday mornings (See the CHEM 212L weekly schedule pp. 2-8). All of the assigned reading is to be done and the electronic pre-lab assignment submitted by e-mail before 10:00 PM on Sunday of each week. Come to the Monday discussion ready to suggest answers to the QOW and bring any questions you have so that we can solve problems before they arise. At the end of each lab period your laboratory notebook may be collected, it will be checked by your instructor and returned to you by the following morning. This check is designed to give you assistance in keeping appropriate laboratory records.

The listing of laboratory report due-dates in the laboratory schedule (See pp. 2-8) should provide you with sufficient notice to organize your group to complete required work, so the deadlines for laboratory reports are firm. (Note: http://www.doodle.com/ can be very helpful for scheduling group meetings) Since you are now familiar with several techniques, you should be able to work efficiently so that you will be able to keep several different procedures going at once. You have experience with recognizing when your data are good enough to support conclusions and when you need to repeat a procedure that did not yield data that are good enough to fulfill your needs. As you should have found last semester, it is more efficient to work with care and produce good results than to rush through a procedure just to get it finished. Remember, the purpose of each experiment is to answer a specific question. Be sure to ask for help if things seem confusing. You are here to learn; we do not expect you to be able to do everything perfectly at once. Enjoy yourself as you learn.

Post-lab Routine
At the end of each lab period:
- Wipe off your personal bench-top area.
- Clear any debris from your sink.
- Check that the common drawer and sink items are in place (see equipment lists on the next page).
- Wash your hands.
- If requested, submit your laboratory notebook and data binder to your instructor. They will be checked and left on the shelf outside 213 Collier hall of Science for you to pick up.

Use, Care and Replacement of Laboratory Equipment.
- At the end of each lab day, equipment that is left around the lab will be placed on a table at the back of the lab where it will be available for any student in the course. If you lose or break a piece of equipment check the bin for a replacement. If none is available, ask your lab assistant for a replacement. There is no charge for replacement of broken equipment; however, materials used in this laboratory are expensive so try to be careful. Also, excessive loss or breakage can be an indication of poor organization, technique or lack of preparation and can adversely affect your lab grade.

Labeling
All samples that are stored in your tote tray or turned in to your instructor must be labeled according to the following format:

<table>
<thead>
<tr>
<th>Identification of Substance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lab Notebook page</td>
</tr>
<tr>
<td>Date</td>
</tr>
<tr>
<td>Student Name</td>
</tr>
<tr>
<td>Lab Section Day</td>
</tr>
</tbody>
</table>

Figure 1: Sample Compound Label
### Personal Tote Tray Contents

- **5** Beakers, 100, 250, 400, 600, 1000 ml
- **1** Büchner or Hirsh funnel w/ rubber adapter
- **1** Conical funnel
- **5** Droppers
- **8** Erlenmeyer flasks, 50, 3x125, 2x250, 2x500 ml
- **1** Filter flask, 500 ml
- **2** Graduated cylinders: 10, 50 ml
- **1** Powder funnel
- **1** Ruler, 6 in.
- **1** Scupula
- **1** Separatory 250 ml funnel w/ stopper & stopcock
- **1** Spatula
- **10** Test tubes, 10x75 mm
- **6** Test tubes, 13x100 mm
- **6** Test tubes, 15x150 mm
- **2** Test tubes, 25x175 mm
- **3** Vials, w/ caps
- **2** Watch glasses
- **1** Stemless funnel
- **1** Stirring rod
- **1** Test tube clamp
- **1** Test tube rack
- **1** Test tube block
- **10** Test tubes, 10x75 mm
- **6** Test tubes, 13x100 mm
- **6** Test tubes, 15x150 mm
- **2** Test tubes, 25x175 mm
- **Goggles ($5 replacement fee if lost)**

### Common Drawer Equipment

- **3** Ring stands (bench top)
- **1** Current regulator
- **1** Heating well
- **1** Iron ring
- **1** Jar, glass w/ screw top
- **1** Magnetic stirrer
- **1** Mortar and pestle
- **1** pH paper vial
- **4** Rubber tubings, including 1 w/ thick wall
- **1** Tongs
- **4** Utility clamps w/ fasteners
- **2** Wood blocks &/or cork rings
- **1** Wire gauze

### Sink Area Equipment

- **2** Cleaning brushes (large and small)
- **1** H₂O Wash bottle
- **1** Soap Wash bottle
- **1** Acetone Wash bottle, (shared with other sink)
- **2** Water baths
- **1** Roll of labeling tape

See Lehman pp. 276, 279 for pictures of most of the equipment on this list.
**Safety Regulations**

*Laboratory Neatness.*

Neatness is essential for safety and for efficient work in the laboratory.
- Keep the lab uncluttered by leaving book bags and all non-essential books in the front of the laboratory. Outer-clothing should be hung on the pegs in the hall or the front or back of the laboratory.
- If you spill anything anywhere in the laboratory, clean it up immediately and leave a clean space for your neighbors. This applies particularly to the balances and melting point apparatuses.
- If problems arise, then each week specific students will be given responsibility for seeing that certain areas are clean and orderly at the end of the period. Please cooperate.
- If you spill acids, bases or other corrosive chemicals, inform the instructor and wash contaminated surfaces with copious amounts of water, and then neutralize as directed by the instructor.
- For reasons of safety and obtaining dependable results, all glassware must be thoroughly clean. After disposing of contents responsibly (see waste disposal instructions for each exploration), wash glassware with hot soapy water and a test tube brush. In some cases, organic compounds are most effectively removed by an acetone pre-rinse followed by a soap and water wash.

**Use of Reagents.**

- Most of the reagents used in this laboratory are irritants and/or toxic. Be careful handling reagents. Gloves are available should you wish to use them, but remember that gloves do not give you 100% protection from all lab reagents. If reagents come in contact with your skin or gloves, wash them off immediately with soap and water. It is also a good practice to wash your hands periodically to remove any material that may have been left on your hands by incidental contact. Finally, be sure to wash your hands with soap and hot water before leaving the laboratory.
- Use reagent bottles only in the areas where they are provided. Solid reagents for this course will be set out on benches at the side of the laboratory near the balances, and occasionally under the hood. Volatile or corrosive liquid reagents will be under the hood.
- Try to take no more of the reagents than you need.
- If by accident you take an excess amount of a reagent, share it with a fellow student or dispose of the excess as instructed (see Table 1 below). Never pour anything back into a reagent bottle.
- Always dispose of chemicals properly.

In general, organic wastes are divided into two classes: "halogenated", compounds containing one or more atoms of F, Cl, Br, or I; and "non-halogenated", compounds containing no halogen atoms. For each exploration all reagents will be assigned to waste disposal categories.

For disposal purposes we have five categories of chemical wastes:

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<thead>
<tr>
<th>Category</th>
<th>Compound Type</th>
<th>Disposal</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Non-halogenated organic solids</td>
<td>Labeled waste containers in waste hood</td>
</tr>
<tr>
<td>2</td>
<td>Halogenated organic solids</td>
<td>Labeled waste containers in waste hood</td>
</tr>
<tr>
<td>3</td>
<td>Water-insoluble - halogenated organic liquids</td>
<td>Labeled waste containers in waste hood</td>
</tr>
<tr>
<td>4</td>
<td>Water-insoluble non-halogenated organic liquids</td>
<td>Labeled waste containers in waste hood</td>
</tr>
<tr>
<td>5</td>
<td>Acidic or Basic aqueous solutions</td>
<td>Labeled waste containers in waste hood</td>
</tr>
<tr>
<td>6</td>
<td>Water-soluble non-halogenated organic liquids</td>
<td>Down drains with a flow of cold water</td>
</tr>
<tr>
<td>7</td>
<td>Inorganic solids</td>
<td>Varies with compound</td>
</tr>
</tbody>
</table>

**Table 1: Laboratory Waste Disposal Categories**

As indicated in Table 1, compounds in categories 1-5 go into appropriately labeled waste containers in the waste hood at the back of the lab while category 6 compounds go down lab drains with a flow of cold water. Category 7 disposal varies with compound and is specified in each exploration.
Part III: Laboratory Record & Report Format

Notebook (You may continue with your CHEM211 if you have remaining space)

General Format and Procedures

On the front cover of your notebook, write your name and laboratory day.
Number all of the pages (both left- and right-hand) at the top of the page.

Reserve the first four numbered pages of each book for the table of contents. As the semester proceeds, enter the title of each experiment and designation of each activity (Part A, Part B, etc.) into your table of contents, along with the pages on which they are recorded. Note that the titles of experiments are required. The experiment and part designations are not sufficient.

Dating Records:
• Be sure to date the pages you use for the Pre-laboratory Discussion Notes.
• In the laboratory, insert the date at the top of each page used to record results obtained.
• At the end of each laboratory period date and initial your last data entry in each activity with newly recorded data.
• If you must insert data on an already dated page, initial and date the insertion.

Laboratory Notebook Records

Diagrams and descriptions are given below to illustrate where information must be entered into your laboratory notebook. Some experiments may not require all possible sections (see individual experiment descriptions). In those cases, simply omit unnecessary parts, but keep the others in the order and position (left- or right-hand page) as indicated below.

<table>
<thead>
<tr>
<th>Left-hand Page</th>
<th>Right-hand Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>p. #</td>
<td>p. #</td>
</tr>
<tr>
<td>Title of the Experiment</td>
<td>Notes (Continued)</td>
</tr>
<tr>
<td>Name of Groupmate(s)</td>
<td></td>
</tr>
<tr>
<td>Question of the Day</td>
<td></td>
</tr>
<tr>
<td>Pre-lab Discussion Notes</td>
<td></td>
</tr>
<tr>
<td>Continue on the right-hand page</td>
<td>Always go to next pair of clear facing pages to start your Table of Compounds and Waste Disposal Instructions.</td>
</tr>
</tbody>
</table>

Figure 2. First Set of Pages of an Experiment (Always starts on a clear set of left- and right-hand pages):

Title of the Experiment

Each new experiment or part should always begin on a clean pair of facing left- and right-hand pages. The title of the experiment should be at the top of the left-hand page. If an experiment has more than one part (as with Experiment 1), the work for each part should be reported separately with the titles of both the experiment and the part at the beginning of each new part. Experiment numbers are not sufficient.

Names of Partners or Groupmates:

When you will be working with labmates, enter their full names below the title of the experiment or activity.

Question of the Week (QOW)

Each experiment will start with a question that will be explored in the pre-lab discussion. The QOW will often be the title of the experiment.

Pre-lab Discussion Notes

Your notes from the pre-lab discussion are to be recorded on this first set of pages for the experiment and each page is to be dated.
Objectives:

Each experiment has one or more objectives. They should be enumerated in this section, which is placed at the top of the first left-hand page following the pre-lab notes.

Table of Compounds:

This is a list of names as well as important physical (mp or bp, density, solubility in acid, base and common organic compounds) and chemical properties (acidity, basicity or flammability) of the compounds used in the experiment. When required for an experiment, this table should be located on the left-hand page immediately following your pre-lab discussion notes. Unless otherwise directed, never put the Table of Compounds in your data binder; it must be in your notebook.

Waste Disposal Instructions:

Most of the compounds that you will encounter in this course are irritants or toxic. To avoid polluting you, your classmates, and our environment, we must be careful to dispose of chemical waste properly. Thus, each experiment will provide instructions for disposal of excess reagents. These instructions should be written in your notebook, at the top of the right-hand page opposite the table of compounds. Follow these instructions carefully.

Chemical Equations:

When experiments involve chemical reactions, chemical equations for the reactions should be written using structural formulas of the organic compounds. Equations should be on the right-hand page below the waste disposal instructions.

Results Step #'s must be opposite the corresponding Procedure Steps.

↓ Continues to the next left-hand page.

↓ Continues to the next right-hand page.
III: Laboratory Record & Report Format

Procedure: (Figure 4) (Always starts on next clear set of left- and right-hand pages):

- Procedure consists of sequentially numbered steps (1, 2, 3, etc.) to be carried out in the laboratory. These steps should represent your understanding of the procedure you followed in collecting your data. The steps should be separated by at least one line to allow for any modifications that might be necessary as you work in the laboratory. Steps need not be written in complete sentences, but should be concise, complete and clear enough that someone else could repeat your work. This section should be organized to facilitate your work in the lab. Procedure should be written after the pre-lab discussion and before you start work in the laboratory.

NOTE: When using a procedure for the first time (e.g. distillation), include the complete procedure in your notebook, including diagrams of apparatus. When you repeat the same procedure in a later experiment, include a reference (with experiment and notebook page number) to the original time you used the procedure.

- Begin the Procedure at the top of the next available left-hand page after the Waste Disposal Instructions or Chemical Equations.

Results: (Figure 4) (always starts on the right-hand page opposite the beginning of the Procedure):

- Consist of observations that may be used as indications that an experiment is proceeding properly or data collected as the result of a procedural step. Observations such as color changes, pH, evolution of gas and/or heat, violent reactions, dissolution of a solid, etc. and data such as wts., volumes, mp's, bp's, etc. should be recorded in your notebook Results section as the work proceeds.

- Each entry in your Results section should be directly opposite the procedure step to which it refers and be designated with the number of that step. (As illustrated in the diagram above) When data cannot be conveniently attached to the results section, it should be kept in the appropriate section of your data binder and a note to "see data binder - Experiment #" should be included at the appropriate position in your results section. (See the Data Binder section below).

Data Binder

General Description
Your data binder needs to be a 1.5-inch, 3-ring, loose-leaf notebook binder with your name on the spine and front cover (lab label tape works for this). It must have a pocket sufficient to accommodate your lab notebook on the inside of its front cover and contain at least 6 tab dividers that separate the sections described below. Your data binder will be used to store data (e.g. thin-layer chromatography plates, infrared, mass and NMR spectra, etc.) that don't fit conveniently into your notebook. Also place returned lab reports in their appropriate section.

Sections (Tab Dividers)
- Lab Manual (Place 1st tab after this.)
- Weekly Post-lab Notebook Checklists: All checklists are to be kept in chronological order in this section.
- Experiment 1
- Experiment 2
- Experiment 3
- Experiment 4
- Experiment 5

General Format
On the front cover and spine of your data binder, write your name and laboratory day.

Organization of Sections
Each section should be labeled as indicated above. Materials to be included in each section must have 3-holes that match the rings of the binder or be permanently attached to a sheet that has the appropriate holes. Specific suggestions for certain types of items to be stored in the Experiment sections are:
• The CHEM 212 Experiment sheets describing the experiment
• Flow Diagram (see Appendix A, pp. A-1 – A2): Some laboratory procedures profit from being presented in a diagram that outlines the procedure followed. When such a "flow diagram" is appropriate, it should be prepared in the process of devising the procedure and included in the appropriate experiment section.
• Spectra collected from the experiment: They will be produced on punched paper or paper that can be punched.
• Thin-layer plates produced in the experiment: Must be taped or stapled to 8.5 X 11 inch punched paper, which will fit your data binder. Three-hole paper is available in the laboratory.

**Labeling and Cross Referencing Data:**
Each piece of data placed in your binder must be labeled with your name and a description of the data and a reference to the page of your notebook and number of the procedure step that produced the item. Descriptions must be sufficient to identify the data without reference to the notebook. (e.g. "A. B. Smith notebook page 36, step 4.-IR spectrum of Unknown X")

In addition, your notebook results section should have an entry to indicate that the data from a procedure step is in your data binder. (e.g. For the spectrum shown above, write next to step 4 on p. 37 of your notebook, which is a Results page, "Spectrum of X can be found in Experiment 3 of my data binder.")

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Obtain 2.2 g A.</td>
<td>3. 2.351 g A</td>
</tr>
<tr>
<td>5. Add A to 25 mL 2 M HCl.</td>
<td>4. White gas and fine pink ppt. form</td>
</tr>
<tr>
<td>7. Obtain IR spectrum of X</td>
<td>6. Spectrum of X can be found in Experiment 3 of my data binder.</td>
</tr>
</tbody>
</table>
**Group Laboratory Reports**

**General Description**

After completing all activities in an experiment you will collaborate with your groupmates to compile and analyze your data and data from the whole class and then write a report on your findings. Your analyses will usually be assisted by in-lab and post-lab questions distributed for most experiments. Each report will have its own specific issues that must be addressed and questions to answer as part of your group report; however all reports will follow the same general format that is outlined below.

**Required General Format**

Fonts and Spacing

All reports are to be produced with word processing software using the following parameters:

- **Font:** 12 point
- **Text Color:** Black
- **Margins:** 1 Inch (left, right, top & bottom)
- **Spacing:** Double Space

Headers (on all pages after the first page) including: your group name, page numbers and Experiment # in this form:

| The Distillers | 3 | Experiment 4 |

**Required Sections:**

**First Page:**

**Description**

First line: (centered near the top of the page) - your lab day

Second line: your lab group name

Third & Fourth lines: complete names of all group members (two or more on each line)

Fifth line: date the report is submitted

Next few lines: The experiment number and title of the experiment

**Question of the Week section**

See the Figure 4.

**The Question of the Week:**

In this section, state The Question of the Week and then provide a brief (100 words or less) statement of your group’s initial claims concerning the QOW, the evidence supporting your initial claims and warrants explaining how your evidence leads to your initial group claims. Then briefly describe the experimental plan that was developed to answer to the QOW. There should also be some discussion of how the experimental plan was developed during your pre-lab work. In experiments that covered more than one QOW, include all Questions of the Week sequentially with a separate description of the experimental plan for each week. (150 words total)

**Second Page:**

**Summary of Results:**

BEFORE preparing your Summary of Results, you must analyze your data and determine your group’s final claims concerning the QOW for the experiment. (Much of this analysis may be developed in the Post-lab discussions.) Then, organize your data parallel to your final claims and warrants. Include graphs and/or tables that summarize your results in an organized manner such that it can be easily cited in your warrants.
Types of Data Presentations: Summaries of spectral data should include the specific spectral characteristics (peak positions, shapes and/or multiplicities) that are important in interpreting the spectra. When creating tables, use page breaks to keep tables from being split between pages of your report. When a table is too long to fit on one page, repeat the header row, which contains the column definitions, at the top row on each new page. If you need assistance with page breaks or other word processing techniques, consult your instructor before submitting your report.

Each item in this section should have:
- A designation (e.g. Table 1, Figure 1, etc.) to facilitate citing in your discussion.
- A descriptive title to indicate what data is being presented (e.g. Boiling Points of Products).
- Specific references to laboratory notebook and/or data binder pages containing the original data. (Indicate both group member’s name and pages containing the data.)

Next New Page:

Discussion and Conclusions:
In this section provide your group’s final claims that are based on all results available from the experiment and warrants needed to show how each claim is supported by specific data entries in the Summary of Results section. The warrants, directly supported by specifically cited data entries, are most important, since unsupported claims are worth very little. Statements such as "The IR and mass spectra from table 1 indicate that unknown # 3 is 4-hydroxybenzoic acid," and "As indicated in Figure 2, the mp of compounds is unaffected by their molecular masses," are not acceptable warrants since they are too vague and lack specific interpretations of the data that lead to the claim. You must explain the reasoning process that allowed you to discern your claim from the cited data. E.g. "The IR absorptions 3300 cm⁻¹ (Br & St)(O-H stretch) and 1715 cm⁻¹ (C=O stretch) suggest the presence of a carboxylic acid and the M⁺ ion at m/e = 138 are consistent with unknown # 3 being 4-hydroxybenzoic acid" or "The plot in Figure 2 shows no correlation between the mp and molecular mass of the compounds studied, so our claim is that mp is unaffected by changes in molecular mass."

Remember that your warrants should be clear and concise. Excessively long and wandering responses, which attempt to include all information that might be relevant to the question in hopes of hitting something that is correct, will not be graded.

Next New Page:

Reflections:
This section provides an opportunity for you to look back on the experiences in the experiment to think about how they have affected your understanding of the concepts developed from answering the QOW and how they provided warrants justifying the claims based on data and other evidence. First compare your group’s initial and final claims, the data or evidence that supported each and the warrants justifying each set of claims. Finally, briefly explain your current understanding of concepts developed or supported by your experience and provide warrants to justify your positions.

Appendix
This section includes:
- One copy of all CHEM 212 Experiment sheets provided to you for the experiment.
- All primary data record pages from all group member data binders. These sheets must be numbered and have appropriate titles and references to notebook pages. They are attached to the lab report with a binder clip. When your graded lab report is returned to you, place the report and the data binder materials back in the proper binder tabs.

Personal Electronic Blog Comment for the Week
For weeks when group lab reports are due, your weekly personal blog comment (See course Syllabus) will be dedicated to your lab report experience. In this comment you will assess your contributions and those of your group mates toward the data analysis and preparation of the group lab report. You will rate each group member’s contributions (including your own) on a scale of 0 to 5. (5 is highest) These ratings will be used to give each group member an appropriate grade for the group report.
COLLABORATION AND ACADEMIC HONESTY

Collaboration among students in class and in preparation for class discussion is generally encouraged and required for most classes. Educational research indicates that students learn best when they engage in discussions and analyses of class material with their peers. However, the final version of all written work submitted for evaluation must be prepared without consultation with other students. To be fair to all students in the course and to assure maximum learning for each student, we follow all the guidelines for academic honesty spelled out in the Moravian College Student Handbook (See College Website http://www.moravian.edu/studentLife/handbook/academic/academic2.html).

DISABILITY SUPPORT

Students who wish to request accommodations in this class for a disability should contact Mr. Joe Kempfer, Assistant Director of Learning Services for Disability Support, 1307 Main Street (extension 1510). Accommodations cannot be provided until authorization is received from the office of Learning Services.
Experiment 1

How Can We Tell the Difference Between Stereoisomers and Why is it Important for NSAID Drugs?

Introduction:
Most of us have taken Advil, Midol IB, Motrin, Nuprin, Actron, Orudis, Aleve, Anaprox or Naprosyn as a pain releaver at some time or other. These drugs are a sub group of the Non-steroidal Anti-inflammatory class of drugs (NSAIDS) that also incudes aspirin, celebrex, vioxx and bextra among others. NSAIDS have a range of medicinal effects: analgesic (pain relief) anti-inflammatory (reduction of inflammation in wounds and joints) and antipyretic (reduction of fever). They are often recommended or prescribed for chronic problems such as arthritis. More information on NSAIDS is available from the following website and its links (http://www.medicinenet.com/nonsteroidal_antiinflammatory_drugs/article.htm). There has been considerable controversy as to the safety of some NSAIDS, with two drugs vioxx and betrex having been removed form the market in recent years.

NSAID produce their effects by inhibiting the class of enzymes called cyclooxygenases, which catalyze the formation of prostaglandins and thromboxane from arachidonic acid. One such reaction is provided in Equation 1. There are many prostaglandins that have various physiological effects.

\[
\text{Arachidonic Acid} + 2 \text{O}_2 \xrightarrow{\text{COX}} \text{Prostaglandin PGH}_2 + \text{H}_2\text{O} 
\]

In this experiment we will explore a subclass of NSAIDS that are derivatives of propanoic acid (Sometimes also referred to as propionic acids or proprionic acids). The structures of these drugs, ibuprofen and naproxen are provided at the beginning of this handout. As is illustrated by the structures, these two drugs have one stereogenic center and therefore have two configurational isomeric forms (label \(S\) and \(R\)). Because enzymes also contain stereogenic centers and only one configurational isomer of each enzyme is formed in a living system, the two different stereoisomers of the NSAID drugs have different medicinal effects. For the two drugs we will explore, the \(S\)-form inhibits the cyclooxygenases while the \(R\)-form does not. Unfortunately, chemical synthesis generally produces an equal mixture (racemic mixture) of the two stereoisomeric forms and the separation of the isomers can be difficult and expensive. So often drugs are sold as mixtures of the active and inactive isomers. With NSAIDS, some preparations are pure \(S\)-isomers and others are racemic mixtures of \(R\) & \(S\)-isomers.

In this experiment we will isolate the drugs from several brands of over the counter NSAID tablets, determine whether they contain the \(S\)-stereoisomer or a racemic mixture of the \(R\)- and \(S\)-stereoisomers and explore how racemic mixtures of stereoisomers might be separated.
Part A

What are chiral compounds and how can we recognize them?

Pre-lab Preparation Assignment:
1. Read:
   Lab Manual: Part A of these Experiment pages (pp. EX-1 & Ex-2)
   CGWW: Stereogenic Centres (pp. 384-385)
2. Bring this Laboratory Manual, your model kit and your proposed answers to the QOW to your afternoon lab section.

Objectives:
1. To define the structural requirements for a stereogenic center and how it can create configurational isomers.
2. To distinguish chiral molecules from achiral molecules.
3. To recognize stereogenic centers in complex molecule and use them to predict the number of possible configurational isomers of a given constitutional isomer.
4. To write and interpret Fischer Project representations of structures with multiple stereogenic centers.
5. To understand the relationships among different types of configurational isomers.

Question of the Week:
What are stereogenic centers and how do they lead to chirality in organic compounds?

Appendix A of the lab manual provides activities to help you to recognize a new class of stereoisomers, configurational isomers and how they relate to each other as well as to learn the terminology used in talking about them. (See p. A1)

Key Terms/concepts/techniques:
Stereogenic center
Chiral
Achiral
Fischer Projections
Enantiomer
Diastereomer
Epimer
Experiment 2

How Can We Determine if Acid and Base Catalysis Work Equally Well for Acyl Substitution Reactions?

Introduction:
In class we have found that all types of reactions of carbonyl compounds can be catalyzed by either acid or base. Acetic anhydride (See Scheme above) readily undergoes acyl substitution reactions with a variety nucleophiles under both acidic and basic conditions. Relatively acidic phenolic OH groups (pK_a ~10) such as that on vanillin in the scheme above usually serve as effective nucleophiles for acetic anhydride reactions. However, as the reaction scheme above indicates, reports suggest that the reaction of vanillin with acetic anhydride gives different products under basic conditions than under acidic conditions. This result is surprising; our mechanistic studies predict that both reactions should give vanillin acetate. Figure 1 shows the expected mechanism under basic conditions.

Figure 2 shows that the formation of vanillin acetate is equally reasonable under acidic reaction conditions.

The reaction of vanillin with acetic anhydride under basic conditions is reported to give the expected vanillin acetate (4-acetoxy-3-methoxybenzaldehyde) product. However, the reaction under acidic conditions has been reported to produce a different product. In this experiment, we will explore whether reactions of vanillin with acetic anhydride under acidic and basic conditions yield different products and, if so, which products are formed and what causes the difference in reactivity.
Part A

What experiments will allow us to determine the cause of different reaction outcomes for vanillin acetylation in acidic vs. basic reaction mixtures if they occur?

Pre-lab Preparation Assignment:
1. Read: These Experiment pages.
2. Review the Summaries of Class Discussions for all class activities on Carbonyl Reactions.
3. Complete the Prelab activity on the course website by 10:00 PM on Sunday, February 5.
4. In your lab notebook: (See Lab Manual pp. 14-16 for format)
   a. Update the Table of Contents
   b. Enter the title of this experiment and the Question of the Week.
6. Bring your notebook and ideas on answers to the Question of the Week and proposed structures to the Monday Lab Discussion period.
7. After the lab discussion, complete pre-lab assignment on the procedure handout to be provided on the course website on Monday.

Objectives:
1. To use previous experience to select appropriate experimental techniques to answer questions in the lab.
2. To analyze experimental results to obtain as much information about the outcome of a reaction as possible.
3. To use initial data analyses to devise experimental plans for additional studies of a reaction system.

Question of the Week:
What experiments will allow us to determine the cause of different reaction outcomes for vanillin acetylation in acidic vs. basic reaction mixtures if they occur?

How can we determine experimentally if the report of differences in outcomes of vanillin reactions in acid and base are correct? Specifically, what experiments should be done and how should the results be analyzed? What additional experiments might allow us to determine what aspects of vanillin’s structure might be responsible for vanillin’s apparently unexpected reactivity under acidic conditions? You have considerable experience with laboratory techniques for separating mixtures and determining structures of compounds. How can your experience and expertise be used to advantage on this problem?

Key Terms/concepts/techniques:
• Acyl substitution reaction mechanisms
• Acid & Base Catalysis
• Problem Solving in the Laboratory
Experiment 3

How Can a Complex Alkene be Synthesized?

R–Br $\rightarrow$ R–Mg–Br $\rightarrow$ R–O$^+$

Introduction:
In our Monday discussions we have been working on understanding how syntheses of organic compounds are devised. This experiment presents you with a relatively simple example of how one of the syntheses we developed can be carried out. As you recall, the syntheses that we devised involved three steps,

- Formation of a Grignard reagent, which is not isolated,
- Reaction of the Grignard reagent with an aldehyde or ketone to form an alcohol,
- Dehydration of the alcohol to form the final product alkene.

These syntheses illustrate how successive reactions can be linked together to produce an alkene with a particular carbon chain structure. The one question that we didn’t consider in our retrosynthetic analysis is the lack of specificity of double bond positioning in the dehydration reaction. Thus, the final aspect of this experiment is the determination of the relative amounts of the various possible alkene products that are actually formed in the reaction.

Part A
A. How can we choose starting materials for the synthesis and get the synthesis started?

Pre-lab Preparation Assignment:
1. Read:
   These Experiment pages.
2. In Padías: Review: Extraction (pp. 116-125) & Drying Agents (pp. 125-126).
3. In CGWW read:
   a. How to make a Grignard reagent (pp. 211-212)
   b. Secondary and tertiary alcohols: which organometallic, which aldehyde, which ketone? (pp. 220-222).
4. Complete the Prelab activity on the course website by 10:00 PM on Sunday, February 26.
5. In your lab notebook: (See Lab Manual pp. 14-16 for format.)
   a. Update the Table of Contents
   b. Enter the title of this experiment and the Question of the Week.
6. Bring your notebook and ideas on answers to the Question of the Week to the Monday Lab Discussion period.
7. After the lab discussion, complete pre-lab assignment on the procedure handout to be provided on Monday.
Objectives:
1. To develop techniques for running air sensitive reactions.
2. To implement a retrosynthetically devised synthesis in the laboratory.
3. To successfully complete a Grignard reaction.
4. To successfully complete a multistep synthesis.
5. To use gas chromatographic analysis to determine product distributions and yields of an organic reaction.

Question of the Week:
How can we choose starting materials for the synthesis and get the synthesis started?

In our retrosynthetic analyses activities we have used Grignard reagents to advantage in creating carbon structures. Our discussions have emphasized the need for absolute exclusion of water from Grignard reaction mixtures until the carbon-carbon bond forming reaction is complete. This experiment will give you an opportunity to experience the techniques required to successfully use a Grignard reagent in a multi-step synthesis of an organic compound. As we will discover, getting the synthesis started requires some special precautions. Reading the assigned sections in Padías and CGWW should give you some sense of the important factors that might affect the reaction, but you will need to think specifically about how an apparatus can be constructed to provide the appropriate environment for the reaction. You have had nearly two years of college chemistry laboratory experience. So, before coming to the Monday lab discussion, draw on your experience as well as the information from your class experience and reading in CGWW and Padías to devise an apparatus that could accomplish:

• Combining magnesium metal, dry ether and an alkyl halide in a dry atmosphere so that they can react to form a Grignard reagent.
• Successfully adding an aldehyde or ketone to the apparatus containing the newly synthesized Grignard reagent without admitting any moisture.
• Finally exposing the reaction mixture to an acidic aqueous solution to complete the formation of the alcohol product.

Be prepared to draw and explain the workings of your apparatus when you arrive at the Tuesday lab discussion.

Key Terms/concepts/techniques:
• Grignard Reaction.
• Organic Synthesis
• Retrosynthetic Analysis
Ex4-1

Experiment 4

What Can Identities of Products Tell Us About Mechanisms of Elimination Reactions of Alcohols and Alkyl Halides?

In Class Group Activities on Elimination Reactions, we saw that both aliphatic alcohols and alkyl halides can undergo elimination reactions to form alkenes. We discovered that eliminations appear to occur by two general mechanisms, E₁ and E₂. We used the dehydration of alcohols as a tool in our retrosynthetic analysis to develop syntheses of alkenes and applied the process in Experiment 3 to synthesize 2-methylheptenes. In our studies, we have some general structural and reaction condition considerations that could help us predict which mechanism might be operating in the elimination reaction of a specific compound under specified conditions. In this experiment we will employ some of the reactions and analytical techniques we learned in Experiment 3 and explore:

• The reaction conditions necessary to promote eliminations of alcohols and alkyl halides.
• How analysis of product mixtures can be used to determine the mechanism that is operating in different elimination reactions.

Pre-lab Preparation Assignment:
1. Read: This Experiment page.
2. Review the material in the Class Group Activities on Elimination Reactions and the procedure used for the final reaction step in Experiment 3.
3. Complete the Prelab activity on the course website by 10:00 PM on Sunday, April 1.
4. In your lab notebook: (See Lab Manual pp. 14-16 for format.)
   a. Update the Table of Contents
   b. Enter the title of this experiment and the Question of the Week.
5. Bring your notebook and ideas on answers to the Question of the Week to the Monday Lab Discussion period.
6. After the lab discussion, complete pre-lab assignment on the procedure handout to be provided on Monday.

Objectives:
1. To select appropriate reactants to explore the potential mechanism of an organic reaction.
2. To interpret product distribution data in terms of reaction mechanism.

Question of the Week:
What reactions should be studied and how might we analyze the products?

After reviewing our discussions of E₁ and E₂ reactions, consider what general structural characteristics might lead to differences in product identities for each mechanism. You need not propose specific compounds to use as reactants, but should propose parts of structures that would have different effects on the outcomes of E₁ and E₂ reactions.

Key Terms/concepts/techniques:
• E₁ and E₂ reactions
• Product distributions
Part A: What Structures Favor Reactions?

In the Class Group Activities Substitution at Saturated Carbon-1 and Substitution at Saturated Carbon-2, we saw that alkyl halides can undergo substitution reactions with nucleophiles. In those activities we used differences in the structures of the reactants and reaction conditions to determine that the substitution could occur by two different mechanisms, \( \text{S}_1 \) or \( \text{S}_2 \). We discovered that the mechanism of substitution was dependent on structures of the halide and the nucleophile, and the reaction conditions. As indicated by the titles of the class activities, all of the organic halides we studied had the halogen attached to a saturated (sp\(^3\)) carbon atom. The halogen atoms of aromatic halides are attached to sp\(^2\) carbons. In class, we are considering the reactivity of aromatic compounds with electrophiles, strongly acidic conditions. This experiment explores their reactivity toward nucleophiles?

Pre-lab Preparation Assignment:
1. Read: This Experiment page.
2. Review the material in the Class Group Activities Substitution at Saturated Carbon-1 and Substitution at Saturated Carbon-2.
3. Complete the Prelab activity on the course website by 10:00 PM on Sunday, April 15.
4. In your lab notebook: (See Lab Manual pp. 14-16 for format.)
   a. Update the Table of Contents
   b. Enter the title of this experiment and the Question of the Week.
5. Bring your notebook and ideas on answers to the Question of the Week to the Monday Lab Discussion period.
6. After the lab discussion, complete pre-lab assignment on the procedure handout to be provided on Monday.

Objectives:
1. To determine if aryl halides will react and, if so, how aryl halides will react with nucleophiles;
2. To determine if substituents on the aryl halide can influence reactivity;
3. To determine if a correlation exists between the basicity and nucleophilicity of a series of aromatic and aliphatic amines.

Question of the Week:
What Can Structural Effects on Reactivity Tell Us About The Mechanism of the Reactions that might occur?

After reviewing our discussions of \( \text{S}_1 \) and \( \text{S}_2 \) reactions, consider what general structural characteristics might help us define the mechanisms of any reactions that might occur. As with Experiment 4, you need not propose specific compounds to use as reactants, but should propose changes in structures that might affect \( \text{S}_1 \) & \( \text{S}_2 \) reactions differently.

Key Terms/concepts/techniques:
- \( \text{S}_1 \) and \( \text{S}_2 \) reactions
- Relative Reactivity
Part V: Theory

A. Stereisomers

A. Introduction.

1. Geometrical Isomers:
   In Chem 211 we discovered that some molecules could have the same molecular formula and same atom connectivity but be superimposable upon each other. We classified such structures as stereoisomers. We recognized that the differences in the stereoisomers were the result of the orientations of atoms with respect to a double bond or ring. These stereoisomers are only one sub-class of stereoisomers called Geometrical Isomers.

2. Configurational Isomers
   There are many biomolecules that have the same constitutional structure (e.i. the same molecular formula and same connectivity of atoms), have no double bonds or rings, but are not superimposable and exhibit different reactivities or functions in nature.

   a. Carbohydrates (sugars – molecules with the formula C\textsubscript{n}(H\textsubscript{2}O)\textsubscript{n}) provide particularly spectacular examples of the effects of configurational isomerism.
   e.g. Glucose, mannose and galactose are configurational stereoisomers that all can be described by the constitutional structure shown in Figure 1, however, glucose is the major energy source for the vast majority of living organisms while mannose and galactose are not metabolized by many organisms.

   ![Figure 1: Bond-Line (Skeletal) Structure of six carbon sugars](image)

b. Stereospecificity of Reactions in living systems:

   ![Equation 1](image)

   \[
   \text{CH}_2\text{C-O-H} \xrightarrow{\text{Oxidation}} \text{CH}_3\text{C-O-H} \\
   \text{lactic acid} \rightarrow \text{pyruvic acid}
   \]

<table>
<thead>
<tr>
<th>Lactic Acid Source</th>
<th>Reaction Conditions</th>
<th>Maximum Yield of Pyruvic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Synthesis</td>
<td>Chemical Oxidation</td>
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</tr>
<tr>
<td>Chemical Synthesis</td>
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<td>Muscle</td>
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</tr>
<tr>
<td>Muscle</td>
<td>Muscle Extract</td>
<td>100 %</td>
</tr>
</tbody>
</table>

   Table 1: Results of Lactic Acid Oxidations

There are two configurational isomers of lactic acid (R-lactic acid and D-lactic acid). Chemical synthesis produces a mixture of both configurational isomers of lactic acid and chemical oxidation converts both configurational isomers of lactic acid to pyruvic acid, which has no configurational isomers. Reactions in muscle extracts are catalyzed by enzymes, which selectively synthesize and catalyze reactions of only one configurational stereoisomer of a molecule like lactic acid.

B. References:
   CGWW CH 16
Figure 2: Configurational isomers of CHClBrF

Figure 2 provides structures of two simple configurational isomers.

a. Build models of the two configurational isomers in Figure 2. (Note that simple lines represent bonds that are in the plane of the paper, dashed-bonds extend below the paper plane and wedge-bonds extend above the paper plane.

b. Compare the two structures and verify that they are not superimposable.

c. Determine the structural relationship between the two structures. Define the relationship and provide your warrant for the definition. Structures with this relationship are called chiral compounds.

d. Use the models to determine the structural changes needed in the R-isomer to convert it into the S-isomer. Explain the required conversion process and provide your warrant for how you recognized the needed changes. Could the conversion be accomplished by any other structural modification of the R-isomer? Provide your warrant.

e. How many other configurational isomers can you make with the molecular formula CHClBrF? Use your models to verify your prediction.

f. The carbon atoms in the structures in Figure 2 are known as Stereogenic Centers. Based on your experience with the structures in Figure 2, predict the total number of configurational isomers possible for a molecule with a stereogenic center. Provide your warrant.
A3

V A. Stereoisomers

Figure 3: Simple Molecules with No Stereogenic Center

g. As indicated in section f, the carbon atoms in the isomers in Figure 2 are **Stereogenic Centers** (also known as centers of chirality, stereogenic atoms or stereocenters) while the carbon atoms in all of the structures in Figure 3 are NOT **Stereogenic Centers**. Based on your analyses of structures in Figures 2 & 3 describe the required characteristics of a stereogenic center and provide your warrant for your claims.

Figure 4: Lactic Acid

Configurational Isomers

2. Recognizing Stereogenic Centers (Also called Chiral Atoms)

   a. Lactic Acid (See Eq. 1) has one stereogenic center illustrated in Figure 4 with wedges and dash-wedges. Thus it has two possible configurational isomers. Note that the three carbon carbohydrate in Figure 5, glyceraldehyde, also has one stereogenic center and can exist as two configurational isomers. Put a checkmark (✓) on the stereogenic center in the glyceraldehyde structure in Figure 5 and draw wedge dash-wedge structures of its two configurational isomers below.

   b. The four-carbon carbohydrate in Figure 5 also has configurational isomers. How many stereogenic centers does the four carbon carbohydrate have? Indicate each stereogenic center with a checkmark (✓) and provide your warrant for identifying stereogenic centers.

   c. How many configurational isomers are possible for the four-carbon carbohydrate structure in Figure 5? Provide your warrant. Draw wedge dash-wedge structures for all of the configurational isomers of the four carbon carbohydrate.

   d. Identify the stereogenic centers in the five-carbon carbohydrate in Figure 5. How many configurational isomers are possible for this five-carbon carbohydrate? Provide your warrant. Draw wedge dash-wedge structures for all of the configurational isomers of the five-carbon carbohydrate.
V A. Stereoisomers

e. Based on your experience with the structures in Figure 5, propose a relationship between the number of stereogenic centers in a molecule and the maximum number of configurational isomers for that molecule. Provide your warrant.

3. Drawing Fischer Projections: See also CGWW p. 395.

As you may have noted in devising structures in 2., when a structure can have multiple stereoisomers, representing them on paper can be cumbersome. Fischer Projections are relatively simple two-dimensional representations of three-dimensional structures and are particularly useful for representing the configurations of atoms in molecules with multiple stereogenic centers.

Fischer Projections require that the molecule be oriented in a specific manner so that a flat representation (projection or shadow in two-dimensions) can give three-dimensional information.

Using the examples in Figure 6 as models, draw the Fischer Projection structure of:

Provide your warrant for determining your Fischer Projection.

b. Using Fischer Projections:

Figure 7 provides the Fischer Projections of D-glucose, D-mannose, and D-galactose as well as L-glucose.

Using the numbering system illustrated for D-glucose, explain how the four structures differ.

(1.) How many stereogenic centers are there in each of the structures in Figure 7? Using the numbering system illustrated for D-glucose, indicate which atoms are stereogenic centers in each sugar molecule. Provide your warrant for recognizing the stereogenic centers?

(2.) Using the numbering system illustrated for D-glucose, explain how the four structures differ.
4. Defining and Recognizing Relationships Among Configurational Stereoisomers:
Explorations of terms that define relationships among configurational isomers: 
**ENANTIOMERS, DIASTEREOMERS & EPIMERS** See also CGWW pp. 382-396 

a. ENANTIOMERS:

![Figure 8: Examples of ENANTIOMERS (Enantiomeric Pairs of Compounds):](image)

(1.) Place a checkmark (✓) next to all stereogenic centers in the structures in Figure 8.

(2.) How are the configurations of the stereogenic centers of the enantiomeric stereoisomers in Figure 8 related to each other? Provide your warrant.

(3.) How are the configurations of the stereogenic centers of non-enantiomeric stereoisomers in Figure 8 related to each other? Provide your warrant.

(4.) Definition: On the basis of the structures in Figure 8, define, as specifically as possible, the relationship between the structures of a pair of enantiomers. Provide your warrant.

(5.) Application: Identify all of the pairs of compounds in Figure 9 that are enantiomers. Provide your warrant.

![Figure 9: Structures for enantiomer & diastereomer problems.](image)
b. **DIASTEREOMERS:**

These sets of stereoisomers are **DIASTEREOMERS**

<p>| | | |</p>
<table>
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<td>Cl</td>
<td>Cl</td>
</tr>
<tr>
<td>CH₃</td>
<td>CH₃</td>
<td>H</td>
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</table>

These sets of stereoisomers are **NOT DIASTEREOMERS**

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<td>Cl</td>
</tr>
<tr>
<td>CH₃</td>
<td>CH₃</td>
<td>H</td>
</tr>
</tbody>
</table>

**Figure 10: Examples of DIASTEREOMERS: (Diastereomeric Sets of Compounds)**

1. Place a checkmark (✓) next to all stereogenic centers in Figure 10.

2. How are the configurations of the stereogenic centers of the diastereomeric stereoisomers in Figure 10 related to each other? Provide your warrant.

3. How are the configurations of the stereogenic centers of the non-diastereomeric stereoisomers in Figure 10 related to each other? Provide your warrant.

4. Definition: On the basis of the structures in Figure 10, define, as specifically as possible, the relationship between structures that are diastereomers. Provide your warrant.

5. Application: Identify all the all pairs of compounds in Figure 9 that are diastereomers. Provide your warrant for your classifications.
c. EPIMERS:

These pairs of stereoisomers are EPIMERS

These pairs of stereoisomers are NOT EPIMERS

Figure 11: Examples of EPIMERS (pairs of epimeric compounds)

1. Place a checkmark (√) next to all stereogenic centers in Figure 11.

2. How are the configurations of the stereogenic centers of the epimeric stereoisomers in Figure 11 related to each other? Provide your warrant.

3. How are the configurations of the stereogenic centers of the non-epimeric stereoisomers in Figure 11 related to each other? Provide your warrant.

4. Definition: On the basis of the structures in Figure 11, define, as specifically as possible, the relationship between structures that are epimers. Provide your warrant.

5. Applications:
   - Which structures in in Figure 7 are epimers of D-glucose? Provide your warrant.
   - Identify all of the pairs of compounds in Figure 12 that are epimers. Provide the warrant for your classifications.

Figure 12: Structures for epimer problems.
5. Defining and Recognizing Types of Stereoisomers

**CHIRAL COMPOUNDS:**

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<th>These compounds are CHIRAL</th>
<th>These compounds are NOT CHIRAL (achiral)</th>
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</thead>
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<tr>
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<td><img src="image" alt="Structure E" /></td>
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<tr>
<td><img src="image" alt="Structure B" /></td>
<td><img src="image" alt="Structure F" /></td>
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<tr>
<td><img src="image" alt="Structure C" /></td>
<td><img src="image" alt="Structure G" /></td>
</tr>
<tr>
<td><img src="image" alt="Structure D" /></td>
<td><img src="image" alt="Structure H" /></td>
</tr>
</tbody>
</table>

**Figure 13: Examples of CHIRAL and ACHIRAL (not chiral) Compounds**

1. Place a checkmark (√) next to all stereogenic centers in Figure 13.

2. Do all chiral molecules in Figure 13 contain stereogenic centers?

3. Do any achiral molecules in Figure 13 contain stereogenic centers? If so which molecules?

4. Definition: On the basis of the structures in Figure 13, define, as specifically as possible, the characteristics required for a compound to be CHIRAL. Provide your warrant.

5. Application: Using the definition you derived in (4), identify all of the chiral compounds in the Figure 14. Provide the warrant for your classifications.

**Figure 14: Structures for chiral and meso molecule problems.**
### D. General Applications:

1. Draw the required structure in each item below and briefly explain how your structure fulfills the requirements of the item:

<table>
<thead>
<tr>
<th>a. Enantiomer of</th>
<th>b. Diastereomer of</th>
<th>c. C3 epimer of</th>
</tr>
</thead>
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<tr>
<td><img src="image1" alt="Enantiomer Structure" /></td>
<td><img src="image2" alt="Diastereomer Structure" /></td>
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<table>
<thead>
<tr>
<th>d. Achiral diastereomer of</th>
<th>d. Chiral diastereomer of</th>
<th>e. Enantiomer of</th>
</tr>
</thead>
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<td><img src="image5" alt="Chiral diastereomer Structure" /></td>
<td><img src="image6" alt="Enantiomer Structure" /></td>
</tr>
</tbody>
</table>

2. Is it possible for a molecule to have more than one enantiomer? Provide your warrant using an example.

3. Is it possible for a molecule to have more than one diastereomer? Provide your warrant using an example.

4. Is it possible for a molecule to have more than one epimer? Provide your warrant using an example.

5. Is it possible for a molecule with one stereogenic center to be achiral compound? Provide your warrant using an example.

6. Is it possible for a molecule with two stereogenic centers to be achiral compound? Provide your warrant using an example.
V A. Stereoisomers

E. Nomenclature of Chiral compounds

References:

1. CGWW: pp. 387-388
2. Tutorials:
   http://www.cem.msu.edu/~reusch/VirtualText/sterism3.htm#isom13
   Developed By William Reusch at Michigan State University
   Provides naming rules and examples
   http://www.acdlabs.com/iupac/nomenclature
   Developed by Advanced Chemistry Development Laboratories
   (Gives detailed IUPAC rules for nomenclature.)

Recommendations 1993
R-7 Stereochemical Specification

R-7.2 Chiral Compounds Specification of Absolute Configuration

R-7.2.1 The R/S convention

(5.) Out of Class Applications of Nomenclature.

(a) Name the following:

(b) Draw structural formulas for the following compounds:

   R 2-iodobutane                   (2S,3R) 3-methyl-2-pentanol
   S ethyl 2-hydroxypentanoate     R 2-bromobutanoic acid
F. Out of Class Applications.

1. Designate all stereogenic centers in the compounds below as having either an $R$ or $S$ configuration. Then classify each of the following compounds into ALL applicable categories listed below:
   a. Compounds that have no stereoisomers.
   b. Chiral compounds.
   c. Achiral compounds.
   d. Epimer of another compound in this group. Indicate the letter of the epimeric compound. Provide warrants for your choices.

<p>| | | | |</p>
<table>
<thead>
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  \text{H} \\
  \text{CH}_3
\end{array}
\] | b. | \[
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  \text{HO} \\
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  \text{CH}_2\text{OH}
\end{array}
\] |
| c. | \[
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\] |

2. Now look back at all of your classifications above.
   a. Do ALL CHIRAL compounds contain at least one stereogenic center? Write the structures of all chiral compounds that do not contain at least one stereogenic center.

   b. Do ANY ACHIRAL molecules contain one or more stereogenic centers? Write the structures of all achiral compounds that contain one or more stereogenic centers.

   c. Does the presence of a stereogenic center allow you to identify chiral compounds dependably? If so, provide your warrant? If not, can you devise a way to use the existence of stereogenic centers to select only chiral compounds? If so, provide your warrant.
Part V: B. General Structure Determination Problems

Devise structures for the compounds that yielded the sets of data below. For each compound, indicate how your structure was determined and how it accounts for all of the spectral data.

Data Set 1.

$^1$H-NMR:

$^{13}$C-NMR
Data Set 1. (Continued)

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IR:

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\text{doublet} & \\
\text{multiplet} & \\
\end{align*}
\]

$^1$C-NMR
Data Set 2. (Continued)

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IR:

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Data Set 3.

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Data Set 3. (Continued)

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</tr>
<tr>
<td>117.0</td>
<td>2.9</td>
</tr>
<tr>
<td>146.0</td>
<td>9.2</td>
</tr>
<tr>
<td>164.0</td>
<td>20.9</td>
</tr>
<tr>
<td>165.0</td>
<td>2.4</td>
</tr>
</tbody>
</table>

**IR:**

![IR Spectrum](image_url)
A. Introduction:
The retrosynthetic approach to organic synthesis starts from the product (the target molecule) and attempts to determine what reactant molecules might be used to synthesize it in one reaction step.

B. Grignard Reactions in Synthesis of Organic Molecules:
In class we have seen that Grignard reagents react with aldehydes and ketones to form alcohol products. We will now consider the synthetic utility of Grignard reactions for synthesizing specific alcohols.

1. What is the relationship between the products of Grignard Reactions a. & b.?

2. What bonds are made in reaction a? Mark them on the product structure.

3. What bonds are made in reaction b? Mark them on the product structure.

4. How are the bonds made in the two reactions similar? How are they different?

5. What is the relationship between the C-C bond formed in each reaction and the OH group of the alcohol in the product?

6. If the C-C bonds made in reactions a. & b. were removed (disconnected) from the product, what additional structural changes would need to be made to convert the pieces of the products into the reactants of each reaction?

This process of modifying the product to reveal the reactants is called a Retrosynthetic Step and is represented by a new kind of arrow (⇒) called a Retrosynthetic arrow. Since retrosynthetic steps for revealing alcohols involve disconnecting a C-C bond they are designated as C-C Grig for a C-C Grignard Disconnection.

7. Considering your discoveries in 1->6, suggest structures for starting materials that would produce the target alcohol 3-ethyl-2-methyl-3-hexanol. Provide the warrant for devising your starting materials.
C. Synthesis of Grignard Reagents:

c. \( \text{CH}_3\text{CH}_2\text{Cl} + \text{Mg}^+ \xrightarrow{\text{Dry Ether}} \text{CH}_3\text{CH}_2\text{MgCl} \)

d. \( \text{C}_6\text{H}_5\text{Br} + \text{Mg}^+ \xrightarrow{\text{Dry Ether}} \text{C}_6\text{H}_5\text{MgBr} \)

1. What does the symbol \( \text{Mg}^+ \) represent in reactions c. & d.?

2. What bonds are made and broken in the two reactions?

3. Considering the outcomes of reactions c. & d., write the reaction equation for the formation of the Grignard reagent provided below and provide your warrant:

\( \xrightarrow{\text{Dry Ether}} \text{C}_6\text{H}_5\text{MgI} \)

In the terminology of Retrosynthetic Analysis, a process such as the formation of the Grignard reagent is a Functional Group Interconversion (FGI) step since it changes the nature of the functional group but does not change the carbon structure. So the retrosynthetic step for formation of a Grignard reagent is symbolized by FGI Grig, since it is the formation of a Grignard reagent.

C. Synthesis of Alcohols:

1. The Retrosynthetic Analysis Process:
   a. Look at the product molecule, find the alcohol OH and identify the bonds around the carbon holding the OH. These are the bonds that could have been made by a Grignard reaction.
   b. Disconnect each bond (C-C Grig) in turn to reveal each potential carbonyl compound and Grignard reagent precursors for the product.
   c. Use FRI Grig to reveal the precursors of the Grignard reagent.

**Full Retrosynthetic Analysis for the synthesis of 3-ethyl-2-methyl-3-hexanol**

(Starting materials in **bold**)

---

V: C Retro Synthetic Analysis C2
2. Devising a Synthesis from a Retrosynthetic Analysis:

**Synthesis based on retrosynthetic analysis b for 3-ethyl-2-methyl-3-hexanol**

a. What is the relationship between the retrosynthetic steps and the synthetic steps for synthesis of 3-ethyl-2-methyl-3-hexanol by retrosynthetic analysis b?

b. What additional information is provided in the synthesis that was not required in the retrosynthetic analysis?

c. Write a synthesis for 3-ethyl-2-methyl-3-hexanol based on retrosynthetic analysis c.

3. An Additional Example of an Alcohol Synthesis:

4. Synthesis based on Retrosynthetic Analysis c:
5. Class Discussion Problem on Alcohol Synthesis:

Use Retrosynthetic Analysis to devise a synthetic pathway for the following compound from smaller molecules.

Then write a complete synthetic path, including reagents and reaction conditions based on your retrosynthetic analysis.
6. **Out of Class Exercises on C-C disconnections in alcohol syntheses.**

For our next lab discussion period, use retrosynthetic analysis to devise at least two syntheses for the following compounds.

Then write complete synthetic paths, including reagents and reaction conditions based on your retrosynthetic analyses.

Be prepared to discuss both the retroanalysis and the synthesis.
C. Alkene Synthesis by Dehydration of Alcohols

1. Dehydration of Alcohols:

Dehydration of alcohols is induced by acidic conditions and, as we will see later, usually occurs by a 2-step mechanism.

\[
\begin{array}{ccc}
\text{H}_2\text{SO}_4 & \text{or} & \text{H}_3\text{PO}_4 \\
\text{H} & \text{C} & \text{O} \\
\text{H} & \text{C} & \text{H} \\
\text{H} & \text{C} & \text{H} \\
\text{H} & \text{C} & \text{H} \\
\end{array}
\rightarrow
\begin{array}{ccc}
\text{H} & \text{C} & \text{H} \\
\text{H} & \text{C} & \text{H} \\
\text{H} & \text{C} & \text{H} \\
\text{H} & \text{C} & \text{H} \\
\text{H} & \text{O} & \text{H} \\
\end{array}
\]

Major Product

a. Why is it reasonable to refer to the above reaction as a dehydration of an alcohol?

b. What bonds are made and broken in forming product 1? Mark them on the product structure.

c. What bonds are made and broken in forming product 2? Mark them on the product structure.

d. How are the bonds made and broken in the formation of the two products similar? How are they different?

e. What is the relationship between each bond made or broken and the OH group of the alcohol reactant?

f. What structural changes would need to be made in each product to convert it to the starting material?

Dehydration is another reaction, like FGI Grig, that changes the functional group without altering the sequence of the carbon chain. This retrosynthetic step is designated as FGI Dehyd for Functional groups interconversion dehydration.

g. Considering your discoveries in a -> f, suggest structures for starting materials that would produce the target alkene given below. Provide the warrant for devising your starting materials

\[
\begin{array}{ccc}
\text{FGI dehyd} & \text{starting material} & \text{FGI dehyd} \\
\end{array}
\]

h. How might the starting materials revealed in g. be synthesized from smaller molecules? Provide your warrant with at least one example.
2. An Example of a Retrosynthesis of an Alkene

Write a synthetic path for the synthesis of the target molecule above by retrosynthetic analysis a.

3. Out of Class Application:
For our next lab discussion period devise at least 2 different syntheses for each of the following compounds from simple monosubstituted aromatic compounds and non-aromatic compounds with four or fewer carbon atoms.

Then write complete synthetic paths, including reagents and reaction conditions based on your retrosynthetic analyses.

Be prepared to discuss both the retroanalysis and the synthesis.
D. Oxidation of Alcohols to Ketones

1. Introduction:
   
   In the previous section we learned how to use C-C disconnections, FGI’s of Grignard reagents and FGI dehydrations to synthesize larger alkenes and alcohols from smaller ketones or aldehydes and organic halides. This unit introduces methods for synthesizing ketones from alcohols, another FGI, since these reactions change functional groups, but do not alter the carbon structure of the reactant. The addition of this reaction to our synthetic repertoire greatly increases our abilities to build larger molecules from a number of smaller molecules.

2. Oxidation of 2’ Alcohols to Ketones:
   
   Chromium Trioxide (CrO₃) in acidic aqueous solution (H₂SO₄) is a common reagent for oxidation of alcohols. This metal oxide reagent is a relatively strong oxidizing reagent. It smoothly converts 2’ alcohols to ketones.

   ![Reaction Equation]

   3. FGI-oxidation:
   
   The following FGI Retrosynthetic step indicates that the ketone can be synthesized from the corresponding alcohol by oxidation.

   ![Retrosynthetic Analysis]

   Consider the retrosynthetic analysis of the complex target molecule shown below. One Grignard of the possible C-C disconnection reveals that the target molecule can be synthesized from phenyl magnesium chloride and 2,5-dimethyl-4-heptanone.

   ![Retrosynthetic Analysis with Grignard Reagents]

   With only the Grignard C-C disconnection, we were able to disconnect the carbon structure of an alcohol only once. How might FGI oxn allow us to synthesize 2,5-dimethyl-4-heptanone from simpler molecules? Provide your warrant with at least one example.
4. Retrosynthetic analysis based of the C-C Grignard in 3. above:

\[
\begin{align*}
\text{C-C disconnection} & \quad \text{Grignard} \\
\end{align*}
\]

Write a synthetic path for the synthesis of the target molecule above from this retrosynthetic analysis.

4. Out of Class Application:
For our next lab discussion period use retrosynthetic analysis to devise **syntheses** for the following compounds **from monosubstituted aromatic compounds** and **non-aromatic compounds with four or fewer carbon atoms**.

Then write complete synthetic paths, including reagents and reaction conditions based on your retrosynthetic analyses.

Be prepared to discuss both the retroanalysis and the synthesis.