

ANSLYN GROUP SAFETY MANUAL

Every group member must read and sign that they understand the content of this manual before starting work in the Anslyn laboratories. This includes undergraduate students, graduate students, post-doctoral associates, and all visiting scholars. Once you have read this manual, please see Eric Anslyn to make a record of your understanding of the content herein.

Key phone numbers:

Eric Anslyn: 512-289-8372

EHS: 512-471-3511

To Start Out, please realize the following -

No closed toed shoes,

No long pants,

No goggles,

No lab coat

Then No Lab Work!

Table of Contents

Section I: Personal Safety and Responsibility

1. Safety Glasses
2. Lab Coats
3. Working in Lab Alone
4. Pressure
5. Glove use in Laboratories
6. Fume Hood Use
7. Monthly Chemical Hazard Assessment
8. Waste Disposal

Section II: Chemical Hazards

1. Base Bath
 - a. Minimum PPE
 - b. Procedure
 - i. Pre-Washing Soiled Glassware
 - ii. Preparation of Base Bath
 - iii. Using the Base Bath
 - iv. Maintenance
2. Pyrophorics
 - a. What are Pyrophorics
 - b. How to Handle Pyrophorics
 - c. Storing Pyrophoric Reagents
 - d. Pyrophoric Solids
3. Sodium Metal
4. Lithium Aluminum Hydride

5. Tert-Butyl Lithium
6. NaH (Sodium Hydride)
7. Potential Peroxide-Forming Solvents
 - a. Use and Storage of Peroxide-Forming Solvents
 - b. General Handling Considerations for Peroxidizable Solvents
 - c. Peroxide Detection
8. Perchlorates
9. Azides
 - a. Potential Health Effects
10. Liquid Oxygen
11. Picric Acid
12. Sodium Benzophenone Ketyl Stills
13. Na(CN)BH₃ Work-Up
14. Handling of Inorganic Cyanide Salts
15. Teratogens
16. Ethidium Bromide and Other Cancerous Agents
17. Chromates
18. Haloethers
19. Mercury (Hg) Spill Response
20. CO (Carbon Monoxide)
21. OsO₄
 - a. Potential Health Effects
 - b. Handling and Storage
 - c. Personal Protective Equipment (PPE)
 - d. Accidental Release Measures
22. Spills of Nitrogenous Bases
23. HCN and HN₃

Section III: Appendix

1. Using Pyrophorics in General
 - a. Key Elements for Handling Pyrophoric Solids
 - b. Pyrophoric Liquids
 - i. Transferring Liquid Pyrophoric Reagents Outside the Inert Atmosphere of a Glovebox
 - ii. When a Syringe is used, the Best Practice for Transferring a pyrophoric reagent is shown in Method A
 - iii. When a Double-Tipped Needle is used, the Best Practice for transferring pyrophoric reagents are shown in Methods B or C
 - c. Titration of alkyllithiums
2. Sodium Benzophenone Ketyl Stills
 - a. Introduction
 - b. Before Getting Started
 - c. Setting Solvent Stills
3. tert-Butyl Lithium - Handling Procedure
 - a. How to Use t-butyl Lithium
 - i. Preparation
 - ii. Reagent Handling Set-Up

BEFORE you enter the lab, you MUST be wearing the following.

Lab coat

Safety glasses

Long pants*

Closed Toed Shoes

*if you have religious requirements for clothing, please talk to Eric Anslyn prior to entering the lab.

BEFORE you start work in the lab, please find for YOURSELF, each of these items.

Location of Laboratory Safety Equipment

Chemical safety showers: 5.120 and 5.110 hallways

Fire extinguishers: 5.120 and 5.110 hallways. Please know that once used, these MUST be replaced. Contact EHS for help with this.

Eyewashes: 5.120 and 5.110 hallways, 5.120 and 5.110 labs on each aisle, 5.120F (HPLC room), 5.110A (peptide synth room), 5.110G (bio room)

Spill kits: 5.120 and 5.110 on supply shelf in yellow bag

First aid kits: 5.120 and 5.110 on supply shelf in white metal box

Telephones: 5.120 and 5.110 labs, grad student offices

Sand: 5.120 lab against wall

Glass waste: 5.120 and 5.110 labs on each aisle, 5.120F (HPLC room), 5.110A (peptide synth room), 5.110G (bio room)

Sharps containers: 5.120 and 5.110 labs against wall, 5.110A (peptide synth room), 5.110G (bio room)

Flame resistant lab coat: stored on shelf in 5.120E (UV-VIS room), also coat hooks in 5.120 and 5.110 labs (please ask before using these as they belong to certain group members)

Respirator: stored in labeled drawer in 5.120E (UV-VIS room)

Liquid waste containers: 5.120 and 5.110 labs against the wall, 5.120F (HPLC room), 5.110A (peptide synth room)

Solid waste containers: 5.120 and 5.110 labs against the wall

Ethidium bromide solid and liquid waste containers: 5.110G (bio room)

Biological waste: 5.110G (bio room)

Emergency contact numbers: plaques inside/outside each doorway or area of the labs

Section 1: Personal Safety

1) Safety Glasses

Safety glasses must be worn in labs at all times to ensure protection of the eyes and prevent eye trauma, vision loss, and blindness. Safety glasses are required once an individual crosses the threshold into the laboratory environment.

Extra safety glasses are located in the hallways of 5.110 and 5.120 on the bottom shelf of the small table. Additional safety glasses may be purchased in the Fisher Store Rooms.

Safety glasses guidelines from the ANSI (American National Standards Institute) website (www.ansi.org):

- Protective eyewear should include side protection unless there is no possible chance of injury from side impact, splashes, or sparks.
- Always put on protective eyewear before entering an area where hazards may be present.
- Eye protection must fit properly and comfortably, including when worn over prescription glasses.
- Eyewear should always be checked for damage and replaced if there is any defect.
- When there is doubt, assume that eye hazards are present.

If individuals prefer to wear corrective lens eye glasses, then additional safety glasses protection must be worn in the laboratory environment. The safety glasses should fit over the corrective lens eye glasses and provide side protection from impact and splashes. (See an example below of safety



glasses which can be worn over corrective lens eye glasses, which can be ordered from the website www.crossfiresafety.com, product number 3111 or 3114 - depending on size of glasses. These can also be purchased in the Fisher Store Room downstairs.)

If you are interested in acquiring prescription safety glasses, please contact US Safety.

2) Lab Coats

Each person is responsible for maintaining their own personal lab coat. Lab coats must be fully buttoned. Each new group member will be supplied one upon joining; additional lab coats are available for purchase at several locations on campus, such as the Fisher store room. Lab coats are to be stored on the coat hooks provided at the entrance to the lab, and should never be worn while working at your desk or outside laboratory space. If your lab coat gets damaged through general wear and tear or through contact with some chemical, it is extremely important that the lab coat is replaced. Remember, your lab coat is your barrier between your skin and potentially hazardous compounds. In the event that your lab coat comes in contact with a compound that requires special disposal, it is important that you coordinate with the lab member in charge of waste and EHS when disposing of the coat. In the event that you are working with a particularly flammable compound there is a flame resistant lab coat available on NHB 5.120K as well as flame resistant lab coats of all sizes on the coat hooks. If a lab coat becomes damaged you need to coordinate with the appropriate lab members to acquire a replacement.

3) Working in Lab Alone

No hazardous reactions should ever be performed in the lab alone. If it is your first time running a reaction, another person **must** be present in lab. If you are using potentially hazardous reagents in your experiment, you must wait until another person is present.

The use of organolithiums and other hazardous chemicals alone in lab is prohibited. If you have questions, please talk to the safety officer or Eric Anslyn.

4) Pressure

Pressure can build up in a separatory funnel due to solvent evaporation, which in extreme cases can result in the separatory funnel exploding. There was an incident on UT campus where a graduate student quenched sodium hydroxide with hydrochloric acid in a large separatory funnel containing diethyl ether, and the funnel exploded, resulting in permanent damage to

the tendons in the student's hands. Thus, it is important to be mindful of the potential for pressure to build up in the separatory funnel during use.

It is important to check all glassware for defects, such as star cracks, before employing the glassware in a situation where the glassware will experience a pressure differential across the glass surface. Such situations include, but are not limited to, heating a closed system, flash chromatography, removing solvent under reduced pressure, and vacuum filtration. If the glassware has a defect, it should be taken to the glass shop or disposed of, and another piece of defect-free glassware should be used in its place.

5) Glove Use in Laboratories

Gloves must be worn at all times in the lab. Gloves must also be changed regularly as the material can deteriorate. No one type of glove may be used as protection from all chemicals. A glove may protect against a specific chemical, but it may not protect the wearer from another. Therefore, the following must be considered when choosing which gloves to be worn to protect against chemical exposures.

Factors to consider when choosing gloves:

- Chemical to be used: Consult the glove chart listed below or the ones posted on the supply shelves in the lab to ensure that the gloves will protect you.
- Dexterity needed: The thicker the glove, typically the better the chemical protection, as the glove will be more resistant to physical damage, like tears and cracks, but it will be harder to handle and feel the work.
- Extent of the protection required: Determine if a wrist length glove provides adequate protection, or if a glove that extends further up the arm will be required.
- Type of work to be done: gloves are specific to the task. Ensure the correct glove is chosen to avoid injuries. Examples: A nylon cryogenic glove will be damaged if a hot item is handled, whereas a "hot mitt" will not protect the wearer when liquid nitrogen is used, as it may be too porous.

Rules for glove use in the labs:

- Wear the correct gloves when needed.

- Wear gloves no longer than 2 hours.
- Wash hands once gloves have been removed.
- Disposable gloves must be discarded once removed. Do not save for future use.
- Dispose of gloves into the proper container (biologically contaminated gloves will need to go into a red bag); while other chemically contaminated gloves may not.
- Non-disposable/reusable gloves must be washed and dried, as needed, and then inspected for tears and holes prior to reuse.
- Remove gloves before touching personal items, such as phones, computers, pens and one's skin. Remember the "designated area rule" where "science" does not mix with personal space (one's desk or lunch space). Gloves used in research are considered "science".
- Do not wear gloves out of the lab. If gloves are needed to transport anything, wear one glove to handle the transported item. The free hand is then used to touch door knobs, elevator buttons, etc. If you are wearing gloves to "protect your sample from you" and are in the hall, no one else understands this and will be concerned about the items you have contaminated with those gloves.
- If for any reason a glove fails, and chemicals come into contact with skin, consider it an exposure and seek medical attention.

Nitrile gloves are the most preferred over latex and rubber gloves. If you are unsure about what gloves to use during what circumstances, please refer to the glove chart mentioned below. Also, if you are allergic to latex gloves but the situation demands the use of latex gloves, it is advised to wear the latex over the nitrile gloves.

Glove charts are also posted next to the supply shelves in each lab.

Glove Chart

Type	Advantages	Disadvantages	Use Against
Natural rubber	Low cost, good physical properties, dexterity	Poor vs. oils, greases, organics. Frequently imported; may be poor quality	Bases, alcohols, dilute water solutions; fair vs. aldehydes, ketones.
Natural rubber blends	Low cost, dexterity, better chemical resistance than natural rubber vs.	Physical properties frequently inferior to natural rubber	Same as natural rubber

	some chemicals		
Polyvinyl chloride (PVC)	Low cost, very good physical properties, medium cost, medium chemical resistance	Plasticizers can be stripped; frequently imported may be poor quality	Strong acids and bases, salts, other water solutions, alcohols
Neoprene	Medium cost, medium chemical resistance, medium physical properties	NA	Oxidizing acids, anilines, phenol, glycol ethers, halogenated solvents
Nitrile	Low cost, excellent physical properties, dexterity	Poor vs. benzene, methylene chloride, trichloroethylene, many ketones	Oils, greases, aliphatic chemicals, xylene, perchloroethylene, trichloroethane; fair vs. toluene
Butyl	Specialty glove, polar organics	Expensive, poor vs. hydrocarbons, chlorinated solvents	Glycol ethers, ketones, esters

6) Fume Hood Use

All work with hazardous chemicals should be performed in a fume hood. To prevent chemical exposure and save energy, the sash should be kept as low as possible when working and should be completely closed when not in use. If the sliding panels are used, these should also be kept closed when not in use. Work should be performed at least six inches from the front of the fume hood and one's head should not be in the hood at any time. Clutter and chemical storage should be minimized.

This is a useful video for setting up and using a fume hood.

http://chem-courses.ucsd.edu/CoursePages/Uglabs/143A_Weizman/EHS/Episode1720p.html

7) Monthly Chemical Hazard Assessment

Each month group members are required to fill out the monthly chemical hazard assessment form. Any chemicals that you have not used before need to be included on the form. This form is to be signed and dated and turned into Eric Anslyn at the first group meeting of every month.

8) Waste Disposal

Waste containers are located in the 5.110 and 5.120 labs. Waste is separated into non-halogenated organic, halogenated organic, acid, base, and metal waste. There are also solid waste containers and sharps containers. Please familiarize yourself with proper waste disposal protocol and ask the group member in charge of waste for help if you need it. All waste containers need to be closed when not in use and properly labeled. There also must be some kind of secondary containment for each waste container.

Section 2: Chemical Hazards

1) Base Bath

Warning:

The solution in the base bath is extremely corrosive and can cause serious burns. Therefore, neoprene gloves with long cuffs (elbow length) must be worn, as latex gloves will not provide adequate protection to the hands.

a. Minimum PPE:

- Safety glasses
- Elbow length neoprene gloves
- Lab Coat - VERY IMPORTANT!

b. Procedure:

I. Pre-washing soiled glassware.

- All soiled glassware should be prewashed with appropriate solvents to get the glassware as clean as possible, being sure to collect the solvents in a container, then put the used solvent into the appropriate waste container.
- Wash the glassware with detergent and rinse with distilled water.

II. Preparation of Base Bath

- Mix 1 L DI H₂O with 4 L isopropanol.
- Carefully add about 500 g KOH

III. Using the base bath.

- Before working with the base bath, be sure that your gloves are in good condition. Replace them if you have any doubt as to their condition.
- While wearing safety goggles and neoprene gloves, glassware that has been prewashed according to the above procedure is gently lowered into the base bath allowing the solution to completely fill the glassware.
- Allow the glassware to remain in the solution several hours or overnight.

- While wearing safety goggles and neoprene gloves, remove glassware from the base bath allowing as much of the solution to drain as is possible.
- Rinse the alcoholic solution from the glass with tap water.
- Rinse with distilled water.
- Rinse with acetone and place on the drying rack.
- After 15 min. the glassware may be placed in a drying oven.

Cautions:

- Glassware can be etched from prolonged exposure to the basic solution. Quartz glassware is too expensive to routinely expose to this risk. It should not be cleaned with a base bath
- Base bath will enlarge the pore size of glass frits and should only be used on fritted glassware as a last resort.

VI. Maintenance

- Base baths should be disposed of properly and replaced with new base/alcohol solutions as the cleaning ability decreases, normally the base bath is useable for several months.

And, Remember to Maintain a Clean Sink

- Excess dirty glassware should not be stored in your sink. Glassware used during chemistry should be cleaned soon after its use. Keeping dirty glassware in your sink provides a safety concerns because glassware can shift and break leaving potential for puncture hazards.

2) Pyrophorics

What are pyrophorics?

Pyrophoric reagents are substances that ignite instantly upon exposure to oxygen, and in most cases are also water-reactive, where heat and hydrogen (flammable gas) are produced. For example, *tert*-butyllithium (*t*-BuLi), and a variety of alkyllithium derivatives, will catch fire if exposed to air at modest humidity. Failure to follow proper handling techniques could result in serious injury or even death to the person handling the materials or to others in close proximity.

Although there are some pyrophoric gases, most pyrophoric reagents fall into the category of solid, pure liquid, or a solution. Examples of pyrophoric reagents are metal hydrides, finely divided metal powders, nonmetal hydride and alkyl compounds, white phosphorus, alloy of reactive metals, and selected organometallic compounds; including alkyllithiums.

Most of pyrophoric reagents fall into the following categories:

- Alkyl aluminum reagents
- Alkyl lithium reagents
- Alkyl zinc reagents
- Alkylphosphines
- Alkylsilanes
- Metal hydrides
- Iron pentacarbonyl
- Sodium/Potassium Alloy (NaK).

a. How to handle pyrophorics - more details in Appendix

Wear proper PPE at all times. This includes a flame resistant lab coat, clothes that are made of natural fibers (these won't melt to your skin), gloves, and safety glasses. Consult Eric Anslyn before using any pyrophoric reagent. Neutralization of excess reagents should be done carefully. When a syringe or a double-tipped needle (cannula) is used in handling pyrophoric reagents, the assembly should be rinsed with an inert (non-reacting) solvent and the rinse transferred to a flask under an inert atmosphere for subsequent neutralization.

This is a useful link that includes technique for handling pyrophoric reagents and how to use a cannula. A cannula should be used for transferring a large amount of pyrophoric solution or liquid (>10 mL).

http://chem-courses.ucsd.edu/CoursePages/Uglabs/143A_Weizman/EHS/EHS.html

b. Storing pyrophoric reagents

It is **highly** recommended that pyrophoric reagents are purchased in quantities that will be used in each experiment to avoid the storage of excessive amounts of these hazardous chemicals. If storage is needed, make sure that the head space above the reagent is purged with an inert gas before storage.

c. Pyrophoric Solids

Although pyrophoric solids are more stable to air than pyrophoric liquids, caution must be exercised during handling, storage, and disposal. In general, pyrophoric reagents are usually handled in a glovebox or by using a Schlenk line under an inert gas. Some pyrophoric solids, such as lithium and sodium, are sold as dispersions in mineral oil to reduce the rate of oxidation to oxides/hydroxides and the pyrophoric character of the reagents. Removal of the mineral oil is accomplished by cutting a piece of the alkali metal and transferring it to a flask containing a hydrocarbon solvent such as hexanes to rinse off the oil. Other mildly pyrophoric solids, such as dispersions in oil of sodium hydride (NaH) and lithium aluminum hydride (LiAlH_4), can be handled in air for short periods of time. The dry solid forms should be handled under inert atmosphere. In addition, the containers must be kept under a blanket of inert gas during storage.

For instructions in dealing with pyrophorics please see the appendix before you use them and follow those instructions.

3) Sodium Metal

Na reacts violently with water. Store in mineral oil in a sealed container kept away from water. Do not touch the metal directly. Handle with tweezers/tongs which have been washed with hexanes, and cut into smaller pieces with a razor blade which has also been rinsed with hexanes. Rinse the mineral oil off the desired amount using hexanes. Work away from any source of water. Keep away from heat sources.

In case of fire, never use water. Do NOT use CO_2 fire extinguishers, only Class D metal fire extinguishers or sand. Cover the flame with dry sand and let the fire extinguish itself, adding additional sand as needed.

It is very hazardous for skin and eye contact. Wear sufficient protective clothing/gloves/goggles at all times.

Here is a useful video for working with sodium metal.

http://chem-courses.ucsd.edu/CoursePages/Uglabs/143A_Weizman/EHS/Episode3720p.html

Caution: If sodium amalgam ($\text{Na}[\text{Hg}]$) needs to be prepared and used, use extreme caution. Dissolving sodium into liquid mercury results in a very exothermic reaction; producing the intermetallic compound NaHg_2 with enough heat to cause localized boiling of the mercury. The preparation of sodium amalgam should be performed in a hood under an inert atmosphere. The benefit of obtaining sodium amalgam is that it has the reducing potential of sodium, a larger surface area, and is more air stable.

Note: Potassium metal is more reactive than lithium and sodium. During prolonged storage, potassium can be oxidized to form a potassium superoxide (KO_2) coating; a yellow, shock-sensitive peroxide that can explode

on handling. **Do not use potassium metal without consulting Eric Anslyn first!**

4) Lithium Aluminum Hydride

This is a strong reducing agent and water reactive substance. It is incompatible with oxidizing agents, air, water, and carbonyl-containing solvents (acetone, ethyl acetate, etc). Reacts violently with water and moisture in the air, producing hydrogen gas. Causes severe burns in all cases of exposure. Store under nitrogen. Light and heat sensitive. Wear sufficient protective clothing/gloves/goggles at all times. For solutions in THF, keep nitrogen or argon balloon pressure, and draw up the appropriate amount with a glass syringe. When your reaction is complete, quench excess LAH by cooling solution to -78 C with acetone/dry ice and adding water drop wise slowly. This will produce precipitates of aluminum oxides, as well as LiOH. Saturated solutions of ammonium chloride can be used to aid in neutralization. Do NOT use acidic solutions to quench LAH.

In case of fire, use dry sand. Never use water or CO₂ fire extinguishers.

5) *tert*-Butyl Lithium

UNDER NO CIRCUMSTANCES SHOULD ANYONE EVER USE TERT-BUTYL LITHIUM FOR ANY REACTION WITHOUT CONSULTING ERIC ANSYN FIRST!

Full fire protective gear must be worn and fire prevention and extinguishing equipment needs to be present when using this compound.

See the Appendix for a detailed discussion of how to use this compound; HOWEVER, you first must have permission from Eric Anslyn.

6) NaH (Sodium Hydride)

NaH can ignite in air, especially upon contact with water to release hydrogen, which is also flammable. Hydrolysis converts NaH into sodium hydroxide (NaOH), a caustic base. In practice, most sodium hydride is dispensed as a dispersion in oil, which can be safely handled in air.

A. HANDLING AND STORAGE

I. Handling

Keep away from heat and sources of ignition. Avoid contact with skin, eyes and clothing. Wear suitable protective equipment. Avoid contact with water. Wash thoroughly after handling. Ensure adequate

ventilation. Keep container tightly closed. For proper needle technique see Appendix.

II. Storage

Storage conditions: Keep containers tightly closed in a dry, cool and well-ventilated place. Keep away from heat and sources of ignition.

Storage temperature: < 30.00 °C (< 86.00 °F)

III. Quenching of NaH

It is recommended that you cool the reaction down to 0 °C. A small piece of dry ice can be added to the solution to create a blanket of CO₂ inside of the flask. This will provide an inert atmosphere and prevent ignition. Then, quench the solution with t-butanol or methanol, followed by the addition of a weak acid like water.

B. FIRST AID MEASURES

In any case immediate medical attention is required.

Inhalation: Move to fresh air. If breathing is irregular or stopped, administer artificial respiration.

Skin contact: IMMEDIATELY get under a safety shower. Wash off with plenty of water. Do not take clothing home to be laundered. Wash contaminated clothing before re-use.

Eye contact: Rinse immediately with plenty of water for at least 15 minutes.

Ingestion: IMMEDIATELY see a physician. Do NOT induce vomiting. Rinse mouth and drink 1 or 2 glasses of water. Never give anything by mouth to an unconscious person.

7) Potential Peroxide-Forming Solvents*

All chemicals that have the potential to form peroxides must be labeled with the date once opened.

Group A: Chemicals that form explosive levels of peroxides without concentration (ex: rotary evaporation). Severe peroxide hazard after prolonged storage, especially after exposure to air.

Test for peroxide formation before using or discard after 3 months.

- Isopropyl ether

Group B: Peroxide hazards can form with concentration (ex: rotary evaporation).

Test for peroxide formation before distillation or evaporation. Test for peroxide formation or discard after 1 year.

- Acetal
- Acetaldehyde
- Benzyl Alcohol
- 2-Butanol
- Dioxanes
- Chlorofluoroethylene
- Cumene(isopropylbenzene)
- Cyclohexene
- 2-Cyclohexen-1-ol
- Cyclopentene
- Decahydronaphthalene(decalin)
- Diacetylene(butadiyne)
- Dicyclopentadiene
- Diglyme
- Diethyl ether
- Ethylene glycol ether acetates
- Furan
- 4-Heptanol
- 2-Hexanol
- Methyl Acetylene
- 3-Methyl-1-butanol
- Methyl-isobutyl ketone
- 4-Methyl-2-pentanol
- 2-Propanol
- 4-Penten-1-ol
- 1-Phenylethanol
- Tetrahydrofuran
- Tetrahydronaphthalene
- Vinyl Ethers
- Sec. Alcohols

* Materials other than those listed may form peroxides. Applies only to pure materials.

a. Use and Storage of Peroxide-Forming Solvents

The solvents most commonly used in the laboratory solvents, such as diethyl ether, tetrahydrofuran, cyclohexene, glycol ethers, decalin and 2-propanol are shown in Group B of the previous section. These compounds produce organic peroxides that are significantly less volatile than the solvent in which they are formed; as a result, evaporative concentration or distillation can produce dangerous levels of peroxides. In fact, most Group B solvents are sufficiently volatile that multiple openings of a single container can result in significant and dangerous peroxide concentration. The next section contains a list of key aspects to consider when handling peroxide-forming solvents.

b. General Handling Considerations for Peroxidizable Solvents:

- Materials should be stored away from light and heat with tightly secured caps and labeled with dates of receipt and opening.
- All peroxide-forming solvents should be checked for the presence of any peroxides prior to distillation or evaporation. Use KI starch paper to test for the presence of strong oxidizers such as peroxides.
- Peroxide-forming solvents should be purchased in limited quantities and older material in inventory should be preferentially selected for use.
- Solvents containing low levels of free radical scavengers such as BHT should be used whenever the presence of the stabilizing species does not interfere with intended application.

- Uninhibited materials should be stored with care and frequently checked for peroxide formation.

c. Peroxide Detection

- At present, 100 ppm is widely used as a general control point with respect to minimum hazardous peroxide concentration in a solvent; however, this value lacks scientific validation and is likely too liberal or conservative depending on the solvent in question and intended application. If there are visible crystals, visible precipitate or an oily viscous layer present in the material, these are extremely dangerous, immediately contact EH&S department to manage this hazardous situation and to dispose of this material.

Information above was taken from Sigma-Aldrich chemical learning center. To see the original website, go to <http://www.sigmaaldrich.com/chemistry/solvents/learning-center/peroxide-formation.html>

8) Perchlorates

Salts derived from perchloric acid are known as perchlorates. These compounds find use in a variety of places, such as rocket fuel, fireworks, and airbags. Perchloric acid is an explosive compound itself, and its salts can be equally as explosive. The majority of these compounds are sold as hydrates, which diminishes the explosiveness of these agents. **EVEN THE HYDRATES OF THESE PERCHLORATE SALTS SHOULD BE HANDLED WITH EXTREME CARE.** The dry crystals of perchlorate salts are shock sensitive, and potentially explosive if disturbed. As oxidizers, these salts can ignite or detonate if they are exposed to heat or shock.

If you have any questions about this compound, or are unsure about its safe use, please consult the MSDS for picric acid (which can be found online from Sigma-Aldrich).

9) Azides

Explosion Hazard!!

Organic azides can be explosive, but the risk of explosion is particularly high for sodium azide. The azide anion can react with acids to form the explosive hydrazoic acid. It can react with chloroform or dichloromethane to form di- and triazidomethanes, which are explosive as well. It can also form explosive salts with transition metals.

Toxicity

Sodium azide is a toxin that binds to iron in heme cofactors. In solution, it can be absorbed through the skin.

Precautions

- Use the smallest amount of azide possible; do not run large-scale reactions without carrying them out on a smaller scale first.
- When weighing out sodium azide, do not scrape at the sides of the container or try to break up clumps. Weigh out the solid with a plastic spoon, not a metal spatula.
- When using sodium azide with ground glass joints (either in the reaction flask or with the rotary evaporator), use solvent to wash the joint to make sure there is no azide present. Then use a Teflon sleeve to line the joint. This prevents azide from getting trapped and also prevents “locking” of the joint.

Quenching

Excess azide should be quenched in a fume hood before disposal according to the following procedure:

- Dilute the azide to 5% in water.
- Add a 20% solution of sodium nitrite such that the total mass of sodium nitrite added is equal to 1.5 times the mass of azide present.
- Add sulfuric acid dropwise until gas is no longer evolved and the solution is acidic.
- Test for excess nitrite (indicates quenching is complete) with iodine-starch paper.
- Dispose of the solution into aqueous waste.

The reactions taking place in this quenching method are as follows:



10) Liquid Oxygen



Liquid oxygen poses a great safety hazard. It is a strong oxidizing agent. When using a liquid nitrogen trap under vacuum, liquid oxygen can

condense in the trap. If organics are present, the trap can explode when combined with the liquid oxygen.

If you notice a bluish liquid in a liquid N₂ trap, please check for a leak that allowed oxygen into the system. Close the manifold leak and then drop the trap to allow the liquid oxygen to warm up with the pump running. Once this has been done, evacuate the area and let your principal investigator know of the situation.

11) Picric Acid

Consult Eric Anslyn prior to use! Picric acid is one of the most acidic of the phenol derivatives, owing to its three proximal electron withdrawing nitro groups at the 2,4, and 6 positions. This compound is referred to as a flammable solid when it is wetted by at least 30% water, while it is considered a high explosive when the amount of water is less than 30%. PICRIC ACID IS AN EXTREMELY HAZARDOUS SUBSTANCE BECAUSE IT IS SO EXPLOSIVE. This compound is highly sensitive to external stimuli such as friction, heat, and shock. The wet product is less sensitive than the dry acid, but should still be handled with extreme care. Keep away from hot surfaces, open flames, and any other source of heat. Picric acid can form salts with a variety of metals, and these salts are as explosive as or potentially more explosive than the dry form. Picric acid should not be allowed to contact concrete floors, as this can form a friction-sensitive salt with calcium in the concrete. Ammonia, reducing agents, strongly basic substances, and metals should be avoided when working with picric acid. Dates that containers were received and opened should be maintained for picric acid, and bottles should be discarded when they reach two years old. The bottles should be inspected, and water added as needed at least once every six months. When water is added the container should be gently rotated so as to evenly distribute the added water.

If you have any questions about this compound, or are unsure about its safe use, please consult the MSDS for picric acid (which can be found online from Sigma-Aldrich).

12) Sodium Benzophenone Ketyl Stills

Benzophenone-sodium ketyl still is a widely used purification method to produce moisture-, oxygen-, and peroxide-free organic solvents, especially for tetrahydrofuran (THF). The soluble benzophenone ketyls can be formed as radical anions by one-electron reduction of carbonyls with sodium. The ketyl molecule is intensively colored (deep blue) and reacts quickly with the water, oxygen, and peroxide dissolved in organic solvents. The deep blue coloration indicates dry and oxygen free conditions. The procedure to prepare such a still is given in the Appendix.

The stills are known to have certain dangers. On very rare occasions they will explode, likely due to the accumulation of peroxides. Hence, our group has switched to solvent delivery systems. If you ever need to have a sodium benzophenone ketyl still, make sure you first contact Eric Anslyn before constructing it.

The largest danger with such a distillation is fire due to spillage. THF is quite flammable and THF vapor is about two and a half times the density of air. Be aware of the risks inherent to the reaction you will perform and appropriate countermeasures. Do you know where the nearest chemical shower is located? When creating the still, at least one carbon dioxide or dry-chemical fire extinguisher should be readily available when working with sodium. In addition, when quenching the still, at least one carbon dioxide or dry-chemical fire extinguisher should be readily available.

Sodium metal is reactive to water. Never under any circumstances, should you pour a quenched still into water or a sink.

13) Na(CN)BH₃ work-up

In acidic conditions, Sodium Cyanoborohydride [Na(CN)BH₃] releases highly toxic gas HCN; work in a hood or a well-ventilated place. Do not work alone in case you are exposed to HCN(g).

HCN is a gas that you can easily breathe into your lungs. It smells like almonds. Cyanide bonds (irreversibly) to the site where oxygen usually binds to hemoglobin causing death from suffocation.

For small scale uses (<100mg) of Na(CN)BH₃, simply leave it stirring inside of the hood, and wait until all the HCN(g) has evaporated. For larger scale uses, aqueous work-up in water or pH 7 buffer solutions is recommended. It is important to add quenching solution **SLOWLY**. Work-up in ice bath for extra safety precaution is optional.

14) Handling of Inorganic Cyanide Salts

Inorganic cyanide salts, such as KCN, NaCN, are highly toxic if ingested. Never use them near or around food. Most importantly, they are deadly when reacting with acid to generate HCN. Recall that the addition of sulfuric acid to NaCN is how the Nazis killed people in the WWII concentration camps.

NEVER, UNDER ANY CIRCUMSTANCES SHOULD ACID BE ADDED TO A CYANIDE SALT!

When handling inorganic cyanide salts, always wear gloves and wash your hands immediately after usage.

For the waste solution containing cyanide salts, treat the solution with excess of aqueous $\text{Cu}(\text{SO}_4)$ (to generate stable complex) and store the solution in a labeled designated container (not general solvent container!).

15) Teratogens

Teratogens are substances that have been found to lead to birth defects or fetal demise. There are many of these types of compounds found in both industrial and academic chemistry labs. Perhaps the most famous example of teratogens is thalidomide. This was a drug prescribed to women in the 1950 to help combat morning sickness; many of the children born to these women had malformed appendages. Pregnant women may face special challenges in the lab. Not only do they need to strive for personal safety they must also consider the safety of their unborn child. Knowledge is the number one tool a pregnant woman can use to protect her and her child's safety. If you are a pregnant woman or are trying to become pregnant you should familiarize yourself with the teratogenic properties of the chemical you are working with. Furthermore you should identify if any of your lab mates are using potential teratogens, especially if they share space with you. A list of compounds (not all teratogens may be listed here) with known teratogenic properties can be found here: <http://www.purdue.edu/rem/ih/terat.htm>. A pregnant woman may wish to consider limiting her potential exposure if she finds that one of her chemicals has a significant teratogenic effect. This could include using alternate chemicals, limiting laboratory time, asking lab mates for assistance when working with these compounds and/or using additional PPE (double glove for example.)

16) Ethidium Bromide and Other Cancerous Agents

When working with potentially cancerous agents such as ethidium bromide or other intercalators proper PPE must be worn. These include: double gloves, safety goggles, and a lab coat.

For chemical exposure of intercalators to the skin: Wash affected area thoroughly with soap and water for 15 minutes and remove contaminated clothing. If the exposure is small, use the sink; if the exposure is large, use the safety shower. Safety showers are located in the hallways of 5.120 and 5.110, next to the oven. If the chemical was ingested, call the poison control center at 1-800-222-1222 or call 911.

All solid ethidium bromide waste, such as agarose or polyacrylamide gels, should be put in the solid waste bucket in the Bio Room (5.110F). All liquid ethidium bromide waste, such as electrophoresis buffer, should be put in the ethidium bromide waste container in the Bio Room.

17) Chromates

Chromium reagents are commonly used as strong oxidizing agents in organic synthesis. Chromates should be stored away from combustible or flammable materials, any heat or ignition sources, and reducing agents. When working with chromates, one should always wear safety glasses and appropriate lab attire. Furthermore, it is recommended that nitrile, neoprene, or PVC gloves be worn when handling chromates. One should avoid skin or eye exposure, ingestion, or inhalation of chromates. Chromates should always be handled in a fume hood to avoid accidental inhalation. Chromates are toxic, carcinogenic, and teratogenic. Contact with the skin can cause chronic dermatitis, while contact with the eyes can cause eye damage and blindness. Ingestion or inhalation results in burns to the digestive or respiratory tracts, respectively. If skin or eye exposure to chromates occurs, wash affected area thoroughly with water for at least 15 minutes. If chromates are ingested and the victim is conscious, the victim should rinse their mouth and drink 2-4 cups of water or milk. If chromates are inhaled, artificial respiration and/or oxygen should be provided to assist in breathing if necessary, and the victim should be removed to fresh air. For any exposures, immediate medical attention should be sought. If a fire involving chromates breaks out, water (**not** a chemical or carbon dioxide fire extinguisher) should be used to put the fire out. Water should be used to douse any chromates that have not yet

ignited to cool them and prevent them from exploding. A respirator should be worn to avoid breathing toxic fumes from the burning chromates. Finally, it is very important to dispose of chromate waste properly because it is extremely harmful to aquatic wildlife. Anything containing chromates should **never** be put down the drain.

References:

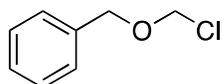
Groce, D. F. Keep the Gloves On! *Occupational Hazards*, June 2008, pp 45-48.

Potassium Chromate. MSDS No. 216615 [Online]; Sigma Aldrich: Saint Louis, MO, March 13th, 2010. <http://www.sigmaaldrich.com> (accessed February 6th, 2012).

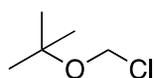
Pyridinium Chlorochromate. MSDS No. 190144 [Online]; Sigma Aldrich: Saint Louis, MO, April 6th, 2011. <http://www.sigmaaldrich.com> (accessed February 6th, 2012).

18) Haloethers

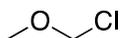
Haloethers are chemicals that are commonly used as alkylating agents and industrial solvents. This class of chemicals is known to be carcinogenic to humans. Consult Eric Anslyn before using. Inhalation of these chemicals should be prevented. If these chemicals must be used, appropriate respiratory protection must be worn (respirator). The following structures are examples of haloethers:



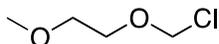
Benzyl chloromethyl ether
CAS = 3587-60-8



tert-Butyl chloromethyl ether
CAS = 40556-01-2



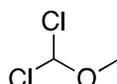
Chloromethyl methyl ether
CAS = 107-30-2



Methoxyethyl chloromethyl ether
CAS = 3970-21-6



Bischloromethyl ether
CAS = 542-88-1



Dichloromethyl methyl ether
CAS = 4885-02-3

Methyl chloromethyl ether (also known as MOMCl for short) is often used as an alcohol protecting group in organic chemistry. The structure of MOMCl is shown above. As previously mentioned, this chemical is carcinogenic and respiratory protection must be worn if using this chemical.

19) Mercury (Hg) Spill Response

If you have a Hg spill, contact Eric Anslyn immediately, irrespective of the size of the spill and the time of day.

After consulting with Eric, if he recommends it, contact UT hazardous materials department (OEHS) if the mercury spill is more than $3 \mu\text{g}/\text{m}^3$. If the spill is significantly larger, we may need to call 911 after office hours, but only do so after consulting with Eric Anslyn. The following is the procedure for cleaning up an Hg spill.

For a small spill, please follow the steps as written:

- Evacuate spill area.
- Ventilate as much as possible.
- Wear safety goggles, rubber gloves, apron and cover your shoes with plastic bags to prevent contamination on other area of the room.
- Set aside everything you think might be contaminated with mercury.
- Use syringe without needle or eye-dropper to pick up the mercury.
- Pour the mercury in a plastic/glass container with lid.
- Close the lid, label the container with date.
- Inspect the spilled area with a bright light to help to illuminate any hidden droplets.
- Then, after your clean up of the small spill, contact EHS to come and check the area for Hg levels.

20) CO (Carbon Monoxide)

Carbon monoxide (CO) is an odorless, colorless, tasteless gas that is slightly lighter than air. It is sometimes called carbonic oxide, exhaust gas, or flue gas. Under high pressure it becomes a liquid. It can also kill within minutes in high concentrations.

In the workplace, carbon monoxide buildups can occur in operations near furnaces, ovens, generators, forges and kilns when they are being fired up to operating temperatures.

If you suspect CO:

- Immediately move outside to fresh air.
- Call your emergency services, fire department, or 911.
- After calling 911, do a head count to check that all persons are accounted for. DO NOT reenter the premises until the emergency services responders have given you permission. You could lose consciousness and die if you go in.
- If the source of the CO is determined to be a malfunctioning appliance, DO NOT operate the appliance until it has been properly serviced by trained personnel.

21) OsO₄

a. Potential Health Effects

Sublimes at room temperature. May be fatal if inhaled. Material is extremely destructive to the tissue of the mucous membranes and upper respiratory tract. May be fatal if absorbed through skin. Causes skin burns. Corrosive. Causes eye burns. Lachrymator. May be fatal if swallowed. Target Organs: eyes, central nervous system, male reproductive system, kidneys.

b. Handling and storage

Precautions for safe handling: **Talk to Dr. Anslyn before starting any experiment that involves the use of OsO₄.** Avoid contact with skin and eyes. Avoid formation of dust and aerosols. Provide appropriate exhaust ventilation at places where dust is formed.

Conditions for safe storage: Keep container tightly closed in a dry and well-ventilated place. Recommended storage temperature: 2-8 °C.

c. Personal protective equipment (PPE)

Hand protection: Handle with gloves. Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good laboratory practices. Wash and dry hands.

Eye protection: Face shield and safety glasses. Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN 166(EU).

Skin and body protection: Complete suit protecting against chemicals, the type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

Hygiene measures: Avoid contact with skin, eyes and clothing. Wash hands before breaks and immediately after handling the product.

d. Accidental release measures

Personal precautions: Wear respiratory protection. Avoid dust formation. Avoid breathing vapors, mist or gas. Ensure adequate ventilation. **Evacuate personnel to safe areas. GET OUT OF THE LAB.** Avoid breathing dust.

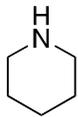
Environmental precautions: Prevent further leakage or spillage if safe to do so. Do not let product enter drains.

22) Spills of Nitrogenous Bases

Nitrogenous bases, such as pyridine, triethylamine, and piperidine (shown below), are chemicals that can be respiratory irritants. In case of a spill, the MSDS of piperidine recommends:

SPILL AND LEAK RESPONSE: Appropriately trained personnel using pre-planned procedures should respond to uncontrolled releases. Proper protective equipment should be used. Remove all sources of ignition. Ventilate area of leak or spill. Keep unnecessary and unprotected people away from area of spill. Wear appropriate protective equipment. Spill kits are located on top of the supply shelves in each lab. They are in bright yellow bags. Alert Eric Anslyn and EHS in the instance of any spills.

Spills: Pick up and place in suitable container for reclamation or disposal, using a method that does not generate dust. Alert Eric Anslyn and EHS in the instance of any spills.



Piperidine

23) HCN and HN₃

Both HCN and HN₃ are lethal chemicals. HCN was used in the Nazi concentration camps during WWII. It is a gas that smells like almonds (some people cannot smell it), and upon inhaling it the sensation is like getting hit on the head with a sledge hammer. Thus, it is a particularly dangerous chemical.

HN₃ is a solid, and is an irritant to the eyes and skin. But, its real lethal power is that it is a dangerously explosive material. It is a friction and bump hazard.

Our group uses Na⁺ and K⁺ salts of both cyanide and azide anions. The pK_a of HCN is around 9, while the pK_a of hydrazoic acid is around 5. Thus, under no circumstances do you ever lower the pH of a solution of these salts to approach their pK_a, or go below their pK_a values.

Lastly, you should specifically alert Dr. Anslyn before the use of any cyanide so that these precautions can be discussed.

Section 3: APPENDIX

1. USING PYROPHORICS IN GENERAL

a. Key Elements for Handling Pyrophoric Solids

- In case of emergency, notify the safety officer, Eric Anslyn, the building manager, and EHS.
- Before working with any pyrophoric, familiarize yourself with the appropriate fire-fighting measures.
- Many pyrophoric solids release flammable and harmful gases. Therefore, it is required to handle these chemicals in a fume hood and use proper personal protective equipment (flame resistant lab coat, clothing made of natural fibers, safety glasses, and gloves) to reduce the release of vapors in the laboratory, eliminate skin contact with the chemical, and prevent injuries.
- Store pyrophoric solids under an inert atmosphere and avoid areas of heat, oxidizers, flammable solvents, and water sources. To avoid uncontrollable ignition, do not leave containers with residues of pyrophoric materials open to the atmosphere.
- All containers must be labeled appropriately with the chemical name and hazard warning.
- Do not cut pieces of sodium metal or other active metals on paper towels or other combustible materials and do not clean up residues from these procedure using paper towels, unless the reactive materials have positively been quenched. A common problem is subsequent ignition when these contaminated towels are disposed into waste receptacles.
- Make sure that the pyrophoric residues in empty containers, spatulas, and other contaminated items are carefully quenched before disposal. After significant dilution of the residues with a non-reacting solvent under an inert atmosphere, place a cooling bath (dry ice/acetone) under the reaction vessel to dissipate the heat, and slowly add isopropyl alcohol to quench the materials.
- Slowly add methanol followed by copious amount of water (stronger neutralization agent) to complete the quenching.
- In case of a small spill (controllable) during the quenching or transfer of the pyrophoric solid, smother the spill with compatible materials or dry sand, place an appropriate fire extinguisher nearby, and mark-off the area with warning signs. Call Eric Anslyn, the building manager, and EHS. Collect the mixture and quench as stated above before disposal.
- In case of a large spill (uncontrollable) during the quenching or transfer of the pyrophoric solid, warn others to leave, and pull the fire alarm, call Eric Anslyn, the building manager, and EHS.

- Provide emergency personnel with technical information about the chemical if needed.
- Contact EHS for assistance with disposal

b. Pyrophoric Liquids

I. Transferring Liquid Pyrophoric Reagents Outside the Inert Atmosphere of a Glovebox

If an inert atmosphere glovebox is not available and a pyrophoric reagent such as *t*-butyllithium solution needs to be used, the solution can be transferred by either a syringe or double-tipped needle (cannula) outside the glovebox **only** if the transfer takes place under an inert atmosphere using proper handling techniques (see methods A-C below).

Important: The following list contains very key elements for transferring pyrophoric reagents **outside** the inert atmosphere of a glovebox.

- Do not work *alone* when handling pyrophoric reagents. Laboratory policy recommends that a colleague be present (the Buddy System) while working with hazardous chemicals. For example, if you become unable to respond to a situation due to an injury, the colleague can provide immediate assistance and make the calls to your emergency contact and building manager, EHS, and Eric Anslyn.
- Fire-resistant apparel (PPE) and safety glasses must be worn at all times when working with pyrophoric reagents. Fire-retardant laboratory coats are mandatory, and fire-retardant gloves are highly recommended. **Note:** Fire resistant gloves can also absorb hazardous liquids and consideration should be given to using the gloves in conjunction with appropriate chemically-resistant gloves. In other words, extreme caution must be exercised to mitigate skin exposure or spillage when handling pyrophoric reagents. Avoid wearing synthetic clothing while working with pyrophoric reagents as they do not provide the required protection. Natural fiber clothing tends to char instead of melt when exposed to flames or high temperatures and is preferable to synthetic fibers.
- Be prepared for the worst when handling pyrophoric reagents. These reagents can catch fire very easily when exposed to air. It is therefore advisable that extreme caution be used. Know the location of the safety shower, a blanket, a sand bucket, and how to use a fire extinguisher in case of emergency.
- If uncertain of how to handle pyrophoric reagents, users must consult a knowledgeable staff member prior to performing the experimental task, read

the manufacturer's MSDSs, and understand the technical information associated with handling the materials.

- Perform the work inside a fume hood with the sash down as far as possible for protection against chemical splashes and unexpected ignition events.
- Remove all other flammable materials from the hood to reduce the hazard in case of a fire.
- Secure the pyrophoric reagent bottle to a stand with a clamp before use to prevent it from tipping over. Controlling the bottle with one hand while handling the syringe with the other hand is strongly discouraged.
- Use a long needle to reach the solvent level. Do not invert the bottle as such action dislodges sediments that may clog the needle.
- Use a wide bore needle of 18-gauge or larger. The use of a smaller bore needle can slow down the transfer process and cause the needle to clog.
- Use a luer-lock syringe with long needle when possible and be sure that the assembly does not leak. Make sure that the needle is secured in the luer-lock and does not separate from the barrel during the transfer. It may help to use parafilm on the outside of the syringe to ensure an air-tight seal.
- When disposable plastic syringes are used, it is highly recommended that the transfer is performed within the confinement of a glovebox. The syringes must be rinsed with non-reacting solvent, neutralized as appropriate, and disposed of safely at the conclusion of the transfer.
- All equipment, such as syringes and glassware, should be free of moisture and purged with an inert gas prior to use.
- Slowly add the pyrophoric reagent to the reaction vessel in a cooling bath to control reaction rate and heat dissipation.
- A container with residual pyrophoric reagents must never be opened. The containers must be rinsed with inert solvent and neutralized with adequate cooling prior to disposal. If uncertain of how to safely neutralize residual pyrophoric reagents, consult with an experienced staff member prior to neutralization.
- Products from pyrophoric reagents should be handled as potentially highly-reactive materials.
- If a person is splashed with chemicals and catches fire, the use of the stop, drop, and roll method, safety shower, a fire blanket, or fire extinguisher (H₂O, CO₂ or A, B, C) are the most effective means of controlling clothing on fire. If a safety shower is available, keep the person under the shower for at least 15-20 minutes to make sure that all chemicals are washed away. Contact Eric Anslyn and EHS immediately.

II. When a Syringe is used, the Best Practice for transferring a pyrophoric reagent is shown in Method A below.

Note: When a syringe is used, extreme caution must be exercised to prevent the plunger from separating from the syringe. Use luer-lock, airtight syringes for the transfer. Avoid the transfer of a large volume (> 10 mL) from the pyrophoric reagent bottle when using syringes. For transferring larger volumes, used the double-tipped needle (cannula) methods described below. At the conclusion of the transfer, the syringe needs to be clean to minimize the chance of the plunger from sticking/freezing in the barrel. The residue should be diluted with non-reacting solvent and remain under an inert atmosphere until rinsed with non-reacting solvent and the rinse and other residues are neutralized as appropriate.

Method A

Figure 3.1 shows the complete assembly of reagent transfer using an airtight glass syringe and a bubbler, for pressure release, under an inert atmosphere. The volume of reagent to be transferred is not to exceed 10 mL. Amounts above this should be transferred using a cannula.

- Make sure that the syringe and the needle attached to the inert gas line needle, equipped with a bubbler and a shut-off valve, are purged prior to reagent transfer.
- Insert the needle, connected to the inert gas line (bubbler), through the septum into the headspace above the reagent to maintain a slight positive pressure inside the Sure/Seal™ pyrophoric reagent bottle.
- Insert the long needle of a luer-lock, airtight, dry syringe through the septum into the reagent.
- Pull the plunger back slowly to fill the syringe with the required volume of reagent. Always keep the plunger in your grasp and avoid pulling back the plunger quickly as this action causes leaks and creates gas bubbles.
- Once the required volume is attained, slowly pull up the syringe needle from the pyrophoric reagent to the overhead space above the liquid.
- Pull the plunger up slowly and allow the inert gas to push the reagent trapped in the needle into the syringe.
- Shut the inert gas line off and slowly pull the needle out from the assembly to complete the transfer.
- At the conclusion of the transfer, the syringe and needle need to be rinsed with a non-reacting solvent such as hexanes and the residue quenched as appropriate. For alkyllithiums, use hexane (this dilutes the reagent), and carefully add the hexane washes to ethyl acetate. Flush the syringe and needle with this mixture a couple of times, and then wash both as usual with acetone (or toss the disposable syringe). For Grignard reagents, use ether

for flushing, then follow the rest of the procedure above. For large amounts, be sure to quench under inert atmosphere as shown below.

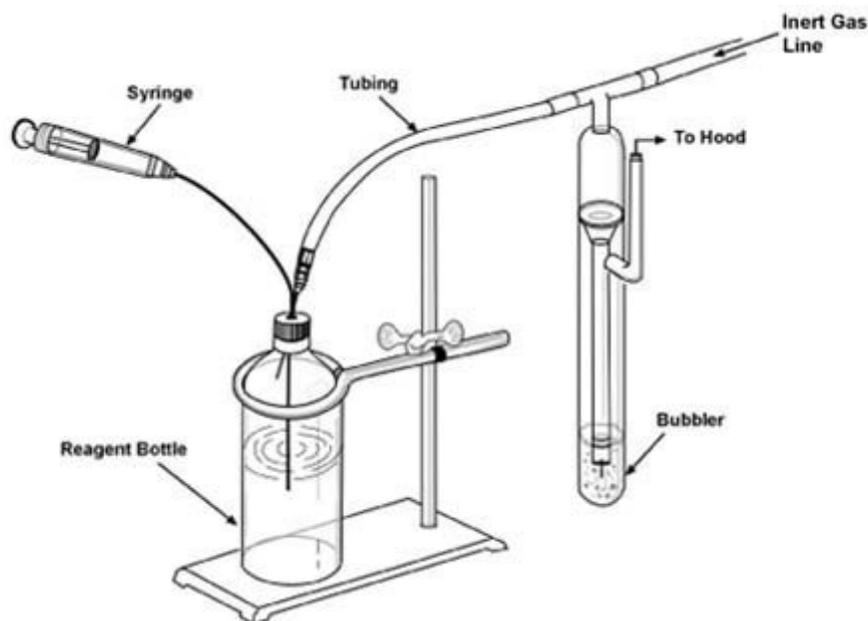


Figure 3.1. Syringe Transfer Assembly Equipped with an Inert Gas Line and a Bubbler during Reagent Transfer

III. When a Double-Tipped Needle is used, the Best Practices for transferring pyrophoric reagents are shown in Methods B or C.

Note: At the conclusion of the transfer, the needle needs to be clean to minimize clogging. The residue should be diluted with non-reacting solvent and remain under an inert atmosphere until the rinse and other residues are neutralized as appropriate.

Method B

Figure 3.2 shows the complete assembly for reagent transfer using a double-tipped needle under low pressure (< 1 PSI) from an inert gas line. Note that a bubbler is connected to the reaction vessel to avoid pressure build up in the assembly.

- Make sure that the glassware being used is dry, and the assembly is purged and maintained under an inert atmosphere prior to reagent transfer.

- Insert one end of the double-tipped needle through the septum into the reaction vessel or addition funnel in order to flush the needle with inert gas.
- Insert the other end of the double-tipped needle through the septum of the reagent bottle into the headspace above the liquid.
- A needle attached to a very low pressure inert gas line (< 1 PSI) is inserted through the septum into the headspace and kept above the solution of the pyrophoric reagent bottle.
- Transfer the liquid from the reagent bottle into the reaction vessel or the addition funnel by pushing down the end of the double-tipped needle in the reagent bottle into the liquid. **Note:** At all times during the transfer, the reaction vessel must be vented through a mineral oil bubbler and kept under a positive pressure of an inert atmosphere to prevent air from entering the system.
- Once the required volume is transferred, pull up slowly on the end of the double-tipped needle in the pyrophoric reagent so that it is no longer in the liquid, but still through the septum and in the headspace above the liquid. Allow the inert gas to flow through the needle to push the trapped reagent in the needle to reaction vessel or the addition funnel.
- At the conclusion of the transfer, the double-tipped needle needs to be rinsed with non-reacting solvent and the residue quenched as appropriate (see method A for details).

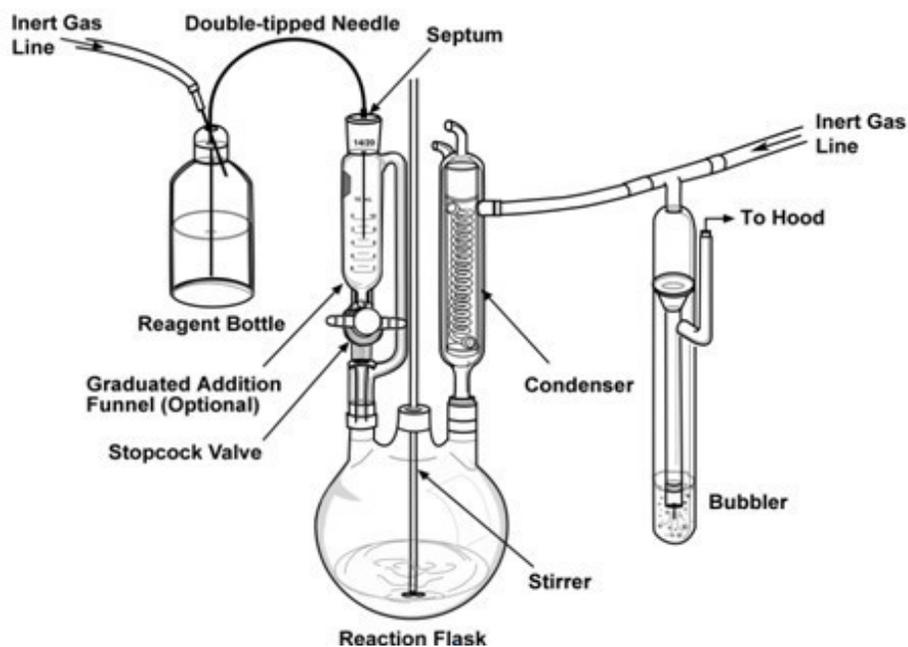


Figure 3.2. Double-Tipped Needle Assembly Equipped with a Bubbler and Kept Under an Inert Atmosphere during Reagent Transfer

Method C:

Figure 3.3 shows the complete assembly for reagent transfer using the double-tipped needle under slight vacuum and connected to an inert gas line through a bubbler.

- Make sure that the reaction vessel being used is dry, and that the assembly is purged and maintained under an inert atmosphere prior to reagent transfer.
- Insert the double-tipped needle through the septum into the reaction vessel or addition funnel to purge the needle with inert gas.
- Insert the other end of the double-tipped needle into the head space above the liquid of the pyrophoric reagent bottle.
- Connect a vacuum line with a shutoff valve to the reaction vessel (as shown below).
- Insert the needle connected to the inert gas line (bubbler) through the septum into the headspace of the Sure/Seal™ reagent bottle to keep the space above the solution under a blanket of an inert gas.
- Make sure that the assembly is in proper configuration, and the inert gas is flowing through the bubbler.
- Push the end of the double-tipped needle in the reagent bottle down into the pyrophoric reagent.
- Apply a slight vacuum to the reaction vessel assembly by opening the vacuum valve slowly to transfer the desired volume from the reagent bottle to the reaction vessel through the double-tipped needle.

Caution: The vacuum line will only need to be opened intermittently in order to transfer the pyrophoric reagent. High and continuous vacuum may allow air to enter the system through the bubbler.

- Once the required volume is transferred, pull up slowly on the end of the double-tipped needle in the pyrophoric reagent so that it is no longer in the liquid, but still through the septum and in the headspace above the liquid. Allow the inert gas to flow through the double-tipped needle to push the trapped reagent in the needle to reaction vessel.
- Close the vacuum valve and connect the reaction flask to an inert gas line.

- At the conclusion of the transfer, the double-tipped needle needs to be rinsed with non-reacting solvent and the residue quenched as appropriate (see method A for details).

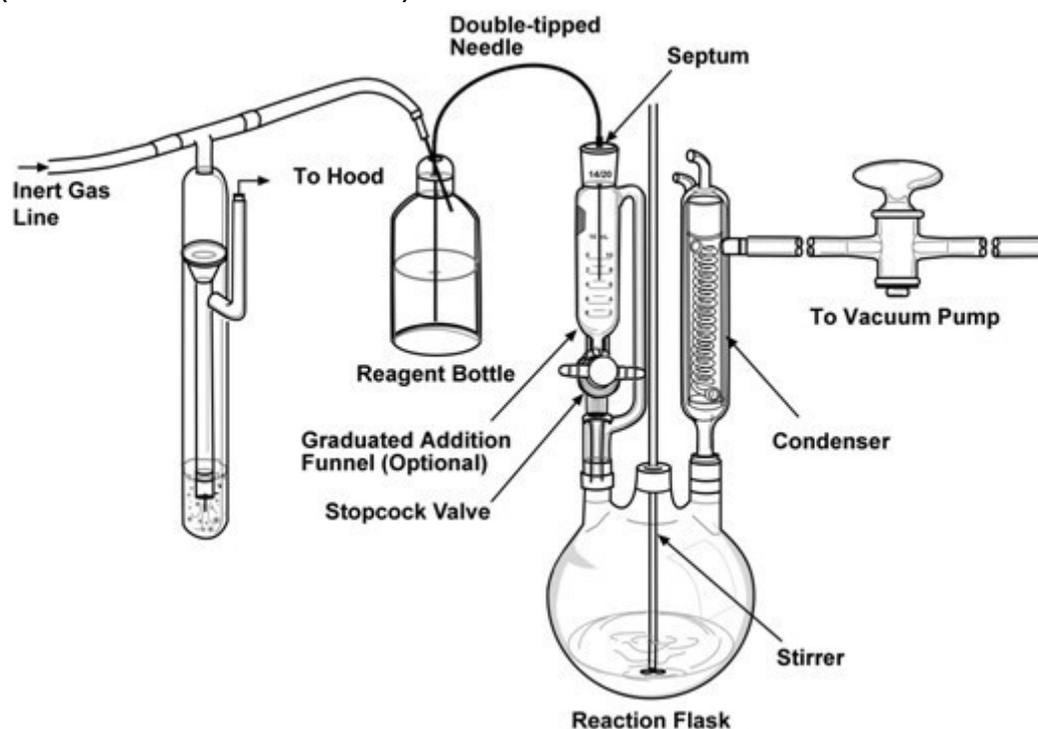


Figure 3.3. Double-Tipped Needle Assembly Equipped with a Vacuum Pump and Kept Under an Inert Atmosphere during Reagent Transfer

2. *tert*-Butyl Lithium - HANDLING PROCEDURE

The following is a detailed account of the accident at UCLA from the CE&N article *Learning from UCLA* - <http://pubs.acs.org/cen/science/87/8731sci1.html>

When Sangji had done the reaction in October, she added 28 mL of anhydrous ether to a flame-dried 200-mL flask. Next, she added 3.0 mL of vinyl bromide and stirred the mixture for 15 minutes at -78°C . She then charged the flask with 53.79 mL of 1.67 M tBuLi in pentane. She further stirred the mixture for two hours, then moved it to a 0°C bath for 30 minutes, and finally took it back to -78°C .

Separately, she added 6 mL of ether and 3.90 mL of 4-undecanone to another flame-dried flask and cooled the mixture. She then used a double-tipped needle to transfer the material to the tBuLi flask. She stirred the reaction at -78°C for two hours, then warmed it to -10°C before quenching the reaction with 80 mL of NaHCO_3 . Her crude yield was 3.60 g of 4-hydroxy-4-vinyldecane, or 86.75%.

Sangji was working on a nitrogen manifold in a fume hood in a lab on the fourth floor of UCLA's Molecular Sciences Building. She had titrated the tBuLi twice to determine its concentration—1.69 M—and needed 159.5 mL of the reagent to react with 9.0 mL of vinyl bromide. She was drawing up the tBuLi in roughly 50-mL aliquots in a 60-mL plastic syringe equipped with a 1.5-inch, 20-gauge needle.

For unknown reasons, the syringe plunger came out of the barrel and the tBuLi was exposed to the atmosphere. Although it wasn't part of her experiment, an open flask of hexane was also in the hood and Sangji knocked it over. The tBuLi ignited and the solvent caught fire, as did Sangji's clothes. She was wearing nitrile gloves, no lab coat, and no one remembers if she was wearing eye protection.

Key problems with this account: no flame-resistant lab coat, synthetic (and flammable) clothing, and using a large syringe instead of a cannula.

How to use *t*-butyl lithium:

I. Preparation:

- **Talk to Dr. Anslyn** - The scale of the reaction is the priority. Discuss alternate options (i.e. using a Grignard reagent instead)
- Double-check your math and stoichiometry.
- Put on flame-resistant lab coat, gloves and eye-protection with the side guards (this goes for people who wear prescription eye glasses also). Ask yourself if you are wearing non-cotton clothing (including undergarments such as brassieres) - if so you should wait until you can change clothes or go home and change clothes. Synthetics will burn much faster and will adhere/melt to your skin more quickly increasing the severity of injuries.
- Have a distraction-free mind. Be able to be fully present to your experiment.
- Clear your hood space of unnecessary clutter, solvents, hoses, glassware, ironware, or anything else that you could bump or spill, or anything that you could snag your lab coat on.

This bench is clear and accessible. The researcher is ready to handle *t*-butyl lithium



- Make sure your nitrogen manifold is set up properly without excess tubing, and that the bubbler and is clearly in sight and working properly.
- Obtain clean (or new), oven-dried, undamaged glassware and needles.
- Set up the reaction space so that the hood sash can be open as little as possible.

II. Reagent handling set-up



- Inform someone you are about to begin handling t-butyl lithium and have them nearby with sand to quench any fires.
- Have the t-butyl lithium destination (i.e. reaction flask), secured by ironware and charged with Argon or Nitrogen, the necessary reagents and solvents, and cooled to $-78\text{ }^{\circ}\text{C}$.
- Have a small beaker filled with hexane (not anhydrous) or toluene (not anhydrous) on the other side of the reaction flask than the t-butyl lithium bottle (this will be used to clean/quench the t-butyl lithium in the syringe after it has been dispensed).
- Obtain at least one glass tray or bowl for secondary containment.
- Support the reagent bottle with a clamp within the glass bowl or tray in close proximity to the reaction flask/destination (this will minimize the time the needle is exposed to the atmosphere).
- Turn on the nitrogen flow through you manifold making sure the bubbler is working properly.
- Remove the cap and insert the syringe needle of the nitrogen line into the center of the septum on the lithium reagent bottle making sure to not penetrate the reagent liquid surface (the amount of bubbles in the bubbler should increase- albeit slightly). Be sure to use a wide gauge needle.

- After assembling your needle (a wide gauge needle) and syringe, draw a blanket of nitrogen through the needle and into the syringe and push it out. Repeat twice. Then draw up some nitrogen and slowly expel this as you prepare to insert the needle into the alkyl lithium bottle. (You want to minimize the time that air has to get into the needle.)
- Insert your reagent syringe needle (make sure the plunger on the syringe is completely depressed prior to insertion). Draw your reagent up slowly (at the rate the nitrogen can replace it) so as not create a vacuum in the flask while maintaining a good grip on the plunger. Once the amount needed is in the syringe, lift the needle out of the solvent level and draw a bit of nitrogen into the syringe. Remove the syringe and invert it quickly to maintain the nitrogen in the head space of the syringe between the solvent level and the needle. Insert it quickly into the reaction flask via the septum and begin a drop wise addition. The bottle of butyl lithium should be stable while you are performing your addition, in that it is still under nitrogen flow. **Caution:** It is common for the tip of the needle to spark even with proper technique.
 - o Making an airlock?: This is an [interesting idea](#) that I've never tried: Plug both ends of a short length of glass tube with septa, flush with Ar, then use it as a needle "air lock" pushing the needle through both septa, then into the BuLi bottle. Take what you need then withdraw the needle through the first septa only - if this is pressed up against the septa of the bottle then the tip shouldn't catch fire. (taken from: <http://chemjobber.blogspot.com/2009/05/if-i-were-working-with-tert.html>)
- When you are finished adding your reagent, take the needle out of the reaction flask. Slowly draw up hexane from the beaker that was set up in step 3, and expel it into an empty beaker. Do this multiple times to insure complete quenching of the residual reagent. The syringe is now ready to be cleaned by standard methods.
- Remove the nitrogen line from the t-butyl lithium bottle and promptly replace the cap.
- Secure the cap tightly, wrap with parafilm and return the reagent to the refrigerator.

***WE STRONGLY SUGGEST YOU WATCH THE VIDEO ON USING ORGANOLITHIUM REAGENTS FOUND HERE:**

http://chem-courses.ucsd.edu/CoursePages/Uglabs/143A_Weizman/EHS/EHS.html

For a description of proper syringe technique, look here.

http://chem.chem.rochester.edu/~nvd/pages/how-to.php?page=use_syringe

For advice on titration of alkyllithiums, look here.

http://chem.chem.rochester.edu/~nvd/pages/how-to.php?page=titrate_alkyllithiums

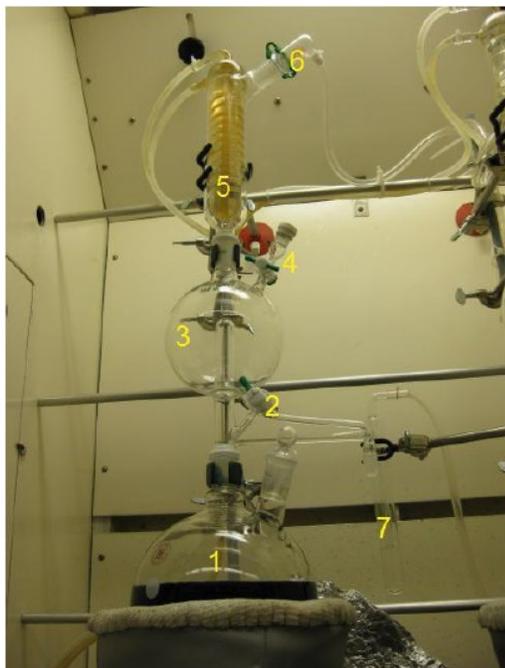
3. Sodium Benzophenone Ketyl Stills

a. Introduction

The benzophenone-sodium still is a widely used method to produce moisture, oxygen, and peroxide free organic solvents, especially for tetrahydrofuran (THF). The soluble benzophenone ketyls can be formed as radical anion by one-electron reduction of carbonyls with sodium. The ketyl molecule is intensively colored (deep blue) and reacts quickly with the water, oxygen, and peroxide dissolved in organic solvents. The deep blue coloration indicates dry and oxygen free conditions.

b. Before getting started

Appropriate safety measures should be in places during all steps of solvent distillation. The largest danger with this distillation is fire due to spillage. THF is quite flammable and THF vapour is about two and a half times the density of air. Be aware of the risks inherent to the reaction you will perform and appropriate countermeasures. Do you know where the nearest chemical shower is located? Sodium metal is reactive to water and it is recommended to have a 500 mL beaker of isopropyl alcohol to remove small pieces of sodium generated during chopping. Have sand or a class D fire extinguisher nearby to extinguish any fires. Perform all work inside an operating fume hood.



The distillation setup pictured to the left is fairly common. The boiling flask 1 is a 3000 mL, two necked variety with the secondary neck stoppered during normal operation. Use this neck to add additional THF. The stopcock 2 is used to collect THF or return the condensate to the boiling flask. Note the T marked on the stopcock. This T indicates the bored openings. The distillate trap 3 collects THF when the stopcock is closed. The second stopcock 4 is used to withdraw THF using a syringe. This is the preferred method of withdrawing THF since there is little opportunity to introduce water vapor or oxygen into the apparatus. To withdraw THF insert a sufficiently long needle into the septum above the stopcock. Open the stopcock and thread the needle through the bore, then withdraw the necessary amount of THF that has collected in the distillate trap. When finished be sure to close the stopcock. The condenser 5 should receive a steady supply of water but

not too much. Take note of the argon inlet 6 and bubbler 7. When in doubt ask for assistance.

c. Setting solvent stills

All glassware you use in this reaction should be oven-dried and your work area should also be free of water. Tetrahydrofuran (THF) should be pre-dried overnight over potassium hydroxide (KOH) or molecular sieves (3 or 4 Å). Extract a block of sodium metal from the container and rinse with a minimum amount of hexanes to remove the oil or kerosene. Slice the sodium into pieces small enough to fit in the neck of the flask; smaller pieces allow more surface area. Add sodium pieces equivalent to approximately 5 grams to the boiling flask, seal the flask and clean up any shavings you missed. Add about 30 g of benzophenone and 2 liters of THF to the boiling flask and restopper. Double-check the flow of water and argon then turn on and slowly ramp up the Variac until the THF starts to simmer. The heating mantle and Variac pictured work well at about 40V. Reflux the mixture under argon until the deep blue color of benzophenone ketyl forms ($\text{Na}[\text{Ph}_2\text{O}]$). If, after refluxing for several hours, the deep blue color does not develop, try to scratch the sodium with a glass rod until it shows partly blue color and continue to reflux it for several hours. The solution should be kept under argon atmosphere at all times. Do not distill it without sodium because THF will form peroxides which are an explosive hazard. The loss of the blue color in 2 or 3 days indicates the decomposition of the ketyl. It can be regenerated by addition of more benzophenone. The deep blue color of the ketyl does not necessarily indicate super dry condition (less than 10 ppm).