Harvard Department of Chemistry and Chemical Biology

Laboratory Safety Manual

Revised January 2012

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This document describes the safety training required and policies that must be followed to conduct laboratory research in the Department of Chemistry and Chemical Biology. It is intended to augment existing CCB and University policies and procedures. Researchers can refer to the Harvard Environmental Health and Safety (www.uos.harvard.edu/ehs) and CCB Safety (www.chem.harvard.edu/safety/index.php) websites for additional safety information and policies. Working safely and following Harvard and CCB safety policies are necessary conditions for conducting laboratory research.

1. Regulations

Occupational Safety & Health Administration (OSHA) *Occupational Exposure to Hazardous Chemicals in Laboratories: 1910.1450* was written to enhance the safety of laboratory personnel through better information and work practices.
www.osha.gov/SLTC/laboratories/index.html

Harvard University Laboratory Chemical Hygiene Plan addresses the general hazards of common chemicals that may be present in the laboratory and describes work practices, procedures and controls that are in place to protect you from those hazards. It also includes information on compliance and administrative responsibilities regarding lab safety.
www.uos.harvard.edu/ehs/ih/lp_chemical_safety_chp.shtml

2. Emergency Contact Information

This information is available from the Emergency Response Guide flipchart hanging near most hallway phones in the CCB Department.

Emergency Dispatcher **911**
Call to report emergencies that require police, fire fighters, and/or paramedics. Follow up with call to Operations Center.

Operations Center (617) 49**5-5560**
Harvard dispatch center staffed 24/7/365. Call for after hours facilities problems, spills, or if you don't know what to do.

CCB Safety Office (617) 49**6-8285**
Contact Mathieu Lalonde, lalonde@fas.harvard.edu, for lab safety and hazardous waste issues.

Environmental Health and Safety (617) 49**5-2060**
Contact for hazardous waste and environmental health and safety issues. Scott Ide is the main EH&S contact for CCB (617-384-8264, scott_ide@harvard.edu).

CCB Facilities (617) 49**5-3076**
Contact Mike Paterno, paterno@chemistry.harvard.edu, Mallinckrodt 020, to report CCB facilities issues (e.g. leaks, fume hood problems) (~8AM-4PM).

Harvard Police (617) 49**5-1212**
Call for security and crime related issues.

3. CCB Safety Committee

The Department of Chemistry and Chemical Biology Safety Committee is composed of representatives from CCB Faculty, Graduate Students, Postdoctoral Fellows, and Administrative Staff as well as members of Harvard Environmental Health & Safety and the Cambridge Fire Department. Each laboratory group nominates at least one Graduate Student or Postdoctoral Fellow to serve as their Group Safety Officer and sit on the Safety Committee.

The CCB Safety Committee:
- Meets monthly.
- Receives input from CCB researchers and staff members regarding safety and health concerns.
- Identifies workplace hazards.
- Reviews accident reports in CCB and other departments.
- Updates departmental safety and health policies.
- Schedules and conducts regular laboratory inspections.

Each Group Safety Officer:
- Attends the monthly Safety Committee meetings and disseminates safety information to their group.
- Coordinates annual group clean-ups and safety inspections.
- Performs weekly surveys of hazardous waste Satellite Accumulation Areas.
- Assists with collection of data for various safety and regulatory compliance requirements.
- Conduct laboratory safety orientations with all new group members.

4. Laboratory Safety Orientation

The group safety officer is charged with conducting and documenting laboratory safety orientations for all group researchers (undergraduate, graduate, post-doctoral, and associate). The orientation will familiarize incoming researchers with the safety features of the laboratory and determine the appropriate additional training required (e.g. laser or radiation safety training). An orientation checklist is attached below and can be found online: http://www.chem.harvard.edu/safety/forms.php

The group safety officer and the trainee must both sign the laboratory safety orientation checklist. The original checklist should be archived by the group's administrator advisor while a copy be forwarded to the CCB Safety Office. Current group members must be oriented, and the appropriate documentation forwarded, by March 31st, 2012.

FAS Laboratory Safety Orientation Checklist

Laboratory Safety Training Review

☐ Register for required general laboratory safety training.
All personnel working within CCB must complete the department's Laboratory Safety Training. Consult the CCB website for dates and times (http://www.chem.harvard.edu/safety/training.php).

☐ Determine and register for additional safety training
http://www.uos.harvard.edu/ehs/training/TARA_Cambridge_Lab_Researcher.pdf
Review research program with PI and/or Safety Officer to determine if any additional safety training is required (e.g. biosafety/blood-borne pathogens, radiation safety, laser safety, liquid pyrophoric, solid pyrophoric, etc…).

☐ Review laboratory-specific training/SOPs for highly hazardous materials, equipment, or processes that pertain to the research program.

Laboratory Orientation. Review the following safety features:

☐ Location and information in Emergency Response Guides (next to wall phones)
☐ Emergency evacuation route and meeting area
☐ Location of fire extinguishers and closest pull station
☐ Location and proper use of safety showers
☐ Location and proper use of eyewash stations
☐ Location of first aid kit
☐ Location and use of spill kits (if applicable)
☐ Basic & lab-specific PPE Policy and location of required PPE (goggles, lab coats, gloves, etc.)
☐ Location of fume hoods and/or biosafety cabinets (if applicable)
☐ Location and use of hazardous waste accumulation areas
☐ Location of Material Safety Data Sheets: http://www.uos.harvard.edu/ehs/msds/
☐ Location of Chemical Hygiene Plan:
http://www.uos.harvard.edu/ehs/ih/lp_chemical_safety_chp.shtml
☐ Location of highly hazardous materials, equipment, or processes and their rules for use.

Trainee Information & Signatures

☐ Undergraduate	☐ Post Doctoral Fellow	☐ Intern	☐ Visitor
☐ Graduate Student	☐ Staff	☐ Core Customer	☐ Vendor

Trainee Name: ______________________________ Signature: ________________________________

Orientation given by: __________________________ Signature: ________________________________

Date: ____ Laboratory/Core: __________________________

By signing here I acknowledge that I have been briefed on the safety features of the laboratory and informed of required additional safety training. I pledge to attend CCB's Laboratory Safety Training and, in the interim, read CCB's Safety Manual in its entirety and understand its contents. I realize that the CCB Safety Manual does not contain comprehensive information regarding every hazard I will encounter in my research. I recognize that I must proactively inform myself about the hazards associated with every process I undertake and every substance I use in my research. I agree to follow the safety policies and principles described in the CCB Safety Manual while conducting research in the Department of CCB.

List of Available Training

CCB Laboratory Safety

Incoming graduate students receive this training during their orientation week in the Fall. Other researchers (e.g. post-docs, undergraduates, inter-departmental visitors) must attend one of the monthly training sessions. Topics discussed include emergency procedures, hazardous waste management, and chemical and physical hazards in the laboratory.

•CCB Laboratory Safety Training
www.chem.harvard.edu/safety/training.php

•ENV 201 Hazardous Waste
After receiving initial hazardous waste training as part of the lab safety training, Harvard laboratory researchers must complete a 'refresher' training annually. Visit the link below, sign in using your Harvard PIN, and select "FAS-Chemistry and Chemical Biology." Review all of the material presented and take the "challenge" at the end.
This online course must be repeated every year following CCB laboratory safety training.
https://www.uos.harvard.edu/cgi-bin/training/training_enter.pl

Subsequent to the general CCB Laboratory Safety training, researchers may need to take specialized safety training depending on the nature of their work. These specialty trainings are listed below.

Laser Safety

Required for researchers who wish to work with lasers (both class IIIB and IV) as well as laser microscopes. The training may be completed by attending a classroom lecture.

•RPO 102 Laser Safety (initial) for class IIIB and IV lasers
http://www.uos.harvard.edu/ehs/radiation/rad_training_laser.shtml

•RPO 201 Laser Safety (refresher)
This course must be repeated every 2 years.
http://www.uos.harvard.edu/ehs/radiation/rad_training_refresher.shtml

•RPO 104 Laser microscope safety training
please call 496-3797 for information about the training

Radiation Safety

Required for researchers who wish to work with radioactive materials or X-ray diffractometers.

•RPO 101 Radiation safety (initial)

Online initial radiation safety training
http://www.uos.harvard.edu/cgi-bin/radsafety/training/training_enter.pl

Initial radiation safety classroom schedule
http://www.uos.harvard.edu/ehs/radiation/rad_training_initial.shtml

•RPO 201 Radiation safety (refresher)
http://www.uos.harvard.edu/ehs/radiation/rad_training_refresher.shtml

•RPO 103 Irradiator Training (instructor–lead training)
Required for researchers who need to use or access an irradiator. Contact RPO at 617-496-3797 for scheduling information.

Biosafety/Bloodborne Pathogens Training
Required for all researchers who work or may come in contact with rDNA, infectious agents and/or established human cell lines, primary cells, or human blood tissue in a research or animal laboratory.

•LAB 103 Biosafety/Bloodborne Pathogens
http://www.uos.harvard.edu/trainingv2/course_schedulex.jsp

•HIS 103 BBP
This is the annual refresher required for LAB103
https://www.uos.harvard.edu/cgi-bin/training/training_enter.pl

Individuals taking LAB 103 will also get credit for LAB 110 NIH Recombinant DNA.

•LAB 110 NIH
Must be repeated online every three years after taking LAB 103 Biosafety/Blooborne Pathogens.
http://eureka.harvard.edu/Eureka/course_template/course.cfm?CourseID=435&categoryID=50

Use of Animals in Research and Teaching
The use of animals in research or teaching must be reviewed and approved by the Harvard University/Faculty of Arts and Sciences (HU/FAS) Standing Committee on the Use of Animals in Research and Teaching.
www.fas.harvard.edu/~research/greybook/animals.html

LISE/CNS Safety Cleanroom Training

•Lab 105 CNS/Lise Safety Orientation
Required of researchers who want to gain access to the CNS Facility (cleanroom and imaging suites). Contact Jim Reynolds at CNS (Reynolds@cns.fas.harvard.edu, 494-7411) for information on signing up for this course.

Shipping Regulated Biological Materials
Required for individuals involved in shipping biological material (e.g., BL2 or BL3 materials and recombinant microorganisms)

•LAB 104 Shipping Regulated Biological Materials (instructor–lead training)
This course must be repeated every 2 years. For more information, please contact Sid Paula, Biosafety Manager, at 495-2345 or spaula@mcb.harvard.edu.

Individuals completing LAB 104 will also get credit for LAB 112

Shipping Dry Ice
Required for individuals involved in shipping dry ice for material other than regulated biological.

•LAB 112 Shipping Dry Ice (instructor–lead training)
This course must be repeated every 2 years. For more information, please contact Sid Paula, Biosafety Manager, at 495-2345 or spaula@mcb.harvard.edu.

Individuals completing LAB 104 do not need to take LAB 112

Shipping Non-Regulated Biological Materials
Required for individuals involved in shipping only non-regulated biological material (e.g., plasmids, proteins, BL1 non-recombinant microorganisms, or fixed material).

•LAB 109 Shipping Non-Regulated Biologicals (instructor–lead training)
For more information, please contact Sid Paula, Biosafety Manager, at 495-2345 or spaula@mcb.harvard.edu.

Shipping Liquid Nitrogen
Required for individual involved in shipping liquid nitrogen

•LAB 106 Shipping Liquid Nitrogen (instructor-lead training)
This course must be repeated every 2 years. For more information, please contact Cathy Thomas, Health and Safety Officer, at 617-512-6813 or catherine_thomas@harvard.edu

Shipping Ethanol
Required of individuals involved in shipping ethanol in quantities less than 1.0 liter

•LAB 107 Shipping Ethanol (instructor-lead training)
This course must be repeated every 2 years. For more information, please contact Cathy Thomas, Health and Safety Officer, at 617-512-6813 or catherine_thomas@harvard.edu

Shipping Formaldehyde
Required for individuals involved in shipping solutions of less then 25% formaldehyde

•LAB 108 Shipping Formaldehyde (instructor-lead training)
This course must be repeated every 2 years. For more information, please contact Cathy Thomas, Health and Safety Officer, at 617-512-6813 or catherine_thomas@harvard.edu

Shipping Chemicals/Hazardous Materials
Required for individuals involved in shipping chemicals or other hazardous materials (e.g., lithium ion batteries) not identified in previous "shipping" selections.

This training is specific to the chemical or hazardous material and the quantity shipped. Laboratory personnel, except those in CCB, who need to ship these materials should contact Cynthia Blais, EHS Environmental Engineer, at 494-5591 or cynthia_blais@harvard.edu. Laboratory personnel in CCB should contact Chris Perry, Facilities and Operations Specialist, at 617-495-4279 or perry@chemistry.harvard.edu. In Chris Perry's absence, CCB personnel should contact Cathy Thomas, Health and Safety Officer, at 617-512-6813 or catherine_thomas@harvard.edu.

Respirators
Required of individuals who must, or choose to, wear any type of respirator.

•IHS 107 Respiratory Protection (instructor-lead training)
This course may be repeated annually. The use of a respirator must be evaluated by an EH&S representative in order to determine training requirements. Contact the EH&S representative in your department or contact Howard Herman-Haase, Senior Industrial Hygienist at 617-495-2186 or howard_herman-haase@harvard.edu.

Ergonomics
Optional for individuals who routinely use a computer more than 4 hours per day or 20 hours per week.

•IHS 104 Computer Ergonomics (instructor-lead training or online training)
Online computer workstation ergonomics training
https://www.uos.harvard.edu/cgi-bin/training/training_enter.pl

To arrange a classroom session contact Mary Streeto, Assistant Industrial Hygienist, at 617-496-0991 or mary_streeto@harvard.edu.

Fire Extinguishers
Required for individuals who regularly work with flammable liquids or solids.

•IHS 110 Fire Extinguishers (instructor-lead training)
Includes hands-on training. For more information regarding this training contact Mark Collins, Life Safety Officer, at 617-496-7168 or mark_collins@harvard.edu.

CCB organizes a fire extinguisher training session for incoming G1s every year.

5. Hazardous Chemicals Training

The policy described below is intended to ensure that researchers 1) are able to identify classes of hazardous substances and common examples therein and 2) receive documented training on the proper use of such substances.

A. Highly Hazardous Substances

All persons who wish to conduct experimental research in the Department of Chemistry and Chemical Biology must complete CCB's Laboratory Safety Training with the CCB Safety Officer (offered monthly and during orientation week for incoming G1s). General laboratory training sessions offered by other departments will not be considered adequate substitutes. Researchers will receive a personal training log during the training session. The training log is attached below and available online: http://www.chem.harvard.edu/safety/forms.php

The CCB Laboratory Safety Training session authorizes researchers to work with 3 categories of hazardous chemicals:

•*Highly Toxic Solids, Liquids, and Gases*
•*Highly Corrosive Compounds*
•*Stench Chemicals and Lachrymators*

Subsequent to the general CCB Laboratory Safety training, researchers may need to obtain specialized safety training depending on the nature of their work. Specialized training is required for the following categories of hazardous chemicals:

•*Pyrophoric Liquids*
•*Pyrophoric Solids*
•*Pyrophoric Gases*
•*Potentially Explosive Substances*

Prior to handling any substance within one of the above four classes, researchers must read the appropriate training material then demonstrate their mastery of the required skills and procedures to safely use the chemical while being observed by a CCB Trainer. Training is required regardless of prior experience at other institutions. Current researchers will be expected to complete training before March 31st, 2012.

Training shall be recorded on the "Personal Chemical Training Log" which will be visibly displayed in each researcher's work area (e.g. on their desk or on a fume hood sash) at all times. The trainee's personal training log will be signed and the training documented if the hazardous substance was handled in the prescribed manner. The CCB trainer may refrain from signing the personal training log and request another instance of training if the researcher is deemed insufficiently safe and/or adept at handling the hazardous chemical.

Completed training for a chemical in any of the seven hazard classes permits the careful, non-supervised, use of all chemicals in that class. Even after training has been completed, a nearby researcher must always be informed prior to and be present during the use of hazardous chemicals. This ensures that at least one person will be able to provide assistance or notify emergency personnel if an accident or injury does occur.

B. Responsibilities and Consequences for Policy Violations

Preventing workplace injuries and illnesses is the responsibility of every member of our campus community. Any researcher, administrator or faculty member may report policy violations. Documented noncompliance with the policy must be sent to the next higher-level member of the campus community for review and possible enforcement action.

Repeated violation or the failure to promptly address policy violations may result in the suspension of research privileges or more severe consequences.

First violation: The Science Safety Officer and next higher-level members of the campus community will be notified and a written warning will be sent to the individual responsible for the violation. If the appropriate training is lacking, a completed training session will be required in order to continue laboratory research.

Second violation: The individual responsible for the violation will be suspended from laboratory research. The Science Safety Officer and next higher-level members of the campus community will be notified and a written warning will be sent to the individual responsible for the violation. A consultation with the Science Safety Officer is required to reinstate research privileges.

Third violation: The individual responsible for the violation will be suspended from laboratory research. The Science Safety Officer and next higher-level members of the campus community will be notified and a written notice will be sent to the individual responsible for the violation. A petition before the Director of Laboratories, Science Safety Officer, and Faculty Chair will be required to determine whether or not research privileges may be reinstated. A report will be filed with the divisional dean's office to inform them of the safety policy violation.

C. Examples of Hazardous Substances

THE ABSENCE OF A SUBSTANCE OR COMBINATION OF SUBSTANCES FROM THIS POLICY CANNOT BE TAKEN TO IMPLY THAT NO HAZARD EXISTS.

This list is intentionally and necessarily abridged, thus it is not a comprehensive catalog of hazardous substances. Chemicals are assigned to one of eight hazard classes based on a subjective determination of a substance's primary hazard. For example, perchloric acid is listed as an explosive hazard although it is also a corrosive and toxic hazard.

Pyrophoric Liquids
Compounds that may spontaneously ignite upon exposure to oxygen, moisture, or both.

- neat trialkyl aluminums (e.g. Me_3Al) or alkylaluminums in solution
- *t*-butyllithium, *sec*-butyllithium and other alkyl- and arylyllithium reagents
- diisobutylaluminum hydride (DIBAL-H)
- Grignard reagents (alkyl- or arylmagnesium halides)
- borane•THF
- diethylzinc
- other substances of comparable properties

Pyrophoric Solids

Compounds that may spontaneously ignite upon exposure to oxygen, moisture, or both.

- alkali metals (Na, K, Rb, Cs)
- high purity, powdered metal hydrides (e.g. NaH, KH, $LiAlH_4$)
- Raney nickel, Palladium on carbon, and other spent catalysts that have been exposed to hydrogen
- Barium manganate
- other substances of comparable properties

Highly Corrosive Compounds

- acid chlorides
- halogens (F_2, Cl_2, Br_2)
- hydrofluoric acid
- nitric acid
- perchloric acid
- phenol
- piranha solution ($H_2SO_4 + H_2O_2$)
- strong organic acids (e.g. methane sulfonic acid)
- other substances of comparable properties

Highly Toxic Solids, Liquids, and Gases

- acrylamide
- alkyltins
- benzyl halides
- carbon tetrachloride
- dimethylcadmium
- dimethylmercury
- dimethylsulfate
- ethidium bromide
- formaldehyde
- hexamethylphosphoramide (HMPA)
- mercury salts
- methyl fluorosulfonate (magic methyl)
- methyl and trimethylsilyl triflate
- nickel carbonyl
- osmium tetroxide
- trimethylsilyl cyanide (TMS-CN)
- trimethylsilyl diazomethane (TMS-N_2)
- tetramethylammonium hydroxide
- other substances of comparable properties

Gases that possesses toxic, pyrophoric, corrosive, and/or flammable characteristics.

- carbon monoxide (CO)
- chlorine (Cl_2)
- hydrogen cyanide (HCN)
- phosphine (PH_3)
- germane (GeH_4)
- diborane (B_2H_6)
- silane (SiH_4)
- other substances of comparable properties

Stench Chemicals and Lachrymators

- butyric acid
- valeric acid
- selenium compounds
- tellurium compounds
- thiols (e.g. ethane thiol, hydrogen sulfide, bis(trimethylsilyl) sulfide)
- isonitriles
- alkyl phosphines
- alkyl halides
- other substances of comparable properties

Potentially Explosive Substances

Substances that undergo a chemical reaction that releases a large amount of heat and a rapidly expanding volume of gas.

- acetylenes
- azides
- diazonium salts and diazo compounds (e.g. diazomethane)
- nitrogen triiodide
- organic peroxides
- oxygen (liquid)
- ozone
- ozonides
- perchlorate salts, perchloric acid
- peroxyacids
- poly-nitro compounds (e.g. picric acid)
- triacetone triperoxide (TATP)
- other substances of comparable properties

Other explosive hazards

- Dess-Martin Periodinane precursor compound (IBX)
- liquid O_2 from N_2-cooled vacuum traps
- nitric acid + organic substances

Notes on Organic Peroxides
They are sensitive to shock, sparks, or other accidental ignition. Ethers such as tetrahydrofuran, ethyl ether, diisopropyl ether, especially when purified (i.e. not containing stabilizers, or inhibitors of autooxidation), may form high concentrations of peroxides within a short period of time when exposed to the air. Diisopropyl ether forms a crystalline bis-peroxide that explodes with deadly force. Also note: exposure of peroxidizable solvents to peroxides or other oxidants, especially in the air, can generate hazardous levels of peroxides. For example, a detonation has been reported from a hydroboration-alkaline peroxide oxidation conducted in THF (see: Meyers, A. I.; Schwartzman, S. *Tetrahedron Lett*. **1976**, *28*, 2417-2418). In this case, washing with sodium thiosulfate solution was insufficient to quench the peroxide formed. The homogeneous reductant dimethylsulfide is reported to be effective. Note also that all substances with weak carbon-hydrogen bonds should be considered as potentially peroxidizable and, therefore, hazardous.

Compounds Known to Autooxidize to Form Peroxides
These compounds can readily form peroxides when exposed to atmospheric oxygen and light:

•aldehydes.
•ethers, esp. cyclic ethers and those containing 1° and 2° alkyl groups.
•compounds containing benzylic hydrogens.
•compounds containing allylic hydrogens (C=C-CH), including most alkenes, vinyl, and vinylidene compounds.
•compounds containing a 3° C-H group (decalin and 2,5-dimethylhexane).

If you encounter a reagent that you suspect has peroxides present, contact the CCB Safety Office to have it removed. Do not handle the reagent yourself.

Peroxidizable Materials Labels
•Available in the CCB Mailroom and on the shelves near the Safety Office.
•Should be attached to all peroxides and peroxide forming materials in the laboratory.
•When storage time limit is nearly exceeded, label the peroxidizable substance as hazardous waste and dispose of it.

Peroxide Test Strips
•Purchase from VWR.com.
•Follow instructions to get semi-quantitative peroxide levels in ~15 seconds.
•Never distill an ether until it has been shown to be free of peroxides.

E. Prior Approval

The use of certain particularly hazardous substances requires the prior approval in writing from the relevant Faculty Advisor and a consultation with the Departmental Safety Officer before EVERY time the chemical is used. The use of these substances should be avoided altogether if at all possible. Faculty may add additional compounds and procedures to this list at their discretion.

Restricted chemicals requiring prior approval:

- dimethylmercury
- dimethylcadmium
- hydrofluoric acid (anhydrous)
- phosgene gas
- fluorine gas
- arsine gas
- diborane gas
- phosphine gas
- silane gas
- sodium potassium alloy (NaK)
- tetramethylammonium hydroxide

Researchers intending to undertake work with any of these substances must prepare a standard operating procedure (SOP) that contains the following elements:

1) Procedures for the safe storage and handling of the hazardous substance.

2) A detailed experimental procedure.

3) Plans detailing first aid in case of exposure and a response in case of a spill.

4) Procedures for the safe collection and management of hazardous waste.

5) The name(s) of the researcher(s) that will be working with the restricted substance, the location(s) of the designated area in which it will be used, the time and date of the operation, and the approximate amounts that will be used.

The SOP should be submitted to the relevant Faculty member for approval. A copy of the SOP signed by the Faculty member must be submitted to Mathieu Lalonde in the CCB Safety Office, after which a personal consultation must take place.

Any changes to a SOP must be submitted in writing to the Faculty member and the CCB Safety Office.

6. Working in the Laboratory

A. Working Alone in the Laboratory

Hazardous materials are found in every research laboratory. Researchers must recognize that risk of serious accident or injury in the laboratory is minimized by the presence of two or more people in the laboratory at all times. This ensures that at least one person will be able to provide assistance or notify emergency personnel if an accident or injury does occur.

Policy

- No researcher is permitted to carry-out a hazardous procedure alone in the laboratory. In order for a researcher to carry-out a hazardous procedure, the operator must notify one or more laboratory personnel of his/her intention to carry-out a hazardous procedure and the details of that operation. At least one person must be designated to remain within visible and audible distance throughout the duration of the hazardous operation. Working alone in the laboratory at anytime is strongly discouraged.

- Undergraduate students and minors are not permitted to work alone in the laboratory at any time.

Responsibility Of The Next-To-Last Person To Leave The Laboratory
The penultimate person to leave the laboratory has a responsibility to notify the remaining person that they are leaving. Thus no one should unexpectedly find himself or herself alone in the laboratory.

Responsibility Of The Last Person(s) To Leave The Laboratory
The last person(s) to leave a laboratory for the day should carry out the following procedures:

1) Walk through the laboratory, inspecting for unsafe conditions and injured persons.
2) Turn off all equipment and instrumentation that can be shut down without compromising safety or the outcome of experiments.
3) Ensure that all hood sashes are lowered.
4) Turn off the lights.
6) Close and lock all doors.
7) Visit a neighboring research group on the way out to check on colleagues there.

B. Minors Conducting Research or Working in the Laboratory

Persons under 18 years of age (minors) wishing to work or conduct research in a CCB laboratory must be sponsored by a member of the CCB Faculty. In no case are minors under 16 years of age permitted to work in a laboratory. A detailed policy description and associated documents are available online: www.chem.harvard.edu/safety/forms.php.

C. Non-Harvard Personnel Using Harvard Research Laboratory Facilities

Any individual without a Harvard Appointment (e.g. visiting scholar or collaborator) that intends to use CCB research laboratory facilities must read, sign, and submit the “risk and release” form posted online: www.chem.harvard.edu/safety/forms.php.

D. Music In The Laboratory

While in the laboratory researchers must be fully aware of their surroundings and the events taking place around them. The volume of sound may never be allowed to impede awareness of laboratory activities. The use of headphones is prohibited when performing chemical procedures and highly hazardous operations.

E. Good Lab Practices

Proactively make your work environment a safer place.

Housekeeping
•Keep your work area well-organized and clean.
•Avoid storing empty cardboard boxes in the lab.
•Keep needles capped or stuck into a silicone rubber stopper to prevent accidental pricks.

Food and Drink
Food and drink should not be present in the laboratory.

Solvent and Reagent Bottles
•Do not place chemical or solvent bottles on the floor where they can be kicked over.
•Transport solvent and acid bottles in rubber carriers.
•All 4L bottles of solvents or acids must be plastic or plastic-coated glass.
•Store bulk solvent containers (4L and above) in flammable material cabinets.

Label Everything
•Ensure that you clearly label all wash bottles, base baths, solvent bottles, and chemicals.
•Label research samples with chemical names and/or chemical structures and/or the relevant laboratory notebook number and page number.

Safety Equipment
•Know the location and operation of eye wash stations, safety showers, fire extinguishers, and emergency exits.
•Maintain unfettered access to safety equipment.

Running a Reaction in Lab
1) Plan ahead of time and read procedures in their entirety.
2) Understand the hazards of the chemicals and procedures you are about to employ.
3) Store and transport the chemicals properly.
3) Choose the appropriate equipment and reaction vessel sizes.
4) Use the appropriate Personal Protective Equipment (PPE).
5) Dispose of hazardous waste properly.

Reaction Scale
Hazards increase exponentially with scale.

a. Controlling reaction temperature can become very difficult.
b. Efficient stirring can be hard to accomplish.
c. Large volumes of chemicals contain a significant amount chemical potential.

d. Flammable solvent vapors, which are denser than air and tend to sink, are a fire hazard.
e. Reagents should be added dropwise with rapid stirring. Overcooling must be avoided, as a dangerous buildup of unreacted reagents may occur. When the reaction mixture is warmed, a violent reaction may result.
f. Scale-up should be avoided and should only carefully occur in stages if absolutely necessary. Reaction scale should increase by no more than a factor of 3 at each iteration. It is preferable to run a reaction at small scale several times to make a desired quantity.

Malodorous Compound Log
Before the use of any volatile, malodorous compounds (e.g. thiols), an entry must be made in the online "Stench Chemical Log." Access the Log and information on the use of stench chemicals at: www.chem.harvard.edu/safety/malodor.php

7. Personal Protective Equipment

A. Eye Protection

To minimize the risk of eye injury, eye protection must be worn at all times by all persons in the laboratory. This includes researchers, faculty, administrators, cleaning staff, and visitors. Depending on the circumstances and the substances being used, appropriate eye protection could consist of safety glasses, safety goggles, or a full-face shield.

Contact Lenses
The American Chemical Society Committee on Chemical Safety does not discourage wearing contact lenses in the laboratory as long as they are worn in conjunction with the appropriate eye protection.

Prescription Safety Glasses
Regular prescription eyeglasses are not acceptable safety glasses. They provide neither splash protection nor impact resistance. However, safety goggles or OTG ('over the glasses') safety glasses may be worn over prescription glasses in the laboratory.

Prescription safety glasses may be worn if they meet ANSI Z87.1-2003 impact resistance standards and have side shields. Because prescription safety glasses may not fit tightly against the forehead, safety goggles can be worn in conjunction with them to provide better splash protection.

The CCB Department will pay for the purchase of one pair of prescription safety glasses for graduate students, post-doctoral fellows, undergraduates, and research staff/associates performing work in a CCB research laboratory. Individuals are responsible for eye examinations, prescription changes, and for replacing lost or broken glasses at their own expense. The prescription safety glasses must:
- be obtained at the UHS Optical Shop.
- have side shields.
- have lenses and frames that meet ANSI Z87.1-2003 impact resistance standards.

To obtain prescription safety glasses, visit the CCB Finance Office with your Harvard ID to obtain a signed authorization form. Take the completed form and an eyeglass prescription to the UHS Optics Shop (617-495-5728) in Holyoke Center to order a pair of glasses. The current cost for standard prescription safety glasses is $200. Contact the CCB Safety Office (617-496-8285) for instructions should the cost exceed this amount (e.g. for custom frames, bifocal lenses).

Safety Goggles
Indirectly-vented goggles provide better eye protection than safety glasses and should be worn when working with lachrymators or when there is potential for a chemical splash or flying debris (e.g. when working with glassware under reduced or elevated pressure). Directly-vented goggles do not protect against chemical splashes. When working with the following substances, safety goggles should always be worn: concentrated acids, concentrated bases, corrosive chemicals, and any concentration of hydrofluoric acid.

safety glasses

OTG safety glasses

indirectly-vented safety goggles

Full-Face Shields and Safety Shields
Full-face shields provide additional protection to the face and neck and should be worn when conducting particularly hazardous operations. Safety glasses or goggles must be used in conjunction with a full-face shield. When possible, a safety shield should be placed around potentially dangerous experiments. Full-face and safety shields are available from the CCB Safety Office.

full-face shield

safety shield

Laser Goggles
Specialized eye protection is necessary when working with lasers. See the Harvard University Radiation Safety Manual (www.uos.harvard.edu/ehs/radiation/hazard_classification.shtml) for more information.

B. Gloves

Gloves that are resistant to the substances being worked with must be worn when in the laboratory. Disposable nitrile gloves, though useful in laboratory operations requiring manual dexterity, may not provide adequate protection against many chemicals. Although latex gloves effectively protect against pathogens, they offer little if any protection against most chemicals.

Glove manufacturers and other organizations have provided many "glove compatibility" and "glove selection" charts that are readily available online. All gloves should be inspected for discoloration, holes, and tears prior to use.

Glove References

For general chemical compatibility of glove materials:

- Lab Safety Supply: www.labsafety.com/refinfo/ezfacts/ezf191.htm
- Oklahoma State University: http://ehs.okstate.edu/MODULES/PPE/Gloves.htm
- Forsberg, K.; Mansdorf, S. Z. *Quick Selection Guide to Chemical Protective Clothing, 5th ed;* John Wiley & Sons: Hoboken, NJ, 2007.

For links to specific glove manufacturer's websites:
www.ehs.ufl.edu/Lab/CHP/gloves.htm

Gloves Outside of the Laboratory

Due to potential chemical contamination, which may not always be visible, researchers must remove gloves before leaving a laboratory and entering a hallway. Do not wear gloves while performing common tasks such as answering the phone, touching a door handle, typing on a keyboard, or operating an elevator.

If you have a contaminated object or chemical to transport you may:

- Place the object or substance in a clean container (preferably with a lid) or on a cart, remove your gloves, then transport.
- Obtain the assistance of a colleague to open doors for you.
- Remove a single glove. Your bare hand can operate door handles, while the gloved hand can carry the object.

Cryo/Temperature-Resistant Gloves

When working with cryogenic liquids and dry ice, waterproof cryo-gloves (e.g. Cryo-Gloves Low-Temperature Gloves from Tempshield) should be worn to protect the user from skin burns. Similarly, when working with hot objects, temperature resistant (e.g. autoclave gloves) gloves should be worn.

Cut Resistant Gloves

Researchers should wear cut resistant gloves when working with sharp objects, blades, and when adding or removing tubing from glassware.

C. Laboratory Attire

Clothing

Skin is less susceptible to chemical exposure when properly covered. As such, the use of full-legged pants and a laboratory coat or apron are necessary in the laboratory when working with chemicals. Shorts are not proper laboratory attire and should not be worn when working with chemicals.

Shoes

Sandals, flip-flops, and other open-toed shoes expose the feet to chemicals as well as sharp objects and are not permitted.

Lab Coats

CCB offers a department-wide lab coat service. Researchers can help themselves to the lab coats found on racks in various areas throughout CCB. If a lab coat of the proper size cannot be found on a particular rack, researchers should not hesitate to take a lab coat from another group's rack and inform Mike Paterno's office such that the lab coat order can be modified accordingly. The plastic shell covering the lab coats can be placed in a recycling bin whereas the hangars should remain on the rack for reuse or recycling.

Lab coats should be worn for one week and then placed in the laundry bin next to the rack. Lab coats in these bins will be laundered on a weekly basis and placed back on the racks.

Flame resistant Nomex lab coats are currently available in limited quantities and can be found outside the safety office. These blue flame resistant lab coats should be employed during the handling of pyrophoric reagents.

Lab coats are to be worn at all times while conducting experiments. Lab coats should remain in the laboratory and should never be worn in common areas (e.g., computer rooms, conference rooms, the NMR facility, cafeteria, etc…).

D. Respirators

The ideal scenario is one where engineering controls (e.g. containment, ventilation) make the use of respirators unnecessary. However, researchers who believe using a respirator is appropriate for their specific laboratory endeavors should contact the CCB Safety Office to arrange for a work process evaluation performed in coordination with EH&S. The researcher will also be required to take the IHS 107 Respiratory Protection training.

With the exception of voluntary users of dust masks, respirator users must be medically evaluated by a physician or other licensed health care professional prior to using a respirator. Though exempt from medical evaluations, voluntary users of dust masks must be provided a copy of an OSHA-required information sheet prior to wearing a respirator:
www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9784

For more information on respirators visit: www.uos.harvard.edu/ehs/ih/rpp_selection.shtml

8. Safety Equipment

Eye Wash and Safety Showers

•Tissue damage begins immediately when a corrosive chemical comes in contact with the eyes or skin.
•The affected area must be irrigated immediately with copious amounts of water for a minimum of 15 minutes.
•Contaminated clothing must be removed; spare clothing is available in the lockers outside of the CCB Safety Office
•Lab coworkers are encouraged to guide the victim of a chemical splash to the appropriate emergency shower. Multiple copies of the relevant chemical material safety data sheet (MSDS) should be printed out and presented to emergency responders. Affected lab workers should obtain medical assistance if necessary.
•Bathing showers should not be used instead of an emergency shower.

Fume Hoods

•Set-up work 6” behind the plane of a fume hood sash.
•Never put your head inside of a fume hood.
•Do not clutter or use a fume hood for storage.
•Face velocity should be in 80-110 fpm range, depending on the type of fume hood.
•Immediately contact CCB Facilities or the Operations Center if a fume hood is not functioning properly.
•Work with the fume hood sash in the lowest possible position.
•Keep the sash closed when not working in the fume hood. It is safer and can offer tremendous energy savings.

9. Health Hazards

Categories

•Irritants (e.g. ammonia)
•Sensitizers (e.g. formaldehyde)
•Corrosives (e.g. sulfuric acid)
•Carcinogens (e.g. benzene)
•Target Organ Effects (e.g. methanol)
•Reproductive Health Effects (e.g. carbon disulfide)
•Acutely Toxic (e.g. hydrogen cyanide)
•Physical (e.g. explosives, machine shops)

Routes of Exposure

•Inhalation
•Skin and Eye Contact
•Ingestion
•Injection
•Combination Routes

Contact poisons

Solvents such as acetone and dimethylsulfoxide render the skin permeable to many compounds that otherwise would not be absorbed. Thus, solutions of toxic compounds in these solvents represent a significant hazard.

***Acute Exposure*:** short duration of exposure, short latency period for symptoms (e.g. hydrogen cyanide). Often case- and animal-studies exist, which are used to derive short-term human exposure limits.

***Chronic Exposure*:** repeated or long duration chemical exposures, long latency period for symptoms (e.g. dust inhalation). Poor clinical data often exists. Researchers must minimize their exposure to all research chemicals.

Exposure Limits*

Occupational Safety and Health Administration (OSHA)
•Permissible Exposure Limits (PELs)
American Conference of Governmental Industrial Hygienists (ACGIH)
•8 hour Time Weighted Average (TWA)
•Short Term Exposure Limit (STEL)
National Institute for Occupational Safety and Health (NIOSH)
•Immediate Danger to Life and Health (IDLH)

*Many chemicals do not have established exposure limits.

10. Fire Safety

A. Definitions

Flammable substances: solid, liquid, or gaseous materials that ignite easily and burn rapidly when exposed to an ignition source.

Flash point: the lowest temperature at which a liquid has sufficient vapor pressure to form an ignitable mixture with air near the surface of the liquid. All common organic solvents have flash points well below room temperature.
Vapor density: the relative weight of a gas or vapor compared to air, which has an arbitrary value of one. Common organic solvents possess a vapor density that is > 1, thus vapors will generally sink in air.

Explosive limits: the limiting concentrations in air necessary for a gas to ignite or explode.
•Lower Explosive Limit (LEL)
•Upper Explosive Limit (UEL)

B. Laboratory Fire Prevention

•Minimize the use of open flames: Bunsen burners should not be hooked up to a fuel supply such as natural by using tygon tubing. Thick rubber tubing should be employed instead. Bunsen burners and propane torches must be employed in areas that are free of chemicals and flammable clutter.
•Be aware of sparking sources in the laboratory: heat guns, variacs, electric motors, and frayed electrical cords.

•Ovens must be elevated from the floor to minimize the risk of setting off a fire in the event of a solvent spill.
•Minimize the volume of flammable solvent being stored in a particular laboratory space at any given moment. Place smaller solvent orders more frequently.
•Store bulk solvents (containers greater than or equal to 4 L) in flammable material cabinets.

C. Fires in the Laboratory

If a fire occurs, researchers do not have to attempt to extinguish it. The default action should be to call 9-1-1 and pull the building fire alarm. A back-up call to the Operations Center (5-5560) will assist with Fire Department coordination and response.

The Harvard EH&S Fire Safety website: www.uos.harvard.edu/ehs/fire_safety

In the event of a fire:
Rescue or **R**elocate
Alert
Confine fire by closing doors in the area
Evacuate or **E**xtinguish if trained and it is safe to do so

Fire Extinguisher Classes
A = ordinary combustibles (e.g. wood and paper)
B = flammable liquids (e.g. gasoline and oil)
C = electrically energized fires
D = combustible metals (e.g. potassium, magnesium)

The CCB Dept. has multiclass (i.e. some combination of A, B, C) fire extinguishers throughout the laboratories. Class D extinguishers are located in laboratories that work with combustible metals.

To use a fire extinguisher:
Pull the pin
Aim at base of fire
Squeeze handle
Spray from side to side

Researchers should never attempt to extinguish a large fire or jeopardize their own health or safety to fight a fire.

Emergency Evacuation
•Know 2 ways out.
•Check floor plans and maps.
•Use stairs.
•Assist disabled persons to a stairwell and inform the Fire Dept. of their location.
•Proceed to designated meeting site.
•Communicate helpful information to the Fire Department.
•Do not re-enter until advised by Fire Department.

11. Chemical Spills

Read the CCB Chemical Spill Policy at: www.chem.harvard.edu/safety/labsafety.php

The hazards resulting from a chemical spill depend on variables that include the spilled material's chemical and physical properties, location, and quantity. Researchers must use knowledge and experience in evaluating when a chemical spill can be addressed by local researchers (minor spills) and when outside help is necessary (major spills).

Major Spills

- Someone has been injured.
- A fire or explosion has occurred or is likely to occur.
- The volume of spilled material is large.
- The type or quantity of chemical released poses an immediate health risk.
- There is an impact on public spaces or spaces adjacent to the area where the spill occurred.
- You and/or your lab-mates are unable to address the spill without assistance.

If the accident involves personal injury or chemical contamination:

1) Attend to the injured or contaminated person and move them to safety if it is safe to do so.
2) Locate nearest eyewash or safety shower, remove any contaminated clothing, and thoroughly flush all areas of the body contaminated by chemicals for 15 minutes.
3) Administer first aid as appropriate (e.g. calcium gluconate for hydrofluoric acid exposures, amyl nitrate ampoules for hydrogen cyanide exposures) and seek medical attention (immediately call **911** with a follow-up call to the Operations Center at **5-5560**).
4) Print out Material Safety Data Sheets for chemicals involved in the exposure and ensure the attending Fire Department/medical personnel receive them.
5) As soon as practically possible, report the injury to your supervisor and the CCB Safety Office.

To evacuate the area and obtain outside help:

1) Alert nearby coworkers and evacuate to a safe distance.
2) If a fire, explosion, or toxicity hazard exists, pull the fire alarm and follow building evacuation procedures. A person familiar with the situation should greet firefighters on Oxford Street when they arrive and provide the relevant MSDS.
3) If you have not pulled the fire alarm, close doors to affected areas and prevent re-entry. Put up Do Not Enter signs or barrier tape (available outside CCB Safety Office).
4) Call the Operations Center at **5-5560** to obtain assistance (they will contact EH&S, a hazardous waste vendor, and/or the Fire Department). Call the CCB Safety Office at **6-8285** to inform them of the situation.
5) Do not re-enter the area until instructed to do so by the Fire Department or emergency response personnel.

Minor Spills

A spill may be considered "minor" if the assessment reveals the spill to present relatively low hazards and no one has been injured or chemically contaminated.

1) Alert nearby coworkers of the spill and request their help (if they are qualified). Contact the CCB Safety Office at **6-8285** for additional assistance.
2) Isolate the area. Close lab doors and evacuate the immediate area if necessary.

3) Remove ignition sources (e.g. no open flames, turn off hot plates and heat guns).
4) If the spill *is not* in a laboratory with strong ventilation (e.g. fume hoods present and working), establish exhaust ventilation to the outside (e.g. open windows, use fans to force air outside).
5) Consult MSDS for hazard information and cleanup instructions.
6) Locate applicable spill kit.
6) Don appropriate personal protective equipment. At a minimum this should consist of safety glasses, gloves, and a lab coat.
7) Control the source and confine the spill using spill kit supplies.
8) Absorb/neutralize free liquid using appropriate absorbent. Sweep solid material into a plastic dustpan.
9) Place debris in an appropriate container (e.g. wide mouth bottle or 5 gallon waste bucket), close the container, attach a Hazardous Waste Tag, and place in a Hazardous Waste Accumulation Cabinet or a fume hood if ventilation is needed.
10) Notify the CCB Safety Office of all spill incident.

Spills Requiring Special Procedures

Call 911 and/or the Operations Center as appropriate

•Flammable metals (sodium, lithium, potassium, magnesium)
•White or yellow phosphorus
•Bromine
•Hydrofluoric acid
•Mercury
•All radioactive materials
•Biological/Blood

12. Physical Hazards

Compressed Gas Cylinders

• Cylinders must always be secured with chains as they pose a mechanical and a chemical hazard.
• The rupture of a high-pressure cylinder or valve results in a high velocity projectile. Thus, cylinders must always be securely lashed to a stationary object.
• A gas cylinder cart with cylinder restraints must be used for transport.
• The gas itself may be reactive, flammable, toxic, or capable of causing asphyxiation.
• Use the appropriate regulator to prevent mixing of incompatible gases.

See Appendix D for the safe use of toxic, pyrophoric, corrosive, and flammable gases.

Cryogens

•Boiling point of liquid N_2 = -196 °C and Ar = -186 °C
•Tissue damage can result from the extreme cold.
•Enormous pressure can result from the warming of a cryogenic liquid: 1 volume of liquid N_2 = 694 volumes of gaseous N_2 at 1 atm and 20 ºC.
•If sufficient cryogenic liquid is vaporized in confined or poorly ventilated areas, the expanding gas will displace oxygen, presenting an asphyxiation hazard.

•Use vacuum insulated dewars and the appropriate cryo-glove protection.

High Pressure Reactions (above 1 atm)

•Danger of explosion.
•Use only thick-walled glass sealed reaction tubes or steel pressure reactors designed for high-pressure work.
•Use a lab safety shield.

Vacuum Work

•Hazard does not depend on magnitude of vacuum as almost all vacuum pressure is relatively low with respect to external pressure of 1 atm.
•Star cracks and imperfections in glassware may lead to a vacuum implosion. Shards of flying glass and exposure to the chemical formerly contained in the vessel may result.
•Only thick-walled glassware designed for vacuum work should be placed under vacuum. Never place volumetric glassware under vacuum.

Distillations

•Inspect glass for cracks before a vacuum distillation.
•Use only glassware appropriate for vacuum distillation (no volumetric flasks).
•Do not heat above the liquid level because the vapors can superheat.
•At the end of a distillation, never release air into a hot distillation apparatus. The hot organic vapors could ignite upon introduction of oxygen. Allow the apparatus to cool or release to an inert gas such as nitrogen or argon.
•Tubing that delivers water for cooling should be clamped down in order to prevent leaks that may potentially flood the fume hood and surrounding area.

UV Lamp Radiation

•Hg lamps used for photochemical reactions can cause severe eye and skin damage.
•Ensure that non-UV transmissive eye protection is worn, skin is covered, that the set-up is contained in a lamp box where no radiation escapes, and that the set-up is well labeled when in use.
•Lamps often generate a tremendous amount of heat, thus ensure proper cooling is provided when necessary, that it is fail-safe, and that no solvent vapors reach the apparatus.

Electrical Hazards

•Check all electrical cords for fraying or exposed wires. Contact CCB Facilities to repair damaged cords.
•Plug heating mantles into variacs NOT a wall outlet.
•Consider how a loss of electricity will affect any reaction or equipment that you set-up and take precautionary measures.
•Contact the CCB Facilities Office whenever changes to electrical wiring or outlets are needed.

Magnetic Fields

•NMR instruments have very powerful superconducting electromagnets.
•No one with a pacemaker may approach.
•Objects made of ferromagnetic materials can accelerate toward an NMR magnet.
•Credit, debit, ATM, and ID cards will be erased by a strong magnetic field.

Lifting, Slipping, Tripping, Cutting

•Most common laboratory injuries: strained back from lifting, cut flesh from broken glass, an injury from slipping or tripping.

•Use care and correct laboratory procedures. Get help when lifting heavy objects and use proper lifting techniques.

•Keep your laboratory surroundings organized and uncluttered.

13. Chemical Storage

•Store large volume containers (4L and larger) of flammable solvents inside of a flammable materials cabinet.

•Only “flammable material storage refrigerators/freezers” (with no internal sparking sources) may be used to cool chemicals.

•Segregate incompatible chemicals (i.e. acids and bases, oxidizing and reducing agents, nitric acid and organic chemicals).

•Ensure all chemical containers are properly labeled.

•Use acid cabinets when appropriate.

Secondary Containment Trays

•Use to keep incompatible chemicals separated. Must be able to accommodate the volume of the largest container held.

•Reagent bottles stored on shelves and in refrigerators/freezers must reside in plastic secondary containment trays. This prevents bottles from toppling and provides containment for spills and leaks.

•All hazardous waste containers must reside in secondary containment.

14. Shipping of Hazardous Materials

Read the CCB policy at: www.chem.harvard.edu/safety/hazmat_shipping.php

The shipment of hazardous materials and/or dangerous goods must conform to the many regulations stipulated by the US Department of Transportation (DOT) (http://hazmat.dot.gov/index.html) (ground transport) and the International Air Transport Association (IATA) (www.iata.org) (air transport). The DOT Hazardous Materials Regulations are detailed in 49 CFR parts 100-185 (www.myregs.com/dotrspa) and the IATA regulations are published in *Dangerous Goods Regulations*, 48th ed, 2007.

These regulations must be followed by a researcher wishing to:
1. ship a research sample for testing.
2. send hazardous materials to a collaborator in industry or at another university.
3. return a hazardous material to the manufacturer.
4. ship a sample packaged in dry ice.

The regulations are complex, thus Chris Perry in Shipping and Receiving should be contacted for assistance with the shipment of hazardous materials from CCB.

15. Hazardous Waste

www.uos.harvard.edu/ehs/environmental/hazardous_waste.shtml

The following may never be poured into a laboratory sink or drain:

- Acetone or alcohols
- Volatile Organic Compounds (e.g. organic solvents)
- Organic chemicals
- Mercury and other heavy metals
- Strong acids (solutions with pH<5.5)
- Strong Bases (solutions with pH>12.0)
- Infectious/biological waste
- Radioactive waste (unless under maximum radiation levels in an approved sink)
- Malodorous substances

Hazardous Waste Container Labeling

All hazardous waste containers must be labeled from the time that waste is first placed into them. Waste labels are available from the CCB Mailroom and Safety Office. Labels must include:

- the chemical name in words (e.g. sulfuric acid).
- the associated hazards of the waste (e.g. corrosive).

The date should only be affixed onto the label once the container becomes full and/or is ready for disposal.

Container Closure

Hazardous waste containers must be closed at all times, except when waste is being added. Regulations DO NOT permit open funnels in waste containers. "Eco-Funnels" may be fitted to hazardous waste containers to make waste addition and container closure convenient.

Container Storage

- Hazardous waste must be stored in a designated "Satellite Accumulation Area," (e.g. fume hood, cabinet).
- Containers must reside in secondary containment trays. Hazardous waste and virgin chemicals (reagents to be used) must not be stored in the same secondary container.
- Satellite Accumulation Areas are inspected weekly by Group Safety Officers for container compliance.
- Containers must be removed from the Satellite Area within three days after the container becomes filled and the label is dated.

Hazardous Waste Reactivity

- Incompatible chemicals (e.g. nitric acid and organics, acids and bases) must be segregated.
- If two waste containers contain incompatible chemicals, they must be stored in separate secondary containers.
- Vented caps (available outside of the CCB Safety Office) must be used on any waste bottle containing piranha solution (sulfuric acid + hydrogen peroxide) or nitric acid. This will help ensure that pressure build-up from off-gassing is safely vented.

The Hazardous Waste Life Cycle

1) A researcher generates hazardous waste and transfers it to a waste container located in the *Satellite Accumulation Area* near the point of generation.
2) A Group Safety Officer conducts a weekly inspection of all waste containers.
3) A hazardous waste vendor conducts quarterly inspections of all waste containers.
4) The waste container is filled, dated, and placed in the *Mini-Main Accumulation Area*.
5) Triumvirate Environmental picks up the Mini-Main waste weekly.
6) The waste is temporarily staged in Naito Lab.
7) The waste is shipped to a hazardous waste disposal plant where it is treated, incinerated, fuel blended, or otherwise properly disposed of.

16. Nanomaterials

- Nanomaterials or nanoparticles are human engineered particles with at least one dimension in the range of 1 to 100 nanometers.
- Understanding of the health effects of nanomaterials is limited. Nevertheless, there is a body of evidence demonstrating that nanoparticles are more toxic than larger particles of the same substance. The toxicity is related to the compositions, size, surface area, and surface reactivity of the particles.
- Given the uncertainty of the research on the health effects, it is prudent to take precautions when working with these substances.
- EH&S can assist with recommended work practices and procedures.
- Contact the CCB Safety Office to arrange for an EH&S visit to add nanomaterials work to the University's inventory.

Visit the link below for additional information and resources:
www.uos.harvard.edu/ehs/ih/nanotech.shtml

17. Reactive Hazards

See the Use of Hazardous Chemicals section below for more comprehensive information about reactive hazards.

Avoid Quenching Reactive Chemicals

Researchers should avoid quenching unwanted reactive chemicals if at all possible (e.g. an old bottle of butyllithium or sodium hydride). The act of quenching is time consuming and often leads to unintended fires. Simply affix hazardous waste tags to unwanted reactive bottles and have the hazardous waste vendor remove them as waste.

Catalytic Hydrogenation

- Do not add more catalyst to a hydrogen atmosphere, as the very fine carbon particles may combust. First, flush the reaction with an inert gas, add catalyst, and then reintroduce hydrogen.
- Keep used catalyst moist when disposing of it.

Incompatible Chemicals

•Consult reference materials for a partial list of incompatible chemicals:
http://msds.chem.ox.ac.uk/incompatibles.html
www.biosci.ohio-state.edu/safety/safety/IncompatibleChemicals.htm

•Do not store incompatible (i.e. reactive) groups of chemicals near each other. For example, store acids separately from bases and segregate nitric acid from organics.

18. Guidance on the Use of Highly Hazardous Chemicals

The appendices that follow provide guidance on the proper use of highly hazardous substances.

Appendix A: Chemical Hazard Information Sources

I. Introduction

Both researchers and faculty advisors must thoroughly investigate the hazards of any compound they work with or intend to synthesize. When working with substances that may be particularly hazardous (e.g. explosive, pyrophoric, toxic), even greater investigative diligence must occur.

The resources described below are intended to be a starting point for the exploration of the properties of a chemical substance. An investigation should in no way be limited to the sources described herein.

II. General Sources of Information

A. Harvard Websites

CCB Safety: www.chem.harvard.edu/safety/index.php
Harvard Environmental Health and Safety: www.uos.harvard.edu/ehs
Harvard SEAS: http://safety.seas.harvard.edu

B. Material Data Safety Sheets (MSDS)

A material safety data sheet (MSDS) is a form containing basic information regarding the chemical and physical properties of a substance and guidelines on how to safely use it. MSDS may be obtained from:

- databases available at www.uos.harvard.edu/ehs/msds
- manufacturer websites.
- internet search engines (e.g. enter "acetone msds" as a search query).

C. Laboratory Safety Texts

The texts below may be found in the CCB Library and Safety Office:

Accident Prevention for College and University Students, 7th ed.; Safety In Academic Chemistry Laboratories; American Chemical Society, Washington, D.C., 2003; Vol. 1.

CRC Handbook of Laboratory Safety, 5th ed.; Furr, A. K., Ed.; CRC Press: New York, 2000.

Handbook of Chemical Health and Safety; Alaimo, R. J., Ed.; Oxford University Press: New York, 2001.

Prudent Practices in the Laboratory; National Academy Press: Washington, D.C, 1995.

Urben, P.G., ed. *Bretherick's Handbook of Reactive Chemical Hazards*; 6th ed.; Butterworth Heinemann: Boston, 1999.

D. Internet Searches

As an increasingly large amount of laboratory safety information is being placed on the Internet, an Internet search for the compound or procedure of concern should be conducted. Although the information collected must be critically evaluated, useful content is often easily accessible.

Possible search strategies:
- Google search of "chemical_name"
- Google search of "chemical_name safety"
- Google search of "use of chemical_name"
- Search of "chemical_name" within Wikipedia.com

Among the types of information you may find are:
- Wikipedia entries
- journal articles
- patents
- MSDS websites
- University health and safety websites
- medical websites
- scientific websites

III. Specialized Sources of Information

A. The Chemical Literature

The ability to efficiently find and extract useful information from the chemical literature is an essential part of any experimental endeavor. Both safety information and proper experimental protocols for working with hazardous substances have been published within the chemical literature (i.e. journals, monographs, reviews, reference works). While searching for 'literature precedent' has existed as long as chemical publications have, digital archiving and electronic data retrieval methods have revolutionized the process.

The Chemistry Department Library web page (www.chem.harvard.edu/library) is a portal to a variety of useful electronic resources. Even more resources can be accessed from the E-Research @ Harvard Libraries website (http://eresearch.lib.harvard.edu/V). You will be prompted to enter your Harvard ID and PIN when attempting to access most of these electronic resources.

Scientific Databases, Reference Volumes, and Encyclopedias
A growing list of databases, reference volumes, and encyclopedias are available via the CCB Library website. Among these are the CRC Handbook of Chemistry and Physics, Encyclopedia of Reagents for Organic Synthesis (EROS), Houben-Weyl Methods of Organic Chemistry, Science Citation Index, and Hazmat Navigator.

Electronic Journals
Almost all scientific journals are now available online and most have digitized all of their past issues so that comprehensive content is now available electronically. Scores of chemistry and chemistry–related journals can be accessed directly from the CCB Library website.

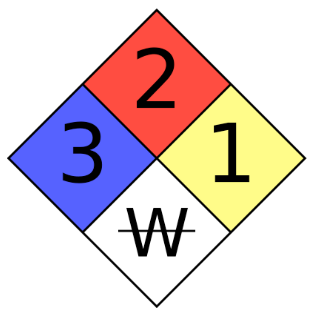
SciFinder Scholar
SciFinder Scholar is a "a research discovery tool that allows college students and faculty to access a wide diversity of research from many scientific disciplines, including biomedical sciences, chemistry, engineering, materials science, agricultural science, and more."

SciFinder Scholar has moved to a web-based interface and the client described above will no longer be updated. Instructions on how to access this tool can be found here: http://www.chem.harvard.edu/library/infosoft.php

Reaxys
Reaxys is a single architecture for convenient searching of chemistry data and combines the power of the CrossFire Beilstein, Gmelin and Patent Chemistry databases:
https://www.reaxys.com

B. National Fire Protection Association (NFPA) 704 Hazard Identification Ratings

The NFPA hazard labeling system consists of a multicolored diamond broken into four sections: health (blue), fire (red), reactivity (yellow), and special hazards (white). Numbers in the three colored sections range from 0 (least hazard) to 4 (most severe hazard).



NFPA ratings can be found on most Material Safety Data Sheets and via ChemTracker (see below). The NFPA ratings for some commonly encountered hazardous chemicals are shown below.

Select NFPA Hazard Identification Ratings

Chemical	Fire	Health	Reactivity
m-CPBA	0	3	3
t-BuLi	4	3	3
DIBAl-H	4	3	3
NaH 95%	3	3	2
diphosgene	0	3	2
BH_3•THF	3	2	3
$HClO_4$	0	3	3
NaN_3	0	4	2
$Fe(CO)_5$	3	3	1
HO_3SCF_3	0	3	0
Cl_2	0	3	3
$(CF_3SO_2)_2O$	0	3	2

A larger list of NFPA ratings can be found here:
www.nmsu.edu/safety/programs/chem_safety/NFPA-ratingA-C.htm

Flammability	
4	Will rapidly or completely vaporize at normal atmospheric pressure and temperature, or is readily dispersed in air and will burn readily (e.g., propane). Flash point below 23°C (73°F)
3	Liquids and solids that can be ignited under almost all ambient temperature conditions (e.g., gasoline). Flash point between 23°C (73°F) and 38°C (100°F)
2	Must be moderately heated or exposed to relatively high ambient temperature before ignition can occur (e.g., diesel fuel). Flash point between 38°C (100°F) and 93°C (200°F)
1	Must be heated before ignition can occur (e.g., soybean oil). Flash point over 93°C (200°F)
0	Will not burn (e.g., water)

Health	
4	Very short exposure could cause death or major residual injury (e.g., hydrogen cyanide)
3	Short exposure could cause serious temporary or moderate residual injury (e.g., chlorine gas)
2	Intense or continued but not chronic exposure could cause temporary incapacitation or possible residual injury (e.g., ethyl ether)
1	Exposure would cause irritation with only minor residual injury (e.g., Acetone)
0	Poses no health hazard, no precautions necessary. (e.g., lanolin)

Instability/Reactivity	
4	Readily capable of detonation or explosive decomposition at normal temperatures and pressures (e.g., nitroglycerine, RDX)
3	Capable of detonation or explosive decomposition but requires a strong initiating source, must be heated under confinement before initiation, reacts explosively with water, or will detonate if severely shocked (e.g. ammonium nitrate)
2	Undergoes violent chemical change at elevated temperatures and pressures, reacts violently with water, or may form explosive mixtures with water (e.g., phosphorus, potassium, sodium)
1	Normally stable, but can become unstable at elevated temperatures and pressures (e.g. Sodium hydroxide)
0	Normally stable, even under fire exposure conditions, and is not reactive with water (e.g. helium)

Be aware that many substances not possessing a NFPA hazard rating of 4 are quite dangerous, even deadly. For example, neither dimethyl mercury (fire 0, health 3, reactivity 0), nor methyl fluorosulfonate [i.e. magic methyl] (fire 2, health 3, reactivity 0) have a hazard rating of 4.

C. Hazmat Navigator

Hazmat Navigator is an excellent online resource for chemical safety information. Detailed chemical reactivity, toxicity, and handling information is available for several thousand chemicals.

The edited content in this resource is drawn from *Bretherick's Handbook of Reactive Chemical Hazards*, *Sittig's Handbook of Toxic and Hazardous Chemicals and Carcinogens*, *Sittig's Handbook of Pesticides and Agricultural Chemicals*, *Encyclopedia of Toxicology, and Fire Protection Guide to Hazardous Materials*.

Hazmat Navigator can be accessed by visiting the CCB Library Database and E-Resources page: www.chem.harvard.edu/library/databases.php

D. Toxicology Searches

There are several useful online databases that have a great depth of toxicology information on a limited number of chemicals.

Agency for Toxic Substances and Disease Registry: www.atsdr.cdc.gov

TOXNET: www.toxnet.nlm.nih.gov

Appendix B: Working With Potentially Explosive Reagents

This policy provides general guidance on the safe use of potentially explosive reagents. Researchers must thoroughly investigate the specific properties of the substance(s) they are working with and modify this guidance as appropriate.

I. Definition

"An explosive is any chemical compound, or mechanical mixture that, when subjected to heat, impact, friction, detonation, or other suitable initiation, undergoes rapid chemical change, evolving large volumes of highly-heated gases that exert pressure on the surrounding medium."[1]

II. Guidance On Working With Potentially Explosive Substances

A. Information Collection (see Appendix A)

1) Both researchers and faculty advisors must thoroughly investigate the hazards of any potentially explosive chemical they plan to work with or synthesize.

2) Some particularly hazardous substances will not have a significant presence in chemical journals due to the challenges and/or dangers inherent in working with them. The consultation of laboratory safety references in these cases is imperative. The following references should be consulted when working with any potentially explosive compound:

   Hazmat Navigator, accessed by visiting the CCB Library Database and E-Resources page: www.chem.harvard.edu/library/databases.php

   Urben, P.G., ed. *Bretherick's Handbook of Reactive Chemical Hazards*; 6th ed.; Butterworth Heinemann: Boston, 1999. (Copies of this reference are available in the CCB Library and the CCB Safety Office.)

3) As an increasingly large amount of laboratory safety information is being placed online, an Internet search for the compound or procedure of concern should be conducted. Although the information collected must be critically evaluated, useful content is often easily accessible.

B. Alternative Substances

1) The use of a potentially explosive substance should be avoided if a safer alternative is available.

C. Notification

1) Researchers must verbally notify their labmates of the substances they intend to use and the hazards associated with them.
2) The Faculty Advisor must be notified prior to the use of especially hazardous substances.

D. Personal Protective Equipment

1) At a minimum, the following must be worn: safety goggles, full-face shield, NOMEX laboratory coat, and sturdy protective gloves.

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[1] *Prudent Practices in the Laboratory* (National Academy Press: Washington, D.C, 1995), p. 54.

E. Laboratory Procedures

1) Never work alone or after hours with a potentially explosive substance.
2) Work must be done within a fume hood. A laboratory safety shield must be placed around the reaction and/or reagents of concern.
3) The initial preparation of the substance must be made on the smallest scale possible. Scale-up should be avoided and should only carefully occur in stages if absolutely necessary. It is preferable to run a reaction at small scale several times to make a desired quantity.
4) For exothermic reactions, reagents should be added dropwise with rapid stirring. Overcooling must be avoided, as a dangerous buildup of unreacted reagents may occur and lead to a violent reaction upon warming.
5) Researchers should avoid concentrating any potentially explosive substance. Some substances can be set off by the action of their own crystal formation. The substance should remain 'wet' and not be allowed to become 'dry.'
6) The substance must never be scraped with a spatula. Friction from ground glass joints may initiate an explosion.
7) Plans for the safe destruction or proper disposal of unused/unreacted material must be made ahead of time.

III. References

Prudent Practices in the Laboratory; National Academy Press: Washington, D.C, 1995.

Urben, P.G., ed. *Bretherick's Handbook of Reactive Chemical Hazards*; 6th ed.; Butterworth Heinemann: Boston, 1999.

Handbook of Chemical Health and Safety; Alaimo, R. J., Ed.; Oxford University Press: New York, 2001. Chapter 59, p. 404.

Appendix C: General Procedure for the Transfer of Pyrophoric Reagents[2]

I. Informing Yourself About The Hazards

Aldrich Technical Bulletin AL-134: Handling air-sensitive reagents
www.sigmaaldrich.com/chemistry/aldrich-chemistry/tech-bulletins.html

Schwindeman, J. A.; Woltermann, C. J.; Letchford, R. J. "Safe handling of organolithium compounds in the laboratory" *Journal of Chemical Health & Safety*, **2002**, *May/June*, 6-11.

Alnajjar, M.; Quigley, D.; Kuntamukkula, M.; Simmons, F.; Freshwater, D.; Bigger, S. "Methods for the Safe Storage; Handling; and Disposal of Pyrophoric Liquids and Solids in the Laboratory" *Journal of Chemical Health & Safety* **2011**, *January/February 18(1)*, 5–10.

FMC Lithium: "Butyllithium Safe Handling Guide"
www.fmclithium.com

J. Leonard, B. Lygo, and G. Procter, *Advanced Practical Organic Chemistry*, 2nd Ed. (United Kingdom: Stanley Thornes, 1995).

II. Personal Protective Equipment (PPE)

•**Safety glasses** must be worn at all times when working with pyrophoric reagents. Additional protection in the form of indirectly vented goggles or a full-face shield may be more appropriate depending on the volume of material employed, the nature of the reagents, and the potential for splashing. Face shields must be worn in combination with safety glasses (safety glasses protect the eyes while the face shield protects the face and neck).

•**NOMEX fire-resistant laboratory coats** must be worn at all times when working with pyrophoric reagents. The blue NOMEX lab coats are located next to the CCB Safety Office (Cv226). Wearing clothing that minimizes skin exposure and is made of natural fibers is also highly recommended. Avoid wearing clothing made with synthetic fibers, which have the propensity to melt when exposed to flames or high temperatures.

•**NOMEX fire-resistant gloves** must be worn at all times when working with ≥5 mL of liquid pyrophoric reagents. The NOMEX gloves should be covered with a pair of tight-fitting, chemical-resistant, disposable gloves (e.g. nitrile gloves). One pair of Nomex gloves will be provided for completing the CCB liquid pyrophoric training. Additional pairs can be purchased here.

It is acceptable to wear a cotton glove liner covered with a nitrile or other chemical resistant glove when working with <5 mL of liquid pyrophoric reagents.

III. Labmates and Work Area

[2] Images and much of the content are taken with permission from J. Leonard, B. Lygo, and G. Procter, *Advanced Practical Organic Chemistry*, 2nd Ed. (United Kingdom: Stanley Thornes, 1995). Significant paraphrasing and some reproduction of this text are employed.

Do not work with liquid pyrophoric reagents while alone in the laboratory. A colleague who is capable of providing immediate assistance must be present and informed of the chemical transformation being performed as well as the reagents employed.

Researchers should review appropriate emergency procedures and be familiar with the location of the nearest safety shower and eye wash station in order to be prepared in the event of a spill, splash, injury or fire. Researchers must stand under the shower for 15-20 minutes and remove contaminated clothing when chemicals are spilled on their person. Eyes must be rinsed with water for 15 minutes at the eye wash station in the event of chemical exposure.

A class D fire extinguisher must be wheeled to a nearby location prior to working with pyrophoric reagents. Carbon dioxide-based class A, B, C, and K extinguishers are inappropriate for fires fueled by reagents capable of reacting with CO_2 and should not be employed under these circumstances.

It is imperative that pyrophoric materials be handled in a glove box, glove bag, or fume hood. Chemicals and solvents that are not required for the reaction with the liquid pyrophoric reagent should be removed from the working area. All reagent bottles and reaction flasks must be firmly clamped in place (so that there is no chance of them being knocked over) and reside in secondary containers (to contain a spill should it occur). When working in a fume hood, ensure that reagent bottles and reaction flasks reside 6-8 inches inside the hood, away from the sash. Keeping the sash low and/or using a blast shield will provide additional protection against chemical vapors and splashes.

IV. Preparing A Dry Reaction or Storage Vessel To Receive Pyrophoric Liquids

1. Dry the glass flask in a laboratory oven or by heating under vacuum. If heating under vacuum, back fill the container with an inert gas (nitrogen or argon). Allow the flask to cool in a desiccator.
2. Fit a rubber septum into the neck of the dry flask as quickly as possible.
3. Inject inert gas into the flask using a needle connected to an inert gas manifold (Figure 1a)
4. Quickly insert a needle through the septum to act as a vent. A vent bubbler may be used.
5. Once the flask has been thoroughly purged with inert gas, first remove the vent, then the inert gas needle.
6. The septum should be secured with copper wire to prevent accidental displacement (Figure 1b).
7. For additional protection, a rubber septum without any holes in it can be inverted over the first septum.
8. Parafilm® may be wrapped around the septa for additional protection.

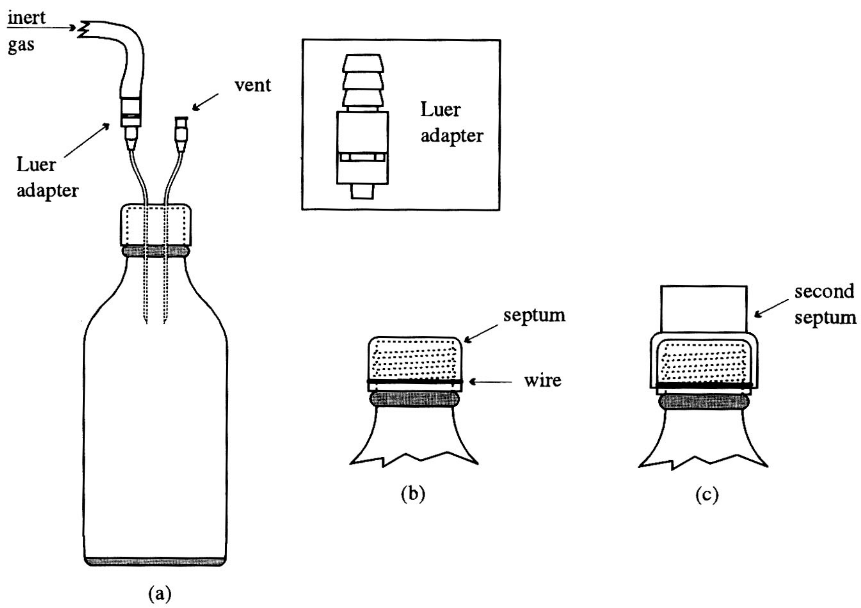


Figure 1: Preparing a dry reaction or storage flask.

V. Syringe Transfer Of Liquids

Syringes may be used to transfer relatively small quantities of pyrophoric liquids, perhaps up to 50 mL in the most favorable of circumstances. A syringe should only be filled to about ½ capacity. Volumes beyond 2/3 of the syringes maximum capacity are unsafe as they increase the risk of the plunger leaving the barrel and the contents spilling over the researcher handling the syringe. Long metal needles should be used to avoid having to tip the reagent bottle when withdrawing material from it.

Types of syringes

Microliter syringes are useful for small-scale synthetic work (Figure 2). For work with pyrophoric reagents, only gas-tight micro syringes with Teflon tipped plungers should be used. The Teflon should remain inert to any reagents used and ensure a tight seal to prevent accidental leaking. Removable needles are preferred as they can be replaced when damaged or clogged.

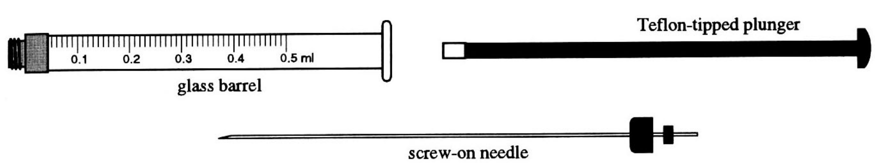


Figure 2: A gas-tight microliter syringe.

Glass Luer syringes range in size from 1 mL to 100 mL (Figure 3). For work with pyrophoric reagents, only gas-tight syringes with Teflon tipped plungers should be used. These syringes are the least likely to leak or jam.

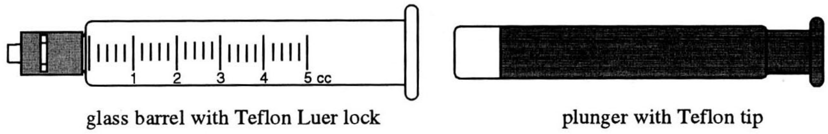


Figure 3: A gas-tight Luer syringe.

Needles may be affixed to a syringe with a Luer type fitting. When working with pyrophoric reagents, a Luer lock fitting with a Teflon tip should be used. The needle must be affixed by a screwing action as this helps ensure that the needle is not accidently displaced during syringing operations.

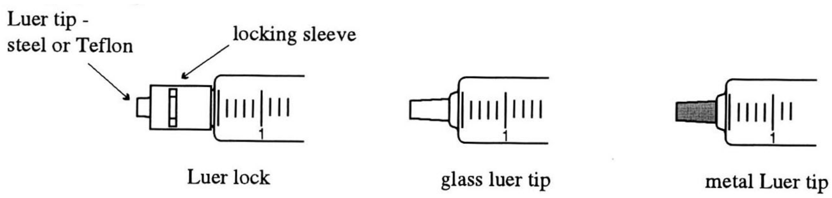


Figure 4: Luer lock tip should be used to transfer pyrophoric reagents.

Plastic syringes should not be used when transferring pyrophoric liquids.

Syringe preparation

The appropriate clean syringe, plunger, and needle combination should be dried in an oven and allowed to cool in a desiccator. Before use, the syringe should be quickly assembled, purged 10 or more times with anhydrous nitrogen (Figure 5 illustrates this process).

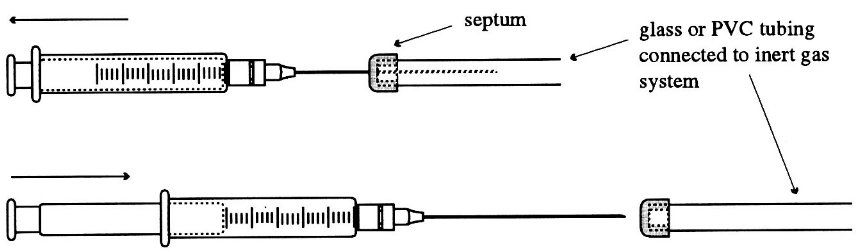


Figure 5: The purging of a syringe with inert gas.

The syringe-needle assembly should be tested for leaks by filling half of the syringe volume with anhydrous nitrogen, inserting the needle tip into a silicone rubber stopper, and attempting to compress the gas to half its original volume. A noticeable loss of pressure will occur in the event of a leak. The needle-luer lock interface can be wrapped tightly several times with Teflon® tape in order to prevent disassembly and leaks. The syringe may be kept for a short while before use if the needle is stuck into a silicone rubber stopper.

Syringe transfer of a pyrophoric reagent

It is essential to fully plan out your syringe transfer operation and to assemble all of the necessary glassware and equipment ahead of time. Syringes and reaction vessels should be prepared as described above.

All reagent bottles and reaction vessels must be securely clamped in place and reside in secondary containers. You may never syringe from or into a container that is not firmly clamped in place.

1. Pressurize the reagent flask with an inert gas line connected to a bubbler (Figure 6a).
2. Carefully insert the needle of the syringe through the rubber septum with one hand while holding the syringe and syringe plunger in place with the other. The pressurized reagent bottle will tend to force the syringe plunger out, with potentially disastrous consequences.
3. Bring the syringe needle below the surface of the reagent and very slowly fill the syringe by pulling the plunger up (Figure 6a). Never fill the syringe to more than two-thirds capacity.
4. Bring the needle above the surface of the reagent, then tip the syringe upside down (Figure 6b). Slowly force bubbles and excess reagent back into the reagent flask. Continue until the exact volume is indicated (Figure 6c).
5. Now that the exact volume is indicated, draw the plunger back a short amount to create a headspace of inert gas in the syringe.
6. Hold the syringe barrel and plunger with one hand and carefully extract the needle through the septum with the other. Quickly insert the needle into the receiver flask, avoiding prolonged exposure to the atmosphere.
7. Slowly dispense the reagent into the receiver flask, which should be connected to an inert gas system with a bubbler.

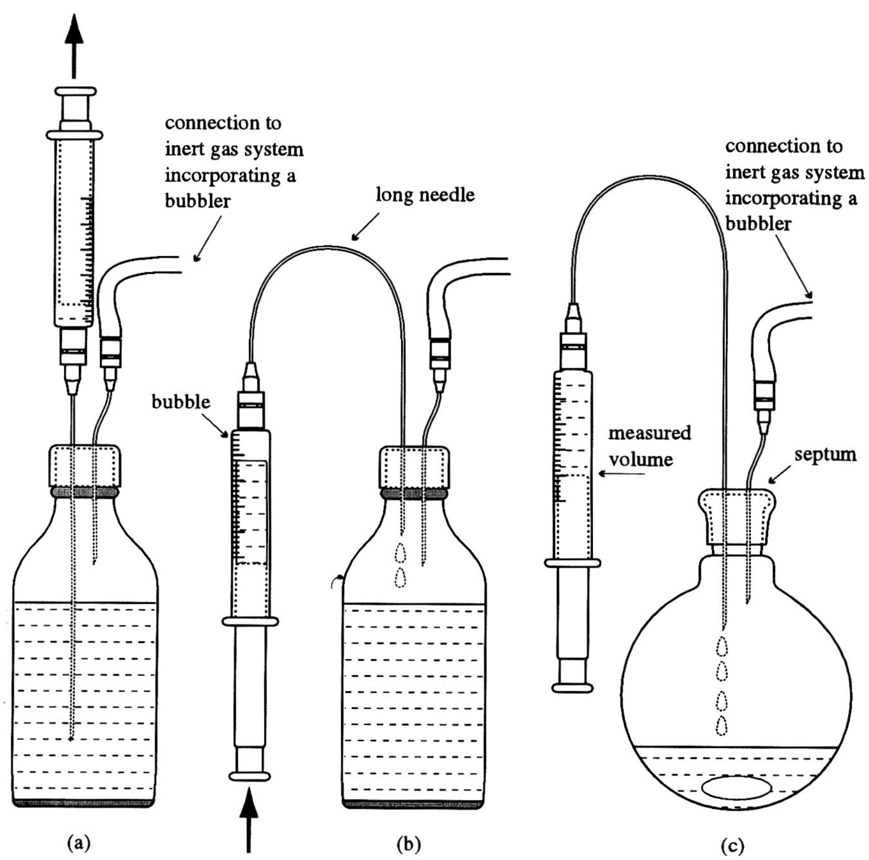


Figure 6: Syringe transfer of a pyrophoric reagent.

Syringe care and cleaning

Syringes and needles should be cleaned immediately after use. After the transfer of a pyrophoric reagent is complete, the syringe should be immediately flushed several times with the solvent in which the reagent was dissolved.

The syringe must be dismantled for final cleaning of the individual components. If the syringe was used to transfer alkyllithiums or other basic reagents, it should be washed successively with dilute HCl, water, then acetone. To clean after a Lewis acid was used, wash successively with dilute sodium hydroxide, water, then acetone.

VI. Bulk Transfer Of Pyrophoric Reagents: Cannula Transfer

Cannula transfer is the process of directly transferring a liquid from one container to another while maintaining an inert atmosphere. A positive pressure is applied to the reagent flask, which forces liquid through a double ended needle into the receiving flask. For liquid to flow, there must be a release of pressure from the receiving flask. When working with pyrophoric reagents, this venting of pressure should take place through a bubbler.

General procedure for cannula transfer

1. The receiving flask should be dried and prepared according to the procedures described in section III above (Figure 1).
2. Securely clamp both the reagent container and the receiving flask.
3. Insert an inert gas line needle into the reagent bottle (Figure 7a). A bubbler should be a part of the gas line.
4. Insert a dry, double ended needle (cannula) into the bottle containing the reagent. The cannula should be allowed to cool in a desiccator if it was recently taken from an oven. Do not place the needle below the surface of the liquid at this time (Figure 7b). Inert gas should be flowing through the cannula into the atmosphere.

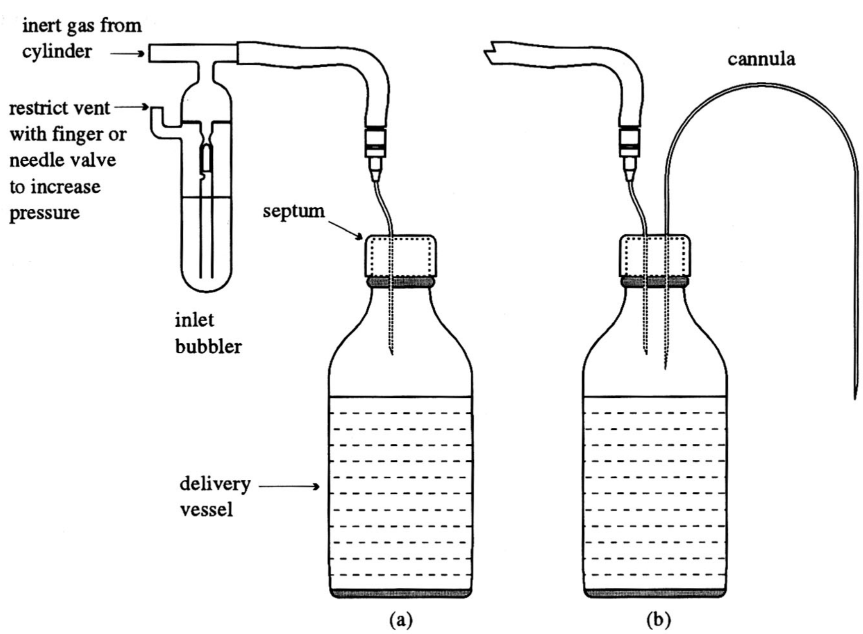


Figure 7: Preparation for a cannula transfer.

5. Insert the other end of the cannula through the septum of the receiving flask. Vent the receiving flask through a bubbler. There should be gas flowing through the cannula and out the bubbler now.
6. Carefully push the inlet end of the cannula below the surface of the liquid in the reagent flask (Figure 8). If the liquid does not begin to flow, increase the pressure in the reagent flask by restricting the vent of the inlet bubbler with a finger or a needle valve.
7. When all of the liquid has been transferred, first remove the vent needle (to bubbler) from the receiving flask and then remove the cannula at the reagent flask end.
8. The remaining apparatus may be disassembled in any order, but exercise extreme caution as there will likely be pyrophoric residue remaining.

If liquid will not flow at an appreciable rate during cannula transfer, consider changing to a wider gauge cannula and/or carefully and securely elevating the delivery vessel above the level of the receiving flask.

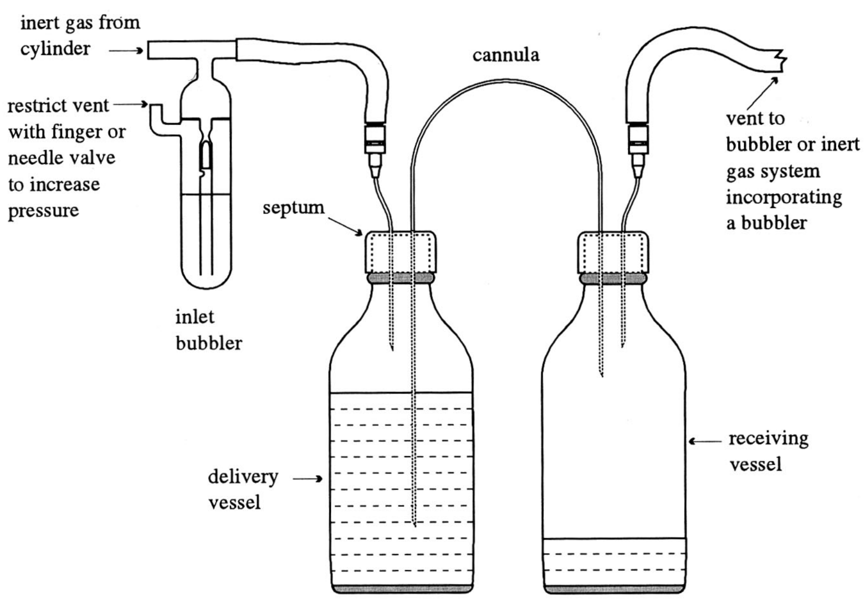


Figure 8: A cannula transfer.

<u>Cannulation techniques to transfer a measured volume</u>

The cannulation technique above can be readily modified to transfer a measured volume of pyrophoric reagent. This is especially useful when a measured volume greater than 50 mL is needed, as a transfer via syringe of this volume is not appropriate.

The technique is identical to that described above, however an oven-dried, graduated cylinder is used as an intermediate container (Figures 9 and 10).

Alternatively, a dry, graduated addition funnel may be fitted to the reaction vessel and the appropriate volume of pyrophoric reagent transferred to it via cannulation.

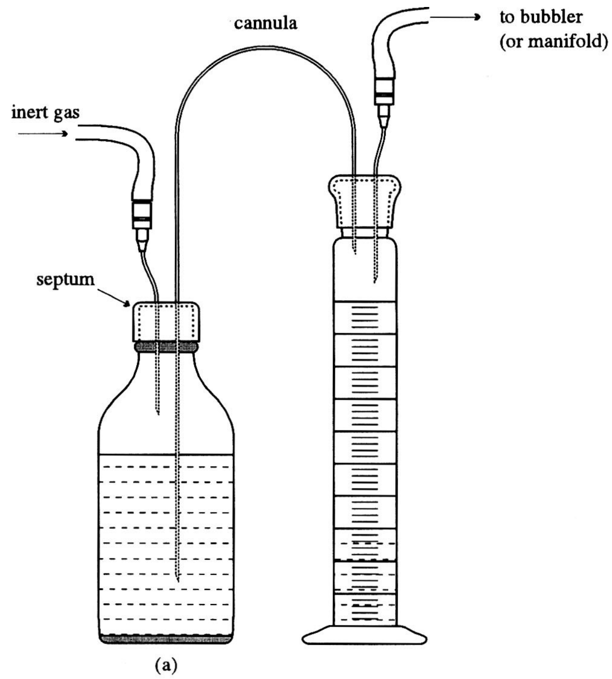


Figure 9: Cannulation into a graduated cylinder.

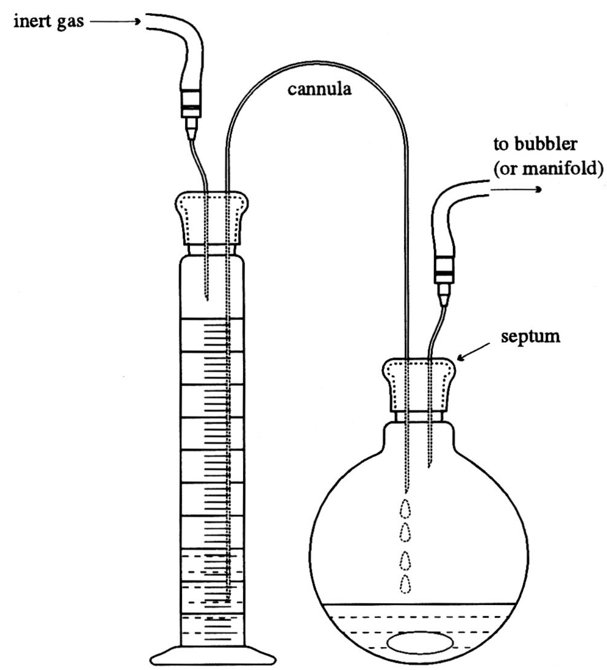


Figure 10: Cannulation of a measured volume of liquid.

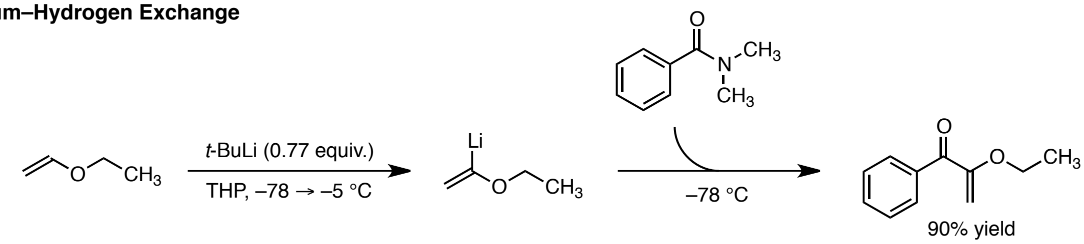
CCB Liquid Pyrophoric Training[3]

I. Introduction to *tert*-Butyllithium

tert-Butyllithium (*t*-BuLi) is a versatile yet extremely pyrophoric reagent employed in a wide variety of chemical transformations (Scheme 1).

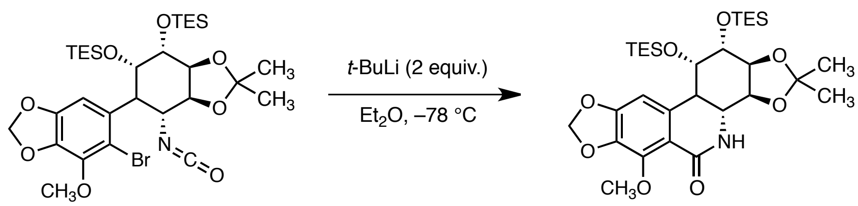
Scheme 1. *t*-BuLi-Mediated Organic Transformations

Lithium–Hydrogen Exchange



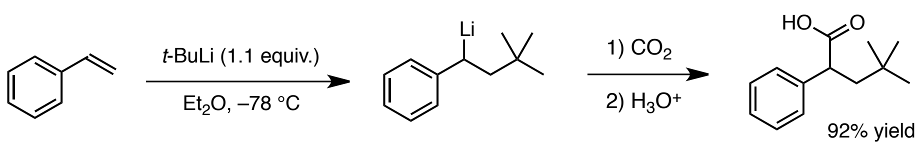
Shimano, M.; Meyers, A. I. *Tet. Lett.* **1994**, *35(42)*, 7727–7730.

Lithium–Halogen Exchange



Trost, B. M.; Pulley, S. R.; *J. Am. Chem. Soc.* **1995**, *117*, 10143–10144.

Additions to Conjugated π-Systems



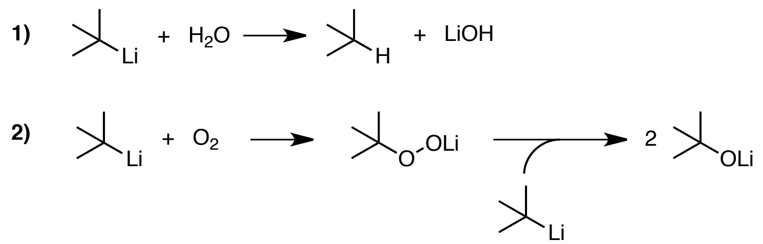
Wei, X.; Johnson, P.; Taylor, R. J. K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1109–1116.

t-BuLi reacts violently with water to release flammable 2-methylpropane (Equation 1) and with oxygen to generate lithium *tert*-butoxide (Equation 2).[4] These reactions explain the pyrophoric nature of *t*-BuLi and, combined with solvent evaporation, the unpredictable shifts in the concentration of *tert*-butyllithium solutions. Titration of *t*-BuLi solutions is essential in order to

[3] (a) Aldrich Technical Bulletin AL-134: Handling air-sensitive reagents www.sigmaaldrich.com/chemistry/aldrich-chemistry/tech-bulletins.html. (b) Schwindeman, J. A.; Woltermann, C. J.; Letchford, R. J. Safe handling of organolithium compounds in the laboratory. *Journal of Chemical Health & Safety*, **2002**, *May/June*, 6-11. (c) Alnajjar, M.; Quigley, D.; Kuntamukkula, M.; Simmons, F.; Freshwater, D.; Bigger, S. Methods for the Safe Storage; Handling; and Disposal of Pyrophoric Liquids and Solids in the Laboratory. *Journal of Chemical Health & Safety* **2011**, *January/February 18(1)*, 5–10. (d) FMC Lithium: "Butyllithium Safe Handling Guide" www.fmclithium.com. (d) Leonard, J.; Lygo, B.; Procter, G. *Advanced Practical Organic Chemistry*, 2nd Ed. (United Kingdom: Stanley Thornes, 1995).

[4] Boche, G.; Lohrenz, J. C. W. *Chem. Rev.* **2001**, *101*, 697–756.

employ adequate amounts of the reagent, which will optimize product yield, and minimize alternate reaction pathways.



In addition to water and oxygen, *t*-BuLi also reacts rapidly with ethereal solvents such as diethyl ether, tetrahydrofuran, and dimethoxyethane (Table 1).[5]

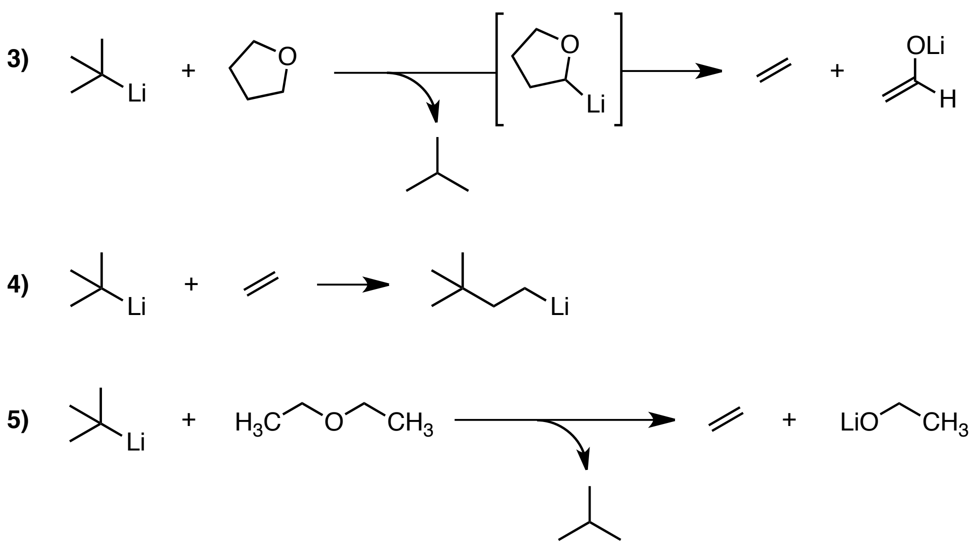
Table 1. Summary of Half-Lives of Butyllithium Reagents in Ethereal Solvents

Butyllithium reagent	$t_{1/2}$ (min)					
	–70 °C	–40 °C	–20 °C	0 °C	+20 °C	+35 °C
t-BuLi in DME	11	<2				
s-BuLi in DME	120	2				
s-BuLi/TMEDA in THF		Stable at $0.4c_0$	28			
t-BuLi in THF		338	42			
t-BuLi/TMEDA in THF			45			
s-BuLi in THF		Stable at $0.4c_0$	78			
n-BuLi in DME			111			
t-BuLi/TMEDA in ether			Stable at $0.8c_0$			
t-BuLi in ether			483	61	Complex kinetics	
s-BuLi/TMEDA in ether			Stable at $0.5c_0$			
s-BuLi in ether			1187	139		
n-BuLi/TMEDA in THF			3314	338	38	
n-BuLi in THF				1039	107	
n-BuLi/TMEDA in ether					603	
n-BuLi in THP					1257	278
n-BuLi in ether					9180	1860

c_0 is the initial concentration of commercially available butyllithium reagent: *n*-BuLi (2.5 M in hexanes), *s*-BuLi (1.3 M in cyclohexane), *t*-BuLi (1.7 M in pentane).

[5] (a) Stanetty, P.; Koller, H.; Mihovilovic, M. D. *J. Org. Chem.* **1992**, *57*, 6833. (b) Stanetty, P.; Mihovilovic, M. D. Half-Lives of Organolithium Reagents in Common Ethereal Solvents. *J. Org. Chem.* **1997**, *62*, 1514-1515. (c) Fitt, J. J.; Gschwend, H. W. Reaction of *n*-, *sec*-, and *tert*-Butyllithium with Dimethoxyethane (DME): A Correction. *J. Org. Chem.* **1984**, *49(1)*, 209–210.

The reaction of *t*-BuLi with ethereal solvents can lead to entirely different compounds that can change the desired course of a chemical transformation. For example, the reaction of *tert*-butyllithium with THF generates ethene and the lithium enolate of acetaldehyde (Equation 3). Ethene subsequently inserts into the carbon–lithium bond of *tert*-butyllithium to yield neohexyllithium (Equation 4). The overall reaction effectively consumes two equivalents of *tert*-butyllithium while generating a lithium enolate and primary alkyllithium: two species with reactivity profiles that differ substantially from that of *t*-BuLi. Similar problems arise when diethyl ether is employed as solvent (Equation 5).



II. Titration of *tert*-Butyllithium

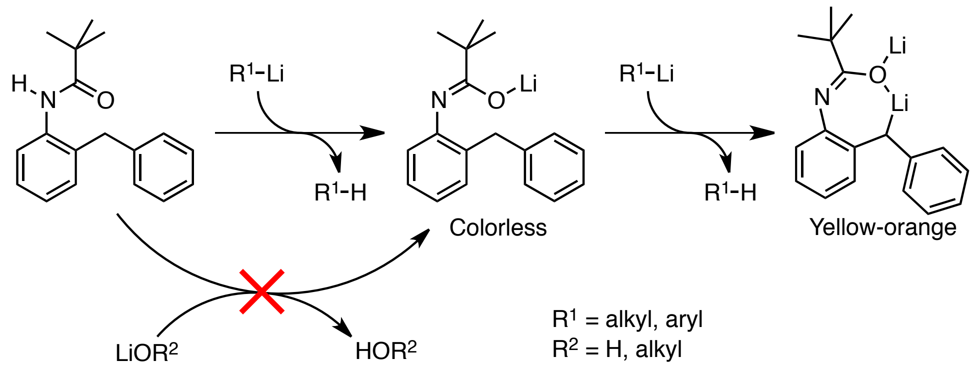
The titration of organollithium reagents is a useful laboratory skill to possess and is an excellent way to assess a researcher's knowledge of appropriate personal protective equipment (PPE) as well as proper technique for handling liquid pyrophoric reagents. The CCB training for handling pyrophoric liquids will require researchers to show proficiency during the titration of tert-butyllithium while wearing the proper PPE.

There are a number of published procedures for the titration of alkyllithium reagents. However, that reported by Jean Suffert[6] is advantageous in two ways: 1) The *N*-pivaloyl-*o*-benzylaniline[7] reagent that is employed provides a more accurate titer given that it is non-hygroscopic and cannot be deprotonated by lithium hydroxide or alkoxides. 2) The titration endpoint is clearly indicated by the appearance of an intense yellow-orange color (Scheme 2). Researchers can employ other titration reagents (e.g. 1,10-phenanthroline/*sec*-butanol, diphenylacetic acid, *N*-benzylbenzamide), solvents (THF), or alkyllithium solutions (*t*-BuLi or *n*-BuLi solutions in pentane) for the training. However, the modified version of Suffert's protocol described below is

[6] Suffert, J. Simple Direct Titration of Organolithium Reagents Using *N*-Pivaloyl-*o*-toluidine and/or *N*-Pivaloyl-*o*-benzylaniline. *J. Org. Chem.* **1989**, *54*, 509–510.

[7] The reagent can be purchased from Sigma-Aldrich: 2'-benzyl-2,2-dimethylpropionanilide, product# 348996-1G and 348996-5G

the preferred method for training as it is safer than the alternatives and provides a more accurate titer.



Scheme 2. Reaction of Alkyllithium Reagents with *N*-Pivaloyl-*o*-Benzylaniline.

Heptane solutions of *t*-BuLi are preferred for the training over pentane solutions. Pentane's high vapor pressure complicates syringe/cannula transfers and increases the likelihood of concentration fluctuations of *t*-BuLi solutions. The latter becomes especially pertinent once the reagent bottle seal has been pierced and/or compromised. Heptane's higher flash point, and lower vapor pressure relative to pentane, circumvents these complications.[8]

Tetrahydrofuran (THF) is rapidly deprotonated and decomposed by *t*-BuLi, even at –40 °C. On the other hand, the deprotonation of tetrahydropyran (THP)[9] by *t*-BuLi is relatively more difficult. In fact, Meyers and Shimano have reported increased yields of *tert*-butyllithium-derived α-alkoxyvinyllithium reagents when employing THP solvent versus THF.[10] As such, THP is preferred as a solvent for the liquid pyrophoric training.

Titration Procedure:

Read the General Procedure for the Transfer of Pyrophoric Liquids prior to performing the titration of t-BuLi.

Three 25 mL round-bottomed flasks (prepared according to the *General Procedure for the Transfer of Pyrophoric Liquids*) were equipped with magnetic stir bars and rubber septa.[11] The septum of each flask was pierced with one nitrogen inlet and one uncapped needle. The flasks were subsequently allowed to cool to room temperature while being flushed with anhydrous nitrogen. Once cooled to room temperature, the venting needles are removed from the flask's septa and the nitrogen inlet flows are adjusted in order to prevent any scattering during the addition of powdered reagents. *N*-Pivaloyl-*o*-toluidine (427.8 mg, 1.6 mmol) is introduced into each flask followed by 8 mL of anhydrous tetrahydropyran. The mixtures were stirred at room temperature until complete dissolution of the *N*-Pivaloyl-*o*-toluidine was observed. The flasks were subsequently cooled with ice baths and a white sheet of paper was placed in the background

[8] Available from Sigma-Aldrich: *tert*-butyllithium (1.6-3.2 M in heptane), product# 94439-100mL-F.
[9] Available from Sigma-Aldrich: Anhydrous tetrahydropyran, product# 293105-100mL).
[10] Shimano, M.; Meyers, A. I. Enolate Free α-Alkoxyvinyllithium Reagents: Improved Preparation and Reaction with *N*,*N*-Dialkylcarboxamides. *Tet. Lett.* **1994**, *35(42)*, 7727–7730.
[11] Triplicate titration is mandatory for the training and highly recommended when attempting to accurately determine the titer of any alkyllithium solution.

in order to facilitate titration endpoint detection. *tert*-Butyllithium (1.6–3.2 M in heptane, handled as described in the *General Procedure for the Transfer of Pyrophoric Liquids*) was added dropwise to the cooled reagent solution using a 1 mL gas-tight syringe equipped with a Luer lock. The end point of titration is reached when one drop of *t*-BuLi solution changes the color of the mixture to a deep yellow-orange, which persists for more than 1 minute while the mixture is stirred. The volume of *tert*-butyllithium solution required to reach the end point of each titration is employed to calculate the molarity (see example below). The average of the results of all three titrations is considered to be the molarity of the *t*-BuLi solution.

Titration	Amide (mg)	*t*-BuLi (mL)
1	430.1	0.74
2	427.2	0.75
3	425.4	0.73

$$\text{Molarity} = \frac{\text{Amount of amide (mg)} \big/ \text{Molecular weight of amide (mg/mmol)}}{\text{Volume of t - BuLi solution (mL)}}$$

$$\text{Molarity \#1} = \frac{430.1\ \text{mg} \big/ 267.37\ \text{mg/mmol}}{0.74\ \text{mL}} = 2.17\ \text{mmol/mL}$$

$$\text{Molarity \#2} = \frac{427.2\ \text{mg} \big/ 267.37\ \text{mg/mmol}}{0.75\ \text{mL}} = 2.13\ \text{mmol/mL}$$

$$\text{Molarity \#2} = \frac{425.4\ \text{mg} \big/ 267.37\ \text{mg/mmol}}{0.73\ \text{mL}} = 2.18\ \text{mmol/mL}$$

$$\text{Molarity}_{\text{av}} = \frac{2.17 + 2.13 + 2.18}{3} = 2.16\ \text{mmol/mL}$$

III. Preparation of *N*-Pivaloyl-*o*-benzylaniline[iV]

o-Benzylaniline (17 g, 0.093 mol), anhydrous dichloromethane (50 mL) and anhydrous triethylamine (13.0 mL, 0.093 mol) were sequentially added to an oven-dried, 250 mL round-bottomed flask equipped with a magnetic stir bar, rubber septum, and nitrogen inlet. The mixture was cooled to 0 °C with an ice bath. A solution of pivaloyl chloride (11.2 g, 0.093 mol) in dichloromethane (10 mL) was added dropwise. Upon complete addition of the pivaloyl chloride solution, the cold bath was removed and the reaction mixture was stirred for 0.5 hours at room temperature. After 0.5 hours of stirring at room temperature, the reaction was poured into 200 mL of ditilled and deionized water. The organic layer was washed with distilled and deionized water (3 x 100 mL) and brine. The remaining dichloromethane fraction was transferred to an Erlenmyer, dried with sodium sulfate, filtered through a medium porosity scintered glass filter funnel and evaporated under reduced pressure. The crude white solid was recrystallized from hot hexanes (200 mL). *N*-pivaloyl-*o*-benzylaniline was obtained as a white crystalline solid in 90% yield (m.p. 83 C, lit. m.p. = 78–80.5 °C).

D. Working With Pyrophoric Solids

The only way to handle solid materials under completely dry conditions is to use a glove box. A less sophisticated method that approximates a glove box is the use of a glove bag. A glove bag is a clear plastic bag, which can be filled with an inert gas and sealed after reagents and equipment are placed inside of it.

For the act of weighing and transferring pyrophoric alkali metals and metal hydride reagents in the laboratory, there are techniques outside of a glove box or bag that may be appropriate.

Handling and weighing reactive metals

Plan this process out ahead of time and ensure you have all of the necessary equipment and a dry receiving vessel under an inert gas prepared.

Alkali metals are often stored under paraffin oil and will likely have a layer of oxide coating the surface. The procedure below should remove both impurities.

1. Place the metal into a beaker, covering it with oil. Use a scalpel and forceps to cut small pieces of metal, removing any coating and leaving only shiny metal exposed (Figure 12). ***Heavily coated potassium has been known to detonate on cutting and should be discarded.***
2. Using forceps, quickly wash a single piece of metal in dry hexane or pentane (Figure 12ii).
3. Remove the metal piece and place it into a tared beaker of oil. You will determine the mass of your metal by weighing this beaker with the metal in it.
4. Repeat the rinse cycle and quickly place the clean metal piece into the dry reaction flask under an inert atmosphere. Minimize the time the rubber septum is off the reaction flask.
5. Neutralize any scraps of metal in the weighing beakers by careful addition of ethanol before washing with water.

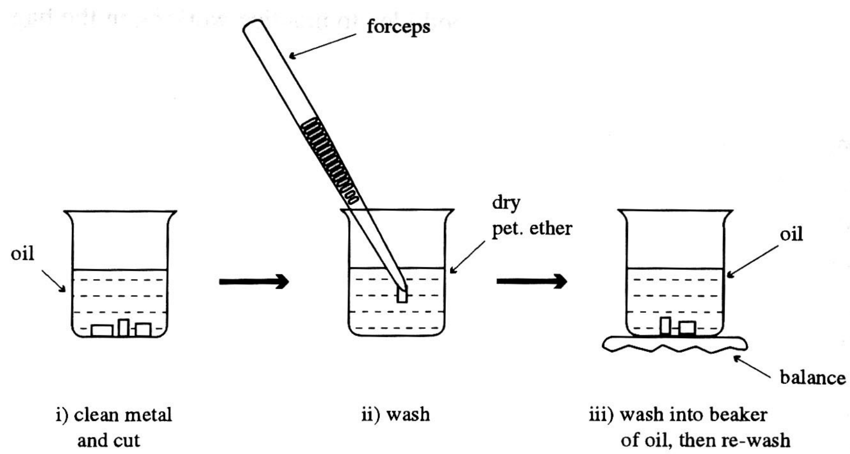


Figure 12: Weighing reactive metals.

Handling metal and metal hydride dispersions

Finely divided metals and metal hydrides are often supplied as dispersions in paraffin oil. These reagents are moderately stable and can often be weighed-out in the laboratory using the techniques described in the next section.

When removal of the oil is required, the following technique may be used. A "Quickfit" 3-way joint is shown in Figure 13, however a two necked flask with a vacuum adapter and rubber septum may be used as well.

1. Weigh the dispersion into a tared flask (take into account the oil) and place under an inert atmosphere (Figure 13a).
2. Add dry hexane or petroleum ether via syringe. Swirl the flask to dissolve the oil and then let it stand so that the metal settles to the bottom (Figure 13b).
3. Carefully remove the solvent above the metal using a syringe. Carefully discard the solvent into ethanol, as it may contain small amounts of the reactive metal.
4. Repeat the washing process two more times.
5. Place the flask under vacuum to remove any residual solvent. The flask may be reweighed to determine the exact amount of metal.

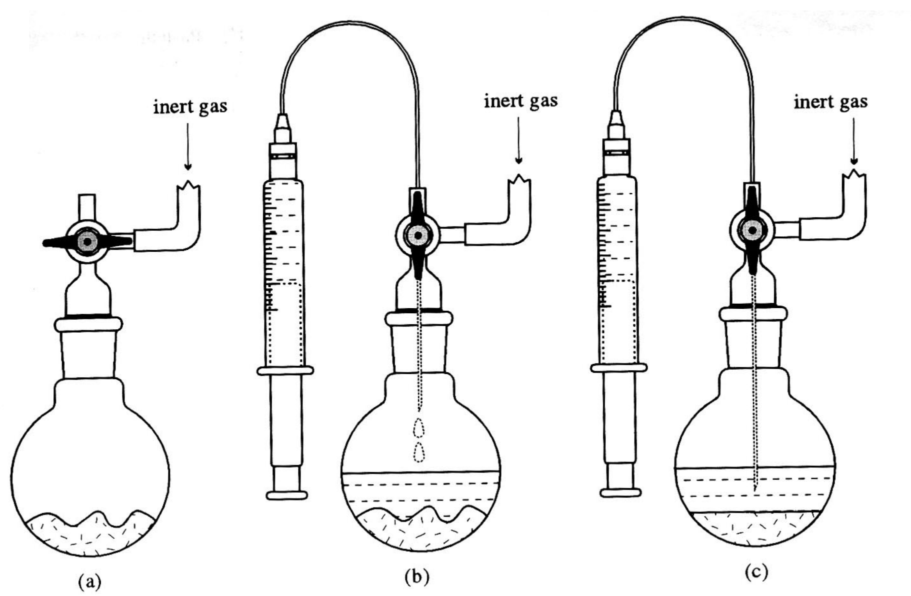


Figure 13: Removing the oil from a dispersion.

<u>Weighing pyrophoric powdered solids</u>

The procedure below may be used with reagents such as sodium hydride, potassium hydride, lithium aluminum hydride, and many finely divided metals. A glove box or glove bag should be used for particularly reactive solids.

Ensure you have a dry receiving vessel under an inert atmosphere prepared.

1. Prepare a balance such that it is blanketed under argon using the inverted funnel setup in Figure 14.
2. Remove the receiving flask from the inert gas system and place on the balance.
3. Keep the top of the container containing the powdered metal under the argon stream and quickly weight the required amount into the flask. **Minimize dispersing the metal through the air as it may lead to a fire.**
4. Reconnect the receiving flask to the inert gas system and carefully evacuate (avoid disturbing the powder). Refill the flask with inert gas.

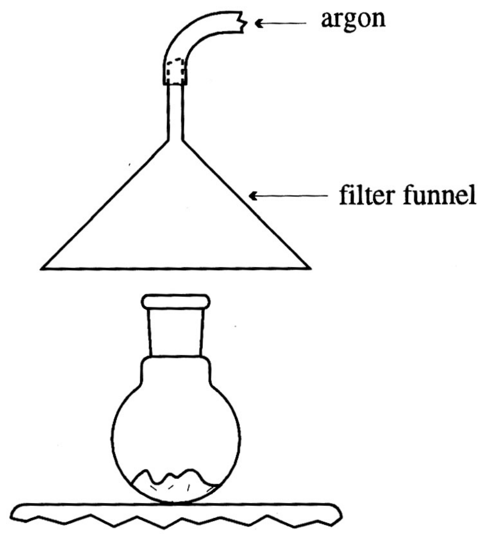


Figure 14: Weighing pyrophoric powdered solids.

V. Emergency Procedures

- If it is safe to do so, a class D fire extinguisher should be used to cover any pyrophoric material that spills.
- If skin exposure occurs, or if anyone catches on fire from a pyrophoric material, immediately begin drenching the person under a safety shower.
- Call 9-1-1 for assistance. A follow-up call can be made to the Harvard Operations Center (5-5560).

Appendix D: Working With Corrosive Reagents

This policy provides general guidance on the safe use of corrosive reagents. Researchers must thoroughly investigate the specific properties of the substance(s) they are working with and modify this guidance as appropriate.

For information on using hydrofluoric acid refer to the document "Guidelines for the Safe Use of Hydrofluoric Acid" at www.chem.harvard.edu/safety/safe_use_of_HF_acid.pdf

I. Preparation

Before any researcher uses a corrosive substance, they should:

- Read the appropriate Material Safety Data Sheet and conduct an informational internet search on the substance. (See Appendix A)
- Know the first aid procedure in case of exposure.
- Know what to do in case of a spill.
- Contact the CCB Safety Office (Mathieu Lalonde, lalonde@fas.harvard.edu, 496-8285) with questions.

II. Personal Protective Clothing

When using a highly corrosive substance, you must wear:

- a laboratory coat. Consider the use of an acid resistant apron and/or protective sleeves.
- close-toed shoes and long pants.
- goggles or full-face shield in conjunction with goggles.
- gloves that are compatible with the substance you are using (see the Glove section of the CCB Safety Manual).
  - disposable gloves (consider double gloving) for brief use of dilute solutions
  - heavy gloves for concentrated solutions or extended use of any solution

III. Safe Laboratory Practices

- Never work alone with a corrosive substance.
- Work within a fume hood.
- Ensure all containers of the substance are clearly labeled.
- Acids and bases must be stored separately from one another.
- Ensure that vials and flasks containing corrosives are securely supported and not likely to tip over. Use secondary containers.
- Keep containers closed to minimize exposure to corrosive vapors.

IV. Managing Corrosive Containing Hazardous Waste

- Corrosive waste should be placed in plastic or glass containers, as metal containers can corrode and leak.
- A vented cap should be used on the hazardous waste container if there is any chance of off-gassing or pressure build-up.
- Dispose of waste containers following the usual hazardous waste disposal procedures.

V. First Aid

For hydrofluoric acid exposures refer to the document "Guidelines for the Safe Use of Hydrofluoric Acid" at www.chem.harvard.edu/safety/safe_use_of_HF_acid.pdf

Skin exposure

1) Immediately proceed to the nearest wash station/safety shower and wash the contaminated area with copious amounts of running water for 15 minutes. Speed and thoroughness in washing off the corrosive material is essential.
2) Remove all contaminated clothing while rinsing.
3) While washing the affected area, have someone call 911 for emergency medical assistance.

Eye exposure

1) Immediately flush the eyes with water at an eyewash station for at least 15 minutes. Gently hold the eyelids away from the eye to fully irrigate the eye.
3) While washing the eye, have someone call 911 for emergency medical assistance.
4) Proceed to a hospital/physician for appropriate follow-up and/or treatment.

Inhalation of vapors

1) Immediately move affected person to fresh air and call 911 for medical assistance.
2) Keep victim warm, comfortable and quiet.
3) If breathing has stopped, start artificial respiration at once.
4) Oxygen should be administered as soon as possible by medical personnel.
5) Proceed to a physician for appropriate follow-up and/or treatment.

VI. Spills

Refer to the "CCB Chemical Spill Policy" available at:
www.chem.harvard.edu/safety/labsafety.php.

Appendix E: Working With Toxic Liquids and Solids

This policy provides general guidance on the safe use of toxic reagents. Researchers must thoroughly investigate the specific properties of the substance(s) they are working with and modify this guidance as appropriate.

I. Preparation

Before any researcher uses a toxic substance, they should:

- Read the appropriate Material Safety Data Sheet and conduct an informational internet search on the substance. (See Appendix A)
- Know the first aid procedure in case of exposure.
- Know what to do in case of a spill.
- Contact the CCB Safety Office (Mathieu Lalonde, lalonde@fas.harvard.edu, 496-8285) with questions.

II. Personal Protective Clothing

When using a highly corrosive substance, you must wear:

- a laboratory coat. Consider the use of a laboratory apron and/or protective sleeves.
- close-toed shoes and long pants.
- safety glasses, goggles, or a full-face shield in conjunction with goggles.
- gloves that are compatible with the substance you are using (see the Glove section of the CCB Safety Manual).

III. Safe Laboratory Practices

- Never work alone with a toxic substance.
- Work within a fume hood.
- Ensure all containers of the substance are clearly labeled.
- Ensure corrosive containing vials and flasks are securely supported and not likely to tip over.
- Keep containers closed to minimize exposure to toxic vapors.

IV. Managing Toxic Hazardous Waste

- Dispose of waste containers following the usual hazardous waste disposal procedures.

V. First Aid

Be familiar with the specific first aid procedures associated with the substance(s) you are working with. In general:

Skin exposure

1) Immediately proceed to the nearest wash station/safety shower and wash the contaminated area with copious amounts of running water for 15 minutes. Speed and thoroughness in washing off the corrosive material is essential.
2) Remove all contaminated clothing while rinsing.
3) While washing the affected area, have someone call 911 for emergency medical assistance.

Eye exposure

1) Immediately flush the eyes with water at an eyewash station for at least 15 minutes. Gently hold the eyelids away from the eye to fully irrigate the eye.
3) While washing the eye, have someone call 911 for emergency medical assistance.
4) Proceed to a physician for appropriate follow-up and/or treatment.

Inhalation of vapors

1) Immediately move affected person to fresh air and call 911 for medical assistance.
2) Keep victim warm, comfortable and quiet.
3) If breathing has stopped, start artificial respiration at once.
4) Oxygen should be administered by medical personnel as soon as possible.
5) Proceed to a physician for appropriate follow-up and/or treatment.

VI. Spills

Refer to the "CCB Chemical Spill Policy" available at:
www.chem.harvard.edu/safety/labsafety.php

Appendix F: Working with Highly Hazardous Gases

General Guidelines for Working with Toxic/Corrosive/Pyrophoric/Flammable Gases

1. Contact the CCB Safety Officer if you plan on using any Toxic/Corrosive/Pyrophoric and Flammable Gases.

2. If toxic, corrosive, pyrophoric, or flammable gases are used, place in a fume hood or in a ventilated gas cabinet.

3. A tubing and gas compatibility chart must be reviewed before choosing the tubing type. The reference can be found in the Air Products web site: http://www.airproducts.com/NR/rdonlyres/D7D98D60-68DF-44A4-AC5A-D541EDCD7899/0/reference_charts.pdf

4. Consider placing all fittings inside exhausted enclosures such as fume hoods, gas cabinets, or local exhaust. Fittings conveying inert gases are excluded form this. Avoid mechanical fittings if possible. If mechanical fittings are conveying toxic/corrosive/pyrophoric gases, then ventilation of the fittings is necessary.

5. Support and protect all tubing.

6. Leak check pyrophoric and highly toxic gas delivery lines before use.

7. Packed valves should be used for corrosive and reactive gases.

8. Diaphragm valves should be used for highly toxic and pyrophoric and high purity gases.

9. Use a purge system for corrosive and highly toxic gases. A vacuum system can be used as a purge system if appropriate regulators are used.

Appendix G: Working With Stench Compounds

I. The "Stench Chemical Log"

Researchers must record their use of all malodorous substances in the web-based "Stench Chemical Log" (www.chem.harvard.edu/safety/malodor.php) before their work begins. This will ensure that the source of any noxious odors reported in the CCB complex will be readily identified.

The use of common amine bases on a small scale (e.g. 1 mL of diisopropyl amine) need not be logged, however their use on a larger scale (e.g. 250 mL) should be.

II. General Guidelines

A. Running Reactions

Extreme caution must be exercised when working with volatile, malodorous compounds. The handling of these compounds should take place inside of a fume hood to prevent the release of noxious vapors into the local laboratory environment. Precautions must also be taken to prevent these vapors from being released within the fume hood and exhausted out of the building. In addition to affecting the outside environment, these vapors can be reintroduced to the laboratory complex via building air intakes and distributed to locations that are distant from the original laboratory source.

1) Use the minimum amount of stench chemical possible (avoid using excess).

2) Rubber septa must never be used as a cap to store stench chemical reagent bottles. The chemical will eventually permeate the rubber.

3) Perform liquid transfers by using a syringe or cannula. Never pour solutions of volatile compounds or transfer via pipette. Consider cooling or freezing the stench chemical before quickly replacing the reagent bottle cap with a rubber septa while working in a fume hood. This should help minimize the vapor that escapes into the atmosphere.

3) Keep the hood sash down as low as possible.

4) A cold trap or a bleach trap should be employed to prevent vapors from exhausting into the fume hood.

5) An oxidizing solution (e.g. bleach) should be present in which to submerge all used labware that has been contaminated with malodorous compounds. See section III.

B. Bleach Traps

Thiols, sulfides, phosphines, and disulfides can be oxidized to less malodorous sulfoxides, sulfones, and phosphine oxides (or other more highly oxidized phosphorous compounds) before venting to the environment. This oxidation can be most easily accomplished using a bleach solution.

The diagram below shows the set-up for a typical bleach trap. The reaction is first vented into an empty trap, to prevent back flow, and then into a bleach solution. An excess (not a large excess) of bleach (Clorox bleach is 6.15% sodium hypochlorite by weight) should be used. The hydrochloric acid generated from the oxidation reaction is neutralized by connecting the bleach trap to a potassium hydroxide trap before venting to the fume hood. The oxidation reaction is exothermic, thus if a large amount of stench chemical is being oxidized then cooling of the traps will be necessary to keep their temperature from rising.

C. Solvent Evaporation

A cold-finger trap (cooled at least to -78 °C) must be used when evaporating solvent under reduced pressure when a stench chemical is present. The collection bulb must be cooled as well. Inadequate cooling of the condenser and collection flask when using the house-vacuum will result in a release of noxious vapors via the vacuum pump exhaust. If a rotary evaporator is used, it should be located inside of a fume hood.

III. Clean-up and Hazardous Waste Disposal

1) Tighten the cap of stench chemical bottles and seal them with Teflon tape.

2) All glassware, syringes, cannula, septa, and other labware that come into contact with malodorous compounds that can be oxidized (e.g. thiols, disulfides, phosphines, etc.) should be rinsed and/or submerged in a bleach solution to oxidize all traces of the noxious chemical. The oxidation reaction can be slow, so soaking for 24 hours may be necessary.

3) If disposable items such as gloves, paper towels, and septa continue to be malodorous, they should be enclosed in a zip-lock bag, placed in a wide-mouth plastic jar, labeled as hazardous waste, and placed in the hazardous waste main accumulation area for removal.

4) The malodorous contents of a cold-trap should be carefully added to a cooled bleach solution and the glassware rinsed and/or submerged in a bleach solution as well.

5) Bleach solutions should be combined into an appropriate container, labeled with a hazardous waste tag, and disposed of as hazardous waste. Potassium hydroxides solution should be added to a separate container, labeled with a hazardous waste tag, and disposed of as hazardous waste.