Sanford Group Welcome Kit

Version 5.0

Guidelines, Procedures, & Requirements

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Laboratory Safety

1.1. General Considerations

1.1.1. Lab goggles or glasses **MUST** be worn at all times while working in the lab! This is extremely important because even things that seem pretty common and safe (e.g., using the rotovap) involve placing glassware under reduced pressure, which can potentially lead to implosions.

1.1.2. Your desk and the group break room are chemical-free areas. In addition, gloves and lab coats should not ever be worn in these areas.

1.1.3. Gloves can and should be reused if they are not contaminated. Carefully remove them and place on your bench for reuse. Unless you are using highly toxic reagents (in which case you should throw out gloves after any chance of contamination – *see toxicity hazards – section 1.4*) or the gloves are damaged, you should not have to use more than two or three pairs of gloves a day. Do not wash gloves with organic solvents (latex and nitrile gloves are permeable to acetone).

1.1.4. Know where all eyewashes are located in each lab.

1.1.5. Know where all safety showers are located in each lab.

1.1.6. Know where all fire extinguishers are located in the lab, what kind they are, and what they can be used for.

1.1.7. Nothing should be stored on the lab floors! Keep the floors free of anything other than lab stools, solid waste buckets, and the 10 L liquid nitrogen dewar.

1.1.8. Don't work in the lab alone! Computer work is okay, but you should plan to have someone else in the lab whenever you need to get something done. This is especially true if you are doing a large scale-up, running reactions with very reactive materials (i.e., strong oxidants or reductants, Grignard reagents, lithium reagents, etc), carrying out reactions requiring high pressure, or running a reaction for the first time. If you do end up working alone, always leave the door open so that someone can get in if there is a problem. Avoid quenching or dispensing large quantities of highly reactive chemicals when no one else is around.

1.1.9. The last person out of the lab should turn all lights out and lock all doors.

1.2. Reaction Safety

1.2.1. LABEL, LABEL, LABEL all your reactions clearly! This is not only for your safety, but for everyone else's as well. Reaction labels should clearly correspond to your notebooks, such that if something goes wrong and you are not available other lab members or safety personnel can take appropriate measures.

1.2.2. Reactions under high pressure (e.g., with condensed gases or in super-heated solvents) are explosion hazards and should be treated with extreme caution. A blast shield should be placed in front any system larger than an NMR tube under pressure. NMR tube reactions should also be treated with extreme caution – the hood sash should always be lowered when working with NMR tubes that are under pressure.

1.2.3. Water condenser hoses should be fastened with copper wire, and water flow should be turned as low as possible at night. Remember that the water pressure will increase at night with fewer users in the building.

1.2.4. Although water aspirators are used all the time in the lab (for filtration, running the rotovaps, etc), you should keep in mind that these involve reduced pressures and are a significant implosion hazard. Use caution when evacuating any flask, especially large round bottoms and large filter flasks (>500 mL), and check glassware regularly for cracks. Star cracks should be sent to the glass shop for repair.

1.2.5. Exercise caution in pulling tubing off Schlenk glassware! If it is too difficult to remove the tubing, carefully cut the tubing away with a razor blade. Excessive jerking, pulling, and twisting **will** snap the glass stopcock off, which may result in an injury. Remember, rubber tubing is cheap and can be cut when necessary.

1.3. Common Explosion Hazards

1.3.1. Oxidants (e.g., bleach, Cr^{VI} and Mn^{VII} salts, hypervalent iodine reagents, H_2O_2, etc) should be placed in separate waste from organic reagents/solvents. The oxidation of organics with these reagents can lead to violent exotherms and explosions.

1.3.2. Oxidizing acids (e.g., nitric acid and aqua regia) can react extremely violently with organics, especially acetone, and the resulting explosions and release of corrosive solutions can lead to serious injury. Acids should *always* be stored in a **separate location** from organic chemicals. Additionally, waste bottles for acids should be clearly marked and placed in a **separate location** from organic waste. This will prevent mistakenly pouring acid waste in with organics, which is the most common cause of this type of explosion.

1.3.3. Perchlorate salts can explode without warning, especially when concentrated in the presence of organics (ClO_4^- is a strong oxidant!). Always use a blast shield when concentrating mixtures containing these salts and avoid the use of the ClO_4^- counter anion whenever possible.

1.3.4. Metallic lithium should **never** be placed in N_2 dry boxes or under a nitrogen atmosphere on your line. A violent and highly exothermic reaction will result from spontaneous "Li_3N" formation.

1.3.5. Remember that even common flash chromatography columns are run under high pressure and can crack or explode unexpectedly.

1.3.6. The condensation of liquid oxygen, liquid nitrogen and solid argon in traps on your vacuum line can lead to explosions. *See the vacuum line safety (section 2) for further details*.

1.4. Toxicity Hazards

1.4.1. Examples of toxicity hazards include thallium salts (*e.g.,* TlOEt), alkyl mercury salts (*e.g.,* $HgMe_2$), tin reagents (especially tetra-alkyl or tri-alkyl aryl Sn compounds) and alkylating agents (*e.g.,* MeI).

1.4.2. Exercise extreme caution when using these reagents!! Clean up spills in your hood and in public areas (balances, dry boxes, etc) immediately, using appropriate procedures and dispose of cleaning supplies and gloves in solid waste containers beneath the hood to avoid fume inhalation.

1.4.3. Dispose of gloves (in solid waste container beneath the hood) whenever you may have come in contact with these reagents.

1.4.4. If any of these compounds are used in the dry box, be sure to (i) use a secondary pair of gloves so as not to contaminate the main gloves, (ii) dispose of all contaminated waste in a separate Ziploc bag before removing it from the box, and (iii) purge the box after the use of these compounds (and before opening the antechamber).

1.4.5. For specific instructions on how to wash glassware that has contacted these reagents, speak with Prof. Sanford directly.

1.5. Disposal of Pyrrophoric Materials

1.5.1. Pyrrophoric materials from commercial sources (e.g, alkyl lithium reagents, Grignard reagents, alkyl zinc reagents, etc.) that are still in their bottles can be given to chemistry waste disposal (Laurie) without quenching if they are still in their bottles. This is the safest way to dispose of these reagents.

1.5.2. If you are quenching pyrrophoric materials before disposal, you should do so with EXTREME caution! Remember that one mistake can be catastrophic and literally burn down the lab and injure a large number of your colleagues (and yourself!). The following general procedure should be followed – WHEN IN DOUBT CONSULT MELANIE OR THE GROUP SAFETY OFFICERS before doing anything like this!

1.5.3. **Locate the appropriate fire extinguisher in the lab before starting this procedure and be sure that you know how to use it. Do not be complacent.** Fires can result even if you have done the same procedure 99 times before. **PLEASE NOTE THAT A SPECIAL FIRE EXTINGUISHER IS REQUIRED FOR FIRES INVOLVING PYROPHORIC MATERIALS!! Know the proper fire extinguisher – this could literally be a matter of life and death!**

1.5.4. Clear your hood **and the area around it** of all flammable solvents (wash bottles, flasks containing solvent, solvent bottles, etc). These can catch on fire very easily and turn a small containable fire into an extremely dangerous fire.

1.5.5. Clear your hood and **the area around it** of any paper materials – this includes Kimwipes, paper towels, etc. Again, these can catch fire easily and turn a small fire into an uncontainable one.

1.5.6. Place the flask containing the material to be quenched into a secondary container. This is important because if your flask breaks – which can happen from vigorous stirring – the pyrophoric material will be contained.

1.5.7. Suspend the pyrophoric material in hexanes or some other inert solvent if there is not solvent in there already.

1.5.8. Fit the flask with a **large** reflux condenser (and put the nitrogen inlet on the top of this). This serves two purposes – (i) it provides additional headspace for when hydrogen gas is generated in the quenching process and (ii) limits exotherms in the quenching process by allowing for the solvent to reflux (thereby cooling the mixture).

1.5.9. Fit the condenser on the flask containing the material to be quenched with a nitrogen inlet and a vent. A nitrogen atmosphere is important for safely quenching these materials because fires are caused by the highly exothermic reaction of hydrogen with oxygen in the presence of heat and a flammable solvent. Without oxygen, a fire is unlikely – although dangerous exotherms can occur which can blow up your flask and/or expell the pyrophoric materials uncontrollably, so be sure to have adequate ventilation and ADD THE QUENCHING AGENT EXTREMELY SLOWLY!!!

1.5.10. Add methanol to this mixture **SLOWLY** over the course of hours or even days. When in doubt about the proper rate of addition, go slower.

1.5.11. Keep in mind that metals (Na, K, Li) get covered in an oxide coating during the quenching process. As a result, there may still be some metal present even after several hours/days stirring in the presence of MeOH. After several days, it is usually safe to add water slowly to quench the final material. But again, use caution and do not do this until there are no noticeable large chunks of metal present.

2. Vacuum Line Procedure—Using the Vacuum Line

You will receive thorough training on vacuum line technique by Prof. Sanford and/or a trained group member before using your line. Remember that many of the techniques involved can be confusing and the consequences of making a mistake can be very dangerous and costly. If you are ever in doubt about how to do something, please be sure to ask Prof. Sanford before proceeding.

2.1. The following references contain useful information on almost all aspects of Schlenk and high vacuum technique (i) **Experimental Organometallic Chemistry**, Andrea L. Wayda and Marcetta Y. Darensbourg, Eds., American Chemical Society: Washington DC, 1987. (ii) **The Manipulation of Air Sensitive Compounds**, D. F. Shriver, Robert E. Krieger Publishing House: Malabar, FL, 1982.

2.2. At liquid nitrogen (LN_2) temperature (–195^{o}C) argon is a solid and nitrogen is, obviously, a liquid. Therefore, it is extremely dangerous to place LN_2 cooled flasks/traps under Ar or N_2 as significant quantities of these gases can condense. The huge pressure increase as the condensed material warms and moves to gas phase can produce extremely violent explosions. **Never** backfill a LN_2-cooled flask with N_2/Ar and/or leave it under a flow of N_2/Ar.

2.3. Oxygen condenses as a bluish liquid at LN_2 temperature (–195 ºC). Liquid oxygen (LO_2) can condense in traps if the line is opened to air for any period of time. This can spontaneously explode when co-condensed with organics. **ALWAYS** evacuate traps before placing them in LN_2 (to remove air) and **ALWAYS** remove LN_2 before venting traps to air. You must carefully monitor your vacuum pressure gauge to ensure that there are not serious air leaks that would allow condensation of LO_2 in the traps.

2.4. Exercise caution when evacuating ***any*** flask on the vacuum line. Large round bottoms and solvent bulbs (>500 mL) are especially significant implosion hazards and should be evacuated with the hood sash down. Regularly check glassware for cracks and remove and clearly label defective glassware. Roy can often fix broken glassware; so don't just throw it away.

2.5. Using solvent pots and flasks on vacuum line: Attach flask or solvent pot to the line via rubber tubing. Be sure to use grease where appropriate. Evacuate the head space (to below 10 mbar on gauge) and refill with N_2. Repeat this cycle three times. At this point all of the air should be out of your system and the flask/solvent pot can be opened to N_2 flow. **Note:** If the system won't pump down below 10 mbar, there is likely a leak, and all joints should be checked and re-greased if necessary. Do not simply proceed – the solvent pots are shared, and contamination will cause problems for everyone!

2.6. Remember that all reactions and flasks that are open to N_2 can and do "see" and cross-contaminate each other via vapor diffusion. For example, if a flask of benzene and a flask of dichloromethane are open on the same Schlenk line, there will be detectable amounts of dichloromethane in the benzene and vice versa. As such, only "compatible" reactions should be open to N_2 simultaneously, and care should be taken to avoid this situation if possible. When in doubt, please talk with Prof. Sanford or Dr. Higgs before proceeding.

2.7. **A critical point:** When using the group solvent pots, ALWAYS close off other reactions from the N_2 and thoroughly flush your Schlenk line with N_2 before exposing the pot to the N_2 atmosphere. If necessary, use the solvent pot on someone else's line rather than risking contamination. Remember – these pots are shared, so we have to keep them clean for everyone!

2.8. The check valves are in place so that you avoid sucking oil and air into your line when you backfill evacuated flasks with N_2. However, they require a significant amount of N_2 pressure to reopen (after they are exposed to vacuum). Therefore, you generally need to turn up the flow through your bubbler when carrying out evacuate/refill cycles.

2.9. Traps

2.9.1. The small trap (closest to the Schlenk line) should be cooled with LN_2 ***whenever*** you are using the vacuum part of the manifold.

2.9.2. The large trap (closest to the pump) should be cooled with LN_2 any time you are removing more than 1 mL of solvent under vacuum.

2.9.3. If you are leaving something on the vacuum line overnight, be sure to fill the traps right before you leave and right when you arrive in the morning. Generally, the LN_2 will only last about 12 hours.

2.9.4. If not being used, the traps should be taken down at the end of the day, and the remaining LN_2 should be returned to the group 10 L dewar.

2.9.5. Before putting traps back up, be sure that they are completely free of solvent (if necessary place them in the oven for 15-30 minutes before proceeding).

2.10. Pumps and Pump Oil

2.10.1. Pump oil should be changed three times a year – in December, April, and August. This will typically coincide with group clean up days (*see group clean up – section 7*). It is your responsibility to keep your pump clean by avoiding contamination with solvents and to change your pump oil on a regular basis. Remember, a clean pump will work smoother, longer, and most importantly it will pump down faster.

2.10.2. For problems with your pump (poor pump performance, leaking, strange noises, etc), immediately shut it down and talk to Prof. Sanford or Dr. Higgs in order to diagnose the problem.

2.10.3. Familiarize yourself with your pump by reading the operating manual. This will be extremely helpful when it comes time to change your pump oil.

3. Cleaning Glassware

***Note**: Cleaning glassware is one of the most important tasks that you will do in lab – contaminated glassware and contaminated solvents are the two most frequent causes of reactions going badly!*

3.1. General Group Glassware

3.1.1.1. Rinse out the flask into organic waste to remove organic material by washing with a H_2O-miscible organic solvent like acetone, ethyl acetate, methanol, or THF, depending on solubility.

3.1.1.2. Thoroughly clean grease off of all joints with hexanes and a Kimwipe.

3.1.1.3. Scrub both the interior and exterior of the flask vigorously with a washing brush and soap and warm water to remove salts and remaining residues.

3.1.1.4. Glass and Teflon stopcocks should be removed from joints before cleaning, NO EXCEPTIONS. They are easily damaged by small particles such as salts and the stopcock bore tends to hold up liquids.

3.1.1.5. Rinse flask with warm water (at least 2-3 times) and with distilled water (at least 2-3 times) to remove all soap residues.

3.1.1.6. Finally, rinse with a small amount of acetone and place on the drying racks.

3.1.1.7. If glassware remains visibly dirty after this procedure **DO NOT** leave it one the drying rack for someone else to take and use!! **ASK** Prof. Sanford or Dr. Higgs about the best way to get it clean – this will usually entail either placing it in the base bath and/or washing with strong acid (e.g. conc. H_2SO_4, HNO_3) to remove residual metal salts.

3.2. Frits

3.2.1. Rinse your frit with solvents that will dissolve the solids in question. Typically this would involve methanol followed by acetone then ethyl acetate then dichloromethane. Then, turn the frit upside-down and rinse with these solvents a second time. You can attach the hose from the nitrogen line to the bottom of the frit to force these solvents through the frit faster, if necessary.

3.2.2. Note that aqueous washes (i.e., water, acid, etc.) are sometimes necessary to remove toxic reagents like tin and other reagents that are soluble in these media. However, these washings need to be separated from the organic washings, and disposed of separately (*see waste – section 1*). Acidic washes should be followed with several water washes before the introduction of organic solvents. Also, washes with water should be followed by copious rinsing with methanol or acetone before the introduction of immiscible organics like dichloromethane or hexanes.

3.2.3. If residue remains, especially metal-based residue, it can often be removed by placing a mixture of 50% conc. HCl and 50% MeOH in the frit and allowing it to drip through slowly, followed by rinses with HCl, H_2O and MeOH.

3.2.4. If *any* particulate matter remains on the frit or it is not completely white, you should place it in one of the bucket in for cleaning with piranha solution (conc. H_2SO_4/H_2O_2) or aqua regia (HCl/H_2SO_4). However, **YOU MUST COMPLETELY REMOVE ORGANIC SOLVENTS** from the frit before subjecting it to piranha solution or aqua regia (highly oxidizing!). Rinse the frits with methanol followed by copious amounts of water before placing them in the bucket.

3.2.5. Strong bases can degrade the quality of the sintered glass of the frits over time by enlarging the pores. For this reason, frits should not be cleaned with concentrated base washes or by soaking them in a base bath.

3.3. NMR Tubes

3.3.1. Rinse the contents of your NMR tubes into organic (or aqueous) waste, depending of the contents of the tube.

3.3.2. Rinse tubes at least one to two more times with a wash bottle into your waste before using the NMR tube cleaner. These steps are important to avoid cross contamination of the NMR tube cleaner with everyone's samples.

3.3.3. Note that you should never stick the tip of a wash bottle into an NMR tube to wash it out. This will inevitably lead to breaking the end off the tube. Instead, always hold the bottle several cm away from the end of the tube to spray the solvent in.

3.3.4. If solids or precipitated metals remain in the tube at this point, clean it out with some solvent (typically acetone) and a pipe cleaner.

3.3.5. Use the NMR tube washer to finish cleaning the tube. Typical solvent rinses might involve methanol followed by acetone, then ethyl acetate then dichloromethane.

3.3.6. Note that aqueous washings (i.e., bleach, water, acid, etc.) are sometimes necessary to remove toxic reagents like Sn and or other water-soluble reagents. However, these washings need to be separated from the organic washings, and disposed of appropriately (*see waste – section 1*). Also, washes with H_2O or aqueous solutions should be followed by copious rinsing with methanol before the introduction of immiscible organics like dichloromethane or hexanes.

3.3.7. Place NMR tubes flat in the oven to dry. Do *not* leave them in the oven for more than ~6-8 hrs (after which they should be placed in a dessicator for storage). Leaving the NMR tubes in the oven for longer than this can lead to warping, which may cause problems with spinning, shimming, and/or result in breakage in the NMR instruments.

3.3.8. For an excellent reference regarding an NMR tube cleaning system see, Org. Process Res. Dev., 2016, 20 (2), pp 319–319.

3.4. Syringes/Needles

3.4.1. **ALL** syringes need to be cleaned directly after use! This prevents them seizing up or clogging (often irreversibly) with dried out residues. Additionally, these expensive pieces of glassware are in limited supply and are shared between many co-workers.

3.4.2. Clean the gas-tight syringes by rinsing them 2-3 times with 3-4 different solvents. Typically this would include methanol, acetone, ethyl acetate, and dichloromethane.

3.4.3. Gas tight syringes should be placed in the oven after cleaning *without their plungers* for 3-4 hrs. Longer times in the oven can lead to cracking and/or damage to the syringe. They should then be placed in a dessicator. Plungers should be wiped off and placed directly into a dessicator after cleaning. This prevents irreversible expansion or contraction of the plunger from repeated heating-cooling cycles.

3.4.4. Non-disposable needles should be rinsed thoroughly using the aspirator vacuum needle cleaner with appropriate solvents (typically methanol followed by acetone then ethyl acetate then dichloromethane).

3.4.5. Once again, note that aqueous washing of both gas tight syringes and needles (i.e., bleach, water, acid, etc.) are sometimes necessary to remove toxic reagents like tin or other water-soluble reagents. However, these washings need to be separated from the organic washings, and disposed of appropriately (*see waste – section 1*). Additionally, washes with water or aqueous solutions should be followed by rinsing with copious methanol before the introduction of immiscible organics like dichloromethane or hexanes.

4. Glove Box

4.1. General instructions – Above all if you have a question, please ask Dr. Higgs or a student in charge of the dry box for help with anything if you are unsure what to do.

4.1.1. Prof. Sanford, Dr. Higgs, or the student in charge of the glove box must check you out before using this piece of equipment.

4.1.2. *Always* sign in the logbook when using the glove box. Please write your initials, which chamber you used (S/L), any solvents or reactive chemicals used, time in and out, purge start and end time. Purge end times are important for glove boxes that share a nitrogen source (i.e. HPLC and GC glove boxes) and for when end purge times are forgotten.

4.1.3. *Always* turn off the circulator before and purge the glove box after using more than 1 mL of solvent or other volatile liquids (in the box. More details about purging are in section 4.4 below.

4.1.4. Flasks being brought into the glove box are subjected to high vacuum and need to be appropriately sealed to prevent them from bursting open in the antechamber. This can be especially dangerous if you are bringing in a reagent that is pyrrophoric or will cause damage to the pump. When bringing a sealed flask into the dry box, ***ensure that it has been completely evacuated on your line.*** All of the joints should be well greased, and the top should be covered with a greased stopper (*not* a septum). Always keep an eye on the pressure in the antechamber when pumping in reactive chemicals. Do not leave the antechamber unattended.

4.1.5. Paper products and most tape (paper towels, Kim wipes, electrical tape, etc.) should not be brought into the box unless properly treated. They must be placed in the dessicator under vacuum for four days before being pumped into the box.

4.1.6. Avoid bringing cardboard materials into the dry box

4.1.7. Cork rings are also filled with air and water and should *never* be brought into the box.

4.1.8. The student in charge of the glove box stocks vials, vial caps, pipettes and Kim wipes. It is your responsibility to refill all other supplies or reagents including solvents.

4.1.9. *Clean up after yourself when using the box!* This means using the dustpan if you spill *and* removing all waste from the box before you leave.

4.1.10. When you are done with an auxiliary vacuum pump it is always your responsibility to take the solvent trap down or find someone that intends to use the pump later.

4.2. Using the small antechamber

4.2.1. Turn the manual valve below the chamber towards “refill”, and refill to atmospheric pressure (0 mbar on the vacuum gauge) with N_2. Make sure that chamber is completely refilled with N_2 before opening doors – if it is still under vacuum when you try to open it *you will break the door*!

4.2.2. ***Set valve to “closed” before opening outer door***. If you don’t close the valve before opening the outer door, then the interior of the box will be directly exposed to the outside atmosphere!

4.2.3. Open outer door, place items in the chamber, and close the exterior door. Be careful not to over-tighten the door when you close it.

4.2.4. Turn valve to “evacuate”, and evacuate chamber (slowly and carefully, especially if there are any powders involved) to –1 mbar (usually takes ~ 30 s to 1 min). Leave it under vacuum for three minutes. Then refill with N_2 to atmospheric pressure (0 mbar).

4.2.5. Repeat the evacuate-refill cycle 3 times.

4.2.6. On last cycle, refill completely to atmospheric pressure (if the chamber is under vacuum, the door will break if you try to open it). Open inner door and take your things into the box.

4.2.7. Note that this entire process takes a minimum of ten minutes. This means that you must plan ahead when setting up your experiments, especially if time constraints are involved. *Glovebox cycling cannot be rushed!*

4.2.8. When you are done working in the box, place your items in the chamber and close the inner door. Again, make sure that the refill valve is **closed** before opening the outer door.

4.2.9. Close the outer door and place the chamber under dynamic vacuum when finished.

4.3. Using the large antechamber:

4.3.1. Use keypad to refill to atmospheric pressure. Make sure that chamber is completely refilled with nitrogen before opening – if it is still under vacuum when you try to open it *you will break the door*!

4.3.2. ***Turn off refill function.*** (Once again, if you fail to turn off the refill function before opening the chamber to air, then the interior of the box will be directly exposed to the outside atmosphere!)

4.3.3. Open outer door, place items in the chamber and close door.

4.3.4. Evacuate the chamber using keypad and leave under vacuum for 15 minutes. Refill with N_2 to –0.5 mbar on pressure gauge (about halfway to atmospheric pressure).

4.3.5. Repeat evacuate/refill cycle 3 times.

4.3.6. On last refill, refill completely to atmospheric pressure (if the chamber is under vacuum, the door will break if you try to open it). Open inner door and take your things in.

4.3.7. Note that this entire process takes a minimum of forty-five minutes. This means that you must plan ahead when setting up your experiments, especially if time constraints are involved. *Glovebox cycling cannot be rushed!*

4.3.8. When you are done working in the box, place your items in the chamber, close the inner door, then open the outer door and take your things out.

4.3.9. Close the outer door and evacuate the chamber to –1 mbar on gauge. Turn off vacuum with keypad when chamber is completely evacuated (leaving it under static vacuum).

4.4. <u>Dealing with liquids in the dry box:</u>

4.4.1. ***You should always turn off the circulator before using a liquid in the box.*** This prevents solvents from getting into the circulator and destroying the catalyst that cleans the atmosphere of the box. Failure to turn off the circulator and to purge after using liquids can ruin the atmosphere of the box and increase the frequency with which the catalyst must be replaced – an extremely costly, labor-intensive, and generally unpleasant task that should be avoided as much as possible.

4.4.2. Remember that the atmosphere of the box is a closed system. This means that any solvent or liquid that you open enters the atmosphere and will diffuse into and contaminate any solvent that you subsequently open until you purge the atmosphere and clear everything out. *As such, solvents are easily contaminated if you don't exercise caution.* You should always open and use deuterated solvents ***before*** using non-deuterated solvents, so that your NMR samples don't get contaminated. Also, always open solvents in order of non-polarity/reactivity (*e.g.,* pentane before toluene before ether before THF before CH_2Cl_2 before acetone, CH_3CN, DMSO, DMF, phosphines) so that the more reactive solvents do not contaminate the less reactive ones. When in doubt about any of this, please speak with the Prof. Sanford or Dr. Higgs before proceeding.

4.4.3. Do not open the freezer after you have used solvents in the box. The solvents will condense in the freezer, leading to contamination of the seals and samples.

4.4.4. When you are done using solvents, remove all pipettes that have touched the solvent along with your flasks and NMR tubes etc from the box.

4.4.5. Individual procedures for purging of the dry box atmosphere vary by dry box manufacturer and model. Please ask for help if you are unsure how to properly purge the dry box in which you are working.

4.4.5.1. To purge the dry box in room 2806 (HPLC box and GC box) first turn the minimum pressure of the dry box up to 11 mmbar and the maximum pressure up to 12 mmbar. Next turn open the purge valve on the top right side of the box. The pressure of the box should drop to about 6-9mmbar once the valve is fully open. After the allotted time shut the valve then turn the pressure down to standard operating parameters (min 4 mmbar max 6 mmbar).

4.4.5.2. To purge the IT boxes in room 2822 (Synthesis box and CO_2 box) first hit the button labeled purge control. Next, set the timer for how long you would like the purge to go and hit start. The purge will automatically shut off after the selected time has passed. Once it is off turn the blower back on by pressing start on the main screen.

4.4.5.3. To purge the satellite box (single MBraun in 2822) simply hit the purge button on the main display interface. To stop the purge, hit the circulation button on the display.

4.5. Specific Dry Box Instructions:

4.5.1. Protic liquids can only be used in the satellite box. Protic liquids are strictly forbidden in all other dry boxes. Always consult Dr. Higgs or a student in charge of a dry box when considering using any protic solvent or gas in a dry box.

4.5.2. Standard operating procedure for the storage of liquids will vary by dry box. Please ask a user of the dry box what the standard procedure is for storing liquids. At minimum, liquids must be stored in an airtight container (Sure-Seal or Schlenk bulb) or a vial with a green cap.

4.5.3. Dimethylamine, a protic gas and potent catalyst poison, is frequently used in the CO_2 box. Despite rigorous purging after use, dimethylamine will often persist. Reactions sensitive to dimethylamine should be performed elsewhere.

4.5.4. Similarly, the GC box is used for electrochemical experiments, which often involve large amounts of acetonitrile. Many of these experiments will run for days and will slowly leach acetonitrile in the atmosphere. Reactions sensitive to acetonitrile should not be performed in this dry box.

5. Dri-Solv System

5.1. Dispensing solvent into group solvent bulbs:

5.1.1. Attach the solvent system to the vacuum immediately adjacent to the satellite box. Ensure that the solvent trap is appropriately connected and chilled with liquid nitrogen.

5.1.2. Attach flask to your vacuum line (***use only Teflon – Krytox – grease***). Evacuate bulb completely (<10 mbar) and refill with N_2. Repeat 3 times. On final cycle leave the flask under vacuum, and close Teflon stopcock.

5.1.3. Attach bulb to solvent system. Evacuate and refill the headspace (between Teflon stopcock and 24/40 adapter) 3 times (by turning the valve to “evacuate” followed by “refill”). You should evacuate for ~ 30 s per cycle. On final cycle leave head space under vacuum and turn valve to “closed” position.

5.1.4. To dispense solvent, open solvent valve (upper valve) to “open” position

5.1.5. Use the metering valve (the one that turns) to dispense solvent carefully into flask.

5.1.6. When complete, close metering valve and solvent valve, and then close Teflon stopcock on your flask.

5.1.7. Use “refill” valve to refill line with N_2 and remove your closed flask.

5.1.8. Flush line with N_2 for ~ 1 minute to remove most residual solvent.

5.1.9. Cap the line with a yellow plug.

5.1.10. Fill the trap (on the left of the system) with LN_2, and evacuate using “evacuate” valve.

5.1.11. After 5 min of evacuation turn “evacuate” valve to “closed”.

5.1.12. If any solvent has condensed in the trap, close off the pump and vent the system (using the three-way valve hanging next to the pump). Allow trap to warm and then empty contents. Then place system under vacuum again.

5.2. Dispensing solvent into round bottom flasks/reaction vessels:

5.2.1. If your reaction requires dry solvent, but is not extremely sensitive, you can dispense directly into the round bottom flask. In this case, simply place the flask below the spigot, and turn on the solvent flow.

5.2.2. When solvent dispensing is complete, purge out the line with N_2 (using “refill” valve) for ~ 1 min. Then carry out steps 5.1.7 to 5.1.11 above.

6. GC/GCMS

6.1. The person in charge of the respective instrument must train everyone before they can use the instrument. See the listing of group jobs to find out whom you should contact for training.

6.2. General guidelines for both GC and GC-MS:

6.2.1. Proper work-up (filtration, extraction, etc) must be done to ensure that your samples do not include any of the following:

6.2.1.1. Strong acids and bases must be quenched

6.2.1.2. No metal salts or any other precipitate can be present

6.2.1.3. No strong oxidants or reductants

6.2.2. Label all vials with your initials

6.2.3. Please remove your samples from the GC and GC-MS after they are complete

6.2.4. If you notice any errors please let someone in charge known ASAP

6.2.5. Be sure to refill the solvents (acetone, DCM, and methanol) prior to submitting your sample

6.3. Specific guidelines for GC-MS:

6.3.1. Samples must be very dilute. If you sample is too concentrated it will saturate the mass spec

6.3.2. Record your information in the notebook (date, initials, how many samples you have, where they are located, and the time).

6.3.3. Edward's pumps use ***ONLY*** Edward's pump oil.

7. Biotage

7.1. The person in charge of the respective instrument must train everyone before they can use the instrument. See the listing of group jobs to find out whom you should contact for training.

7.2. General guidelines for using the Biotage systems:

7.2.1. Be sure the solvents have more than 1L present (ideally, they should be at least half-full). Check the number under the solvent tab and make sure it is an accurate reflection on how much solvent there is. If you are changing the numbers, estimate on the high side. If they are low when you have finished your column, refill them for the person after you (it might be you again!).

7.2.2. Be sure there is acquit space in the waste container.

7.2.3. If you want you use a solvent other than hexanes, ethyl acetate, dichloromethane, and methanol, talk to the person in charge. Once approved be sure to flush the lines after use with the usual solvent for at least 20-50 mL.

7.2.4. Free up the racks as quickly as possible. We only have 10-16 racks that can be used on the Biotage.

7.2.5. After your column is finished, remove the column, remove your test tubes, and purge the solvent lines if necessary.

7.2.6. ALWAYS type your initials in the sample name section

7.2.7. Reuse columns for up to two weeks if possible. Keep the columns capped to avoid drying out.

8. Parr System and Reactors

8.1. No one should use the Parr system or high-pressure reactors/bombs without training. You must be retrained if you leave the lab for a rotation and then join the lab (if your rotation/joining are not consecutive semesters).

8.2. All reactor parts only need to be hand tightened. Do not over tighten the screws or the needle valve (black inlet and outlet valves) on the reactors. Hand tightening is the only way to ensure the needle valves reseal in the future; wrench tightening the valves will result in slow leaking and the eventual need to replace the part.

8.3. All cylinders must be capped or have a regulator on them at all times.

8.4. CO should only be used in a cylinder coffin or in a hood with a CO detector.

8.5. If the CO detector goes off (loud beeping and flashing light) and you are using CO, evacuate everyone from that lab and the adjacent labs on both sides. If possible and safe to do so please, also shut the

doors between the labs to further contain the material. If it is during the day contact Chris Peters and/or Tracy Stevenson. If it is after hours contact DPS either by dialing 911 or 3-1131 and letting them know so they can have OSEH come out and check the area to make sure there isn't an active leak. If you do call DPS after hours please also contact Chris and Tracy and inform them what happened.

8.6. If the CO detector goes off and you are using a gas other than CO, close the tank, open the hood, and go into the hallway to turn off the alarm (key is on top of the blue box). If the alarm does not start beeping again, you may reenter after five minutes. Be sure to check the detector is back to reading 0 ppm. If not, exit the area again. Repeat until the detector reads 0 ppm.

9. HPLC

9.1. The person in charge of the respective instrument must train everyone before they can use the instrument. See the listing of group jobs to find out whom you should contact for training.

10. **Triannual Group Cleanup**

10.1. Group clean up takes place three times a year. Everyone will be responsible for cleaning their own personal workspace (hood, bench, shelves, cabinets, pump, desk, etc.) as well as being assigned to a job cleaning and organizing shared spaces (gloves boxes, instruments, break room, etc.). Prof. Sanford and the student in charge of group cleanup will make these assignments.

10.2. A checklist of duties and expectations for all of these jobs will be distributed before the day of group cleanup. Please consult the list and complete it. Your personal standard of what constitutes and cleaned workspace may not be the same as what Prof. Sanford expects.

10.3. Group cleanup takes the majority of the day, but not all group jobs are created equal. If you finish your responsibilities before other people, you're expected to go help your colleagues with more labor-intensive jobs. No one should start doing chemistry or leave the lab until everyone's group cleanup responsibilities have been completed.

10.4. Lunch will be provided!

11. Lab Notebooks

11.1. Maintaining a clear, well organized, and up-to-date lab notebook is critical for (a) keeping track of your experiments for your thesis, (b) any publications/ patents that you will write and (c) enabling future generations of students to reproduce your work.

11.2. General instructions for keeping a lab notebook are as follows.

11.2.1. Skip 3-4 pages in the beginning for the Table of Contents and update the TOC regularly (monthly, at least).

11.2.2. Use only non-erasable ink in your notebook.

11.2.3. Write the reaction/experiment clearly at the top of each page. If you are following a published procedure, indicate the reference from which the procedure was obtained.

11.2.4. Make a table including each reagent, it's molecular weight, the measured quantity – g (or mL), mol, and eq – used in the reaction, and the commercial source/purity of the reagent.

11.2.5. Write a detailed experimental, including the rate/order/time/temperature of addition of each reagent and solvent, and, where appropriate, any color changes that take place during the reaction. Also, detail all work up procedures and TLC data (where appropriate) for the reaction.

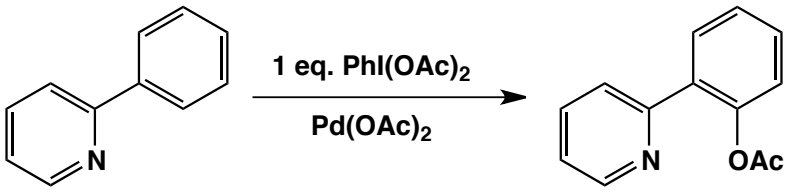
11.2.6. Be sure to weigh the product and determine the % yield for all reactions!!

11.2.7. NMR spectra should be saved and labeled according to the notebook number, page, and sample they refer to. For example, 1mss23.007 would refer to Melanie S. Sanford notebook #1, p. 23, sample #7.

11.3. Everyone is responsible for backing up their data on Zip disks or CD's.

11.4. Sample notebook entry.

Date: 12/07/2016



Chemical	Source	Mol. Weight	Amount	mmol (eq)
$Pd(OAc)_2$	Pressure	224 g/mol	0.014 g	0.064 (0.05)
2-phenylpyridine	Aldrich	155.20 g/mol	0.200 g	1.29 (1.0)
$PhI(OAc)_2$	Acros	322.10 g/mol	0.415 g	1.29 (1.0)
AcOH (Solvent)	Fisher		8.0 mL	

Procedure

Pd(OAc)2, PhI(OAc)2 and 8-methylquinoline were placed in a 20 mL vial in that order. Acetic acid (8 mL) was added. Mixture is a clear suspension with yellow solids at bottom of vial.

Placed in oil bath at 100oC and heated for 1 hr. After 5 min, color changes to black.

Removed vial from bath and allowed to stand at 5 min at room temperature. Opened and removed ~10 mL for GC analysis.

GC (GC1, mss short method) shows 8% starting material (retention time 4 min) and 80% of a new peak at 6 min. Other unidentified peaks were observed at 7 and 9 min (5% each). **GC labeled 1mss27.001**. (Notebook 1, mss, page 27, 1st spectrum obtained)

Rotovapped vial to dryness. Some of the material bumped into the rotovap trap. Recovered material by rinsing the trap with acetone (3 x 5 mL). Some remained stuck in the rotovap trap.

Dissolved reaction mixture in methylene chloride. Ran TLC's in 40%/60% and 50%/50% and 60%/40% hexanes/ethyl acetate. Optimal conditions were 50%/50% hexanes/ethyl acetate (product rf ~ 0.2).

Mistakenly dropped vial on bench and spilled approximately 1/4 of material. Yield is expected to be low as a result.

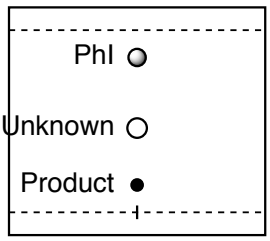
Rotovapped to dryness and redissolved in 50% hexanes/50% ethyl acetate

Loaded onto silica column (50 g silica, wet-packed in 50%/50% hexanes/ethyl acetate), and collected 100 fractions. Every other fraction was TLCed and fractions 7-9, 11-14, and 32-47 (each of the three spots werecollected and rotovapped to dryness. Obtained 114 mg of fractions 7-9, 10 mg of fractions 11-14 and 212 mg of fractions 32-47.

GC's of each set of fractions were obtained: Fractions 7-9: 1mss27.002; Fractions 11-14: 1mss27.003; and Fractions 32-47: 1mss27.004. Each appears to be pure.

^1H NMR spectra of each fraction was obtained in $CHCl_3$. Fractions 7-9: 1mss27.005; Fractions 11-14: 1mss27.006; and Fractions 32-47: 1mss27.007.

Conclusions from 1H NMR and GC analysis:
Fractions 7-9 are iodobenzene with some other solvent impurities.
Fractions 11-14 contain aromatic and aliphatic peaks. Need to do more analysis.
Fractions 32-47 are the expected product. No solvent is present.



Molecular weight of product: 213.2 g/mol
Amount Expected: 275 mg
Amount Obtained: 212 mg
% Yield: 77% yield

12. Reimbursement

12.1. Sanford Lab Reimbursement Policy

12.1.1. LSA policy dictates that reimbursements must be made within 45 calendar days of the end of the trip or within 45 calendar days of the date of purchase. Ideally, expenses should be submitted within 10 days.

12.1.2. All receipts submitted for reimbursement must include the last four digits of your credit card number or be marked as paid in cash. If your receipts do not show the last four digits of your credit card number, but were paid with a card, please submit your credit card statement showing that charge as proof of payment. You should redact any non-essential information on that statement.

12.1.3. Ask Melanie for trip approval BEFORE making any purchases. Best practice includes providing Melanie (cc Kate) with an estimated cost of expenses in writing when requesting permission to attend any conference or workshop. Please keep in mind that the more money we save per trip, the more money we have to go around to other lab members and for other trips.

12.1.4. Airfare – Please choose the lowest airfare possible within reason. We do not expect you to take a red-eye fight with three layovers just to save $50, but you should also not be purchasing a direct flight that costs significantly more than a flight with stops. Please check multiple airlines for the best rates and use your best judgment when purchasing flights. Check with me / Melanie for clarification and approval.

12.1.5. Ground transportation – Lab policy allows ground transportation only to and from the destination site (from the destination airport to the conference site and back). We do not pay for your ground transportation or parking in Ann Arbor / Detroit. Taxis, trains, buses, Uber, etc are all covered under this policy.

12.1.6. Lodging – Lodging is covered. We request that lab members (students and postdocs) attending the same conference who are able to room together do so (i.e. MM / FF / partners) to keep costs low. If you know of a student or postdoc in another group who will be attending the conference that you are able to room with, please try to do so. People at the University also often share lodging with non-University friends and acquaintances. If your room will cost more than $150 per night, please ask Melanie (cc Kate) for approval.

12.1.7. Car rental – We will cover car rental with prior approval. Please request approval from Melanie (cc Kate) before arranging your car. Gas for your rental vehicle will be covered.

12.1.8. Registration - We cover registration fees and abstract submission fees. We do not cover fees associated with memberships, even if you require a membership to register for a particular meeting.

12.1.9. Mileage – We will cover mileage if approved in advance. This is a common mode of transportation for local conferences (Indiana / Ohio).

12.1.10. We do NOT cover per diem, membership fees or baggage fees. If you receive a travel grant or non-UM reimbursement, policy dictates that you use those funds to deduct from your reimbursement of the allowable expenses listed above.

12.2. Reimbursement Procedure

12.2.1. Obtain prior approval for each expenditure from Melanie (copy Kate)

12.2.2. Determine whether you will be able to use Concur (those with regular appointments / appointments funded through the University) or if you will need to submit a hard copy request. Contact Kate for details on how to submit via hard copy.

12.2.3. Concur: Log in to Concur, click Profile, Profile Settings, and on the left side of the screen add Nick Adams (nickad) as approver 1 and Kate (kkdyki) as approver 2.

12.2.4. Draft an email to me (kkdyki@umich.edu) for approval of expenses and shortcode.

12.2.5. Attach receipts. Each receipt must show the last 4 digits of your credit card number or be marked as paid in cash. Please use your credit card statement as backup if you don't have paid receipts.

12.2.6. Step 7: Once you receive the OK from me, please send to Shared Services at expensereports@umich.edu with me copied. They will usually prepare your report within 24 hours. You will receive an emailed link to your report once it has been prepared and from there will be able to submit your expense report for reimbursement. You should receive your reimbursement with approximately 1 week. Note: Policy does allow for multiple reports for one trip. For expenses paid in advance (airfare, registration, etc.) you may wish to file a reimbursement before the trip and then follow up with a second reimbursement after the trip has been completed for the rest of your expenses. Shared Services will complete up to 3 reports per month per individual.

13. General

13.1. Notify Prof. Sanford if you will be out of town for one working day or more.

13.2. Group and subgroup meetings will be held weekly. Check the group calendar for dates, times, and locations as the may change throughout the year. Notify Prof. Sanford if you cannot attend for any reason.

13.3. It is important to keep up on the current literature in organic and organometallic chemistry – particularly as it relates to your project. Additionally, you will periodically be asked to choose a paper from the current literature to present at group meeting. The following are journals that you should read each week and are appropriate sources for group meeting papers:

J. Am. Chem. Soc.
Organometallics
Org. Lett.
J. Org. Chem.
Angew. Chem., Int. Ed.
Science
Nature

Note that reading the literature is critical not only to learn more about your project/area of research but also to get you prepared for upcoming seminar speakers, proposal writing, orals, local and national ACS meetings, writing your own papers, and ultimately getting a job!

13.4. General tips for reading the chemical literature

13.4.1. You cannot expect to read everything.

13.4.2. Try to read papers that are (i) the most interesting to you and (ii) the most relevant to your and the group's research projects.

13.4.3. No one has time to read the entire text of every article. Read the abstract and introduction and then try to discern the major point of the paper from the Figures and Schemes. If you find something especially interesting or unclear consult the text for further details. *Keep in mind when writing your own papers that these are the sections that are usually the most read.*

13.4.4. Whenever possible, discuss with others what you have read! This will solidify your general knowledge as well as improve your understanding of what you have read.

13.4.5. Take particular note of papers that describe selective reactions. These are the most useful in synthetic chemistry and the most difficult to find by traditional searching techniques.

13.4.6. Keep an eye out for molecules that could be assembled using the methodology that you are developing. This will be helpful for those of you who are interested in applying methodology in total synthesis, as well as for writing proposals.

13.4.7. Other journals to keep an eye on (monthly) are:

Org. Process Res. Dev.
Tetrahedron Letters
Tetrahedron
JCS, Perkin 1
JCS, Dalton Transactions
Chem. Comm.
Chem. Reviews
Acc. Chem. Res.
Synlett