Chemistry 146A

Advanced Laboratory in Organic Chemistry

Fall 2018

Table of Contents

This manual is the collaborative effort of the organic chemistry faculty Caitlin Binder, Rebecca Braslau, and Daniel Palleros with the invaluable help of Chris Murphy and Chris Bailey.

CHEM 146A – Advanced Organic Chemistry Lab Schedule

Arrive on time and dress appropriately for every lab meeting, even if no experiment will be performed that day. Bring the lab manual and notebook to every lab.

	Tuesday	Thursday
		9/27 – No Lab Meeting
Chemdraw & SciFinder tutorials in McHenry Library Digital Scholarship Commons. Register for passwords & find the DSC by 10/2 (instructions sent *via* email)		
1	10/2 – ***Orientation & Safety*** **** Students must be present this day to secure their space **** NMR Activity	10/4 - ***Experiment 1*** (dry lab) Group A ***Identification of an Unknown*** Group B – ChemDraw & SciFinder *Exp 1 Pre-Lab Q's due for both groups
2	10/9 - ***Experiment 1*** (dry lab) Group B ***Identification of an Unknown*** Group A – ChemDraw & SciFinder	10/11 – ***Experiment 2.1*** ***Two Base Extraction of Excedrin*** Students work in pairs
3	10/16 – ***Experiment 2*** Complete ***Exp 2.1*** Begin ***Experiment 2.2: Column Chromatography*** Students work in pairs	10/18 – ***Complete Exp 2.2*** Students write draft of reports in lab: Group A – Exp 2.1 Group B – Exp 2.2
4	10/23 – ***Experiment 3*** (dry lab) ***Separation & Identification of Two Unknowns*** **Exp 2.1** report due	10/25 – ***Experiment 3*** (dry lab) ***Separation & Identification of Two Unknowns*** **Exp 2.2** report due
5	10/30 - ***Experiment 4***	11/1 – ***Experiment 4***
6	11/6 – ***Experiment 4***	11/8 – ***Experiment 4***
7	11/13 – ***Experiment 4***	11/15 – ***Experiment 4*** **Progress report**
8	11/20 – TA Office Hours, Cleanup	11/22 – Thanksgiving – no lab
9	11/27 – ***Experiment 4***	11/29 – ***Experiment 4***
10	12/4 – ***Experiment 4***	12/6 – Dry Lab ***Experiment 4*** Draft Due Writing workshop – peer review Lab Clean-up

Revised Exp 4 report due 12/10 by 5 pm in David Delgadillo's mailbox in PSB.

CHEM 146A – Advanced Organic Chemistry Lab
UCSC, Department of Chemistry and Biochemistry

Instructor: Dr. Caitlin Binder **Office Location:** Thimann Labs 313
Email: cambinde@ucsc.edu **Office hours:** M 11am-12pm, W 2-3pm in PSB 145
Teaching Assistants: David Delgadillo – daadelga@ucsc.edu
Patrick Skelly – pskelly@ucsc.edu

Course Prerequisites: CHEM 8L/M, 110L **Course Fees:** $55 materials fee
Lab Meetings: TuTh 1:30 – 5:30 p.m.

Required Materials

- Any Experimental Organic Chemistry textbook, such as…
  - Mohrig, J. R., *et. al* "Techniques in Organic Chemistry" Freeman (any edition)
  - Palleros, D. R. "Experimental Organic Chemistry" Wiley, 2000.
- Lab Notebook – no carbon copies needed, get a fresh new notebook of any kind
- Goggles & Lab Coat (provided) or your own approved safety goggles (no glasses).
- Check email and class website frequently for updates and supplemental materials: https://acrochem.sites.ucsc.edu/chem-146a/

Required Assignments

There are two dry-lab and two wet-lab experiments to be completed and there will be four written assignments to be completed using proper technical writing and specific notes given within each experiment. Structural elucidation through NMR spectroscopy is a key component of this course and is part of each assignment. Students will be given in-class time to gain a more complete understanding of this valuable tool, but this will also require time outside of class. Students are given opportunities to work on, revise, and otherwise get help with reports during lab. The minimum passing grade for each experiment is 70%.

Laboratory Notebook

An up-to-date, current laboratory notebook should be kept while doing experiments. The notebook will be checked periodically and will be turned in with the reports. A table of contents should be kept up-to-date at all times. Students that do not have notebooks completed on experiment days cannot participate in lab and will receive zero points for that day's work. See full details on 'keeping the lab notebook' and specific notes within each experiment.

Absences & Lateness – Communication is Key!

If you absolutely need to be late for or miss a lab or two, *pre-arrange this with the instructor.* Students that are late or absent without notice will lose points on the corresponding reports. Experiments 1 - 3 **cannot** be postponed, however there is some flexibility in Experiment 4. This does not mean that you are free to miss labs on a causal basis: email the instructor the night or morning before at latest. **More than one non-prearranged absence can be grounds for a *Fail* (F) in this class. No make-up laboratory sessions will be arranged.**

Illness. Casts and Crutches. Pregnancy

If you are ill, you **should not attend** lab and, as stated above, should contact the instructor as soon as possible. In the circumstance that you must wear a cast, a sling or use crutches, please contact the instructor immediately, before your next lab section, so we can arrange the best possible accommodations for you. Also contact the DRC (Disability Resource Center 831-459-2089) as soon as possible. If you are pregnant or intend to get pregnant during the course of this quarter, please contact the instructor before your next lab section to obtain important information about chemicals and pregnancy. Also, we recommend that you consult with your physician about this subject.

NMR Activity

Structures of several organic compounds are given for the purpose of predicting the ^{1}H and ^{13}C NMR spectra for each using chemical shift tables and background knowledge of chemical equivalency and splitting patterns. The goal of this activity is to refamiliarize students with NMR spectroscopy in a forward sense (given structure, predict spectra) in preparation for structural elucidation in a backward sense (given spectra, draw structure). Students should begin this before the first class meeting and finish by the end.

Experiment 1: Identification of a Single Unknown

The structure of an unknown compound with no more than nine carbon atoms will be determined by IR spectroscopy, chemicals tests, and provided ^{1}H-NMR. Students work individually on this experiment.

Experiment 2: Column Chromatography & Acid-Base Extraction

In the first two lab periods, students will revisit two techniques from 8M to separate the active ingredients in Excedrin: column chromatography (Exp 2.1) and acid-base extraction (Exp 2.2). Before the experiment, students type responses to pre-lab questions and a summary/introduction paragraph describing the theory behind each experiment. The lab notebook must be prepared with the descriptive, yet concise experimental details. The summary paragraph will be revised for the report, using feedback from the instructors. The main results are typed in another brief paragraph, tying the results back to the theory behind the experiment. Students work in pairs on the experiment and turn in separate reports.

Experiment 3: Separation & Identification of Two Unknowns

Each student will be given a unique mixture of two organic unknowns, which will be separated by acid-base extraction. Students will work in pairs on the separation, then each student will purify and analyze one compound individually. Spectroscopic analyses (IR, ^{1}H and ^{13}C NMR) will be performed to determine the structure of the unknown. The lab report will consist of a record of the separation, purification, and recovery, as well as the fully assigned spectra with discussion of the structural analysis.

Experiment 4: Alkene Epoxidation and Oxidative Cleavage

Students will perform a two-step synthesis, including optimization of the second step and purification of both steps. Products will be analyzed via IR and NMR spectroscopy.

Grading

Punctuality, Preparedness, & Cleanliness (includes intro activity): **15%**
Technical Skill & Safety Compliance (evaluated by the instructor and TA): **15%**
Experiment 1: **10%**
Experiment 2: **15%**
Experiment 3: **20%**
Experiment 4: **25%**

Note: ****All drafts & reports must be printed and in-hand at the beginning of lab**** All experiments and written assignments must be completed on time to pass the course. Please communicate with us if you're having a hard time completing an assignment on time. A minimum grade of 70% will be needed to pass each experiment.

A typical grade distribution is as follows:
A = 90-100%; B = 80-89%; C = 70-79%; D = 60-69%; F = < 50%.

Introduction to Chemistry 146A

This lab manual contains detailed instructions to set you up for success in this course. Attention to detail and safety are emphasized above all else. General and specific details are provided throughout the lab manual, some of which are redundant. Come to the instructors immediately if there is conflicting information. Please read these introductory pages carefully before the first class meeting. Students who do not come properly dressed for the lab will not be allowed in the room. This includes the first day of class or check-in, which may result in you being dropped from the class. Students who do not follow the safety rules during the course of the lab will be asked to leave. This may result in failing the class.

We want to emphasize that a collegial and professional atmosphere is mandatory in these lab sections. The teaching assistant and instructor are here to help you. Our philosophy is that we are here to act as your research advisors and, hopefully, to convey to you some of our own passion for organic chemistry. **Your part of the deal is thinking, preparing and asking questions, no matter how stupid you might think they are.** Collegial interaction and cooperation is encouraged. That means that you should feel free to consult with each other and with the TA about the chemistry that you are doing. It does not mean that the TA or another student does your lab work for you.

Please remember that the amount of time available for laboratory work is limited. The laboratory is the place to make observations; use time outside the lab for planning and consulting the literature. It is essential that you have a plan of action when you arrive at the laboratory. This means that you must plan ahead for the experiments. You cannot afford to look information up as needed, unless the procedures specifically instruct you to do so.

The accurate and concise communication of research results and the ideas generated by these results is paramount in every branch of science. Maintenance of a neat, professional, and **permanent laboratory notebook** is an important objective of this course. Whether you write large or small, neat or not so, if the information in your notebook cannot be read, then that information is worthless. In addition, please remember that "bad results" are at least as important as "good results." All entries in you notebook should be made in ballpoint pen (so it will not “run” if wet). Your lab book must have bound, consecutively numbered pages.

Take good care of your bench space. Keep it clean and tidy at all times. Keep the reagent counters, fume hoods, and the balances clean. If you spill a small amount of a solid when transferring or weighing it, clean it with wet paper towels and dispose of the towels in the solid-waste container; wear gloves during this process. Keep reagent bottles and Erlenmeyer flasks well capped. Do not move reagents around the lab.

There are two main adjoining rooms for the bulk of student work with a third adjoining room with the reagents, waste, and IR. Be considerate of the fact that one TA is primarily supervising 16 students. The instructor (Caitlin) will either be across the hall in her office or in the lab. **Students should stay in the room with their assigned drawer, going into the third room only to get necessary materials then returning to the designated workspace.** *In other words, know what you need before you move to a different room!*

All products made or purified in the lab should be stored in a screw-cap vial or a plastic bag that is properly labeled with the compound's name, melting point (if applicable), mass, your name and the date. The vials or bags are to be turned in immediately after completion of the experiment to the stockroom or your TA unless requested to do otherwise. Any compounds kept for the next lab period must be in clearly labeled vials in the desiccator in your assigned drawer.

Have fun, and learn as much as you can! Again, your TA and instructor are committed and approachable!

LABORATORY SAFETY

A laboratory should be a safe and comfortable place to work, but no environment is safe without the cooperation of its inhabitants. Although the experiments in this class do not involve extremely dangerous substances, the use of hazardous chemicals cannot be entirely eliminated. Before engaging in experimental work, read the following guidelines and observe them at all times in the laboratory. For more information about laboratory safety visit the site for the UCSC Environmental Health and Safety (EH&S; http://ehs.ucsc.edu).

"Safety First!"

Negligent or repeated violation of any of the rules below may result in you being removed from the lab and/or you will receive ZERO for results portions of the lab (credit granted for preparation only – introduction & notebook). A second violation will result in you being dropped from the course. ***No make-up labs for students who violate these rules.***

GENERAL SAFETY GUIDELINES

Attire

Wear safety goggles at all times no matter what you are doing or where you are in the lab. For maximum protection against splashes, safety goggles should not have open holes on the sides; the venting apertures, necessary to minimize fogging, should have splash guards.

Goggles with anti-fog lenses are commercially available. If fogging occurs, clean the lens with a piece of tissue paper and anti-fog lotion available in the laboratories. Repeat the cleaning as necessary. This operation should be performed outside the lab. If you need prescription glasses wear them beneath the safety goggles.

Lab coats are provided in the lab and must be worn over appropriate lab attire (see below). *You will lose points every time you are told to put on or button your lab coat.*

Clothing is only a first line of defense against chemical exposure. Any clothing worn tightly to the skin acts as a sponge to directly deliver chemicals to your skin. Consider this in choosing your wardrobe for the day, along with the following specifics. Students that are not dressed properly cannot participate in lab, cannot go home to change, and will receive zero points for the day.

- **OK LAB ATTIRE:** Pants or long skirt, short or long-sleeve shirt, closed-toe shoes that cover the entire top of the foot. Long hair and loose clothing are confined or tied back.
- **NOT OK:** Shorts or short skirts (no exposed ankles), *leggings/tights*, cropped pants that expose ankles, ripped pants that expose skin, tank tops, sandals, ballet flats, or any other shoes that expose the tops of the feet (Crocs and Tom's are NOT OK!). High heels, baggy clothing, and dangling jewelry are strongly discouraged.

Headphones cannot be used in the lab.

Cell phones cannot be used in the lab and must be turned off.

Bikes cannot be kept, locked or unlocked, inside the building. This includes hallways, labs, instrument rooms and stockroom.

Good Laboratory Habits

Use common sense.

Do not eat, drink, smoke, vape, or apply makeup.

Take a short break if necessary and please let someone know you're leaving. Wash your hands before you go outside or check out the greenhouse and breathe fresh air. A ten-minute break during a 4-hour lab period is refreshing!

Do not bring drinks or snacks into the lab, even if hidden in your backpack. Leave drinks and snacks on the designated table outside. Take off your lab coat and wash your hands before leaving the room and snacking.

Never use laboratory glassware for food or drink. Do not use the ice from the ice machine and the industrial water from the laboratory faucet for a drink.

Never leave an on-going experiment unattended. If you have to leave the lab for a few minutes, notify your TA. Overnight reactions must be in secondary containment

Do not keep your books, backpacks, and coats on the bench-top. Instead, keep them in the designated area.

Do not obstruct the aisles with belongings, stools, or open drawers.

Do not sit on the benches!

Keep exits and aisles free of obstructions at all times.

Do not keep personal electronic devices (laptops, cell phones, etc) on the lab bench, with the exception of dry lab days. If there is a spill they may get damaged and you may loose important data.

Keep your bench space clean and tidy at all times. Make sure to clean it before you leave.

Do not perform unauthorized experiments. Such experiments are strictly prohibited.

Do not invite or receive visitors in the laboratory.

Do not rush. Do not run. Do not push.

Do not engage in horseplay and practical jokes in the lab.

Precautions

Before each experiment, familiarize yourself with the hazards (flammability, reactivity, stability, and toxicity) of the compounds involved. Such information can be found in the Material Safety Data Sheets (MSDS) provided by the manufacturer. They are kept in the stockroom (Thimann 281) and are also available online. Consult also the Merck Index for additional information. Record this information in your lab book.

Be aware of your surroundings. Know what your neighbors are doing. If somebody in the lab appears to be performing an unsafe operation, point out the hazard immediately. Prevention is always the best medicine.

Never use open flames in the laboratory without your instructor's permission.

In case of an emergency evacuation of the building, all the students and instructors should meet outside the building at a spot designated in advance by the instructor. The meeting place for Thimann Labs occupants is the grove between Thimann Labs and Kerr Hall.

If you are pregnant or planning a pregnancy while taking the organic chemistry laboratory, contact your instructor and your doctor. They will provide you with information regarding potential risks to you and the embryo.

If you have to wear crutches or a sling, contact the instructor immediately, before going to your next lab section. Also contact the Disability Resource Center (DRC) (http://drc.ucsc.edu; phone: (831) 459-2089). If contacted with enough time they can arrange for a scribe and/or a lab assistant to help you.

Before Leaving the Lab...

...Clean the bench tops and fume hoods. Other students will appreciate a spotless work area as much as you. First wipe the bench with a wet sponge using elbow grease, then dry with a paper towel. Repeat if necessary. If streaks are left on the bench, you will lose points (the streaks are likely contaminants).

…Perform your community task and initial the table on the door.

...Turn off gas, water, air, steam and vacuum valves at or near your bench space.

...Unplug all electrical appliances (hot plates, heating mantles, water pumps, etc.). Never unplug or turn off GCs, IR instruments, GC carrier gas.)

...Wash your hands thoroughly with soap and water.

* Work together to clean the entire lab as you go along. Just because one personal is assigned a community task, that does not leave you leave all the work to them! Ex. ask around if it looks like everyone's done with the rota-vap and shut it down.

Handling Chemicals
Consider all chemicals poisonous.

Use the fume hood when handling organic solvents and volatile compounds.

Never use your mouth to carry out a chemical operation (fill a pipet, start a siphon, etc.).

Dispose of chemical waste in the containers provided for that purpose. They should be clearly labeled and are usually placed in the fume hood. Follow proper procedures as indicated by your instructor and this lab manual.

Do not contaminate reagents. Most organic chemicals are very expensive. Use clean and dry pipets to dispense them. Take just the amount you need, do not waste them. Never pour unused reagents back into stock bottles.

Keep stock bottles in their designated spots, so everybody can find them easily.

Label all containers. Do not use chemicals from unlabeled containers.

Read labels carefully.

Do not inhale, smell, or taste chemicals. Never touch your face without washing your hands.

Wearing Gloves

Wear gloves prudently. There are several types of gloves offering different levels of chemical protection. Always check their chemical resistance and recommended usage. If they are not worn properly, they will only give you a false sense of security.

In the labs we will provide you with nitrile gloves. Wear them when handling organic solvents and specific chemicals as indicated in the experiments.

Do not wear them while washing glassware.

Remove them when you go outside the lab (even if it is only for a short trip to the stockroom).

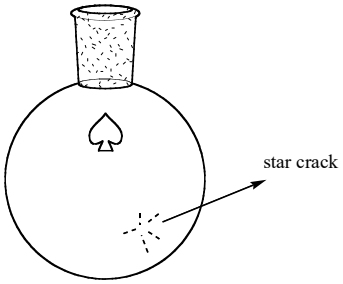
Change them frequently: every time you work with a toxic compounds, especially strong solutions of acid or bases, and definitely when they get soiled or punctured.

Do not handle solid chemicals directly with your gloves, always use a spatula.

Do not reuse contaminated gloves.

Handling Glassware

Check your glassware before use. It is important to check round-bottom flasks and condensers carefully. “Star cracks” may cause glassware to break. Do not use any piece of glassware with a crack; bring it to the stockroom for an exchange.



When inserting (or removing) a piece of glass tubing or thermometer into a stopper or hose, always wrap the tubing with paper towels or a cloth to avoid cutting yourself. Use water, glycerol or grease as lubricants as necessary. Hold the tubing as close to the insertion point as possible and apply a slow rotatory motion. Keep your hands far from your body and face.

Place broken clean glassware in the appropriate disposal container, usually located on the floor. Do not place it in the trash.

Place broken or disposable contaminated glassware (including Pasteur pipets) in the appropriate solid hazardous waste container usually located in the fume hood. Do not place it in the trash. It may puncture the trash bag and cut the person who empties the trash.

If two ground-glass joints get "frozen" do not try to unlock them by applying a torque as they can break and hurt you. Notify your TA instead.

In Case of Accident

If you injure yourself, notify your instructor immediately. Check your local emergency number.

Small cuts can be treated by washing the wound, removing any pieces of glass and applying pressure with a sterile pad. The First Aid Kit is located in Thimann 322.

Do not move injured persons unless they are in further danger.

If chemicals get in your eyes, immediately flush them with water for at least 15 minutes using an eye-wash fountain or eye-wash cup. Seek prompt medical attention.

In case of ingestion of a hazardous chemical contact the local Poison Control Center immediately. The phone number should be posted by the emergency phone (Thimann 281). Meanwhile follow the first aid instructions shown in the MSDS. Never give anything by mouth to someone who is unconscious.

In case of small fire, get your instructor's attention immediately and follow instructions. In case of a large fire evacuate the building immediately. See instructions under In Case of Natural Disaster or Fire Alarm.

If your clothing is on fire, do not run. Use water, a blanket, or a coat to put out the fire. If necessary, the person should roll on the floor. Get prompt medical attention.

Spills

If you spill a chemical on your skin, remove all contaminated clothing and immediately flush with cold water for at least fifteen minutes. Notify your instructor. Check the MSDS for delayed effects. Check for a reaction during the next 24 hours. See a physician.

If you have a chemical spill on a large area of your body, use the safety-shower immediately as you remove any contaminated clothing. Avoid spreading the chemical on the skin. See a physician.

If you spill a nonhazardous solid or liquid, immediately wipe it up using spill mats. If the spill is large (> 100 mL) or if it poses a danger to you or someone else, notify your instructor. Do not attempt to clean up large spills.

If you spill a hazardous material notify your instructor immediately.

Dispose of material used to clean up a spill in the proper waste containers.

In Case of Natural Disaster or Fire Alarm

If the fire alarm goes off stabilize any ongoing experiment by turning off gas, water, vacuum, and any source of heat that you may be using (do this only if it does not pose further danger to you) and exit the building as soon as possible. Do not run.

Do not use the elevators to evacuate the building. Gather outside the building in the pre-arranged spot. For Thimann occupants the meeting place is in the grove between Thimann Labs and Kerr Hall (off the road).

In case of natural disaster such as an earthquake, if possible, find shelter under a desk or a door frame. Duck, cover (at least your head with your arms) and hold (to a sturdy piece of furniture or frame). When the tremor has subsided turn off gas, water, steam, vacuum and any source of heat that you may be using (do this only if it does not pose further danger to you) and exit the building as soon as possible. Always take your personal possessions with you if doing so does not pose further danger. Do not run. Never gather next to a building as falling debris may hurt you.

Community and General Cleaning Descriptions

Keeping a clean and organized lab space is a group effort.! Keep an eye out for items that need to be restocked at all times, not just at the end of lab. Either refill it yourself or ask the TA for assistance, especially in the case of reagents and solutions. Don't assume it'll be magically refilled – the lab fairies do not exist!

*** A table with community cleaning assignments will be posted on the first day of lab. On each day, we'll decide your community cleanup role. Please initial that you've done your task at the end of every lab or you get zero clean-up points for the day ☹**

*** This is in addition to cleaning your own workspace, including a pristine drawer with no extra, missing, or dirty items. Drawers will be checked without warning and points taken off for each infraction. These penalties will increase as the course progresses, if necessary.**

Reagents and Solutions – Check it is at least ¼ of the way full and in the correct place. Notify TA if empty or near empty. Do not re-make solutions.

Gloves, Pipets, Paper Towels – Check all glove boxes in the main labs (314/318). Bring in new boxes from the stockroom (322) if boxes are empty or close to it.

Soap & Sinks – Check all sinks have full dish soap dispensers. Re-fill using stock containers under the sink. Concentrated soap under sink in 322. Notify the TA if the pink hand soap is near empty – do not refill hand soap with dish soap! Remove any debris from sinks.

Waste containers – clean any spills in secondary containment (ask for help if needed, do not lift carboys), cap all containers, notify TA if full

Benchtops clean – Use a wet sponge followed by dry paper towel to clean & dry every benchtop, including fume hood space. Alternate who cleans the benchtops in 322. Bring any stray equipment to the TA or, even better, ask around to find out who it belongs to!

Floors swept – spot sweep every lab, full sweep at once/week. Alternate who sweeps 322.

Drying Rack – beginning or end of lab – put dishes away from the drying rack - applies to shared glassware not in lockers. Bring any stray glassware to the TA or, even better, ask around to find out who it belongs to!

Equipment organization in cabinets – any shared equipment (hotplates, sand baths, clamps, etc.) is neatly organized in each of these cabinets every day

Equipment turned off – rota-vaps unplugged, water pumps off, buckets empty & upside-down in the sink. All other equipment (hot plates, etc.) is unplugged and neatly put away.

Stockroom (322) – check that all benchtops, including the IR station, are clean. Notify the TA if any stock items are missing. Double check that hoods are clean and waste bottles are capped.

LOCKER EQUIPMENT
THIMANN 314, 318

Some items are provided in the room for everyone to share. Extras of locker items are also available. Please come to the stockroom in Thimann 281 for additional glassware.

Beakers
☐ 50mL
☐ 100mL
☐ 150mL
☐ 250mL

Bottle, wash

Bulb, small

Clamp, screw

Cylinders, graduated
☐ 10mL
☐ 25mL
☐ 100mL

Dish, Crystallizing

Filter vac

Flasks, Erlenmeyer
☐ 50mL
☐ 125mL
☐ 250mL

Flasks, filter
☐ 50mL
☐ 125mL

Forceps

Funnels, glass
☐ 25mm
☐ 65mm

Funnel, Buchner

Pluringe
☐ 1mL ☐ 3mL

Rings, cork
☐ 2" ☐ 4"

Rods, glass stirring
☐ regular (3)
☐ micro

Ruler

Scoopula

Spatula
☐ regular
☐ micro

Split stopper

Stir bar
☐ 0.5" ☐ 1"

Watch Glass
☐ 100mm ☐ 125mm

<u>Organic Chem Kit</u>

Round Bottom Flasks
☐ 500mL ☐ 250mL ☐ 100mL ☐ 50mL ☐ 25mL

Adapters
☐ Claisen ☐ 3-Way ☐ Vacuum ☐ Straight tube

Condenser, West

Separatory funnel, 125mL with 19/22 stopper

Neoprene thermometer tip

LAB MAP – Safety & Orientation Activity

After familiarizing yourself with your locker equipment, find the following items in your assigned lab room and make a map in your notebook. Feel free to open any and all drawers and cabinets in your lab room to get to know your space. Check this with your TA.

1. Hotplates, lab jacks, and sand baths
2. Thermowells and rheostats - for heating RBF's
3. Cystallization dishes - for water baths
4. Vials – for product storage
5. Water lines – for water-cooled condensers
6. Rota-vaps – note the one closest to your station
7. Chemical spill mats
8. Glass pipets
9. Filter paper
10. Gloves
11. Parafilm
12. Boiling chips/stones, $MgSO_4$, pH paper, copper wire, scissors & tape
13. Foil and cotton
14. Soap refill
15. Glass waste
16. Fume hoods
17. Beakers
18. Erlenmeyer flasks
19. Test tubes
20. Larger filter flasks
21. Vacuum tubing
22. Clamps, support rings, clamp holders, ring stands
23. TLC plates, chambers, tygon tubing for columns
24. Eye wash station
25. Safety shower
26. Fire alarm, fire extinguisher
27. Evacuation route

In the adjoining stockroom, please find the following but do not touch or move anything in this room. This is a semi-restricted area. For most labs, students will only be allowed in this room with permission and in designated areas only.

28. Fume hoods – these will be designated as waste or reagent hoods
29. Flammable solvents cabinet
30. Acid cabinet
31. Refills of gloves, kim wipes, pipets, etc.
32. IR Spectrometer

KEEPING A LAB NOTEBOOK

Students are required to use a fresh, new notebook for this class.

1. Use a bound notebook (not loose leaf!). Number all pages ahead of time if they are not pre-numbered. Never remove pages from the notebook.

2. Start a table of contents on the last page. Keep this up-to-date for each new page added, starting with the LAB MAP. Otherwise, fill in with the experiment number & title and descriptive but brief subtitle every day (Ex. "Exp 2.1 – Excedrin Column").

3. Use a title for each new experiment and begin each new experiment on a new page. Your title may use chemical structures rather than long chemical names when referring to a specific organic reaction.

4. Start a new notebook page each day. Add the date to the page where you are working as you start lab work each day. Fill out the lab book as you go, rather than after the fact. This will help you keep track of what you have done, and provides a record for others to follow.

5. **When performing a reaction,**
   - **…start a new notebook page and draw the reaction scheme at the top of the page (reactants, arrow, expected products) followed by…**
   - **…a table with chemical info and properties (mmol, mg, mL, MW, bp or mp, density, and hazards). Use the reaction scheme to define abbreviations for chemicals to use in the reagent table for simplicity.**
   - **After the reagent table, give a <u>concise</u> description of what you plan to do and leave space to make changes based on your experience in the lab. With a few exceptions, you may not refer to the lab manual while performing the experiment.**

6. Don't compress multiple parts of experiments onto a single page. There are many pages available in the lab notebook and it should be easy to find everything based on page titles and the table of contents.

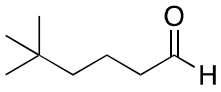
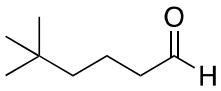
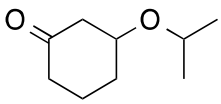
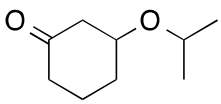
7. Write neatly enough for other people to be able to read what you have written. Don't agonize about being too neat: it just needs to be well organized and legible, not perfect!

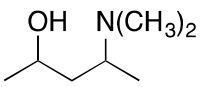
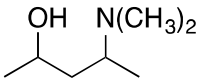
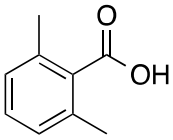
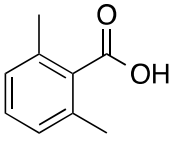
8. There is no need to use complete, grammatically correct sentences in your lab notebook: this should be reserved for your laboratory reports. An example might be: "Isolated amine as 2.3 g off-white solid. Recrystallized from methanol (1 g amine in ~15 mL methanol; recovery: 0.85 g). mp (crude) = 123-129 °C; mp (recryst.) = 130-132 °C."

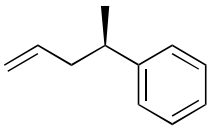
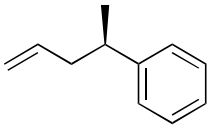
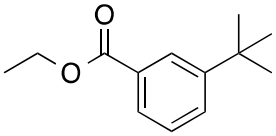
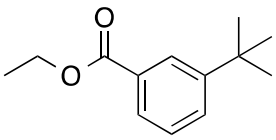
'Reacquainting with NMR' Problem Set

1. Predict the detailed ^{1}H NMR spectrum for each compound below using **Appendix V** of this lab manual and the table format below. Approximate chemical shifts within provided ranges and relative to other signals in the molecule. The correlation tables in the Mohrig or Palleros textbooks can be used as a training tool to calculate more exact values and/or check your work. For best results, students should work independently until working through each molecule.

2. Sketch the ^{13}C NMR spectrum for each compound, including approximate chemical shifts and peak heights relative to other signals within the molecule. Use **Appendix VI**.

Structure (add labels)	**Assignment** (corresponds to label on structure)	**Chemical Shift** (ppm)	**Integration** (# H's per signal)	**Splitting**
 ^{1}H NMR				
 ^{13}C NMR				
 ^{1}H NMR				
 ^{13}C NMR				

Structure (add labels)	**Assignment** (corresponds to label on structure)	**Chemical Shift** (ppm)	**Integration** (# H's per signal)	**Splitting**
 ^{1}H NMR				
 ^{13}C NMR				
 ^{1}H NMR				
 ^{13}C NMR				

Structure (add labels)	**Assignment** (corresponds to label on structure)	**Chemical Shift** (ppm)	**Integration** (# H's per signal)	**Splitting**
 ^{1}H NMR				
 ^{13}C NMR				
 ^{1}H NMR				
 ^{13}C NMR				

3. Structural Elucidation – Choose any molecule on the previous pages and draw a close-ish derivative. Add a functional group, change the branching or substitution pattern, etc. Predict both its ^{1}H NMR and ^{13}C NMR spectra. **Check this with the TA then re-write this as a structural elucidation problem (molecular formula, ^{1}H NMR signals listed, and ^{13}C NMR sketched). TAs will collect your problem and exchange with another student.**

Structure (add labels)	**Assignment** (corresponds to label on structure)	**Chemical Shift** (ppm)	**Integration** (# H's per signal)	**Splitting**
^{1}H NMR				
^{13}C NMR				

EXPERIMENT 1 - Identification of a Single Unknown

In this dry lab exercise, you will identify an unknown organic compound using IR spectroscopy, chemical tests, and ^{1}H-NMR spectroscopy. Each unknown contains nine carbon atoms or less and will have one of the following functional groups: alcohol, alkyl halide, aldehyde, ketone, carboxylic acid, or ester. In addition, the unknown may have an ether or arene group.

You will be given a packet containing the IR spectrum, chemical test results, and ^{1}H NMR spectrum for an unknown. You are required to fully interpret the data and ***solve the unknown before leaving the lab on the same day***. As always, the TA will be there to assist you and to clarify any questions, especially about ^{1}H-NMR. You should come to the lab very well prepared with a good working knowledge of IR and, above all, ^{1}H-NMR.

Notebook Preparation

Prepare 3 tables on 3 separate pages: (1) IR Spectroscopy, (2) Chemical Tests, and (3) ^{1}H NMR Spectroscopy. Don't forget to add each page to the table of contents!

Pre-lab Questions – Read the chemical test descriptions on the following page and consider the questions below. Concise responses should be written in passive voice without personal pronouns, typed and in-hand at the beginning of lab. Responses cannot be changed.

1. What are the expected IR stretches for each of the functional groups that may be present in the unknown? Present your responses in table format.

2. Give an example of the balanced reaction and mechanism for a molecule that gives a positive Lucas test.

3. Give an example of the balanced reaction and mechanism for a molecule that gives a positive 2,4-dinitrophenylhydrazine test.

4. What is the full balanced reaction for the oxidation of a generic aldehyde (R-CHO) to a carboxylate and the reduction of Cu^{2+} to Cu_2O? No mechanism.

5. What is a chelating agent? Look up the structure of tartrate (the conjugate base of tartaric acid) and propose a structure for copper II tartrate.

6. Give an example of the balanced reaction and mechanism for a molecule that gives a positive sodium iodide in acetone test.

7. Give an example of the balanced reaction and mechanism for a molecule that gives a positive silver nitrate in ethanol test.

8. What are the characteristic ^{1}H NMR chemical shifts for each possible functional group? Present your responses in table format.

EXPERIMENTAL PROCEDURE

The ***Lucas test*** is based on the reaction of alcohols with HCl that leads to the formation of alkyl chlorides. The reaction takes place by an S_N1 mechanism. Tertiary alcohols are the most reactive, followed by secondary alcohols. Primary alcohols do not react with Lucas reagent at room temperature.

The test is useful only for alcohols soluble in the Lucas reagent (small alcohols with fewer than six carbons). Tertiary alcohols soluble in the Lucas reagent ($ZnCl_2$ in $HCl_{(c)}$) react immediately and give an insoluble tertiary alkyl chloride that separates as an immiscible layer or as an emulsion. Secondary alcohols soluble in the Lucas reagent react more slowly than tertiary alcohols and cloudiness, or an immiscible layer, forms within 5-10 minutes.

The ***2,4-dinitrophenyldrazine test*** is based on the nucleophilic addition of a hydrazine derivative (H_2N-NH-R), to the carbonyl group of aldehydes and ketones. A positive result is the formation of an insoluble 2,4-dinitrophenylhydrazone. This has a more extended system of conjugation than the original hydrazine and absorbs visible light at longer wavelengths (blue) than the original 2,4-dinitrophenylhydrazine (absorbs violet). The resultant product tends to be orange (the complementary color of blue). Aldehydes and ketones react almost immediately and give a yellow-orange (sometimes red) precipitate when treated with 2,4-dinitrophenylhydrazine.

Esters do not react; they give a negative test as evidenced by the lack of a precipitate. If the 2,4-nitrophenylhydrazine test was positive, the ***Fehling's test*** is performed as well. Aliphatic aldehydes give a positive test (the formation of a brown-reddish precipitate of cuprous oxide) with the Fehling's reagent. Ketones and aromatic aldehydes do not react.

Fehling's test is a redox reaction accompanied by a drastic change in color. Cu^{2+} under basic conditions is deep blue, and the product of the reaction, usually Cu_2O rather than metallic copper, is a reddish precipitate. The reaction is performed in the presence of tartrate to keep the Cu^{2+} in solution under basic conditions. Tartrate is a chelating agent.

Aldehydes, especially aliphatic aldehydes, can be easily oxidized with Cu^{2+}. The aldehyde gets oxidized to a carboxylic acid (or a carboxylate under the basic conditions of the test) and the copper gets reduced to Cu^{+} (in the form of Cu_2O) and occasionally to Cu^0 (metallic copper). Esters do not react with the Fehling reagent.

The ***sodium-iodide-in-acetone*** and ***silver-nitrate-in-ethanol test*** are based on substitution reactions and allow one to distinguish between primary and tertiary alkyl halides.

Sodium iodide in acetone test

Alkyl chlorides and bromides react with NaI in acetone to give an alkyl iodide and sodium chloride or sodium bromide, respectively. The reaction typically takes place by an S_N2 mechanism. Primary alkyl bromides and chlorides react faster than secondary halides. Primary alkyl bromides react at room temperature. Primary and secondary alkyl chlorides and secondary and tertiary alkyl bromides react upon heating at 50°C. Tertiary alkyl chlorides, aryl halides, and vinylic halides do not react even after heating. The formation of a white precipitate of NaCl or NaBr is considered a positive test. This test is based on the limited solubility of sodium chloride and sodium bromide in acetone. NaI (the reagent) is soluble in acetone, while NaCl and NaBr (the possible side products) are not.

Alkyl halides react with silver nitrate in ethanol to give silver halide which separates as a precipitate. The formation of this precipitate is considered a positive test. The by-products are nitric acid and an ether. The reaction takes place by an S_N1 mechanism so tertiary alkyl halides react faster than secondary. Primary alkyl halides react slowly and give a precipitate only upon heating.

After interpreting the IR spectrum and chemical tests, ***check the results with a TA or instructor***. If you are on the right track, move on to ^{1}H-NMR interpretation, otherwise we will help you reorient. The interpretation of the NMR should be done in the lab. These are the recommended steps to follow for structural elucidation:

- Make a table of all NMR peaks: chemical shift, integration, splitting, and assignment.

- Notice the solvent used to obtain the NMR and make sure that you do not assign solvent or impurity signals, such as ***water***, to your sample. Check the table provided at the end of this manual for a list of commonly used solvents and their NMR signals, including water.

- Interpret the integration values in the ^{1}H-NMR spectrum. Since you do not know the molecular formula, your integration will be in relative terms. However, you should try to anchor the integration by making a reasonable assumption about the number of hydrogens under a certain peak. Your assumption should be based on the functional group present in your molecule and knowing that the unknown is a relatively small molecule with 9 or fewer carbons. For example, if you suspect an aldehyde, locate the aldehyde hydrogen. That peak should integrate for only 1H.

- Interpret the multiplicity of the peaks following the n+1 rule. This will tell you not only the number of neighbors for each type of hydrogen, but it may also be helpful in anchoring the integration. For example, if your spectrum shows two triplets and no other multiplet (doublet, triplet, quartet, etc.), it is likely that each triplet integrates for 2H (the 2H that split the neighbor's signal into a triplet).

- Pay attention to the chemical shifts to determine the environment of each hydrogen (shielded or deshielded). Use the correlation tables provided at the end of this manual to calculate the chemical shifts of all the hydrogens. The match between your calculations and the experimental values should be acceptable.

- Keep in mind that contrary to IR, every peak of the NMR spectrum should be accounted for (except for very small peaks that may belong to impurities). If you leave a peak without interpretation, it's very likely that your proposed structure is wrong.

- ***Before leaving the lab, present the name and structure of the unknown to your TA and explain your reasoning.***

EXPERIMENT 2 REPORT GUIDELINES – subject to change, check online
- Read and apply info from ***Appendices 1* & *2*** in the lab manual.
- Include the unknown number as a Header – appears at the top of every page.
- The structures of the unknown should be provided at least twice in the report (abstract & results sections). Look up the name/structure online. Use common name if applicable.
- Keep as concise as possible while still being descriptive.

The lab report will consist of the following sections with the cover page available online.
Abstract – one paragraph summary of the experiment in this order:
(1) purpose – "The purpose of this experiment was to…"
(2) methods – list the methods used to determine the unknown (IR, names of chemical tests, and ^{1}H NMR)
(3) main results – results of *pertinent* chemical tests only (Lucas test was positive for …), one or two distinctive IR stretch(es) and one or two distinctive NMR peak(s)
(4) conclusion - state the identity of the compound (acceptable name).
Include the structure of the unknown below this abstract – no Figure heading necessary in abstract only. Use ChemDraw to present the structure here.

Results – Briefly introduce each method and pertinent chemical tests in one-to-two sentences: what *general* information one could / would get from that part of the experiment? Do not explain the history or inner workings of IR or ^{1}H NMR spectroscopy. State the facts, include all pertinent results for each part of the experiment with limited interpretation, and present the structure at the end of this section. Text should be interspersed with tables, where the text appears before it with a clear parenthetical reference to it (**Table x**). You will likely not list every result from the tables in the text. Instead, re-state a few main findings and refer the reader to the table. Save the logical description of how you solved the structure for the discussion section. Stick to the facts and initial interpretation in the results section. An example of how to organize the results section follows:

- Utility of IR spectroscopy and main findings
  - IR table: Functional group, bond, expected stretch, observed stretch
    - Include each IR active bond in your solved unknown structure (ignoring the fingerprint region)
- Description of each *pertinent* chemical test and results
  - Chemical test table: include ALL given chemical test results. Include a column for the functional group interpretation of each
- Utility of ^{1}H NMR Spectroscopy and main findings
  - Use ChemDraw to present the solved structure above the NMR table. Add letters corresponding to each set of H's on the structure.
  - NMR Table: Assignment (letter corresponding to labeled structure), observed chemical shift, expected chemical shift (use predictor tool or calculate values of solved structure), integration, and splitting.

Discussion – Re-state the goal of the experiment, initial IR findings, and a brief summary of the results obtained in the chemical tests (functional group assignment). Your analysis should be critical, showing how you deduced the structure of your unknown. Include the complete interpretation of IR and ^{1}H-NMR with the chemical shifts, integration, and splitting, comparison with table values and assignments (which bonds gave rise each IR band in the table and to which Hs each NMR signal belongs?). Students should refer to tables from the results section and peaks within (ex. the 3H singlet at 2.0 ppm was assigned to signal A) rather than reproducing the entire table and structure. Conclude with a statement of the methods used and the unknown name.

EXPERIMENT 2 OVERVIEW

The best way to become a master in any technique is practice and repetition. There is always room for improvement. Even the masters acknowledge that they are still students and are open to feedback from students, peers, and teachers. The goal in the first experiment is to re-familiarize students with lab equipment, approaching these techniques with a fresh pair of eyes. Depending on when you were in CHEM 8M, this may be a repeated experiment or it is similar. Do your best to avoid an attitude of "I already know how to do this" or "why are they making us do this again?" Practice patience and humility! Ask questions only after thinking through the problem and discussing with lab-mates. The other goal is to work independently, but knowing when to ask for help is important as well.

It can be relatively easy to set up chemical reactions, but takes far more expertise to work up the reaction and isolate the product with good yield and purity. The first wet lab days in 146A will give students practice in two important separation and purification techniques in synthetic organic chemistry: column chromatography and acid-base extraction. In this context, students also have the following learning objectives.

- Proper safety precautions and lab etiquette (see pages 5 – 11)
- Concise technical writing with proper grammar; following guidelines
- Thin-layer chromatography (TLC, see Appendix IV)
- Infrared (IR) spectroscopy (see Appendix VII)
- Use of the rotary evaporator (rota-vap, see Appendix III)

Lab Report

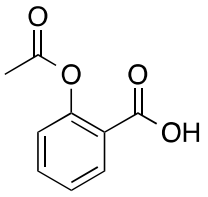
The final Exp 2 lab report consists of three parts: **(1) Introduction, (2) results, and (3) References.** Students assigned to Group A will turn in the Exp 2.1 (columns) report and Group B will turn in the Exp 2.2 (extraction) report. Students are encouraged to work together, with the assigned student taking responsibility for final content and edits. The **pre-lab questions** are included in the report grade, as well as an assessment of each student's **preparedness, safety, cleanliness, and organization** throughout the experiment. Reports will be penalized for being over two pages total, not including IR spectra. The lab notebook will be turned in whole after both parts of the experiment are completed – do not tear out, re-write, or photocopy.

Each student will write separate **introduction paragraphs** with at least one reference to a textbook or scientific paper (no web references here, half page maximum). This paragraph should include the **theory** behind the technique in a *general sense* (what it's used for and how it works, including principles guiding separation) with only the last sentence or two describing how the technique will be applied to the actual experiment. **This paragraph is not the history of the technique or the procedure (no specific amounts used)!** The writing should be descriptive but concise and follow technical writing guidelines (ex. passive voice, no personal pronouns). Instructors will evaluate your writing and provide general feedback. It is your responsibility to incorporate this feedback into the revised report. Students will lose points on the draft for not following the above instructions.

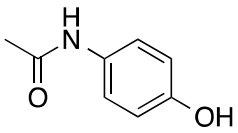
The **main results** (see underlined parts of procedures) should be stated in a few short, concise sentences. This includes ^{1}H and ^{13}C NMR tables for any two components.

At the very least, **reference** the lab text and journal article below using the format given in the appendix at the end of the lab manual. It is not necessary to reference this lab manual.

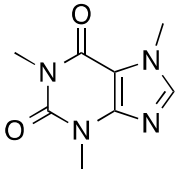
Experiment 2 – Separation of the Active Ingredients in Excedrin



Aspirin (ASP)



Acetaminophen (ACE)



Caffeine (CAF)

The over-the-counter analgesic Excedrin is composed of the three polar organic molecules shown above, which are held together by a starchy tablet binder. Aspirin (ASP), acetaminophen (ACE), and caffeine (CAF) can be dissolved in an organic solvent such as ethyl acetate (EtOAc) or ether and the binder is removed by filtration. In two separate experiments, students will separate the crude mixture of ASP, ACE, and CAF using (1) column chromatography and (2) acid-base extraction. The procedures also contain details on lab etiquette that students are expected to follow in future experiments without needing to be told.

Background Reading: access on campus from pubs.acs.org
Revell, K. D. *J. Chem. Ed.* **2011**, 88, 1413

Pre-lab Preparation

Each student must have the typed responses to the **pre-lab questions** on the first Exp 2 day and the prepared **lab notebook** for the day's experiment. The flow charts must be complete before beginning Exp 2.2. Students cannot participate in lab without a prepared notebook and will receive zero points for that part of the report. No credit will be given to pre-lab questions turned in late. Students will lose 5 points if the responses are not typed. Use ChemDraw to include chemical structures.

Pre-Lab Questions

1. What is the experimental objective common to both Experiment 2.1 and 2.2?

2. Identify each component (ASP, ACE, and CAF) as a weak acid, strong acid, or base. List the functional group in each that imparts the acid/base property.

3. Consider the expected results in the TLC separation of Excedrin components (**Figure 2** of the article referenced above). Report the R_f values of each and the mobile phase used. Explain the relative order of separation and distance each component moved from the origin.

4. Report the three mobile phases that will be used in column chromatography. Why are the solvents added in this order? Which component is expected to elute with each solvent mixture? What would happen if the solvent order were reversed?

5. The active ingredients in Excedrin are dissolved in ethyl acetate and then a mildly basic aqueous solution is added. Where is each component during this part of the extraction (organic or aqueous layer)?

6. The organic layer from #5 is treated with a strongly basic aqueous solution. Where are the remaining components (organic or aqueous layer)?

7. What IR stretches are *unique* to each compound?

Experiment 2.1 – Column Chromatography

In this experiment, students will separate ASP, ACE, and CAF using column chromatography (aka flash or liquid chromatography). This is similar in theory to the separation of spearmint and caraway oils students performed in CHEM 8M.

Notebook Preparation

- *Purpose:* Write the purpose of the experiment in one complete sentence. Draw the process scheme and structures of aspirin, acetaminophen, and caffeine at the top of the page.
- *Reagent Table:* Make a table with the physical properties of silica (SiO_2), aspirin, acetaminophen, caffeine, ethyl acetate, hexanes (*n*-hexane), and acetone. Include amount to be used (g or mL) or leave the space blank if the mass will be determined later, MM, b.p., density, and a one-word hazard description where appropriate (flammable, corrosive, etc. from the safety table).
- *Procedure:* Hand-written, step-wise, and concise. Include a list of materials (chemicals, labeled glassware, equipment, etc.) to obtain at the beginning of lab. Do not copy directly from the procedure below. **You cannot reference the lab manual during this experiment.**
- *Clean-up & Safety:* Copy the table at the end of the procedure into your notebook.

PROCEDURE

Active Ingredients in Excedrin - Obtain the mass of a single tablet of Excedrin® and crush using a mortar and pestle. Add 20 mL of EtOAc to the mortar and mix with a stir rod in the fume hood for 5 minutes. The three active components will dissolve and the starch binder (inactive ingredients) will not. Decant the solution into a small glass funnel with a small piece of cotton using a glass stir rod to aid in the transfer. Collect the filtrate in a 50-mL round-bottom flask (RBF). Transfer a few drops of the filtrate (liquid) to a capped vial labeled "**ORIGINAL MIXTURE + (your initials) + (date)**" and keep for TLC analysis.

Prepare & Load the Column - Add a small amount of silica (about ½ mL) to the RBF and concentrate to dryness using a rota-vap. The result is silica coated with Excedrin! Prepare the following solvent mixtures in the fume hood and keep in labeled, covered Erlenmeyer flasks: (1) 30 mL of 1:1 hexane/EtOAc; (2) 30 mL of 1:2 hexane/EtOAc; and (3) 30 mL of acetone. Spills are almost guaranteed when pouring directly from larger reagent containers. ***Help prevent chemical exposure incidents and spills using the following guidelines…***Use a funnel to transfer the bulk of solvent from the reagent container into a graduated cylinder, then use a pipet to bring the solution up to the proper volume. Students should not be pouring directly from 4-L solvent bottles! Label 6 large test tubes for collection of the column fractions and keep in a test tube rack. A disposable polypropylene column (1.5 x 12 cm) will be used for column chromatography. Securely clamp the column to a ring stand. Add 3 g of silica to the column, then add the silica /Excedrin mixture using a powder funnel.

Running the microcolumn: Carefully add the first solvent portion by pipet without disturbing the silica. Collect the eluent in the test tube labeled "Fraction 1". *Do not allow the column to run dry or test tubes to overflow*. Collect each successive 30 mL portion of solvent in two test tubes.

TLC Analysis: Analyze each fraction by TLC in comparison to the original mixture and standards. TLC analysis of the original mixture and standards can be done at any time during the lab. The spots should be small and dilute enough for 2-3 spots per plate without smearing. The first student to begin TLC should make solutions of the standards and keep in labeled test tubes in the reagent hood. Each standard should have its own designated labeled capillary tube. Conserve capillary tubes for your samples – each group can use just one for the entire lab. Carefully but quickly spot the plate. Best results are obtained when the spots are very small and

tight. Rinse the capillary with acetone to prevent cross-contamination between samples. Before placing the plate in the developing chamber, visualize the spots with a UV lamp to ensure you added enough sample to visualize but not too much to smear. A more complete description of running and analyzing TLC plates can be found on the CHEM 8L website in the Experiment 4 PDF, as well as in your textbook.

Run the TLC plate in the fume hood: All TLC chambers should be kept in the fume hoods and covered at all times. Using tweezers, carefully place the TLC plate into the developing chamber. Be sure to not to disturb the mobile phase as the sample should not dissolve in the solvent. Place the cap on the jar upside down (screwing the cap on will disturb the mobile phase). Allow the TLC plate to run until the solvent is approximately 1 cm from the top of the plate. Remove the plate with tweezers, quickly draw the solvent front on the plate, and wait until the solvent evaporates before visualizing with the UV lamp. Circle the spots, calculate all R_f values, then dispose of the plates in solid waste. Which fractions contain which compound(s)? Was the separation successful?

Isolation of Components: Any fractions containing a single compound, as determined by TLC, can be concentrated using a rota-vap. If two fractions contain the same single compound, those fractions can be combined. Review Appendix III for use of the rota-vap and check with the TA to ensure you are using this equipment properly. Transfer the fraction(s) to an appropriately sized, pre-weighed round-bottom flask and concentrate. The compound may or may not solidify. Record the mass of each component isolated and determine the percent recovery, as compared to the amount of each component in an Excedrin tablet.

IR Analysis – Students will need to coordinate or rotate to share this one instrument. Obtain the IR of any one pure component when the IR is available. If no pure compounds were obtained, take the IR of any one standard. Consult the IR table of values to determine the expected stretches and which peaks to pick. Make a Nujol mull then transfer onto the plate - grind the mull for at least one minute. Honest self-assessment – ask your TA for a refresher on how to use the IR if needed. Does IR analysis confirm the identity of this component?

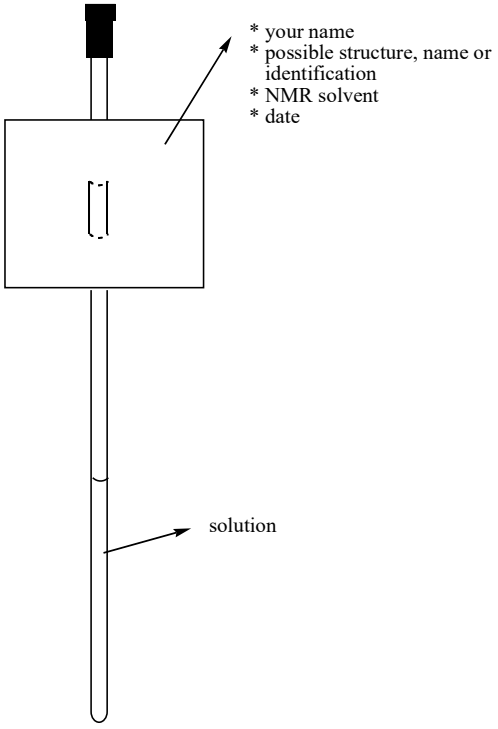
Gloves should be worn when preparing samples but taken off when using the computer. Plates must be rinsed and wiped immediately with acetone saturated with NaCl. Plates must be put back in the metal container and desiccator after each use. The NaCl plates are hygroscopic and can be ruined by the moisture in the air. These expensive plates are delicate so handle with care! The sample prep area should be cleaned after each use.

Table 2.1. Column Clean-up and Safety

Clean-up	**Safety**
Liquid waste: acetone, hexanes, and fractions	Acetone, hexanes, ethyl acetate are flammable
Solid waste: pipets, columns with tubing, dry silica, TLC plates	Caffeine is a *stimulant* and is NOT to be ingested or taken home.
Wash glassware, put away equipment, and wipe benchtops	Silica is an irritant
ALL STUDENTS IN ANY SECTION WITH GLASSWARE (INCLUDING PIPETS) IN ANY OF THE TRASHCANS WILL **LOSE 5 POINTS** FROM THEIR LAB REPORT	

NMR Analysis

Safety First
- Deuterated chloroform is a possible carcinogen.
- Wear gloves when preparing the NMR samples.
- Prepare samples in the fume hood.
- Keep the NMR tubes capped at all times.
- Do not clean the NMR tubes yourself. Return them to the TA or the stockroom for cleaning.



Choose any one pure component (assessed by TLC) and prepare a sample for NMR. For solids, dissolve approximately 15 mg of sample in 800 μL of deuterated chloroform ($CDCl_3$). Transfer this solution using a pasteur pipet into a clean, dry, and labeled NMR tube. For liquids, add 800 μL of deuterated chloroform ($CDCl_3$) into the NMR tube using the shared pluringe. Use a long-stem pipet to transfer one drop of sample into the labeled NMR tube, add the pipet bulb, and draw the solution up and down to dissolve the sample.

Always wear gloves when preparing the NMR samples and do it in the fume hood. Label the NMR tube with a provided paper flag with two holes inserted as shown in the figure below. Make sure that the label contains your name, the identification of the sample (name or possible structure or origin (such as: "basic compound")), solvent used, and date. ***Do not use tape*** to label the NMR tubes. *Samples improperly labeled will not be run and this will set you behind!*

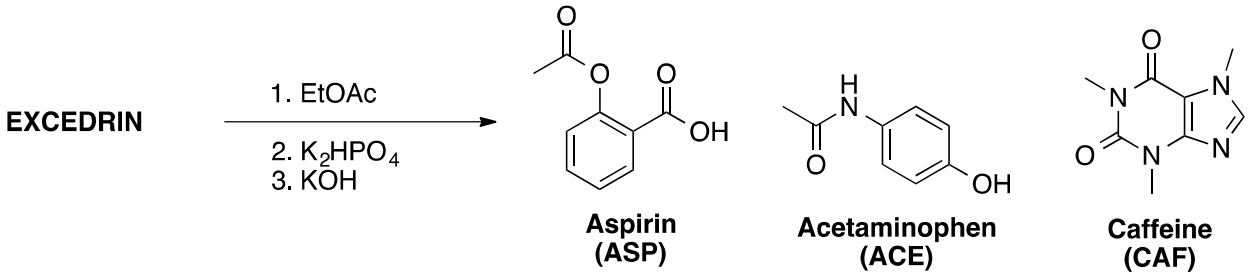
NMR spectra will be available to students in a shared Google Drive folder within a few days. A link to this folder is on the CHEM 146A website. Students must be logged into their ucsc account to access spectra.

Each student should include <u>^{1}H NMR and ^{13}C NMR analysis in table format</u> for one component. The complete structure with labeled H's and C's should be included above each table. The ^{1}H NMR table should include the assignment (letter corresponding to labeled structure), observed chemical shift, expected chemical shift (use predictor tool or calculate values of solved structure), integration, and splitting. The ^{13}C NMR table should include the assignment, observed chemical shift, and expected chemical shift.

Experiment 2.2 Acid-Base Extraction of Excedrin Components

Notebook Preparation

- *Purpose* – one-sentence description of the purpose in addition to the following scheme:



- *Reagent table* – Amount (mg or mL), MW, bp or mp, density, and one-word hazards found in the clean-up/safety table for each of the chemicals in the scheme above. For Excedrin, list only the amount to be used and leave space to write down the actual mass used in lab.
- *Procedure* – hand-written, step-by-step procedure. Include a list of materials (chemicals, labeled glassware, equipment, etc.) to obtain at the beginning of lab. You cannot reference the lab manual during the experiment.
- *Safety & Clean-up* – copy the table at the end of the procedure into your notebook.

EXPERIMENTAL PROCEDURE – Students work in pairs

**This experiment includes many different clear, colorless liquids. Containers must be labeled with the contents, your initials, and experiment date before the material is inside.

Frequently refer to flow charts along with written procedure.

All steps involving ethyl acetate (EtOAc) must be performed in the fume hood. Only one student from each pair should be at the fume hood at a time – rotate different parts of the experiment. Your TA must approve your separatory funnel technique with water before you begin the experiment.

Separation of the active ingredients in Excedrin - Obtain the mass of a single tablet of Excedrin® and crush using a mortar and pestle. Add 20 mL of EtOAc to the mortar and mix with a stir rod in the fume hood for 5 minutes. The three active components will dissolve and the starch binder (inactive ingredients) will not. Decant the solution into a small glass funnel with a small piece of cotton using a glass stir rod to aid in the transfer. Collect the filtrate directly in a separatory funnel secured on a support ring on a ring stand. Carefully drain a few drops of the filtrate (liquid) to a capped vial labeled "**ORIGINAL MIXTURE + (your initials) + (date)**" and keep for TLC analysis next week.

Extraction with weak base - Add 10 mL of $K_2HPO_{4\ (aq)}$ (aqueous dibasic potassium phosphate) to the separatory funnel. Cap then invert the funnel twice, holding onto the cap. Vent into the fume hood by holding the funnel upside-down and open the stop cock with the tip pointing *away from your face*. Continue to mix and vent frequently for at least 3 minutes. A chemical reaction is taking place and proper time must be given for components to travel to the preferred layer. Drain the mildly basic aqueous layer containing deprotonated aspirin into a labeled scintillation vial (**K_2HPO_4 – ASP AQ**) and set aside. The organic layer will remain in the separatory funnel. Extract the organic layer with an additional 3 mL of K_2HPO_4 (add 3 mL of $K_2HPO_{4(aq)}$, mix and vent for several minutes, then drain into the **K_2HPO_4 – ASP AQ** vial). The organic layer remains in the funnel. One student in the pair should move onto "**Isolation of Aspirin**" using the combined **K_2HPO_4 – ASP AQ** extracts.

Extraction with strong base - Add 10 mL of 1 M KOH to the separatory funnel. Mix the layers for 3 minutes (vent early and often into the fume hood). Drain the aqueous layer containing deprotonated acetaminophen into a second small, labeled container (**KOH – ACE AQ**) and set aside. Extract the organic layer with an additional 3 mL of KOH (add 3 mL of KOH, mix & vent for a few minutes, then drain the aqueous layer into the **KOH – ACE AQ** vial). Keep the organic layer in the funnel.

Isolation of caffeine - Wash* the remaining organic layer with 10 mL of *aq*. NaCl (brine). Separate the layers, draining the organic layer into a small, labeled Erlenmeyer flask. The brine wash (aqueous) should be kept in a separate container labeled "waste" and transferred into the liquid waste at the end experiment. Use an additional 2 mL of EtOAc to rinse any residual caffeine from the walls of the separatory funnel. Remove any visible water from the bottom of the Erlenmeyer using a pipet. Dry the organic layer by adding two spatula tips of anhydrous sodium sulfate (Na_2SO_4). Allow the capped organic layer to sit with occasional swirling for 5 minutes (move onto one of the isolation steps below while waiting). Decant the organic layer using a small glass funnel with loosely packed cotton into a pre-weighed 50 mL RBF. Concentrate the dried organic extracts using a rotary evaporator (rota-vap). This concentrated caffeine extract may either be a liquid or solid, depending on purity. Obtain the <u>mass of caffeine</u> by difference with the original flask then transfer into a labeled vial.

Isolation of Aspirin – This step may be performed on the benchtop. Tear a 2-inch piece of pH paper into many small squares to conserve and put the pH paper back where it belongs. Determine the pH of the **K_2HPO_4 – ASP AQ** solution by dipping a stir rod into the solution then touching to a small piece of pH paper on a watch glass. Obtain 10 mL of 6 M HCl in a labeled test tube. Slowly add 6 M HCl drop-wise to the **ASP AQ** solution, swirling and taking pH readings after every 5-10 drops, until the solution is acidic (pH 2 or less). Do not rush this process! Re-label the vial "**Acidic ASP AQ.**" It may be necessary to get additional 10 mL portions of HCl. Please conserve and take only small amounts at a time (how much HCl should be required to neutralize the solution?).

Isolation of Acetaminophen – Carry out the same acidification procedure used to isolate aspirin. Label the vial "**Acidic ACE AQ**."

Acidic aqueous extraction – The neutral protonated compound, either aspirin or acetaminophen, is in the aqueous solution and will be extracted with EtOAc. *If the solution contains a significant amount of precipitate, skip this step and move to the next paragraph.* Transfer the acidic aqueous solution to the separatory funnel and add 15 mL of EtOAc. Mix and vent for 3 minutes, then drain the aqueous and organic layers into separate flasks. Extract the aqueous layer with an additional 15 mL of EtOAc (add 15 mL EtOAc to the aqueous layer, mix & vent for several minutes, then remove the aqueous layer). Wash the combined organic extracts with 10 mL of brine. Separate the layers and dry the organic layer over anhydrous Na_2SO_4 for 5 minutes (remove visible water from the organic layer by pipet, add the drying, and allow to sit with occasional swirling). Filter into a pre-weighed 50-mL round-bottom flask then concentrate using a rota-vap. The concentrated extracts may either be a liquid or solid, depending on purity. Obtain the <u>mass of product</u> by difference, transfer to a labeled vial, and proceed to analysis.

If a significant amount of either ASP or ACE precipitated out of acidic solution, save this in a vial in your drawer until the next lab to allow the crystals to form completely. The solution needs to be opaque to qualify. In the next lab period, collect the product by vacuum filtration and allow to air dry for 10-15 minutes. Obtain the <u>mass of the solid</u> then transfer into a capped vial labeled "**ASP or ACE + (initials)**."

* Wash = add brine to the funnel and mix for 1 minute before draining the aqueous layer

ANALYSIS Perform TLC analysis first then IR of any *one pure* solid when the instrument is available. Calculate the percent recovery of each component from the original mass of Excedrin. You must complete all analysis, have your area clean, and be ready to leave at least 5 minutes before lab ends. Check in with the TA before leaving. There is time to complete analysis during the following lab.

Percent Recovery – Report the percent recovery of each component in comparison to the initial mass of the tablet.

TLC – Begin preparing solutions and plates during down time (dry/rota-vap). Use an analogous procedure to Exp 2.1. Analyze each component by TLC and compare to standards. Assess the identity and relative purity of each fraction.

IR – Obtain the IR of any one solid when the instrument is available. This should be a different component than that analyzed in Exp 2.1 Refer to the procedure in Exp 2.1 for etiquette. Identify the peaks that confirm the identity of the component, including wavenumber, functional group, and bond.

NMR Analysis – Follow the same instructions as in Exp 2.1, using a different component.

Table 2.2. Extraction Clean-up and Safety

Clean-up – leave the lab as you found it!	**Safety**
Glass waste: uncontaminated pipets only	HCl and KOH are corrosive & toxic.
Liquid waste: contents of rota-vap trap, TLC solutions	Acetone and ethyl acetate are flammable. Caffeine is a stimulant and is NOT to be ingested or taken home.
Solid waste: filter paper, used pipets, TLC plates	
Product waste bag: product vials	Do not look directly into the UV lamp.

Experiment 2 report guidelines can be found on page 23.

EXPERIMENT 3 - Separation & Identification of Two Unknowns

You will be assigned a unique mixture of two unknowns – a basic compound (amine) and an acidic compound (carboxylic acid or phenol). This is a dry lab. Each student will independently devise a procedure for separating these compounds before lab and solve the structure using provided IR, ^{1}H NMR, and ^{13}C NMR spectra.

Separation of Acids and Bases by Extraction

Extraction is based on a compound's solubility in different solvents at different pH levels. This phenomenon is most pronounced between ionic compounds, which are generally water-soluble, and non-ionized organic compounds, which are generally soluble in less polar organic solvents and insoluble in water.

We use this principle to our advantage in the separation of acidic and basic compounds. Treating such a mixture with aqueous base converts acidic compounds to salts that travel to the aqueous layer as they are more soluble; separating layers thus separates the compounds. Acidification of the basic aqueous extract converts the salt into the protonated acid form which, because this form is insoluble in water, can be filtered if it is a solid or extracted with an organic solvent if it is a liquid. Similarly, organic bases (amines) can be extracted with aqueous acid, then isolated by basifying the acidic extract.

Separation and isolation of each component

Separation of the components follows the classical extraction procedure with dilute acid and base. After extracting three times with a dilute aqueous solution, back-extract the aqueous solution with the organic solvent—some non-ionized compounds have appreciable water solubility and back-extracting will assure a more efficient separation of the acidic or basic component from the others. The ionized compound in aqueous solution will need to be neutralized then extracted three times with the organic solvent.

When the un-ionized form is regenerated from the aqueous solution, it is best to extract the aqueous mixture with the organic solvent even if the component is a solid. Filtration is often an inefficient isolation procedure due to partial solubility and mechanical material loss.

Notebook Preparation: Procedure

Students will describe how to separate the unknowns with a step-wise written procedure, flow chart, and diagram in the notebook, similar to Exp 2.2. Students must have this procedure approved by the TA before being given unknown spectra. Include all glassware, including size. An inventory of solvents, solutions, and volumes is as follows. It may not be necessary to use each solution below. Other equipment and materials such as drying agents, pH paper, should be included in your procedure as well.

Organic solvent: ethyl acetate, extract with 30 mL portions.

Basic solutions: 1 M NaOH, extract with 25 mL portions; 3 M NaOH, add drop-wise

Acidic solutions: 1 M HCl, extract with 25 mL portions; Concentrated HCl, add drop-wise

Neutral solution: saturated NaCl (brine), use 10 mL to wash combined organic extracts

Clean up & Safety – include within the procedure

- Transfer any unused or to be discarded basic aqueous layer to the container labeled “Aqueous waste - basic.”
- Transfer any unused or to be discarded acidic aqueous layer to a container labeled “Aqueous waste - acidic.”
- The contents of the rota-vap and any unused or to be discarded organic layer should be disposed of in the container labeled “Organic solvent waste.”
- Dispose of the unused unknowns in the bag labeled “Unknowns-waste.”
- Dispose of any Pasteur pipet, filter paper, drying agent in the container labeled “Solid waste.”

EXPERIMENT 3 REPORT GUIDELINES

- Detailed procedure for separation of an acid and base
- Structural determination of two unknowns via IR and NMR spectroscopy
    - Unknown A Results & Discussion
    - Unknown B Results & Discussion
- Read and apply info from ***Appendices I & II***
- Include the unknown number as a Header – appears at the top of every page.
- The structures of both unknowns should be provided at least twice in the report (abstract & results sections). Look up the name/structure online. Use common name if applicable.

Exp 3 Report Formatting & Organization Guidelines

Abstract – one paragraph summary of the experiment in this order:
(1) purpose – "The purpose of this experiment was to…"
(2) methods – general methods for separation and analysis
(3) main results – distinctive IR stretch(es) and NMR peak(s) for the unknown acid (UNK A) and unknown base (UNK B) in separate sentences
(4) conclusion - state the identities of the two compounds (acceptable names).
Include the structures of both compounds below (ChemDraw) – no Figure heading.

Procedure - Your audience for this section is an intro-level (CHEM 8M) student.

Incorporate the written procedure in complete sentences (paragraphs, bullet points, or numbered) with the flow chart and diagrams. Use ChemDraw to make the flow chart and diagrams. Number these as figures and give short, descriptive titles. Refer to each figure parenthetically in the written procedure. You are encouraged to go the extra mile by including photos of experimental setups, additional safety notes, and pro-tips or potential sources of confusion.

Results - Your audience for this section is a fellow 146A student and TAs.

IR – State one or two stretch(es) indicative of the functional group(s) in the solved structure. Include a table with functional group, bond, expected, and observed wavenumbers for each IR active bond in the solved structure.

NMR – State only a few signals in the ^{1}H and ^{13}C NMR spectra – those that were pivotal in your structural assignments. The ^{1}H NMR table should include the assignment (letter corresponding to labeled structure), observed chemical shift, expected chemical shift (use predictor tool or calculate values of solved structure), integration, and splitting. The ^{13}C NMR table should include the assignment, observed chemical shift, and expected chemical shift.

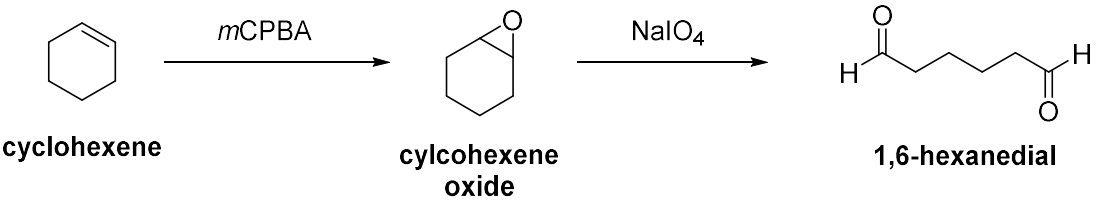
Discussion – Re-state the methods used for structural determination of the unknown. Your analysis should be critical, showing how you deduced the structure of your unknown. Include the complete interpretation of IR and ^{1}H and ^{13}C NMR with the chemical shifts, integration, and splitting, comparison with expected values and assignments (which bonds gave rise each IR band in the table and to which Hs each NMR signal belongs?). Students should refer to tables from the results section and peaks within (ex. the 3H singlet at 2.0 ppm was assigned to signal A) rather than reproducing the entire table and structure. Conclude with a statement of the methods used and the unknown name.

References

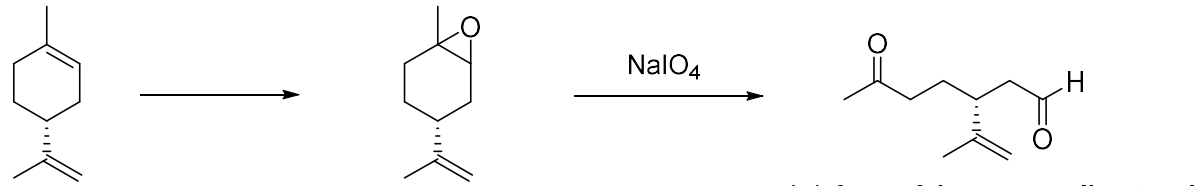
- Refer to **Appendix II** for format
- References should be cited as endnotes – superscripted number goes after punctuation at the end of the sentence. The endnotes are listed in the References section. If a reference is listed at the end of the report, it needs to actually be used and cited in the text.

Experiment 4: Synthetic Methodology - Alkene Epoxidation and Oxidative Cleavage

In this experiment, the class will perform representative procedures for two types of reactions in the literature: **(1)** Epoxidation of an alkene with *m*CPBA and **(2)** oxidative cleavage with $NaIO_4$. Students will look up references and linked supporting information to find the procedure for each reaction. Each pair will be assigned one reaction to perform two-to-three times on a 20 mmol scale with respect to alkene or epoxide. Crude reaction products will be analyzed by ^1H NMR. Further purification may need to be performed *via* column chromatography. Time and reagents permitting, students may collaborate with another group to complete the two-step reaction.



cyclohexene **cylcohexene oxide** **1,6-hexanedial**



(*R*)-(+)-limonene **(+)-limonene oxide** (*cis* / *trans* mixture) **(*R*)-6-oxo-3-isopropenylheptanal**

The procedure will be prepared in the lab notebook before entering lab and includes one-sentence purpose, reaction scheme, reagent table, and abbreviated procedure (mostly copying from literature experimental methods is okay). Each reaction should be started on a new page. Duplicate reactions get new pages as well - complete with purpose, table, etc. where "refer to pg xx for procedure" is appropriate.

(1) Treatment of an alkene *meta*-chloroperoxyacid provides the corresponding epoxide, as demonstrated by in the following reference.
- Constantino, M. G.; Lacerda Jr., V.; Invernize, P. R.; Carlos da Silva Filho, L.; Jose da Silva, G. V. *Synth. Comm.,* **2007**, 37, 3529 – 3539.
- This reaction can be run and worked up in the same day.

(2) Treatment of epoxides with sodium periodate ($NaIO_4$) should yield corresponding aldehydes and ketones, using the procedure in the following reference. The representative procedure gives a range of 2 – 5 molar equivalents of $NaIO_4$. Students will optimize the amount of $NaIO_4$ used.
- Binder, C. M.; Dixon, D. D.; Almaraz, E.; Tuis, M. A.; Singaram, B. *Tet. Lett.*, **2008**, *49*, 2764-2767.
- This is an over-night reaction: set up one day, work up the next.

Background Reading: In addition to the references given above, read the sections within Chapters 8 & 18 of McMurry's *Organic Chemistry* regarding epoxide formation and opening.

Experiment 4 will be completed over nine lab periods. All students must be finished with all wet lab work by 5:10 and ready to leave by 5:25. General cleaning and community tasks should be completed or point penalties will apply.

Students should determine the optimal conditions for TLC separation of product / reactant with hexanes and ethyl acetate mobile phases using an iodine chamber to visualize the plate (read TLC appendix).

The crude reaction mixture for each reaction will be analyzed for percent composition by ^{1}H NMR, which should be available within a few days.

A typed progress report is due at the half-way point (see schedule), including results obtained so far with experimental methods.

All students must have a draft of the Exp 4 report typed and in-hand at the beginning of lab (see schedule for draft due date), including a cover page obtained in lab. Each student should participate in a peer review editing process, referring frequently to all the guidelines in the lab manual (appendices and specific Exp 4 guidelines provided. Experimentation may be performed this day, but students must still participate in the editing process.

Pre-lab questions – typed and in-hand at the beginning of Exp 4, Day 1 (see schedule)

1. Read the mCPBA article posted on the course website. Draw the reaction scheme for the synthesis of *m*-CPBA using ChemDraw and comment on why we are buying this compound rather than synthesizing it ourselves!

2. What is the theoretical yield of each reaction?

    a. Limonene → limonene oxide
    b. Limonene oxide → (cleavage product)
    c. Cyclohexene → cyclohexene oxide
    d. Cyclohexene oxide → (cleavage product)

3. Why is limonene oxide produced as a mixture of diastereomers in the first step? How will this effect the ^{1}H NMR spectrum?

4. Why would this two-step method be preferred to ozonolysis? There is a brief discussion on this topic in the following reference but further research is recommended: Binder, ***et. al. J. Org. Chem***. **2009**, *74*, 2337.

5. Use a SciFinder search to find another method for oxidative cleavage of alkenes. Provide the reference and reaction scheme using ChemDraw along with an approximate cost breakdown of each chemical based on listings on the SigmaAldrich website, if available through that vendor. Calculate the entire cost of reagents on a 20 mmol scale, not including work-up solvents.

EXPERIMENT 4 REPORT

Further details of and clarifications to this report will be announced in class. This depends on the success of the experiment and whether or not students collaborate.

Refer to **Appendices I & II for general formatting and writing style.

Abstract – one paragraph summary of the experiment
Purpose – "*The purpose of this experiment was to…"*
Methods – reaction overviews (chemicals names at least) without specific amounts or mention of reaction workup or purification
Main Results – one sentence per reaction giving product description and highest yield obtained. If products were not pure, list this as "crude yield."
"_____ *was obtained as a clear liquid (xx mg, xx% yield)*."
Conclusion - state whether the reaction(s) were successful and/or gave the expected products.

Include the reaction schemes below with the name under each compound in bold

Introduction – no more than one page of background including but not limited to…
Utility of epoxides and/or cleavage products in organic synthesis
Epoxides or epoxidation reactions – alternate methods or applications
Oxidative cleavage – alternate methods or applications

Results – state the main results (reaction yields – crude and after purification if applicable; include % conversion from ^{1}H NMR if applicable). Refer the reader to tables for spectral data with limited interpretation. Do not list every peak in the table! State one or two distinctive peaks per compound before the table.

Tables to include (numbered with title)…
- One IR table for all 3 compounds with significant stretches
- Two NMR tables for each compound (^{1}H and ^{13}C NMR)

If impure spectra were obtained, it is ok to reference literature chemical shifts, splitting, etc. to make the assignments.

Discussion – 1 page preferred, 2 pages maximum
Complications and sources of error in the reactions
You may briefly describe any mistakes you made, if applicable, but this section is more about ways that the reaction or experimental approach could have been improved.

Experimental Methods – per formatting in sample in the lab manual
General methods
Representative procedure if multiple reactions of same typed performed
One paragraph per compound synthesized, including specific amounts used and yield, plus compound characterization (ok to use literature values)

References – at least 3 scientific literature references using Appendix II format

Appendix I. Organization and Style of Lab Reports

See the schedule for report drafts and revised due dates. The reports are to be organized in a neat and professional manner. ***Write like your job depends on it!*** One of the goals of CHEM 146A is to develop your proficiency in reporting the results of experimental work. The results of scientific research are of little value unless they are known to others who can make use of them. Written reports are more important than oral communications. These take the form of papers in the chemical literature. This body of literature serves as an important repository for past experimental, theoretical, and conjectural results on a variety of topical areas.

A written report should be both concise and clear. Clarity in writing rests on a thorough understanding of the problem undertaken and of the significance of the results. One must be able to convey this understanding to the reader in a coherent, organized, and concise fashion. ***Lab reports written with poor grammar and spelling will be returned for revision, with no extension of the due date.***

Students should be accustomed to the style of technical writing outlined in CHEM 8L/M. Revisit the writing guidelines from your previous courses and/or access this online. The following points are of particular importance in 146A reports.

* Reports should be typed, double-spaced, justified text with adequate margins. Pages should be numbered, including attached spectra (hand-written page numbers are OK for spectra). The report should be printed on paper and securely stapled or bound in a folder.

* Use the cover pages provided online.

* Literature references should be sequentially numbered with in-text citations, and placed at the end of the report. See **Appendix II** for the appropriate format, as used in *J. Am. Chem. Soc*. **If a reference is listed at the end of the report, it needs to actually be used and cited in the text.**

* Common abbreviations may be used: mm, cm, g, mL, Hz, NMR, sec, mp, GC, HPLC. Periods should not be placed after these except in. for inch and no. for number which do require periods. You can (and should) define abbreviations parenthetically for anything else the first time they are used. Thereafter use that abbreviation. Do not switch back and forth!
Ex. “The 2,4-Dinitrophenylhydrazine (DNPH) test…”

* To ensure clarity, it is common to sequentially number compounds and structures with boldface integers: **1**, **2**, **3,** etc. These numbers are used to clearly refer to compounds in the body of the text.

* All reports should use ***grammatically correct, complete English sentences***. While your lab book can be written using phrases, the report should be written professionally, with proper grammar and spelling. The ACS style guide sets the following protocol for scientific writing: use past tense for your experimental findings, and use the present tense for “statements of fact” from the literature. Reference all information retrieved from the literature with footnotes (see 3 above!).

* In *scientific writing*, **avoid the use of the first person (“I” or “we”)**. For example, instead of writing “I recrystallized my neutral unknown from ethanol to give 0.66 g of a solid as white needles;” instead write: “The neutral unknown was recrystallized from ethanol to give a white solid (0.66 g).”

* Include a document header including your name and unknown number so that this information appears on every page.

* EVERY figure, table, and scheme is given a number and descriptive title. EVERY one of these should be referenced in the text, preferably before the figure, table, or scheme.
  - Scheme = reaction; Figure = anything not a reaction or table, ex. mechanisms
  - Ex. **Table 1.** ^{1}H NMR Shifts of Acetanilide
  - "The chemical shifts, integration, and splitting patterns for acetanilide can be found in **Table 1** below." …or…
  - "The structure of acetanilide was confirmed by ^{1}H NMR spectral analysis (**Table 1**)."

* Elements and chemical names are NOT proper nouns.

* Do not start sentences with numbers or abbreviations. Write out the name for numbers below ten (one, two, three…10, 11, 12…).

**** The teaching team (Caitlin, David, and Patrick) are available to help with your reports. Help us help you by reading the lab manual and text carefully before asking for help. It makes a lasting impression when students clearly have taken the effort to work out issues on their own, then discuss the outcome with the instructor. That being said, don't wait too long to ask for help!***

Experimental Methods and Compound Characterization

Experimental methods and compound characterization are found at the end of scientific journal articles, dissertations, and other technical documents to give the reader instructions on how to recreate the experiment and confirm the structure of the newly synthesized compounds. The format and general content differs depending on the field. Students will include this section at the end of the final lab report using the generally accepted guidelines followed by synthetic organic chemists: one General Methods paragraph followed by one additional paragraph per compound synthesized. ***A sample Experimental Methods section is provided online and contains much more information than CHEM 146A students are expected to include.*** *Use passive voice and past tense.*

General Methods

Reagents and by-products do not get full descriptions but are mentioned in the "General Methods" section with the following statement: "All reagents were commercially available, unless otherwise stated." Typically researchers would then describe how reagents and solvents were purified, but *this does not apply to 146A students*. Next, define the abbreviations and list the specifications for NMR (MHz of instrument) and IR (medium for analysis, such as salt plates or Teflon) only if used in the experiment.

Experimental Methods

Following general methods, each organic compound or reaction gets its own paragraph (one paragraph per reaction/compound). Depending on the forms of analysis available to students (based on experimental techniques as well as spectra provided), some or all of the following should be included in the experimental methods and compound characterization section.

- Reaction scheme - including reactants, reagents, products, solvent(s), and % yield (structures and reaction schemes can be hand-written)
- **Full chemical name of product in bold** (common and/or IUPAC)
- Brief description of reaction set up and workup including…
  - Names and amounts of each reactant and reagent (mmol and mL or mg)
  - Name and amount of solvent (mL)
  - Order of addition, if pertinent, and reaction conditions (time, temperature)
  - Description, name, and amount of product obtained and % yield:
    - Ex. "Benzhydrol was obtained as a clear liquid (1.00 g, 87% yield)."

Characterization follows in the same paragraph (after reporting the yield) and includes some or all of the following.

- ^{1}H NMR data – peaks listed downfield to upfield with chemical shift, integration, splitting, and coupling (*J*) values
- Melting point or boiling point
- Optical rotation
- Distinctive IR stretch(es) – one or two distinguishing peaks, such as carbonyl or O-H stretches

Excerpt of Experimental Methods Section (Dr. B's Thesis)

The following is an excerpt of the supporting information for a Ph.D. dissertation and contains significantly more details than are applicable to CHEM 146A students. Follow the general format below and apply to reports where experimental methods sections are required.

General Methods.

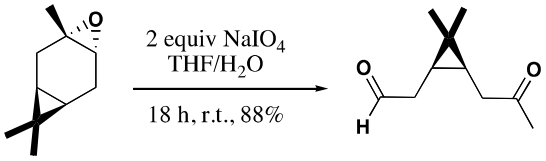
All reagents were commercially available, unless otherwise stated. All air and moisture sensitive reactions were carried out under argon atmosphere using flame- or oven-dried glassware and standard syringe technique. Tetrahydrofuran (THF), dichloromethane (DCM), cyclohexane, triethylamine (Et_3N), morpholine, *tert*-butanol (*t*-BuOH), and dimethyl sulfoxide (DMSO) were distilled over CaH_2. Oxalyl chloride was distilled without drying agent prior to use. Column chromatography was carried out with Silica Gel 60.

Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were carried out at 300, 500, or 600 MHz. Chemical shifts are reported relative to TMS (δ=0 ppm), $CHCl_3$ (δ=7.27 ppm) or DMSO (δ=2.54 ppm) for ^{1}H NMR and $CHCl_3$ (δ=77 ppm) for ^{13}C NMR. The following abbreviations were used to describe peak patterns where appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet, app=apparent, sep=septet, and m=multiplet.

IR spectra were carried out on NaCl plates with ν_{max} in inverse centimeters. Optical rotations were obtained on a digital polarimeter at 20 °C. High resolution mass measurements were obtained on a benchtop ESITOF mass spectrometer.

Representative procedure for $NaIO_4$-mediated cleavage of epoxides. To a round-bottom flask equipped with magnetic stir-bar, finely powdered sodium periodate (99% pure, 2 - 5 equiv) was stirred with the appropriate solvent mixture (2:1 THF/H_2O or CH_3CN/H_2O, 40 mL) for five minutes. The epoxide (10 mmol) was then added and the reaction mixture was stirred at room temperature. Upon reaction completion, as monitored by TLC, the reaction mixture was filtered and solids were washed with 30 mL Et_2O, creating two distinct layers. The aqueous layer was

extracted with Et_2O (2 x 30 mL), washed with water and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Spectra of compounds **2.3**-**2.11** were consistent with literature data.



3.4-(Dimethylcyclopropyl)-heptan-1-al-6-one, 2.7. (3*R*)-3-Carene oxide (11.3 mmol, 1.6 mL) was reacted with sodium periodate (20 mmol, 4.28 g) for 24 h in 2:1 THF/H_2O (30 mL). **2.7** was isolated as an orange oil (1.678 g, 88% yield). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.78 (t, *J*=1.8 Hz, 1H), 2.34 (m, 4H), 2.17 (s, 3H), 1.15 (s, 3H), 0.98 (m, 2H), 0.91 (s, 3H). ^{13}C NMR ($CDCl_3$, 500 MHz) δ (ppm): 208.5, 202.1, 39.7, 39.4, 29.7, 28.5, 21.1, 19.4, 17.2, 15.2. $[\alpha]^{20}_D$ -4.8° (*c* 4.0, MeOH), IR (neat) 1719 cm^{-1}. ESITOFMS *m/z* $[M+H]^+$ 169.1266 (calcd for $C_{10}H_{17}O_2$ 169.1223).

Appendix II

FORMAT FOR LITERATURE REFERENCES

There is a standard A.C.S. (American Chemical Society) format (see http://pubs.acs.org/books/references.shtml) for listing references in the chemical literature that you are required to follow. This format, illustrated below, must be used in the reference section of your report, if appropriate. Be sure to document all assertions and past work described in your reports with a footnote. Footnotes can be referred to more than once. Use superscripts[1] with corresponding numbered references at the bottom of the page or at the end of the report.

BOOKS

Author's last name, first initial, *Title of Book* Publisher: City of publication, Year of pub.; pages used.

Examples

Crews, P.; Rodríguez, J.; Jaspars, M *Organic Structure Analysis, 2nd Ed.;* Oxford University Press: New York, 2010; pp. 67-70.

Palleros, D.R., *Experimental Organic Chemistry;* John Wiley & Sons, Inc.: New York, 2000; pp. 61-70.

JOURNALS

Author's last name, initials; 2nd author's last name, initials *Journal abbrev.* **Year**, *Vol.,* first to last page of article.

Examples

Tansakul, C.; Lilie, E.; Walter, E. D.; Rivera III, F.; Wolcott, A.; Zhang, J. Z.; Millhauser, G. L.; R. Braslau, R. *J. Phys. Chem. C,* **2010**, *114,* 7793-7805.

Sanchez, L. M.; Lopez, D.; Vesely, B. A.; Della Togna, G.; Gerwick, W. H.; Kyle, D. E.; Linington, R. G. *J. Med. Chem.*, **2010**, *53*, 4187-97.

Woehrmann, M. H., Gassner, N. C., Bray, W. M.; Stuart, J. M.; Lokey, S. *J. Biomol. Screen.* **2010**, *15,* 196-205.

WEB SITES

These are not recommended for this class. Use full websites addresses so a reader could locate your referenced material on the web. **Be wary of the content. The info on the web is usually not peer reviewed, and can be erroneous!** If you do cite a website, include the date the website was accessed.

Example

http://organicchemistry.wordpress.com/2007/08/18/tips-for-writing-organic-chemistry-lab-reports/ accessed 7-23-09.

Further Reading on Experimental Organic Chemistry and Structure Determination

There are many excellent textbooks on the art of organic structure determination (using NMR as well as other techniques), and more continue to be written all the time. A few good ones are listed below:

Crews, P.; Rodríguez, J.; Jaspars, M *Organic Structure Analysis, 2nd Ed.;* Oxford University Press: New York, 2010

Silverstein, R.M.; Webster, F.X; Kiemle, D.J. *Spectroscopic Identification of Organic Compounds*. John Wiley & Sons: U.S.A., 2005, 7th ed.

Breitmaier, E. *Structure Elucidation by NMR in Organic Chemistry: A Practical Guide.* Wiley: New York, 2002, 3rd ed.

Palleros, D. *Experimental Organic Chemistry*, Wiley: New York, 2000.

Shriner R. L.; Hermann, C. K.; Morrill, T. C.; Curtin, D. Y.; Fuson, R. C. *The Systematic Identification of Organic Compounds* Wiley: Hoboken, NJ, 2004, 8th ed.

There also many websites on the subject: surf around (but make sure that you use reputable sources!)

Appendix III. Operation of the Rotary Evaporator

Most organic reactions are carried out in solution and are subjected to extraction during the work up, so that isolation of product requires solvent removal. A convenient and fast method to remove solvent from a solid or from a higher-boiling liquid is the use of the rotary evaporator, abbreviated "rotavap".

The rotavap performs a fast, simple distillation of solvent, leaving the organic product as a residue in a round bottom flask where it can be retrieved easily. What makes the separation rapid is the use of a vacuum which significantly lowers the boiling point of the solvent to around room temperature, thus avoiding elevated temperature which takes time to attain and which could alter the desired organic product. Since boiling chips, stones or sticks cannot be used in a rotavap, the boiling mixture is constantly agitated mechanically by rotating the flask, to prevent bumping.

Operation

1. Ideally, round bottom flasks should be no more than half full of solution. Cyclohexane and many other organic solvents have a low boiling point, and bump easily. To avoid bumping, ***never*** fill a round bottom more than half full of cyclohexane solution.

2. Fill the condenser water pump bucket with ice. Plug in the pump.

3. Turn on the rota-vap vacuum ***all the way***.

4. With your right hand, put the round bottom flask on the trap joint and ***hold it there***.

5. With your left hand, rotate the condenser stopcock 180°. This closes the condenser to the atmosphere and creates a vacuum.

6. Turn the motor dial to a med-fast setting ***immediately*** after closing the stopcock.

7. You may cease holding the round bottom flask when a) the flask becomes cold from evaporation; or b) the solution bubbles. Either of these occurrences signals that the vacuum is strong enough to hold the round bottom flask on the trap joint.

8. When the round bottom flask has cooled enough to condense moisture, raise the warm water bath to touch the flask. Gradually raise it throughout the evaporation. Avoid the temptation to warm the flask too soon; premature warming will cause the solution to bump into the trap.

9. Two things signal when evaporation is complete: 1) there is no visible change in the appearance of the material in the round bottom and 2) no more condensate drips from the condenser.

10. Remove your flask in the opposite order of steps: lower the warm water bath; turn the motor dial to "0"; ***hold the round bottom***; open the condenser stopcock to the air (180° rotation); wait until it vents completely, then turn off the vacuum and remove the round bottom flask. Never turn off the aspirator while the system is still evacuated. Unplug the pump if you're the last one using the rota-vap (ask around!).

In the unusual event of your solution bumping into the trap, you can retrieve it by removing the trap; ask the instructor or TA for help. **Lab courtesy demands that you leave the trap clean for the next user.**

Appendix IV. Thin Layer Chromatography (TLC)

Why is TLC so useful?

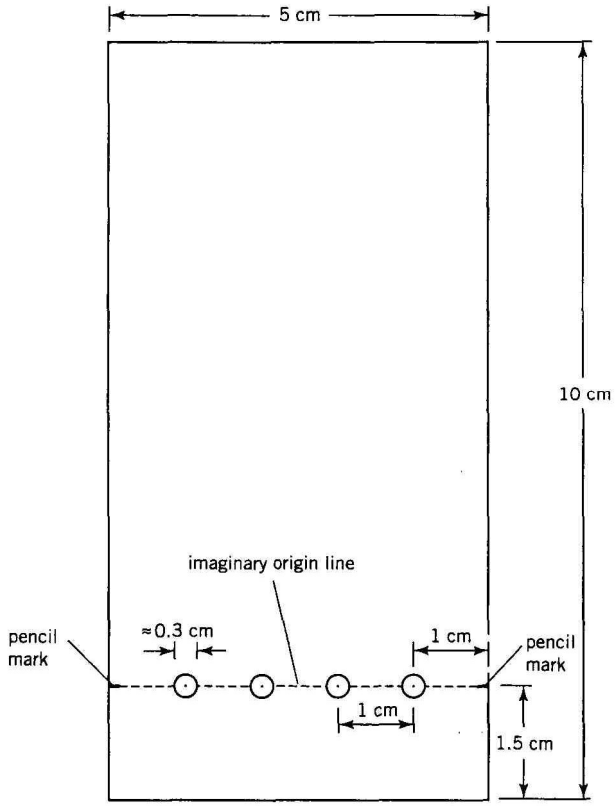
(1) TLC is a fast way to determine the number of components in a sample, provided optimal solvent conditions are determined. This can be used to assess the relative purity of such a sample.

(2) Optimized TLC conditions can be applied to the solvent used for separation of the components using column chromatography. A difference of about 0.5 R_f units is required for good separation on TLC to be applied to a column.

Spotting the plates

A solution of the sample to be analyzed is made in a suitable solvent. The solvent must dissolve the sample completely to ensure an accurate representation of the sample's composition. Volatile solvents such as hexane and ethyl acetate are particularly recommended because they evaporate rather quickly once the sample is spotted on the plate.

A small aliquot of the solution is taken with a capillary tube (with both ends open) and applied on the TLC plate by touching the adsorbent with the tip of the capillary lying flat. Gentle pressure is applied to deliver the liquid, which penetrates the adsorbent. When the size of the spot is about 2-3 mm in diameter, the capillary is raised to stop the flow of liquid. The solvent is allowed to evaporate and another application is made, if necessary.



Ordinary capillary tubes used for melting point determinations and commercial Pasteur pipets are too wide to be used as spotting devices for TLC. Narrow capillary tubes should be used instead.

For regular TLC plates (5 x 10 cm), spots should be applied at a distance of about 1.5 cm from the bottom edge of the plate, and about 1 cm from the sides of the plate. If more than one sample is analyzed per plate, a distance of at least 1 cm should separate the spots. A mark made with pencil on both sides of the plate should indicate the imaginary origin line where all the spots are applied. For microplates (2.5 x 5 cm), the spots should be applied at a distance of about 1 cm from the bottom edge and 0.5 cm from the sides; the separation between spots should be at least 0.7 cm. All marks on the TLC plates should be made with pencil, never with ink because the components in ink may separate during the run and interfere with the TLC analysis.

Determining the Optimum Mobile Phase

This is tricky when the samples are unknown. Begin by spotting the sample (ex. mixture of unknowns) on two plates and running one in a polar mobile phase (ex. hexanes) and the other in a non-polar mobile phase (ex. ethyl acetate). If neither provide good separation (more than 0.5 Rf units), try different mixtures of hexanes/ethyl acetate. If that doesn't work, you may work with DCM solutions with methanol (less than 10% methanol or the plates dissolve). While

toluene may work as good TLC solvent, its high boiling point makes it impractical for use in column chromatography.

Analyzing the Chromatogram

Once the spots have been visualized, the distance traveled by the spot from the origin is measured along with the distance traveled by the solvent front. The ratio between these two distances is called ratio to the front or retention factor (R_f):

R_f = (Distance traveled by spot) / (Distance traveled by solvent) (1)

The distance traveled by the sample is measured from the origin to the middle of the spot. With very large and ill-defined spots, as for example, spots with "tails," Rf values are meaningless because the middle of the spot varies with the amount of sample applied to the plate. If the spot streaks or runs with a tail, it is an indication that too much sample was applied. A decrease in the volume of sample spotted should be tried first; if this does not correct the problem, then a different adsorbent/solvent system should be tried.

The ratio to the front depends on several variables such as:
- the thickness of the adsorbent;
- the nature of the stationary phase and its degree of activation;
- the mobile phase*;
- the amount of material applied*.

* These will be variables in your experiment, particularly the mobile phase.

Table V.1. Selected Solvents in Order of Increasing Polarity

Solvent	Dielectric constant
hexanes	1.89
cyclohexane	2.02
toluene	2.38
diethyl ether	4.34
ethyl acetate"	6.02
methylene chloride"	8.93
acetone	20.7
methanol	32.7
water	80.1

"On the basis of chromatographic data, ethyl acetate is considered more polar than methylene chloride.

Table V.2. Families of Organic Compounds in Order of Increasing Polarity

Family of compounds	Structure
aliphatic hydrocarbons	R–H
alkyl halides	R–X
unsaturated hydrocarbons	R–CH=CH–R
aromatic hydrocarbons	Ar–H
aryl halides	Ar–X
ethers	R–O–R
esters	R–COOR
ketones	R–CO–R
aldehydes	R–CO–H
amides	R–CO–NH_2
amines	R–NH_2
alcohols	R–OH
phenols	Ar–OH
carboxylic acids	R–COOH
amino acids	H_3N^+–CHR–COO^-

Appendix V. ^{1}H NMR Tables*

TABLE 22.1 Deuterated solvents used for NMR spectroscopy

Solvent	Structure	Residual ^{1}H signal (ppm)	^{13}C chemical shift (ppm)
Chloroform-d	$CDCl_3$	7.26 (singlet)	77.0 (triplet)
Acetone-d_6	$CD_3(C{=}O)CD_3$	2.04 (quintet)	29.8 (septet) 206.5 (singlet)
Deuterium oxide	D_2O	4.6 (broad singlet)	—
Dimethyl sulfoxide-d_6	$CD_3(S{=}O)CD_3$	2.49 (quintet)	39.7 (septet)

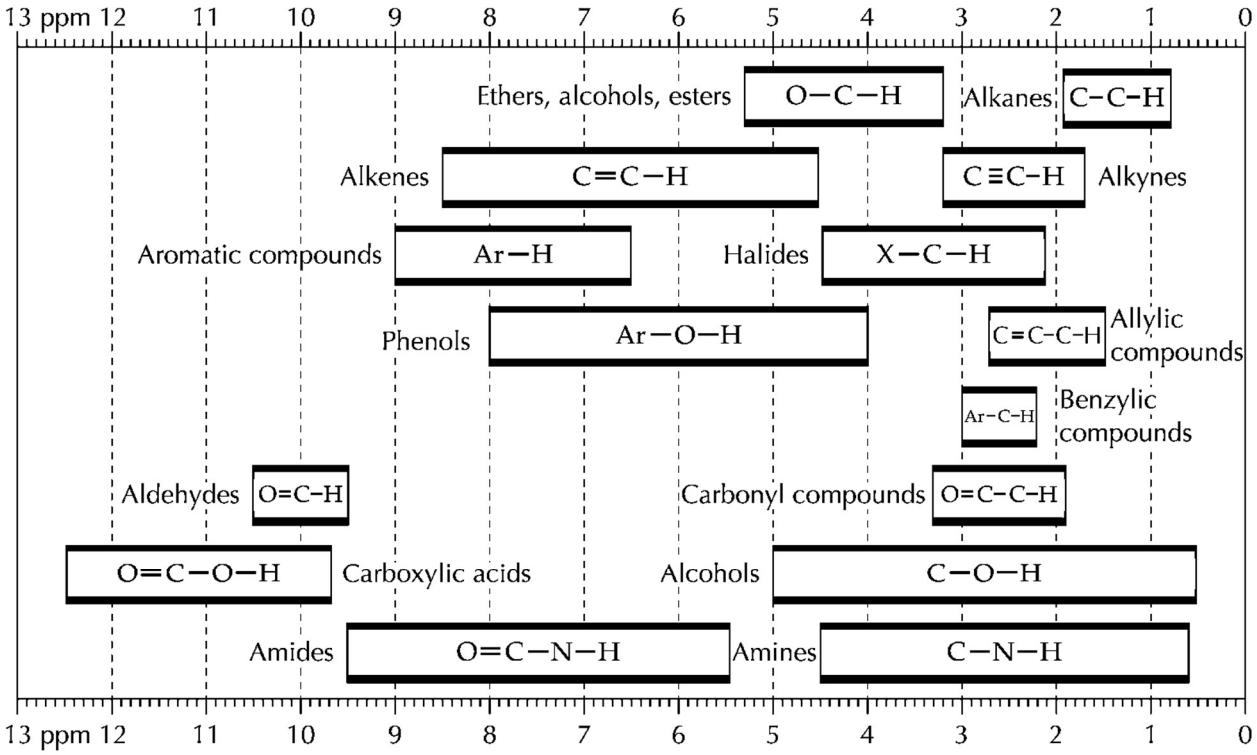


FIGURE 22.13 Approximate regions of chemical shifts for different types of protons in organic compounds.

** The correlation tables provided in this lab manual give general ranges for certain types of protons, not necessarily all of them, and do not include more detailed substituent effects. These tables are useful when determining an unknown structure. More specific chemical shift can be calculated using the correlation tables in the Mohrig or Palleros texts once the structure is proposed or known. Online spectra predicting tools may also perform such calculations. The calculated chemical shifts are to be included in lab reports to confirm the structure. Trying these calculations before you know the structure is impractical and overly complicated – there are too many options!!

* Mohrig, J. R.; Hammond, C. N.; Schatz, P. F. *Techniques in Organic Chemistry, 4th Edition*, Freeman: New York, **2015**.

Appendix V cont'd

TABLE 22.2 Characteristic ^{1}H NMR chemical shifts in $CDCl_3$

Compound	Chemical shift (δ, ppm)
TMS	0.0
Alkanes (C–C–**H**)	0.8–1.9
Amines (C–N–**H**)	0.6–4.5
Alcohols (C–O–**H**)	0.5–5.0
Alkenes[a] (C=C–C–**H**)	1.5–2.6
Alkynes (C≡C–**H**)	1.7–3.1
Carbonyl compounds (O=C–C–**H**)	1.9–3.3
Halides (X–C–**H**)	2.1–4.5
Aromatic compounds[b] (Ar–C–**H**)	2.2–3.0
Alcohols, esters, ethers (O–C–**H**)	3.2–5.3
Alkenes (C=C–**H**)	4.5–8.5
Phenols (Ar–O–**H**)	4.0–8.0
Amides (O=C–N–**H**)	5.5–9.5
Aromatic compounds (Ar–**H**)	6.5–9.0
Aldehydes (O=C–**H**)	9.5–10.5
Carboxylic acids (O=C–O–**H**)	9.7–12.5

a. Allylic protons.
b. Benzylic protons.

Appendix VI. ^{13}C NMR Tables[*]

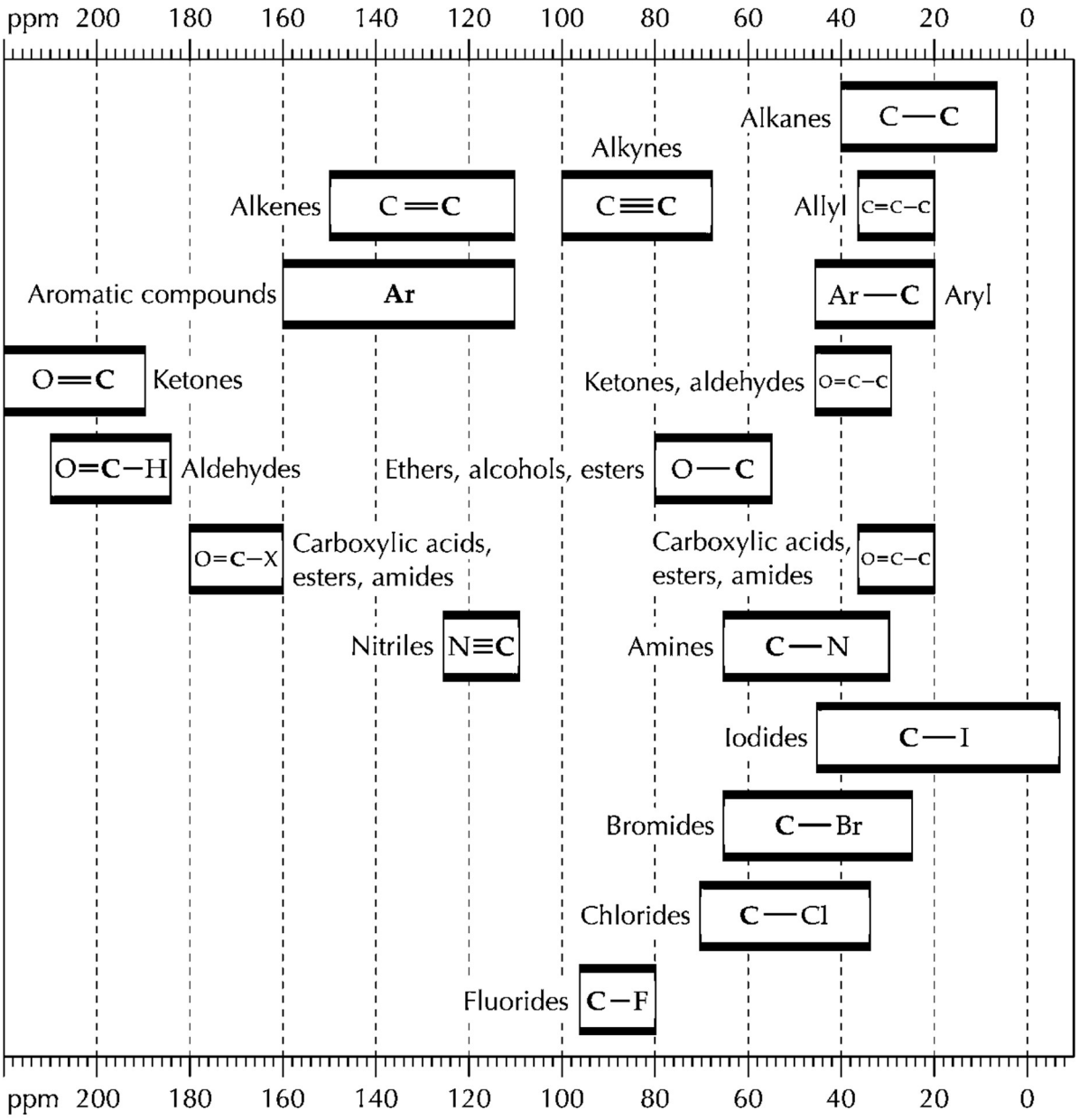


FIGURE 23.4 Approximate regions of ^{13}C chemical shifts for different types of carbon atoms in organic compounds.

[*] Mohrig, J. R.; Hammond, C. N.; Schatz, P. F. *Techniques in Organic Chemistry, 4th Edition*, Freeman: New York, **2015**.

Appendix VI cont'd.

TABLE 23.1 Characteristic ^{13}C NMR chemical shifts in $CDCl_3$

Compound	Chemical shift (ppm)
TMS	0.0
CDCl_3 (t)	77
Alkane (C–**C**H_3)	7–30
Alkane (C–**C**H_2)	15–40
Alkane (C–**C**H) and (C–**C**)	15–40
Carboxylic acids, esters, and amides (**C**–C=O)	20–35
Allyl (**C**–C=C)	20–35
Arene (**C**–Ar)	20–45
Ketones, aldehydes (**C**–C=O)	30–45
Amines (**C**–N)	30–65
Iodides (**C**–I)	–5–45
Bromides (**C**–Br)	25–65
Chlorides (**C**–Cl)	35–70
Fluorides (**C**–F)	80–95
Alcohols (**C**–OH), ethers (**C**–OR), esters (**C**–O[C=O]R)	55–80
Alkyne (**C**≡C)	70–100
Alkene (**C**=C)	110–150
Aromatic	110–160
Nitriles (**C**≡N)	110–125
Carboxylic acids, esters, and amides (**C**=O)	160–180
Aldehydes (**C**=O)	185–210
Ketones (**C**–O)	190–220

Appendix VII. IR Tables

Table VII.1. Characteristic IR Absorption Peaks of Functional Groups

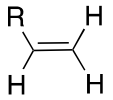
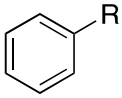
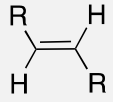
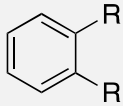
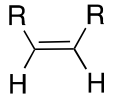
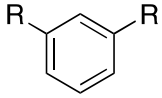
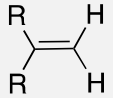
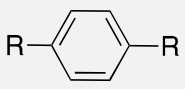
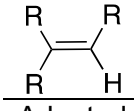
Vibration	Position (cm^{-1})	Intensity*	Notes
Alkanes			
C-H stretch	2990 – 2850	m to s	
C-H bend	1480 – 1430 & 1395 – 1340	m to w	
Alkenes			
=C-H stretch	3100 – 3000	m	
C=C stretch	1680 – 1620 (sat.) 1650 – 1600 (conj.)	w to m	
=C-H bend	995 – 685	s	See Table 2 for detail
Alkynes			
≡C-H stretch	3310 – 3200	s	
C≡C stretch	2250 – 2100	m to w	
Aromatic Compounds			
C-H stretch	3100 – 3000	m to w	
C=C stretch	1625 – 1440	m to w	
C-H bend	900 – 680	s	See Table 2 for detail
Alcohols**			
O-H stretch	3650 – 3550	m	Free (dilute)
	3550 – 3200	br, s	Hydrogen bonded (typical)
Amines			
N-H stretch	3550 – 3250	br, m	Primary (two bands) Secondary (one band)
Nitriles			
C≡N stretch	2280 – 2200	s	
Aldehydes			
C-H stretch	2900 – 2800 & 2800 – 2700	s	H-C=O Fermi doublet
C=O stretch	1740 – 1720 (sat.) 1715 – 1680 (conj.)	s	
Ketones			
C=O stretch	1750 – 1705 (sat.) 1700 – 1665 (conj.)	s	
Esters**			
C=O stretch	1765 – 1735 (sat.) 1730 – 1715 (conj.)	s	
Carboxylic Acids**			
O-H stretch	3200 – 2500	br, m to w	
C=O stretch	1725 – 1700 (sat.) 1715 – 1680 (conj.)	s	
Amides			
N-H stretch	3500 – 3150	m	Primary (two bands) Secondary (one band)

Vibration	Position (cm^{-1})	Intensity	Notes
Anhydrides**			
C=O stretch	1850 – 1800 & 1790 – 1740	s	
Acid Chlorides			
C=O stretch	1815 – 1770	s	
Nitro Compounds			
NO_2 stretch	1570 – 1490 & 1390 – 1300	s	
Thiols[i]			
R-S-H stretch	2550 – 2600		
Alkyl & Aryl Halides[†]			
C-F stretch	1000 – 1400		
C-Cl stretch	< 600 – 840		
C-Br stretch	< 700		
C-I stretch	< 600		

* Abbreviations: s = strong; m = medium; w = weak; br = broad; sat. = saturated; conj. = conjugated

** Alcohols, Esters, Carboxylic Acids, and Anhydrides also absorb in the fingerprint region due to the C-O stretch (1300 – 1000, s).

Table VIII.2. Out-of-Plane C-H Bending Vibrations in Alkenes and Aromatics

Alkene Structure	Position (cm^{-1})	Phenyl Structure	Position (cm^{-1})
Mono-substituted 	997 – 985 & 915 – 905	Mono-substituted 	770 – 730 & 720 – 680
Disubstituted, *trans* 	980 – 960	Disubstituted, *ortho* 	770 – 735
Disubstituted, *cis* 	730 – 665	Disubstituted, *meta* 	810 – 750 & 725 – 680
Disubstituted, symm. 	895 – 885	Disubstituted, *para* 	860 – 800
Trisubstituted 	840 – 790		

Adapted from…Mohrig, J. R.; Hammond, C. N.; Schatz, P. F. "Infrared Spectroscopy" in *Techniques in Organic Chemistry, 3rd Edition*. Freeman: New York, **2006**.