ORGANIC CHEMISTRY III LAB FOR LIFE SCIENCES
CHEM 223

Revised February 2018

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GENERAL SCHEDULE OF EXPERIMENTS

The following is a typical CHEM 223 lab schedule. Please check with your lab instructor for any changes.

You are responsible for the assigned reading listed at the beginning of each experiment prior to the lab meetings.

Week	Experiment	Expt #
1	Check-in; safety	
2 **3**	Synthesis Of Methyl Salicylate: A Fischer Esterification	1
4	Oxidation of Borneol with NaOCl	2
5 **6**	Preparation of Dibenzalacetone	3
7 **8** **9**	Multi-Step Aromatic Synthesis	4
10	Check-out	

REQUIRED MATERIALS

In addition to this lab manual, the following are required for laboratory work. Please confirm this list with your lab instructor.

- Safety goggles (ANSI Z87.1 or Z87+)
- Bound laboratory notebook
- **Companion lab textbook:** *Making the Connections: A How-To Guide for Organic Chemistry Lab Techniques*, Padías, A. B. 3rd edition
- Lock for drawer
- Neoprene and nitrile gloves
- Lab coat (provided in the lab; no personal lab coats are allowed)

LABORATORY SAFETY RULES

CHEMISTRY AND BIOCHEMISTRY DEPARTMENT
CAL POLY STATE UNIVERSITY, SAN LUIS OBISPO

The rules and guidelines listed here are the minimum that apply to all laboratory work in the Chemistry & Biochemistry Department. Your instructor may add others. **Failure to comply with these rules may result in reduction in grade or, in extreme cases, expulsion from the lab.**

PROPER LAB ATTIRE (ACHIEVED BEFORE ARRIVING IN LAB)

1. *The guiding principle for proper clothing in lab is avoidance of exposed skin*.

2. Wear shoes and socks that do not expose skin on the foot and ankles. Shoes with a porous fabric are not recommended. Sandals, clogs and shoes that do not cover the entire top of the foot are not permitted. The stockroom does not provide shoes for student use.

3. Shorts and skirts (unless the skirt is ankle-length) are not permitted. Pants are the best option, but avoid tight fitting pants, which may affect permeation rate in the event of a chemical spill.

4. If you have long hair, bring a hair tie to lab.

5. If you do not follow the above directives, the instructor and staff have the authority to deny entry into the lab.

PERSONAL PROTECTIVE EQUIPMENT (PPE)

1. **GOGGLES.** Chemical splash goggles (**purchased by the student**), must be indirectly-vented or unvented and conforming to ANSI Z87.1 or Z87+. These are the only approved protective eyewear for use in a Teaching Chemistry Laboratory. You must always wear these goggles whenever **anyone** is working with hazardous chemicals or processes in the lab. **UVEX Stealth goggles are best for the organic lab.** These goggles are available at the bookstore or online**.** Tinted goggles are not allowed. Goggles may be stored in the locker provided they are enclosed in a sealed plastic bag, provided by the stockroom.

2. **LAB COATS.** Lab coats will be provided for you in the lab and must always be worn when working in the lab. No personal lab coats are to be worn in the lab. Lab coats must go down to the knees or below, and the sleeves must go to your wrists. You should not have exposed skin between the edge of your glove and the edge of the lab coat sleeve. Lab coats must always be fully buttoned. Lab coats must not be worn outside the lab, unless you are going directly to and from the stockroom window or between instrument rooms. Do not eat, drink, sit on outside furniture, or use the restroom while wearing your lab coat.

3. **GLOVES.** Chemical resistant gloves (**purchased by the student**) must be worn whenever you are handling hazardous chemicals in the lab. No affordable glove

type offers across-the-board protection against a wide variety of chemicals in the lab.

- An **unsupported neoprene or neoprene / latex blend glove** will protect you from most of the organic solvents and chemicals found in the organic chemistry labs. These neoprene gloves also provide protection against acids, bases, and inorganic chemicals. Some manufacturers refer to neoprene as **synthetic rubber** or **synthetic latex**. Buy neoprene gloves at the bookstore or Grocery, Drug and Hardware stores. Look for the words "neoprene" or "synthetic rubber". One drawback of neoprene gloves is diminished manual dexterity.
- **Disposable nitrile** gloves are generally less protective towards chemical contact than neoprene gloves, but offer better manual dexterity. They are purchased by the box and are single use only.
- The Chemistry Department recommends that students purchase both **nitrile and neoprene** gloves to cover a multitude of situations.
- Do NOT wear gloves while touching doorknobs or keyboards.

WHEN IN LAB, OBSERVE THE FOLLOWING:

1. We suggest you report a significant physical or medical condition -- for example, pregnancy or chemical allergy (such as sulfite, iodine) -- to your instructor.

2. If you injure yourself -- for example, if you cut, burn, or spill a harmful chemical on yourself -- tell your instructor at once.

3. Make sure you understand and follow all directions for each experiment, including the safety directions.

4. Be very careful with all heat sources (heat guns, hot plates, ovens, etc.). Keep heat sources away from flammables.

5. Learn the locations of safety equipment -- safety showers, eye wash fountains, fire extinguishers and substances for neutralizing acid spills. Locations of showers and eye wash fountains are especially important because you may need one suddenly. Use of fire extinguishers is limited to faculty; in case of fire, leave the room and go to the lawn between Baker and building 52.

6. If you leave the lab for any reason during an experiment, you must inform your instructor and double check that your experiment and work area are secure before leaving. Keep your equipment locker and work area neat. Clutter creates accidents.

7. Dispose of waste chemicals according to directions stated in your lab manual or given by your instructor. Do not return unused chemicals to their original containers. If you are unsure, ask your instructor.

8. Clean up spilled chemicals or broken glass immediately. Dispose of broken glass in designated glass disposal boxes. If you break a thermometer containing mercury, tell your instructor immediately so it can be cleaned up.

9. Wash your hands before leaving the lab.

WHEN IN LAB, DO NOT DO THESE THINGS:

1. Do not enter a laboratory unless authorized by the instructor.

2. Do not work alone in any lab. Do not perform unauthorized experiments. These rules also apply to project students.

3. No food or drink is allowed in the lab at any time.

4. Do not kneel or stand on lab stools or sit on bench tops.

5. Do not use your cell phone or personal music devices (iPOD, MP3 players) in the laboratory. Do not use headphones in the lab.

6. **Do not remove any reagents, products, or equipment from the department. Theft or intentional misuse of laboratory reagents, products, or equipment will be reported to Judicial Affairs for disciplinary action**.

CONTACT LENS POLICY

CHEMISTRY AND BIOCHEMISTRY DEPARTMENT
CAL POLY STATE UNIVERSITY, SAN LUIS OBISPO

1. Contact lens wearers must use eye protection meeting or exceeding ANSI Z87.1 or Z87+ whenever anyone in the lab is handling hazardous materials.

2. Students wearing contact lenses identify themselves when they fill out the Safety Policy sheet at the first lab meeting each quarter; these sheets are kept on file in both stockrooms.

3. Individuals wearing contact lenses must handle dichloromethane in the fume hood only, regardless of the level of eye protection worn.

4. Any student suffering eye discomfort must inform the lab instructor; in particular, notify the lab instructor if contact lenses are being worn. Students wearing contact lenses will be instructed ***to immediately remove contact lenses while flushing*** both eyes for at least 15 minutes in the eyewash fountain.

5. All individuals are recommended to seek medical attention after suffering a hazardous chemical splash to the eyes; in addition, contact lens wearers must seek professional medical attention under these circumstances.

MEDICAL EMERGENCIES

A medical emergency is a medical condition that is an immediate threat to your life or long-term health. Generally, if your medical condition can wait until the next day for assessment or treatment, it is not a medical emergency.

If you or your lab partner experience or exhibit any of the symptoms or conditions in the following list, call 911 immediately from the landline in the lab and not from your personal cell phone, if possible. If you need to use your cell phone indicate that you are calling from Cal Poly. The Cal Poly dispatcher will help you assess the situation and initiate the appropriate emergency response.

WHEN TO CALL 911:

- Unconsciousness or altered level of consciousness
- Trouble breathing or breathing in a strange way
- No pulse
- Persistent chest or abdominal pain or pressure
- Severe bleeding
- Seizures, severe headache or slurred speech
- Poisoning
- Vomiting blood or passing blood
- Injuries to head, neck or back
- Possible broken bones
- Victim cannot be moved easily

NOTE: You will need to use **private insurance** for ambulance transport, emergency treatment away from campus, hospitalization, and treatment by medical specialists not available at Cal Poly Health Services.

LABORATORY ACCIDENTS / INJURIES

MINOR LABORATORY INJURIES

Minor laboratory injuries (e.g. small cuts, skin irritation) are common in the Chemistry & Biochemistry department. If you suffer a minor injury while working in a laboratory you must report the injury to your lab instructor as soon as possible; if your instructor is not available, seek out any Chemistry & Biochemistry faculty or staff for assistance. If you or your instructor feels that your condition should be evaluated by a medical professional, the following options are available:

FREE SERVICES – ON-CAMPUS HEALTH CARE

Cal Poly Health & Psychological Services: Open MTRF 8:00–4:30 W 9:00–4:30
Free physician and nurse practitioner visits, laboratory and X-ray, low-cost pharmacy and dermatology.

PRIVATE INSURANCE - AFTER-HOURS HEALTH CARE (OFF-CAMPUS)

NOTE: Cal Poly H&P Services ("The Health Center") does not provide any after-hours care. If you wish medical attention after 4:30 pm or during the weekend, you must go to an off-campus facility. You must have your own insurance or pay cash for these services. Your insurance provider may require pre-approval or a per visit co-pay – call the number on your insurance card to find out.

Emergency After-Hours Care (San Luis Obispo)

- **Sierra Vista Regional Medical Center, 1010 Murray St. (805)546-7650 (ER)**
- **French Hospital Medical Center, 1911 Johnson Ave. (805)542-6377 (ER)**

Non-emergency After-Hours Care (San Luis Obispo)

- **Family & Industrial Medical Center, 47 Santa Rosa (805)542-9596**
- **Med Stop, 263 Madonna Road (805)549-8880**
- **Other:** You may see any health care provider that your private insurance allows.

FIRE

Laboratory fires will not occur if necessary precautions are observed consistently (identify flammable materials, control ignition sources, store chemicals properly, use fume hoods). Any fire, however small, must be reported to your instructor immediately. If you are confronted with a large fire (i.e. a fire you cannot smother easily or allow to burn out), you must be prepared to take action to protect yourself and others.

Small Fire (can be smothered easily or will soon burn out)

- De-energize any equipment involved (hot plate, Bunsen burner, etc.).
- Remove any nearby flammable or combustible materials.
- If fire is inside fume hood, let it burn or smother (if easy to do so).
- If fire is on bench, smother (if easy to do so).

Large Fire (too much fuel to smother easily or fire has spread)

- Evacuate the room.
- Pull fire alarm.
- Go to a safe location and call 911.

DO NOT ATTEMPT TO FIGHT A LARGE FIRE!!!
EXTINGUISHERS ARE INTENDED FOR USE BY TRAINED PERSONNEL ONLY.

SPILLS

Small spills

Small spills are spills that can be easily and safely cleaned up by one person. The spilled material must be disposed of properly – hazardous material spills must be handled as hazardous waste.

Large spills

Large hazardous material spills are spills that cannot be handled safely by one person.

- Evacuate the laboratory immediately and lock the laboratory doors.
- Alert your instructor or a stockroom technician, if possible, for instructions.
- If you cannot speak directly with your instructor or a stockroom technician, **you must call 911**. Stand by in a safe location to assist by providing information to emergency personnel when they arrive.

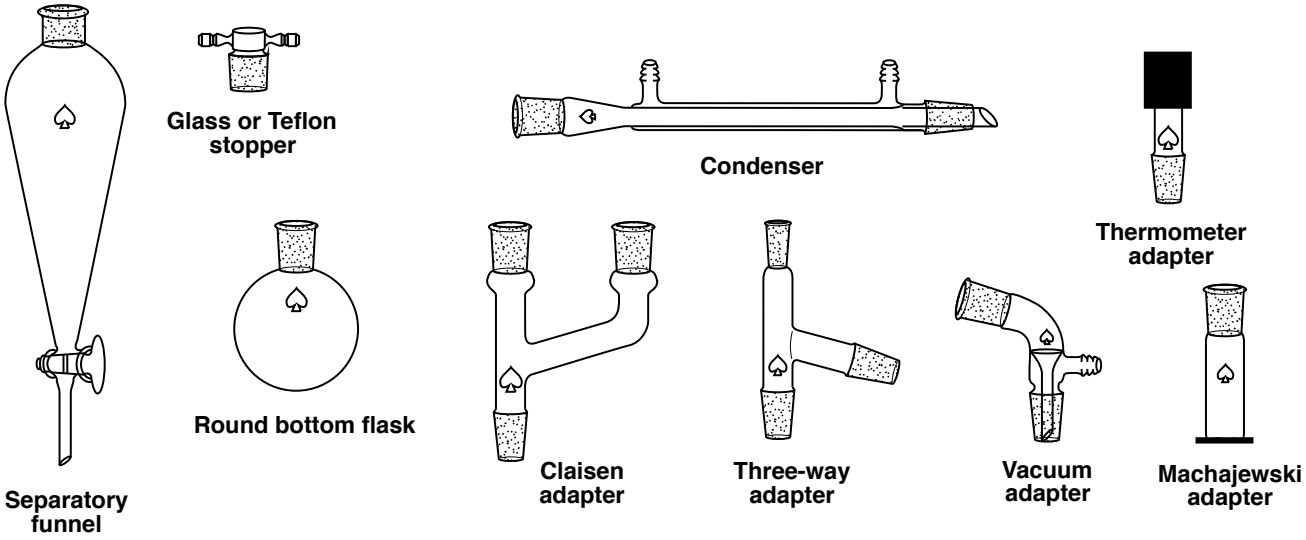
CALIFORNIA POLYTECHNIC STATE UNIVERSITY

Organic Chemistry Locker Contents

Chem 223 Revised 2017

Locker Contents

1 Flask, round bottom, 25 mL, ST*	1 Funnel, powder, plastic
1 Flask, round bottom, 50 mL, ST*	1 Funnel, short stem
1 Flask, round bottom, 100 mL, ST*	1 Funnel, Buchner
1 Separatory Funnel, 125 mL, ST*	1 Graduated Cylinder, 10 mL
1 14/20 Stopper, glass or teflon, ST*	1 Graduated Cylinder, 50 mL
1 Thermometer Adapter, ST*	1 Magnetic stirbar, 3/4 inch
1 Claisen Adapter, ST*	1 NMR tube with cap
1 Three-way Adapter, ST*	1 Spatula, stainless steel
1 Vacuum Adapter, ST*	1 Stirring rod, glass
	1 Watch glass, 90 mm
1 West Condenser, ST*	1 Latex bulb, 2 mL
	2 Medicine droppers
1 Beaker, 150 mL	1 Vial, pH test paper
1 Beaker, 250 mL	4 Vials, 4-dram
	2 Vials, 11-dram
2 Erlenmeyer Flasks, 25 mL	1 Cork ring
2 Erlenmeyer Flasks, 50 mL	Keck clamps
2 Erlenmeyer Flasks, 125 mL	
1 Erlenmeyer Flasks, 250 mL	1 Filter flask (250 mL or 500 mL)
	1 Filter adapter
1 Machajewski adapter	
1 Ruler	*ST = Standard Taper (ground glass joint)



ORGANIC CHEMISTRY LAB CHARGE POLICY

At the beginning of the quarter, you will be assigned a drawer in your chemistry lab. Check the contents of the drawer carefully against the locker list to make sure that it contains all the items listed. Any missing items can be obtained from the stockroom. Once you have been checked in, you are responsible for all the items therein. If you drop the class, even after the first week, you must come to the stockroom to be checked out of your drawer.

Failure to check out will result in a $95 fee along with charges for any missing items and may result in an incomplete ('I') grade for the lab!

During the course of the quarter, there will be times when you need to check additional items of equipment out of the stockroom. Usually this will be handled by signing your name on a sign-up sheet as you pick up the equipment. If you do not cross your name off the sheet when you return the equipment, you will be charged for the items.

You are responsible for your glassware drawer set and will be charged for any piece of glassware that you break or lose. At the end of the quarter, you will check out of your lab drawer any charges under your name will be processed. Any missing items will be replaced from the stockroom and billed to you. Charges will be posted to your student account at the end of the quarter.

Any charges must be paid before the second week of the following quarter to prevent a hold on transcripts and registration.

ORGANIC CHEMISTRY LAB ETIQUETTE

You are assigned a drawer in the organic laboratory. Since this is your individual drawer, you are responsible only to yourself for its condition. You have a community responsibility, however, to those parts of the lab outside of your drawer. Labs will run more smoothly and SAFELY if you show consideration for other lab students through attention to these areas:

Your bench. Return common equipment like clamps, rings, hoses, stir motors, etc., to the appropriate drawer (but leave a HOT hot plate on the bench). Wipe the bench with paper towels or a sponge before you leave. Clean the sink area. Check for extraneous equipment or glassware—it might be yours!

Lab in general. If you find a spill, even if it is not yours, take a few seconds to clean it up. This is especially true of the expensive, electronic balances, which can be damaged by chemicals on them. Put tops on bottles of reagents as soon as you are done dispensing the reagent. Inform the instructor of empty reagent bottles. Refill empty dropper bottles and acetone squirt bottles from the solvent cans below the hoods—READ LABELS. Put waste in the appropriate places—when in doubt, ask. Clean up broken glass with a broom and dustpan, NOT your fingers. Alert the instructor to broken thermometers; mercury is hazardous and must be cleaned up immediately.

Instrument room. The instruments in general and the spectrometers in particular get very heavy use. Keep the sample preparation area clean; cap $CDCl_3$ bottles and throw out used pipettes. Clean the IR sample stage immediately after use (with 2-propanol, NOT acetone). Obey all glove usage signs (keyboards, doorknobs, etc.). Additional printer paper can be found in drawers next to the printers.

Time. It is inconsiderate to your lab instructor and to the next lab students to work past the allotted time. Always start long procedures at the beginning of a lab, not near the end. Begin your cleanup at least 15 minutes before the end of the lab. *Do not go to other lab sections to do your lab work. Toward the end of the quarter, if you find yourself woefully behind, make arrangements with your own instructor to make up the work.*

The keys to hassle-free labs are PREPARATION in advance, EFFICIENT WORK during the lab, and CONSIDERATION for others.

CHEMICAL HYGIENE IN THE ORGANIC LABS

Practice good chemical hygiene in the Organic Labs! What does this entail? The following are some guidelines:

- If you spill anything (especially around a high traffic area such as near balances), clean it up immediately. Consult your lab instructor on how to clean a spill.
- Always clean up broken glassware with broom and dustpan and not bare or gloved hands! Place the broken glass in the broken glass container.
- Do not handle any organic compound with bare hands – always wear gloves!
- Do not touch any door handles, keyboards, phones with gloves on.
- Do not walk outside the lab with your lab coat on, unless you are going directly to and from the stockroom window or between instrument rooms.
- At the end of each lab period, wipe down your half of the fume hood and your bench area with a 50:50 mixture of acetone and water (even if you did not spill anything throughout the lab).

WASTE DISPOSAL IN THE ORGANIC LABS

In the organic labs, the chemical waste is segregated into 3 streams for a number of reasons – the most important of which is SAFETY! We do not want to have a dangerous reaction taking place in our waste bottles inadvertently.

There are 3 separate, color-coded waste bottles in the organic labs:

COLOR CODE	CHEMICAL WASTE
Blue	Non-halogenated
Pink	Halogenated
Yellow	Aqueous

Please be sure not to mix waste streams! If unsure, always check with your lab instructor or staff as to which waste bottle you should use.

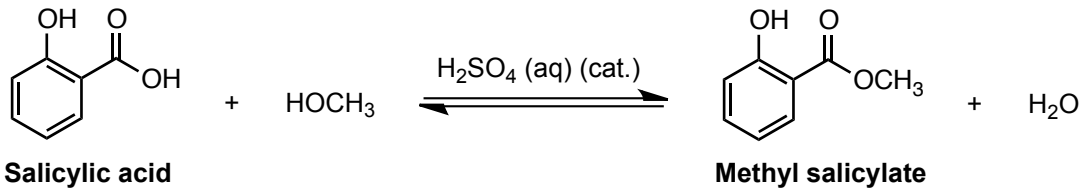
COMMON AQUEOUS SOLUTIONS USED IN ORGANIC LABS

SOLUTION	MOLARITY
5% HCl	1.4 M
10% HCl	2.9 M
Conc HCl	12.1 M
5% NaOH	1.3 M
10% NaOH	2.8 M
Conc. NaOH (50%)	19.1 M
5% $NaHCO_3$	0.6 M
9% $NaHCO_3$ (saturated)	1.1 M
5% Na_2CO_3	0.5 M
10% Na_2CO_3	1.0 M
Sat. NaCl	5.7 M
Conc. HNO_3	16. M
Conc. H_2SO_4	18. M
Conc. H_3PO_4	14.7 M
Conc. NH_4OH	14.8 M
Glacial CH_3COOH (HOAc)	17.4 M

EXPERIMENT 1: SYNTHESIS OF METHYL SALICYLATE: A FISCHER ESTERIFICATION

Reference: Wade 9th ed., pp 961-965.
Preparatory reading: Appendix at the end of this lab manual p. 39 (Experimental Checklist For Every Reaction)

Bananas, oranges, apples, pineapples and many other fruits owe part, if not all, of their flavor and odor to a class of compounds called esters. Today, you will synthesize an ester using the Fischer esterification – one of the most common methods to synthesize esters. A typical Fischer esterification involves the treatment a carboxylic acid with an alcohol in the presence of a catalytic amount of sulfuric acid (H_2SO_4). The reaction is slow at room temperature and proceeds to an equilibrium with about 70% ester. Heating improves the rate of attaining the equilibrium but does not change the ultimate ratios of products and reactants at equilibrium. One can also improve the yield by directing the equilibrium towards the side where the desired product resides through the use of Le Châtelier's Principle (see note at the end of this experiment). *How can you use this principle to direct your equilibrium below toward methyl salicylate?*



Salicylic acid **Methyl salicylate**

SAFETY. Goggles, gloves and an apron or lab coat should be worn at all times. Organic solvents, acids and bases can injure skin and eyes—avoid contact with these materials. **Concentrated sulfuric acid (H_2SO_4) is especially corrosive**. Look up the specific hazards of each compound used in this experiment on www.hazard.com.

WASTE DISPOSAL. Organic layers should be discarded in the Blue "Non-Halogenated" waste. Flasks containing $MgSO_4$ should be rinsed with acetone into the Blue "Non-Halogenated" waste. Any remaining $MgSO_4$ (aka Epsom salt) can then be rinsed with H_2O in the sink. Aqueous waste should be discarded in the Yellow "Aqueous" waste.

Procedure

Reaction. To a 100 mL round bottom (RB) flask add:

- 2-3 boiling stones
- 9.7 g (0.070 moles) salicylic acid
- 25 mL of methanol (MeOH)

USING EXTREME CAUTION, obtain *ca.** 4 mL concentrated sulfuric acid [H_2SO_4 (aq)] into a 25-mL Erlenmeyer flask using a disposable pipet (you can use the graduations on the side of the disposable pipet for volume measurements).

Note: The abbreviation *ca.* stands for *circa*. It means "approximately".

Add *ca.** 1 mL H_2SO_4 (aq) at a time to your reaction mixture of salicylic acid in MeOH. Tremendous heat is generated during addition of H_2SO_4 (aq); swirl the mixture well after each addition to dissipate the heat.

After the H_2SO_4 (aq) addition is complete, rinse the funnel and the graduated cylinder with water in the sink to remove any traces of acid. If any acid spilled on the gloves, replace the gloves with new ones to avoid exposure to this hazardous chemical. **Inform your lab instructor at once if you spill any H_2SO_4 (aq) anywhere.**

Attach a condenser your reaction flask and heat the solution to reflux (see Figure 1 for general glassware set-up for reflux) for 45 minutes.

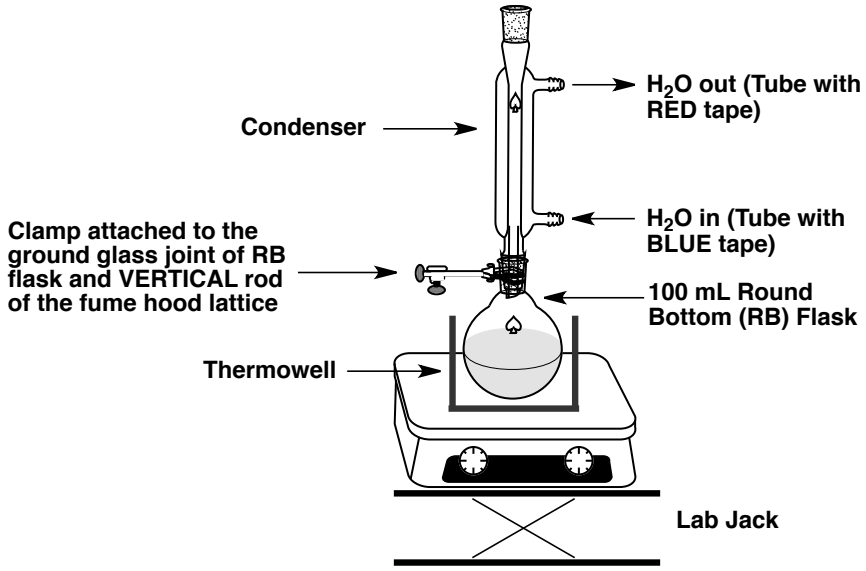


Figure 1. General glassware set-up for reflux

Product Isolation (Work-up). Remove heat and allow reaction mixture cool to room temperature. Remove the condenser and place your reaction mixture in an ice-bath for 10 minutes.

Sage advice: While your reaction mixture is cooling, prepare for the extractions as described below.

In a 250-mL separatory funnel, place *ca.* 50 mL ice, 25-30 mL ethyl acetate (EtOAc), and 25-30 mL saturated NaCl (aq) (aka brine).

Removal of methanol and sulfuric acid: Using a funnel, pour the cooled reaction mixture (but not the boiling stones!) into the separatory funnel. Stopper, shake gently and vent quickly. Shake with increasing vigor until no more pressure is released when you vent. Turn the separatory funnel right side up, remove the stopper, and allow the layers to separate. This may take a couple of minutes. Drain the aqueous layer (is it top or bottom?) into a 250-mL beaker. The combined aqueous layers will contain H_2SO_4 (aq) and should be discarded into the special acid waste bottle – check with your lab instructor.

FROM NOW ON, YOUR PRODUCT WILL BE IN THE ORGANIC (EtOAc) LAYER.

Add 25-30 mL of brine to the EtOAc layer. Shake with venting. Drain the aqueous layer into the same 250-mL beaker.

Removal of sulfuric acid and salicylic acid: Carbon dioxide is produced in the following steps which builds up significant pressure in the separatory funnel.

$$H_2SO_4\,(aq) + 2\,NaHCO_3\,(aq) \longrightarrow 2\,Na_2SO_4\,(aq) + 2\,H_2O\,(l) + \mathbf{2\,CO_2\,(g)}$$

CONSULT YOUR LAB INSTRUCTOR BEFORE PROCEEDING. Add *ca.* 25 mL saturated sodium bicarbonate [$NaHCO_3$ (aq)] solution to the EtOAc layer in the separatory funnel. WITH GREAT CAUTION, stopper, invert gently WITH A FINGER ON THE STOPPER, and vent immediately. If you can, swirl the separatory funnel upside down with the stopper open to release some carbon dioxide. Then close the stopper, shake once and vent immediately. Don't let it go for more than about 3 seconds without venting! When most of the gas has been released, drain the bottom aqueous layer into a 150-mL beaker (different than the beaker than you used in the *Removal of methanol and sulfuric acid*). Add a second 25 mL portion of $NaHCO_3$ (aq) to the EtOAc layer. Mix and vent as carefully as you did above. Drain the aqueous layer into the 150-mL beaker.

Dry your organic (EtOAc) over anhydrous magnesium sulfate ($MgSO_4$). Gravity filter (with fluted filter paper) into a clean, dry, and tared RB flask (what volume should you choose?). Remember not to fill your RB more than halfway for the rotavap. Remove the EtOAc on the rotary evaporator and any remaining EtOAc traces with the high vacuum pump.

Before performing any analyses, weigh your final product and calculate the percent yield.

Product Characterization/Analysis. Check with your lab instructor about what he/she requires you to perform from the list of analyses below:

TLC

Elute a TLC plate [25% Ethyl acetate (EtOAc) in 75% Heptane eluent] with the following spots:

- Starting material (salicylic acid)
- Isolated product (methyl salicylate)

IR

Take an IR of your starting material (salicylic acid) and the isolated product (methyl salicylate).

^{1}H and/or ^{13}C NMR

Prepare a solution of your isolated product in deuterated chloroform ($CDCl_3$) for ^{1}H and/or ^{13}C NMR analysis – check with your lab instructor.

LE CHÂTELIER'S PRINCIPLE: A BLAST FROM THE PAST (aka General Chemistry)

In a generic chemical reaction *at equilibrium*:

$$A + B \rightleftharpoons C + D$$

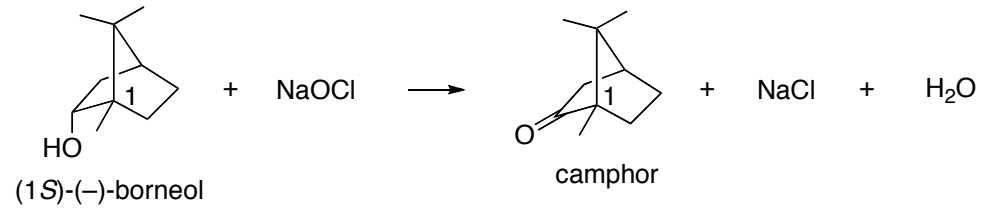
Le Châtelier proposed that "if a stress is placed on a system, the system responds to relieve the stress." A chemical reaction at equilibrium is limited to one of two things: it can move more in the forward direction or in the reverse direction. For example, if more of reactant A is added, the reaction responds by trying to use up the extra A by shifting toward products: the amount of B goes down, and the amounts of C and D increase. The same effect can be achieved by removing one of the products C or D: the reaction shifts toward products to try to replace the missing one, thereby reducing the amount of A and B and producing more C and D. We use this principle to increase yields of products. To produce more D, we could either add more A or B, or we could remove C or D as they are produced. A product can be removed by distillation if the boiling points cooperate, or if one product is water, it can be removed by adding an anhydrous material like sodium sulfate or a special mineral called zeolites, also known as molecular sieves.

EXPERIMENT 2: OXIDATION OF BORNEOL WITH NaOCl

Oxidation of secondary alcohols to ketones is a common and important reaction in organic synthesis and in biochemical processes. The Jones oxidation using Cr (VI) as the oxidizing agent has been a standard lab method for decades, but chromium is not an environmentally friendly element. The procedures below use relatively safe, inexpensive, and environmentally innocuous oxidizing agent, sodium hypochlorite (NaOCl), common household bleach.

SAFETY. Goggles, gloves and an apron or lab coat should be worn. Organic solvents, acids and bases can injure skin and eyes—avoid contact with these materials. Look up the specific hazards of each compound used in this experiment on www.hazard.com.

WASTE DISPOSAL. Organic layers should be discarded in the Blue "Non-Halogenated" waste. Flasks containing $MgSO_4$ should be rinsed with acetone into the Blue "Non-Halogenated" waste. Any remaining $MgSO_4$ (aka Epsom salt) can then be rinsed with H_2O in the sink. Aqueous waste should be discarded in the Yellow "Aqueous" waste.



(1*S*)-(–)-borneol camphor

Procedure

Oxidation. In a 50 mL Erlenmeyer flask, place 2.0 g of borneol along with a magnetic stir bar and 5 mL of glacial acetic acid (HOAc). Clamp a thermometer at an angle so that its bulb is immersed in the solution without contacting the stirbar. Use a thermometer adapter so that a clamp can securely hold the thermometer. Place 30 mL of 6.0% sodium hypochlorite (NaOCl) solution in a graduated cylinder. ***Caution:*** *NaOCl can rapidly bleach cloth and cause damage to the skin; gloves and a lab apron are highly recommended when handling it.* With stirring, add 10 mL of NaOCl to the flask in one portion. At 2 minute intervals, add 2.0 mL of NaOCl using a glass pipette with a latex bulb. Record the temperature just prior to each addition. It is advisable to construct a blank table in your notebook prior to beginning the addition. After all of the NaOCl has been added, continue to record the temperature at 2.0 min intervals. ***Be sure that the mixture is stirred vigorously in order to avoid solid material from clumping in one location in the flask.***

Once the temperature has returned to room temperature, stir the reaction for 10-15 minutes and test for the presence of hypochlorite by using a wetted piece of starch-iodide test paper. Be sure to use a glass stir rod to sample the reaction rather than immersing the paper in the flask. If hypochlorite is still present, the test paper will turn to a dark

purple color. If the result is negative, then add an additional 5.0 mL of NaOCl solution to ensure an excess amount of oxidant. *(Why do you want to confirm that there is an excess of oxidant?)*

Product isolation (Work-up). Vacuum filter the solid and wash well with about 50 – 100 mL of water. Maintain the vacuum for a few minutes allowing air to dry the solid. Spread the crude solid on a piece of medium-sized filter paper. Use your spatula to pulverize any large pieces and blot dry with a second piece of filter paper. The camphor product should be stored in a tightly capped tared vial rather than between filter paper. Determine the crude weight.

Purification (by sublimation). Check with your lab instructor whether this is required. Place approximately ≥ 0.7 g of the crude solid into the bottom of a vacuum sublimator (available from the stockroom). Insert the cold-finger condenser, making sure it does not touch the crude solid. Attach to the high vacuum line (your instructor will demonstrate), and raise a Thermowell to within about 1 cm of the bottom of the sublimator—do not touch the glass with the Thermowell. Heat gradually (Thermowell on ≈3-4). Remove the heat immediately if the remainder of crude material begins to liquefy or bubble. Allow the apparatus to cool for a few minutes and *carefully* release the vacuum by turning the vacuum manifold stopcock into the proper position (ask your instructor, if you are not sure). Scrape the purified camphor from the cold finger, weigh it, and calculate the recovery. Store the camphor in a small, tightly-capped vial; do not store it such that it is open to the atmosphere.

Product Characterization/Analysis. Check with your lab instructor about what he/she requires you to perform from the list of analyses below:

IR

Take an IR of your starting material (borneol) and the isolated product (camphor).

^{13}C NMR + DEPT

Prepare a saturated solution of your isolated product in deuterated chloroform ($CDCl_3$) for the ^{13}C NMR and DEPT analyses.

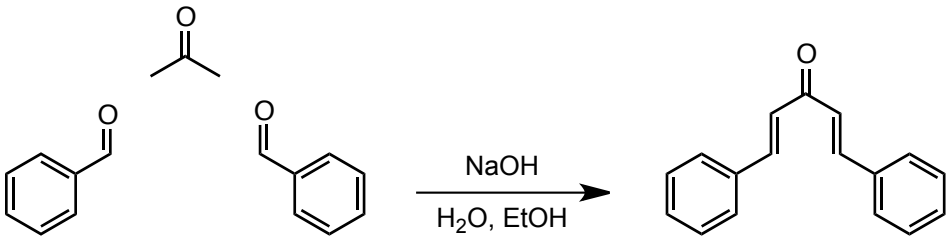
Questions

1. Balance the chemical equation on the previous page.
2. Calculate the number of moles of each reactant used. How can a catalyst be distinguished from a stoichiometric reagent?
3. How many chiral centers does borneol have? How many for camphor? In (1S)-(–)-borneol, what do “1S” and “–” mean? Which camphor is produced from (1S)-(–)-borneol, 1S or 1R? Compare the physical properties in Aldrich for 1S and 1R camphor; are they what you would expect?
4. What is the purpose of the sodium bisulfite wash in the work-up?
5. What property must a solid have before it can be purified by sublimation?

EXPERIMENT 3: PREPARATION OF DIBENZALACETONE

Reference: Conard, C. R.; Dolliver, M. A. *Org. Synth*. **1943**, *2*, 167.

This reaction is an example of a mixed aldol condensation involving nucleophilic addition to a carbonyl by an enolate, followed by dehydration. The sequence occurs on one side of the acetone molecule, then another condensation-dehydration takes place on the other methyl group of acetone.



Dibenzalacetone

Procedure

Reaction. To a 125-mL Erlenmeyer flask add:

- magnetic stirbar
- 3.0 g (75 mmol) NaOH pellets
- 30 mL H_2O
- 20 mL of ethanol (EtOH)

To a capped vial add:

- 30 mmol benzaldehyde (PhCHO)
- 15 mmol acetone

What is the best way to measure the above quantities?

Sage advice: Make sure to cap the vial immediately after the addition of acetone so as not to allow any evaporation of acetone.
How would this affect your reaction stoichiometry?

Place the reaction flask (125-mL Erlenmeyer flask) in a room temperature water bath (aka a bowl filled with cold tap water) and start stirring vigorously. Add (with a disposable pipet) approximately one-half of the PhCHO/acetone mixture. Recap the vial immediately! Stir vigorously for 15 minutes during which a flocculent precipitate forms. Add (with a disposable pipet) the rest of the PhCHO/acetone mixture. Rinse the vial with 2-4 mL EtOH and add this rinse to the reaction mixture. Continue stirring vigorously for another 30 minutes.

Product Isolation (Work-up). Cool the reaction mixture in an ice-bath. Collect the product by vacuum filtration. Use cold water to transfer any remaining solids in your reaction flask. Rinse the collected solids with cold water. Allow the collected solids to dry over vacuum for 5-10 minutes. Transfer your product to a large sheet of filter paper, and store it in your locker to dry until the following lab period.

Before performing any analyses, weigh your final 'dry' product and calculate the percent yield.

Product Characterization/Analysis. Check with your lab instructor about what he/she requires you to perform from the list of analyses below (or any other):

TLC

Elute a TLC plate (*what eluent should you use?*) with the following spots:

- Starting material (PhCHO)*
- Isolated product (Dibenzalacetone)

** Why are we not analyzing acetone by TLC as well?*

Melting point

Use a small sample of your isolated product to determine its melting point. The literature melting point range for dibenzalacetone is 110-111 ºC.

^{1}H NMR

Prepare a solution of your isolated product in deuterated chloroform ($CDCl_3$) and obtain a ^{1}H NMR.

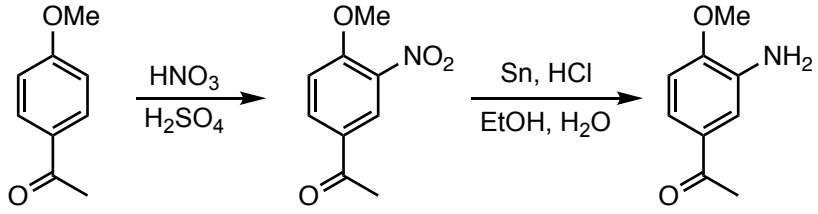
Questions

1. How is NaOH able to remove a proton from acetone? In other words, why is acetone a much stronger acid than an alkane? What are the pK_a values?
2. Why is the order of addition important? What would happen if the NaOH and acetone were mixed, followed by the benzaldehyde?
3. Most dehydration reactions occur under acid conditions, yet this one proceeds rapidly in base. How can this be dehydrated in base? How does the mechanism explain this unusual observation?
4. If the instructions did not suggest a reaction time, how could you determine experimentally when the reaction was complete?
5. Why is the product colored?

EXPERIMENT 4: MULTI-STEP AROMATIC SYNTHESIS

This series of experiments is designed to show you some major types of reactions of aromatic systems, and to expose you to a multi-step synthesis, that is, a sequence of reactions leading to the target molecule. Many areas of organic chemistry, in basic research as well as in industrial and commercial application, rely on principles encountered in this sequence.

Overall Synthesis



Strategy: Perform the reactions according to these procedures. Note that, in some cases, you may have to modify the instructions to fit the amounts you have. Start with the amounts given for Reaction 1; use this product as the starting material in Reaction 2, *etc*., EXCEPT save at least 200 mg from each product for IR, NMR, m.p., TLC, *etc*. At the end of the sequence, hand in all products, product cards, and a report as required by your lab instructor.

SAFETY. Goggles, gloves and an apron or lab coat should be worn. Organic solvents, acids and bases can injure skin and eyes—avoid contact with these materials. Look up the specific hazards of each compound used in this experiment on www.hazard.com.

WASTE DISPOSAL. Non-halogenated organic waste should be discarded in the Blue "Non-Halogenated" waste. Halogenated organic waste should be discarded in the Pink "Halogenated" waste. Flasks containing $MgSO_4$ should be rinsed with acetone into the Blue "Non-Halogenated" waste. Any remaining $MgSO_4$ (aka Epsom salt) can then be rinsed with H_2O in the sink. Aqueous waste should be discarded in the Yellow "Aqueous" waste.

Procedure

3-Nitro-4-methoxyacetophenone: Dissolve 5.0 g of 4-methoxyacetophenone in 20 mL concentrated sulfuric acid* by stirring magnetically at room temperature. Cool this solution to less than 5 ºC and add 2.5 mL of concentrated nitric acid* dropwise at such a rate that the temperature is maintained below 10 ºC. After the addition is complete, stir the mixture for 15 min. Pour the mixture

*Use EXTREME caution with conc. H_2SO_4 and HNO_3.

Be SURE the starting material does not precipitate from the cold solution.

into a beaker containing 70 mL ice and water. Stir the resulting mixture for 10 min and collect the precipitated solid by vacuum filtration. Recrystallize this solid from ethanol (EtOH) to produce pale yellow crystals (literature mp. 99.5 ºC). If your yield is less than 3.5 g, isolate a second crop from the mother liquor. Dry between two pieces of filter paper and/or place in a RB flask and place on the high vacuum line to remove all traces of EtOH. Save a small sample (*ca.* 200 mg) for analyses (e.g., TLC, IR, ^{1}H NMR) as required by your lab instructor.

This mixture of crude product and water may be allowed to set until the next period.

<u>3-Amino-4-methoxyacetophenone</u>:

Dissolve 15.0 g of stannous chloride dihydrate in 15 mL concentrated HCl. With vigorous stirring, add 3.3 g of solid 3-nitro-4-methoxyacetophenone as rapidly as possible. The temperature should increase quickly. Cool *only* if the temperature reaches 95°C. After the exotherm, cool the mixture to room temperature. Filter the precipitated solid by vacuum filtration USING ACID-RESISTANT GLASS-FIBER FILTER PAPER—DO NOT WASH. Transfer the filter cake to a beaker; add 80 mL water and make basic with 50% NaOH* (*Why?*) Extract the precipitated amine three times with CH_2Cl_2, dry over anhydrous $MgSO_4$, and rotavap (literature m.p. = 100-101ºC).

Monitor for complete conversion to desired product by TLC. **Hint:** use a 10% MeOH/CH_2Cl_2 solvent system

*Use EXTREME caution with NaOH.

Product Characterization/Analyses. Check with your lab instructor about what he/she requires you to perform.

Do <u>not</u> cool until 95 °C. Have ice ready.

The solid is a mixture of amine hydrochloride and tin salts. The tin salts are insoluble in CH_2Cl_2.

OPERATION OF THE GOW-MAC GAS CHROMATOGRAPH

Ordinarily, the set-up steps will be done by the time you are ready to inject your sample into the GC. If these steps have not been done, check with the instructor.

Set up

1. Power "On". Thermometer will indicate proper oven temperature within 30 minutes.
2. Detector "On". Current will have been set for you.
3. Open the LoggerPro file named 'CHEM216 Distillation' on the desktop. Graph parameters are set. **Do not reset any of the parameters without asking your lab instructor.**

You should perform these steps when taking a GC:

7. Flush the GC syringe three times (3x) by drawing up a small amount (about 5 µL) of your sample and depositing it on a KimWipe. In addition to cleaning and rinsing your GC syringe with your sample, this will also allow you to detect any clogging in your GC syringe.
8. For each injection, draw up 1.0 µL of sample followed by 1.0 µL of air (to serve as a buffer from material prematurely entering the column). Each injection should be about **1.0 µL**.
9. Check that your baseline is zero. If necessary, adjust baseline to zero on the graph by selecting "Zero…" under 'Experiment' pull-down menu.
10. Inject each sample on **column A**. Immediately use the mouse arrow and click the "Collect" button (it is a green, 'play' button) at the top of the screen. Click the 'erase and continue' option on the ensuing dialog box.
11. When GC trace is complete (i.e., all the components of your mixture have exited the GC column), click the "Stop" button at the top of the screen.
12. **To determine retention times (t_R):** Click the mouse arrow the peak maximum and you can see the t_R at the lower lefthand corner of the screen. Record the retention time (t_R) in your lab notebook.
13. **To integrate peaks:** Click the mouse arrow to the left of the peak (i.e., the beginning of the peak) on the baseline and drag the mouse arrow by holding down the left mouse button to the right of the peak (i.e., the end of the peak). This highlights the peak to be integrated. Click the 'integral' button at the top of the screen. A box linked to the peak will appear with its integration. You can ignore the units of the integration. Record the integration in your lab notebook.
14. **To print a chromatogram:** Click on the 'print' button or select 'print' from the File dropdown menu.
15. Repeat steps #3-7 for each new injection. You can also rinse your GC syringe with acetone when you are done with your GC analyses.

OPERATING INSTRUCTIONS FOR THE AGILENT GC-MS
(A COLLEGE OF SCIENCE AND MATHEMATICS COLLEGE-BASED FEE ACQUISITION)

Sample Preparation – DO NOT inject any sample into the GC-MS that has not been purified or its purity demonstrated. A 0.1 – 0.5 % solution is adequate (GC-MS is very sensitive and requires very little sample). For example, 0.01 – 0.05 g of compound may be dissolved in 10 mL of solvent. Methanol or acetone are ideal solvent choices. The GC-MS is generally run in a split mode with a 2.5 min solvent delay. If you inject □□□□□l of a 0.1% solution into the GC, the mass spectrometer will not begin looking at your sample until all of the solvent has cleared the instrument – this helps extend the life of the detector by saving it from observing an enormous solvent peak. With a split ratio of 50:1, that means the mass spec will be looking at only 2×10^{-2} □g compound! It doesn't take much material, and too much sample will create more downtime for our instrument.

Set-up – As you face the instrument, from left to right the two parts of the instruments are the MSD (mass selective detector) and the gas chromatograph. A computer workstation is located on the opposite bench.

Method Preparation – *Skip to Step 3 if the computer is already on and running the appropriate programs.*

1. Turn on the monitor – button on the lower right corner of the screen. If a logon is required, logon as 'Student' with the password = chem.

2. Open 'Instrument #1' (alias on the desktop – make sure you DO NOT select 'Instrument #1 Data Analysis'). It will take a few moments to open. If a question box pops up, 'Limits fail: Pump Oil (Days), Tune Time (Hours), select OK.

3. From 'Instrument #1', under Method select Load ----> 319.M (the path is MSDChem/1/Methods/319.M), and OK. Individual instructors may have created a subfolder for your specific class. On the MSD the LED readout should confirm 'Method Loaded'. Note that *method files* end with ".M' and *data files* end with ".D'.

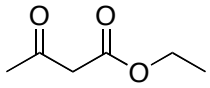
4. From 'Instrument #1', under Method select Run Method. A user interface box appears that requires a Data Path (D:\DATA\319), a Data File Name (e.g., test1.D), an Operator Name, etc. It appears that you can type in a file name and the .D extension will be added automatically. Select 'Run Method' (DO NOT press 'OK'). If the filename has been left unchanged you may be asked 'OK to overwrite?'

5. On the front of the gas chromatograph push 'prep run'. This turns off the gas saver mode and prepares the instrument.

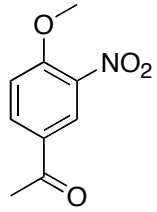
6. From 'Instrument #1', a dialog box will appear saying "Waiting for GC Ready".

Injecting Sample – When the gc 'not ready' light is no longer lit, <u>inject 1□l of your sample</u> into the gc and press <START> (front of the gc). DO NOT override the 2.5 min solvent delay. Select 'NO' when asked. After the 2.5 min delay the trace will begin to appear in the 'Total Ion' window. Sometimes this window is minimized or is hiding behind other windows. You may have to look for it.

Review Data – The run will stop automatically or it may be stopped manually (e.g., ethyl acetoacetate takes 5.7 minutes and 3-nitro-4-methoxyacetophenone takes about 11.5 minutes to pass through the column). It is probably preferable to have the run go to completion so that the elevated oven temperature will have an opportunity to help clear the column.



ethyl acetoacetate
M^+ = 130 (5.7min)



3-nitro-4-methoxyacetophenone
M^+ = 195 (11.5min)

7. After the run is complete, go to 'Instrument #1' and under View, select 'Data Analysis (offline)'. This opens a data analysis window. In this new window, under File select 'Load Data File', choose your file name and select 'OK'.

(If you want to inject a second sample, that may be done now by going back to the 'Instrument #1' window and selecting 'Run Method' under the 'Method' heading, and going through the procedure as before.)

8. The TIC will appear for your injection. You may expand regions by dragging a block around your peak with a left mouse click. A double left click will return your full TIC. Double right mouse click on any peak in the TIC and observe its mass spectrum in the window below.

9. Printing - When you are ready to print go to 'File' ----> 'Print' ----> 'TIC and spectrum' ----> 'OK'.

10. For a mixture you may request a % composition report. From Instrument #1 select 'Chromatogram' ----> 'Percent Report'. Right click with the mouse in your report box and choose 'Print' for a hard copy.

Finishing Up – The gas chromatograph and MSD will take care of themselves in your absence, so no action is required. You may leave the windows open on the computer and turn-off the monitor. Be sure to sign the logbook that is on the table next to the MSD. Please report any anomalies in the book and additionally mention them to your instructor.

Please be careful with this expensive research-grade instrument. Keep organics on the end of the bench behind the instrument and be careful with the GC syringe. Work thoughtfully and don't rush.

OPERATION OF THE HIGH VACUUM SYSTEM (AKA HI-VAC)

Proper care and feeding of a vacuum system

So much of the success of a vacuum distillation depends on proper use of the vacuum system that it is worthwhile reviewing important principles of using vacuum.

Our vacuum systems have three parts: the pump, the trap, and the manifold. The pump is a mechanical rotary pump turned on by the switch on top of the bench. The purpose of the trap is to condense all solvent vapor before it reaches the pump—the trap protects the pump, so correct trapping is critical. The manifold is a "vacuum reservoir" where we "store" vacuum until we need it. You will not do anything with the pump other than to turn it on or off, but here are the important operating procedures for the manifold and the trap:

A. Always have cryogen on the trap when the vacuum pump is on. The "cryogen" is the cooling agent, which is **dry ice in 50:50 ethanol/isopropanol** in your lab. YOUR LAB INSTRUCTOR SHOULD BE THE ONE HANDLING THE CRYOGEN. Before applying the cryogen to the trap, it is a good idea to ensure that the trap is empty and clean. Before applying the cryogen to the trap, be sure the trap is empty and clean.
B. The manifold must be OPEN when the vacuum pump is OFF. (If a gas has condensed in the trap, the liquid will vaporize when the cryogen is removed; if the manifold is closed, the increase in pressure will cause it to explode.)
C. The manifold must be CLOSED when the vacuum pump is ON. (If the manifold is open to the air, liquid oxygen will condense in the trap, and the air will eventually damage the pump.) It is much better for the system to be left on than it is to be turned on and off several times.

Measuring pressure

Each manifold is connected to a Pirani 501 gauge. The stopcock between the Pirani gauge and the manifold should always remain open. To measure pressure in the system, read the inside of the arc (torr). Be careful when making the reading, as the scale is not linear.

OPERATION OF THE BUCHI ROTARY EVAPORATOR

Reference: Padías 2nd ed., pp. 156-157

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". Basically, the rotavap performs a 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 fast is the application of a vacuum to the system 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 decompose the desired organic product. Since boiling 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. To avoid bumping, NEVER fill a round-bottom flask more than two-thirds full of solution.

2. Be sure that the recirculating chiller displays a low temperature (probably between -15 and -5 ˚C). Fill the plastic bucket under the large solvent trap with ice-water.

3. With your right hand, put the round-bottom flask on the trap joint, affix a blue plastic Keck clamp, but continue SUPPORTING THE FLASK with your hand until you complete Step 7.

4. Switch on the mechanical vacuum pump.

5. With your left hand, close the Teflon stopper located at the upper left part of the condenser. This closes the condenser permitting the vacuum to evacuate the system. You will probably hear a difference in the sound coming from the vacuum pump.

6. Turn the motor dial to a setting between 5 and 7 **IMMEDIATELY** after closing the stopcock.

7. You may cease supporting the round bottom flask when one of two things occurs: a) the flask becomes cold from evaporation; or b) the solution bubbles. Either of these events 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, gradually lower it into the warm water bath. 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 further change in the volume 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: raise the flask out of the warm water bath; turn the motor dial to "0"; HOLD THE ROUND BOTTOM; open the condenser stopcock to the air (180° rotation); wait ~10 seconds, then turn off the mechanical vacuum pump; remove the round bottom flask. Never turn off the pump while the system is still evacuating. Additionally, pulling off your flask before the vacuum line is off may cause air to rush in near the joint of the flask and drive a lot of your material out (and onto your hand!).

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

OPERATING INSTRUCTIONS FOR THERMO-NICOLET FOURIER TRANSFORM INFRARED SPECTROMETER
(A COLLEGE OF SCIENCE AND MATHEMATICS COLLEGE-BASED FEE ACQUISITION)

Reference: Padías 2nd ed., pp. 66-76

The two Nicolet spectrometers are operated with the EZ OMNIC software. Open this program.

Preparation of Sample Area

- The sample surface area (Germanium or Diamond) should be left clean. It can be cleaned with a few drops of propan-2-ol (*DO NOT USE ACETONE – IT WILL DAMAGE THE IR CASING!),* followed by wiping with a piece of cotton or a cotton swab. Do not use a Kimwipe!
- To clean the compression tip (used for solid samples) use a propan-2-ol moistened piece of cotton.

Obtaining the Background Spectrum

- Press 'Clear' (see toolbar).
- Press 'Collect Background'. Click OK. After the 4 scans are complete and the dialog opens asking if you want to add to window 1, select 'NO'

Applying the Sample

With the exception of placing your sample on the surface area, keep all chemical samples away from the instrument and computer keyboard, etc.

- Be sure that a background spectrum has been collected. A fresh background usually helps produce a better sample spectrum.
- Liquid Samples: Place one drop of liquid sample on the center or the diamond sample surface. (be careful not to get sample on the instrument casing as it may damage it).
- Solid Samples: Place a very small amount of crystals on the diamond sample surface. Lower the pressure arm down against the sample until a gentle pressure is achieved. Do not force it.

Obtaining the Sample Spectrum

- Depending on how the background was collected, there may be a window on the screen instructing you to collect the sample. If not select 'Collect Sample' and click OK. After the spectrum appears, when a dialog asks if you would like to add to a Window. Click Yes.
- Baseline not flat?? Put spectrum in Absorption view. Under 'Process' select "Automatic Baseline Correction". Click on and highlight original spectrum, then select 'Clear'. Return to Transmittance view.
- To raise the spectrum up higher on the page, left click on the spectrum and drag it higher.
- **If the spectrum seems to have disappeared, type Ctrl-F to display the full spectrum again**.

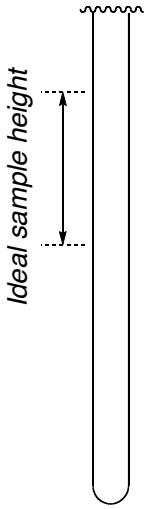
Assigning Peaks

- Click the 'Find Peaks' button on the toolbar. (Or use the T on bottom toolbar. After using the T icon always return to the arrow icon)
- Set the sensitivity threshold by clicking higher on the spectrum wherever you would like prominent peaks identified.
- Click the 'Replace' button when finished. (**Otherwise, you will not be able to print!**)

Printing the Spectrum

- Click the *'i'* (info) button by the message bar.
- On the 'Custom 1' line, put the name of your compound and other information you desire.
- On 'Custom 2' put your name.
- Click OK; you may need to move the window up to find the bottom toolbar.
- Click on the 'Print' icon in the toolbar.

^{1}H NMR INSTRUCTIONS



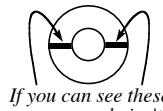
1. Prepare your sample for the NMR

- **Liquids**: In a shell vial, place 0.50 mL of $CDCl_3$ with 1% v/v TMS and about 5 drops of your compound. Use a dropper to transfer to an NMR tube. Cap the tube; clean the outside with a KimWipe.

- **Solids**: Weigh approximately 0.15g of solid into a shell vial. Add 0.50 mL $CDCl_3$ with v/v 1% TMS and swirl to dissolve. With a disposable pipet, transfer to an NMR tube. If there are undissolved particles, filter the sample through a glass pipette containing a small amount of a KimWipe directly into the NMR tube.

2. Place your prepared sample in the magnet.

- Open the lid to the magnet and *smoothly* push the black air ejector button. The previous sample will pop out. Remove that tube, and put your tube in the plastic spinner.
- Adjust the depth of the tube in the spinner using the depth gauge on the magnet housing.
- Push and hold the black air button and carefully insert your sample. Gently release the button and your sample will drop into the magnet. **MAKE SURE THE TUBE IS SPINNING, NOT WOBBLING.** (Use the flashlight to see the tube. If you can see the two lines on the spinner then your sample is not spinning.) Close the lid.


If you can see these, your sample isn't spinning!

IMPORTANT: Never insert an NMR tube without a spinner or a spinner without an NMR tube into the NMR magnet.

3. Obtain the Proton NMR data.

- Open **PNMR** program. (Look in Start Menu if not on the desktop or already open.)

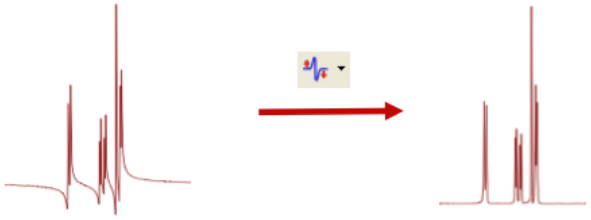
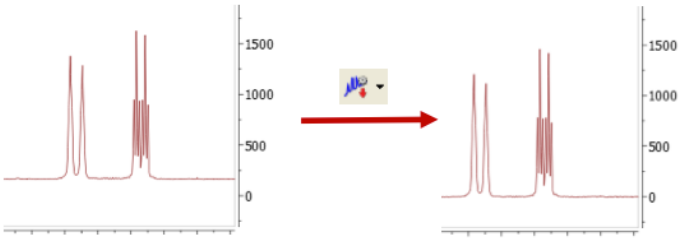
Command	Comment
<nu> <enter> **<H1> <enter>**	Sets spectrometer to observe ^{1}H channel.
<ns> <enter> **<4> <enter>**	Sets **n**umber of **s**cans to 4. Better spectra are obtained with 4 scans vs 1 scan. More than 4 is generally not necessary for ^{1}H NMR.
<**zg> <enter>**	**Z**ero previously stored data and **g**o Enter a file name with the following format: **nmra#####** (for NMR A) or **nmrb#####** (for NMR B) then **<enter>**
	IMPORTANT NOTE: If the FID is red you must lower the receiver gain by typing <**control> <q>** to stop the scan, then <**rg> <enter>.** Try lowering gain by about **2** or **3** units then <**enter>.** Type <**zg>,** fill in the dialog box, and hit **<enter>** to begin acquiring data again.

- Retrieve your sample and **replace the reference sample**!

4. Load your data.

- Go to one of the four NMR remote workstations and open the **MestReNova** program.
- Open your NMR file through File → Open.
- The command buttons are located on the top and their functions can be revealed by leaving the cursor arrow to rest on them.

5. **Phase and baseline correction of the NMR spectrum** (This step may not be necessary.)

Command Button	Comment
	Click this **Phase Correction button** if your peaks are not symmetric. 
	Click this **Baseline Correction button** if your baseline is not at zero. 

6. **Setting reference peak and scaling the spectrum**.

Command Button	Comment
	Click this **Reference button** if your reference peak (e.g., TMS) is not at the correct ppm. Place the cursor arrow on your reference peak and left click on the mouse. Type in the correct ppm value in the "New Shift" field of the dialog box that pops up.
	Click this **Fit To Highest Intensity button** (or press H) to scale your NMR spectrum vertically to the highest peak. Alternatively, you can adjust the vertical scale of your spectrum with the mouse wheel.
	Click this **Manual Zoom button** to define your horizontal scale (spectral window). Type in the range (e.g., –1 to 10 ppm) in the dialog box that pops up.

7. **Peak picking**.

Command Button	Comment
	Click and hold down this **Peak Pick button** and select "Manual Threshold" on the dropdown menu. Define your threshold by holding down the mouse left click, dragging the resultant threshold bar across your spectrum and lowering the threshold to touch your lowest peak. Make your threshold low enough to catch the smallest significant peak, but not so low that a large number of noise peaks are picked. Use your judgment. If you don't like what you see, there is always CTRL-Z (or the undo button). If the 'Manual Threshold' option ends up in excessive peak picking, you can choose 'Peak by Peak' option on the dropdown menu of 'Peak Pick'. In this option, you can pick each peak by dragging the cursor to the individual peak and left-clicking.

8. Integrating the spectrum.

Command Button	Comment
	Click and hold down this **Integration button** and select "Manual". Integrate the peaks by holding down the mouse left click at the beginning (left side) of the peak and dragging to the end of the peak (right side). Double clicking on the actual integral above the peak will bring forth a dialog box where you can set the value of the peak integral.

9. Printing.

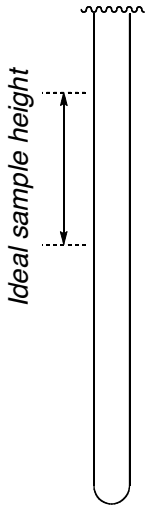
Go to File → Print ; select Landscape.

or

Go to File → Export to PDF

10. Cleaning the NMR Tube. Rinse well with acetone using the NMR cleaning station – ask your lab instructor. Blow dry with nitrogen stream from house N_2. If you don't get the acetone out it will show as a signal in your spectrum at 2.1 ppm.

^{13}C NMR INSTRUCTIONS



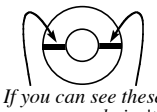
1. Prepare your sample for the NMR

- **Liquids**: Add enough of your sample to reach the ideal height shown at right. This is called "neat". If you do not have enough sample and/or you want a TMS reference peak premix your sample with ~0.25 mL of $CDCl_3$ with 1% v/v TMS in a vial. Use a dropper to transfer to an NMR tube. Cap the tube; clean with a KimWipe.

- **Solids**: Weigh approximately 0.50 – 0.70 g of solid into a shell vial. Add 0.25 – 0.50mL $CDCl_3$ with v/v 1% TMS and swirl to dissolve. With a disposable pipet, transfer to an NMR tube. If there are undissolved particles, filter the sample through a glass pipette containing a small amount of a KimWipe directly into the NMR tube.

2. Place your prepared sample in the magnet.

- Open the lid to the magnet and *smoothly* push the black air ejector button. The previous sample will pop out. Remove that tube, and put your tube in the plastic spinner.
- Adjust the depth of the tube in the spinner using the depth gauge on the magnet housing.
- Push and hold the black air button and carefully insert your sample. Gently release the button and your sample will drop into the magnet. **MAKE SURE THE TUBE IS SPINNING, NOT WOBBLING.** (Use the flashlight to see the tube. If you can see the two lines on the spinner then your sample is not spinning.) Close the lid.


If you can see these, your sample isn't spinning!

IMPORTANT: Never insert an NMR tube without a spinner or a spinner without an NMR tube into the NMR magnet.

3. Obtain the Carbon NMR data.

- Open **PNMR** program. (Look in Start Menu if not on the desktop or already open.)

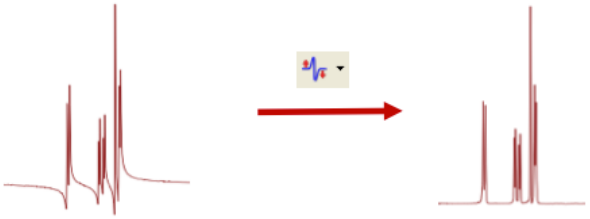
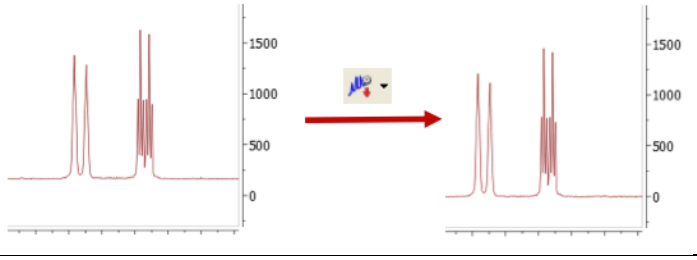
Command	Comment
<nu> <enter> **<C13> <enter>**	Sets spectrometer to observe ^{13}C channel.
<ns> <enter> **<24> <enter>**	Sets **n**umber of **s**cans to 24. Obtaining quality ^{13}C NMR spectra requires many more scans than for ^{1}H NMR. In some cases you may need ≥ 64 scans, but this requires more instrument time; consult your instructor.
<zg> <enter>	**Z**ero previously stored data and **g**o Enter a file name with the following format: **nmra#####** (for NMR A) or **nmrb#####** (for NMR B) then **<enter>**
	IMPORTANT NOTE: If the FID is red you must lower the receiver gain by typing <**control> <q>** to stop the scan, then <**rg> <enter>.** Try lowering gain by about **2** or **3** units then <**enter>.** Type <**zg>,** fill in the dialog box, and hit **<enter>** to begin acquiring data again.

- Retrieve your sample and **replace the reference sample**!

4. Load your data.

- Go to one of the four NMR remote workstations and open the **MestReNova** program.
- Open your NMR file through File → Open or simply dragging your NMR file into MestreNova window.
- The command buttons are located on the top and their functions can be revealed by leaving the cursor arrow to rest on them.

5. **Phase and baseline correction of the NMR spectrum** (This step may not be necessary.)

Command Button	Comment
	Click this **Phase Correction button** if your peaks are not symmetric. 
	Click this **Baseline Correction button** if your baseline is not at zero. 

6. **Setting reference peak and scaling the spectrum**.

Command Button	Comment
	Click this **Reference button** if your reference peak (e.g., TMS) is not at the correct ppm. Place the cursor arrow on your reference peak and type in the correct ppm value in the "New Shift" field of the dialog box that pops up.
	Click this **Fit To Highest Intensity button** (or press H) to scale your NMR spectrum vertically to the highest peak. Alternatively, you can adjust the vertical scale of your spectrum with the mouse wheel.
	Click this **Manual Zoom button** to define your horizontal scale (spectral window). Type in the range (e.g., 0 to 220 ppm) in the dialog box that pops up.

7. **Peak picking**.

Command Button	Comment
	Click and hold down this **Peak Pick button** and select "Manual Threshold". Define your threshold by holding down the mouse left click, dragging the resultant threshold bar across your spectrum and lowering the threshold to touch your lowest peak. Make your threshold low enough to catch the smallest significant peak, but not so low that a large number of noise peaks are picked. Use your judgment. If you don't like what you see, there is always CTRL-Z (or the undo button).

8. Printing.

Go to File → Print ; select Landscape.

or

Go to File → Export to PDF

10. Cleaning the NMR Tube. Rinse well with acetone using the NMR cleaning station – ask your lab instructor. Blow dry with nitrogen stream from house N_2.

DEPT INSTRUCTIONS

Use the same sample that you used for your ^{13}C NMR spectrum. Be sure the # of scans is set to 24.

DEPT sequence

Command	Comment
<dept>	Use the same file name you used for your ^{13}C NMR spectrum except add "dept" to the name then **<enter>.** Allow the entire acquisition to finish (approximately 8 – 10 min). The dialogue box will indicate: "DEPT 135 completed…DEPT 90 completed…DEPT 45 completed"
	You need to use the NUTS program (not MestReNova) to open the file. Open your NMR file by using CTRL-F11. If asked, set the line broadening to 0.5.
	Adjust the vertical scaling of the stacked spectra using the arrow keys. From top to bottom the spectra are: DEPT 135 DEPT 90 DEPT 45
	Go to File → Print or Export to PDF; select Landscape.

COSY NMR INSTRUCTIONS

(COSY = correlated spectroscopy)

1. Obtain the COSY data.

Command	Comment
<cosy>	(Instead of **<zg>)** Enter a file name with the following format: **nmra#####** (for NMR A) or **nmrb#####** (for NMR B) then **<enter>**
	Relaxation delay = 2
	Number of scans = 1

2. Load and process the COSY data.

Command	Comment
	Open your NMR file through File → Open or simply dragging your NMR file into MestreNova window.
	Adjust the vertical scaling of the stacked spectra using the arrow keys.
	Go to File → Print or Export to PDF; select Landscape.

3. Printing.

Go to File → Print; select Landscape; hit **okay** or **<enter>.**

LITERATURE SEARCH USING SCIFINDER SCHOLAR

Throughout your career as a scientist or health professional you will be repeatedly required to conduct many scientific literature searches using the primary literature. In addition, you may also be asked to summarize the information you have learned into actionable tasks or report summaries.

How do I get started?

1) You will need to register through SciFinder on campus. SciFinder registration can be done from the Chemistry Computer lab or from a laptop on campus by logging into your *my.calpoly portal* account and clicking on the "*Library*" tab. Once in the "*Library*" directory, scroll down to "*Top Resources*" and click on "*Databases A-Z*" and find ***SciFinder Scholar*** under the "*S*" subheading. Once in SciFinder, you will be directed on how to create a new SciFinder account. Note: You must use your "calpoly.edu" email address to register for the database.

2) Prior to conducting your search you should watch a short online **YouTube** tutorial on conducting searches in SciFinder using SciPlanner. The YouTube tutorial is called "*How to use SciPlanner to Plan a Synthesis Project*." The url is:

   https://www.youtube.com/watch?v=GSJ_tGbZ-ds&list=UUcXk83ni0MamhrR9zmvdqsg

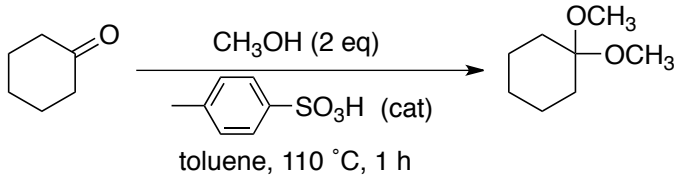
EXPERIMENTAL CHECKLIST FOR EVERY REACTION

1. DETERMINE REAGENT AMOUNTS

- Experimental procedures described in the lab manual (and in the chemical literature) commonly provide amounts in the units of moles (mol) or sometimes millimoles (mmol); chemists find it is more convenient to discuss "20 mmol" rather than "0.02 mol"
- BEFORE LAB: For all reagents to be used in a reaction, convert mol (or mmol) to the more practical units of **mass** (grams) and **volume** (mL)
- You should know how to use molecular mass (MM), molarity, density, and/or % solution values to convert to a mass or volume value (look in your Padiás text if you have forgotten)
    - Think ahead: Will it be better to measure out a reagent in a graduated cylinder, a weigh boat or weighing paper, or in a tared vial?
        - For example, it's more practical to measure 0.80 g of cyclohexanol on an analytical balance (in a tared vial) rather than 0.84 mL of it in a graduated cylinder

2. CALCULATE EQUIVALENTS

- Equivalents (or sometimes molar equivalents) is a measure of the *molar ratio of reagents* and should always be included in your reagent table
    - Equivalents effectively tells you the molecule-to-molecule ratio of each reagent in the reaction (or if a reagent is catalytic)
    - Consider the analogy: *if you build bicycles, it's helpful to know that you need TWO wheels for ONE frame*
- BEFORE LAB: Find the number of mmol of your **substrate** (the organic compound that you're operating on) and divide this number into the mmol amount of the other reagents in the table (this sets your substrate compound as 1.00 equivalent)
- Example:



Reagent	**MW** (g/mol)	**Density** (g/ml)	**Amount** (g or mL)	**mmol** (mmol)	**Equivalents** (eq)
cyclohexanone	98.15	0.948	5.03 g = 5.31 mL	51.2	1.00[a]
methanol	32.04	0.792	3.36 g = 4.24 mL	104.9	2.05[b]
pTsOH	172.20	–	0.70 g	4.09	0.08[c]

[a] This is your substrate (limiting reactant), therefore, 1 eq = 51.2 mmol. Every entry in this column gets divided by 51.2 mmol to determine the equivalents.

[b] Twice as much (i.e., 2 eq) of methanol is used. Typically, we use just a little more.

[c] This reagent is needed in a catalytic amount (in this case, 0.08 eq or 8 mol%).

3. CALCULATE THEORETICAL YIELD

- The theoretical yield expresses you how much material are you preparing
- BEFORE LAB: You must determine how much material you are expecting at the end of every reaction
    - Are you expecting 0.5 g, 10 g, 35 g? What?! You don't know?! This is essential information to know at all times
- This information will help you assess whether or not you have used the rotary evaporator for along enough period of time
    - Does it look like you have the theoretical amount remaining in your flask or is that still a lot of solvent you're seeing?

4. FIND OR PREDICT SPECTRA

- BEFORE LAB: Use the SDBS website **OR** sketch out the expected ^{1}H NMR, ^{13}C NMR, and IR for **every** compound you are using
    - This is especially helpful if your printed spectrum is nothing like you're expecting:
        - Maybe you grabbed someone else's printed spectrum; maybe you processed a different file; maybe you didn't make your compound at all (!)
- Don't forget about solvents!
    - Can you identify if you have any solvent remaining? Did you not leave your sample on the high vacuum pump long enough? Consider every solvent that came in contact with your compound? Did you use THF for the reaction? Did you use CH_2Cl_2 for the workup/extraction? *Spectra that contain solvent peaks demonstrate shoddy work.* It is your responsibility to have your final spectra be solvent-free; you may need to pour your NMR sample back into the flask and re-subject it to rotary evaporation and high vacuum.
    - Look up common solvents (see list below) on the SDBS website and know their ^{1}H NMR information (chemical shifts, splitting, and integration).
    - You should also know their chemical shifts in ^{13}C NMR and absorption frequencies in IR. Refer to this sheet frequently!

Common solvents

1. CH_2Cl_2 (dichloromethane)
2. Et_2O (diethyl ether)
3. $CHCl_3$ (chloroform; residual amounts in $CDCl_3$)
4. EtOAc (ethyl acetate)
5. Acetone
6. Tetrahydrofuran (THF)
7. H_2O