Rubin's group laboratory operating procedure series

1. The Safe Use of Pyrophoric Reagents

REVISION RECORD

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Contents

1. Scope and Applicability

In December 2008, a fatal accident at UCLA occurred while a researcher was working with *t*-butyl lithium, a highly pyrophoric agent. Pyrophoric materials ignite spontaneously on contact with air. Failure to follow proper handling procedures can result in fire or explosion that lead to serious injuries or even death, as well as significant damage to facilities.

This document is to serve as a guide for the group members who currently, or might in the future, use pyrophoric reagents. Reading this guide does NOT mean the completion of the laboratory safety training required for manipulating pyrophoric materials. Only qualified members should ever attempt to use these materials.

Here are some examples of the common pyrophoric reagents:

- Organolithiums: *t*-butyllithium, n-butyllithium, methyllithium
- Organozincs: diethylzinc
- Organomagnesiums: ethylmagnesium bromide, ethynylmagnesium bromide
- Aluminum alkyls: trimethyl aluminum
- Metallic hydrides: lithium aluminum hydride
- Finely divided metals: powders of zinc, aluminum, magnesium, titanium
- Non-metal alkyls: R_3B, R_3P, R_3As
- Potasium, Sodium

2. Hazard Information

Pyrophoric reagents are extremely reactive to oxygen and moisture, and precautions must always be taken to prevent their exposure to air, which usually leads to spontaneous ignition. The danger of this reactivity is often exacerbated by the fact that these reagents are sold in extremely flammable solvents such as ethyl ether, tetrahydrofuran (THF), or pentanes. When possible, compounds stored in pentanes or hexanes should be avoided, as storage in heptanes is *slightly* less hazardous.

The hazards from using these chemicals stem from fires that could result from the chemicals themselves and the solvents containing them, as well as any secondary fires that may spread to nearby flammable or combustible materials. Segregating combustible materials from storage as well as work areas is the best way to prevent dangerous secondary fires that could cause serious property damage and personal injury. Be especially vigilant when using *t*-butyl lithium that is *extremely pyrophoric*. Other common hazards include corrosivity, teratogenicity, peroxide formation, along with damage to liver, kidneys, and central nerve system. For more information, refer to the relevant MSDS(s) (http://www.actiocms.com/chemquik/mainpage.cfm).

3. Hazard Control

3.1. Administrative Control

All users of pyrophoric reagents must first go through the laboratory safety training before working in the lab. Users must be trained thoroughly by a qualified and experienced supervisor on techniques for handling pyrophorics, and must be directly supervised when first starting with these techniques. Also, users must consult with the PI and obtain approval when working with highly hazardous materials.

3.2. Safe work practices

- DO NOT WORK ALONE when using pyrophoric materials. Other members in the lab should be notified of the use of pyrophoric reagent in advance so that they are ready for help in case of accidents.
- Consider performing a "dry run" to identify and resolve possible hazards before conducting the actural procedure.
- Keep combustible materials, including paper towels and Kimwipes, away from pyrophoric reagents.
- Minimize the quantity of pyrophoric reagents used and stored.
- It is better to do multiple transfers of small volumes than attempt to handle larger quantities. Consider using the cannula method when transferring more than 20 mL.

3.3. Personal Protective Equipments (PPEs)

- **Gloves.** Nitrile gloves should be adequate for handling most of these in general laboratory settings but they are combustible. Use adequate protection to prevent skin exposures. Heavy gloves are required for work with large quantities. Sigma-Aldrich recommends the use of nitrile gloves underneath neoprene gloves.

- **Eye protection.** Chemical splash goggles or safety glasses that meet the ANSI Z.87.1 1989 standard must be worn whenever handling pyrophoric chemicals. Ordinary prescription eyeglasses will NOT provide adequate protection unless they also meet this standard. A face shield, worn over safety eyewear, is required any time there is a risk of explosion, large splash hazard or a highly exothermic reaction. All manipulations of pyrophoric chemicals that pose these risks should be conducted in a fume hood with the sash at the lowest feasible position.

- **Lab coat.** All users of pyrophoric reagents must wear a fire resistant lab coat. A chemical-resistant apron worn over the lab coat is required for working with large quantities.

- **Shoes.** No open-toed shoes are allowed

3.4. Safety Equipments and Emergency Responses

- Always know the exact locations of the eyewashes and safety showers, as well as the phone in the office. Keep the areas around them clear from obstruction at all times.
- Keep a container of vermiculite or sand within arm's reach.
- Users may encounter small fires at the tips of needles—know to expect this, and do not panic if you see it. A beaker of sand is useful for extinguishing this "pilot light".
- DO NOT use a class ABC or CO_2 extinguisher to attempt to quench a fire with pyrophoric reagents, since this can greatly exacerbate the situation. Use a class D extinguisher—check where it is and how to use in advance of using pyrophoric reagents.
- For skin exposures, if there are no severe burns, rinse with water for 15 minutes and seek first aid.

4. Operating Procedures

4.1. Equipment Preparation

(1) Make sure the fume hood is clean and absent from combustible materials and heat sources.

(2) Locate a needle of appropriate length and gauge. A sixteen-gauge needle is recommended if one plan to draw from the reagent container several times, as anything larger than this will leave a hole too large for the septum on the reagent bottle to reseal. A long needle is best if using a syringe. A long double-tipped flexible needle can be used for cannula transfer. Luer lock needles, or needles otherwise equipped with a locking mechanism, are highly recommended as a guard against the needles becoming detached.

(3) Flush the syringe-needle assembly, if using one, with dry, inert gas before starting. Ensure that it is leak-free by inserting the needle into a rubber stopper. It should be possible to compress the syringe to half its original volume without any leaks. The needle can be left in the rubber stopper when not in use to prevent the entry of air.

(4) Ensure that all glassware and other equipment involved in the procedure are clean and dry. Glassware should be heated in an oven or by a heat gun to remove moisture, and cooled in an inert atmosphere.

(5) Prepare an inert gas line for supplying positive pressure to the reagent container. Use a dry, inert gas cylinder with a pressure regulator set to the lowest pressure sufficient for your work, attached to flexible plastic tubing. A mineral oil bubbler should be added to the line, typically off of a manifold, to release excess pressure. A hypodermic needle at the end of the tubing can be used to insert the line through the septum of the reagent container. This needle can be inserted into a rubber stopper when not in use to prevent the entry of air.

(6) The reaction vessel will also need to be supplied with a small amount of positive pressure during the reaction to prevent any pressure reversals that could cause air to enter the vessel. An inert gas line equipped with a mineral oil bubbler to relieve excess pressure will be needed for this. Run the reaction in a Schlenk flask or an equivalent flask that is

under positive pressure from the inert gas line, connected via the tubing adapter. If the reaction vessel has a septum inlet, a hypodermic needle attached to the gas line can be pushed through the rubber septum to the reaction vessel, though the Schlenk vessel is better suited for controlling the atmosphere.

4.2. Syringe Transfer

Transfer of pyrophoric reagents via syringe is convenient, but should not be used for 50 mL or more.

(1) Clamp the reagent container firmly. A small amount of positive pressure in the reagent container will be needed in order to draw the reagent into a syringe. Insert an inert gas line with low positive pressure (1-2 psi). Ensure that excess pressure is released through the mineral oil bubbler that is attached to the gas line. Simply sticking a needle through the septum, or using a balloon to relieve pressure, is not safe for pyrophoric reagents.

Fig. 1 Drawing reagent into syringe from reagent container, with inert gas line inserted

(2) Prior to starting the procedure, ensure that the reaction vessel deposit the reagent into has a mineral oil bubbler to relieve pressure (if a bubbler is not already on the gas line), and that it is thoroughly flushed with inert gas prior to use. Again, do not use a balloon, and do not simply stick a needle through the septum to relieve pressure.

(3) Before beginning, set aside an Erlenmeyer flask with the same solvent in which the reagent is dissolved. If it is a neat reagent, use a solvent that is inert and unreactive towards that reagent. Aliquot slightly more than the volume of the reagent that will be transferred with the syringe. This flask will need to be immediately available after the transfer for flushing out the syringe.

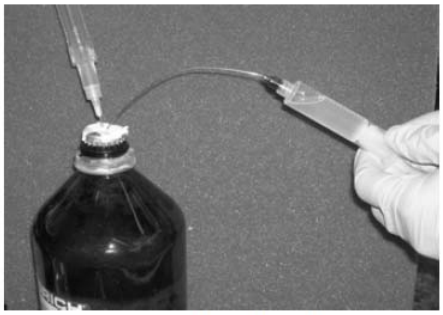

Fig. 2 Syringe is flipped needle-up after drawing liquid to allow inert gas bubbles to rise to needle

(4) Draw the reagent slightly more than you need initially. Be careful to pull only very gently on the plunger as pulling too strongly can cause leaks and create air bubbles. Always keep a good grip on BOTH the needle and the plunger to ensure that neither comes off. The ejection of the plunger with its contents due to excess pressure will result in a dangerous fire on your hands. (Fig. 1)

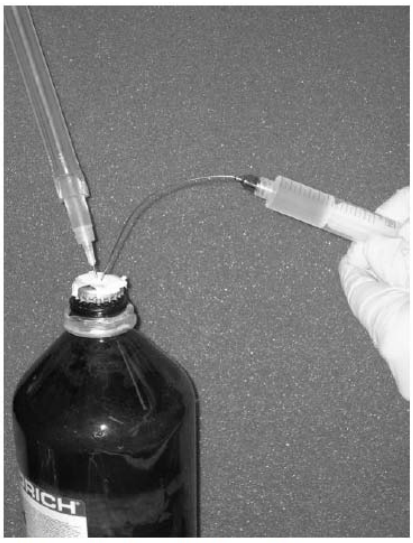

Fig 3. Inert gas bubbles and excess liquid are forced back into reagent bottle

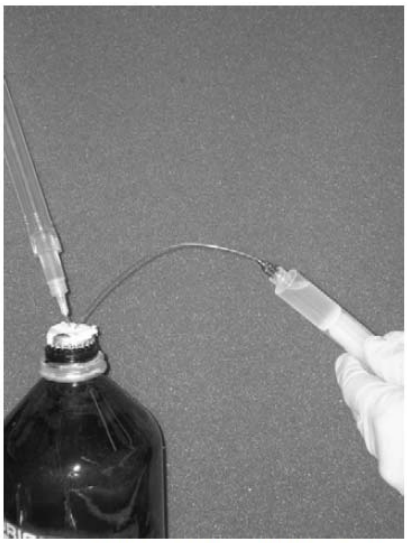

Fig. 4 Needle tip is brought into head-space of bottle, and an inert gas layer is drawn into syringe

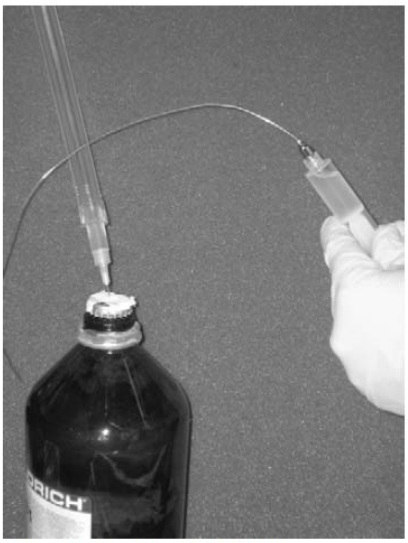

Fig. 5 Needle is carefully with-drawn from reagent bottle. Syringe is kept needle-up to prevent spilling

(5) Flip the syringe needle-up, so that the inert gas bubbles rise to the top (a long needle is needed for this). It is best to avoid allowing the reagent in the bottle to come into contact with the septum to prevent degradation. Tap the syringe a couple of times and look to make sure all the air/gas has been collected at the tip. (Fig. 2)

(6) Push the plunger down to eject the inert gas and excess reagent back into the reagent vessel, stopping once the volume needed for the experiment is reached. (Fig. 3)

(7) Pull the needle into the headspace of the reagent bottle and draw a small amount of inert gas into the syringe. This prevents spilling, and very importantly protects the liquid from exposure to air during transfer. (Fig. 4)

(8) The needle can now be removed from the bottle, keeping the inert gas layer at the syringe tip. If you see a small flame at the tip of the needle, do not panic. Use a beaker of sand to extinguish this. (Fig. 5)

(9) Insert the syringe into the septum of the reaction vessel, keeping the inert gas layer between the syringe and needle. Ensure that the vessel is equipped with an inert gas line to provide positive pressure, and a mineral oil bubbler to relieve excess pressure. Holding the plunger down, inject the inert gas cushion in your reaction first, and then inject your liquid into the flask.

4.3. Cannular Transfer

Transfer of pyrophoric reagents via cannula is recommended for 50 mL or more.

(1) Clamp the reagent container firmly. A small amount of positive pressure in the reagent container is required in order to force the reagent through your double-tipped needle. Connect it to an inert gas line to provide low positive pressure (1-2 psi). Ensure that the line is equipped with a mineral oil bubbler to relieve excess pressure. Using a balloon or

simply sticking a needle through the septum to relieve pressure is not safe for pyrophoric reagents.

(2) Make sure, before starting, that the reaction vessel into which you plan to deposit your reagent has a pressure release mechanism such as a mineral oil bubbler on the inert gas line, and that it is thoroughly flushed with inert gas prior to use. Again, do not use a balloon or simply stick a needle through the septum to relieve pressure.

(3) Insert one end of the double-tipped needle into the headspace of the reagent vessel and allow the positive pressure from the inert gas line to flush the needle free of air.

(4) Insert the other end of the double-tipped needle through the septum of the reaction vessel. To allow for a measured transfer, a sealed, measured funnel attached to the reaction flask can be used with the septum at the top of the funnel.

(5) When ready to transfer, push the needle that is in the headspace of the reagent container down into the liquid. The pressure from the inert gas line will begin forcing the liquid through the double-tipped needle.

(6) When the desired volume has been transferred, pull the end of the needle in the reagent container up into the inert gas headspace and allow it to be flushed with inert gas again. Remove the end of the needle from the reaction flask first, and then from the reagent container. If, upon removal, a flame is lit at either tip, extinguish it in a beaker of sand.

4.4. Equipment Cleanup

(1) If the syringe transfer method is used, the syringe will have a small amount of the reagent remaining. Fill an Erlenmeyer flask with the same solvent in which the reagent was stored, using slightly more than the volume which the syringe was used to transfer. If the syringe was used for a neat reagent, use a solvent that is inert and unreactive toward the reagent.

(2) Ensure that any flame at the tip of the needle is extinguished first, and put the tip of the needle beneath the liquid in the flask, keeping it beneath the solvent.

(3) Carefully draw the solvent into the syringe and eject it to flush the syringe, and repeat for a total of three rinses.

(4) The syringe can be disposed of by putting it into a sharps container, if it is disposable. The solvent in the flask, with trace amounts of the pyrophoric compound, should be quenched by slowly adding a protic solvent (acetone, ethanol etc.), then added to a solvent waste container. Be sure to list all of the components on the chemical/hazardous waste label.

(5) For the cannula transfer, the double-tipped needle should have been purged with inert gas before you removed it. The needle can be placed in a sink in the absence of any solvents or other combustible materials.

(6) Flush the needle with water, collecting the effluent for disposal with aqueous waste. Making sure that there is no longer any reactivity, use a wash bottle to flush the needle with acetone, collecting the effluent.

5. Sources and Further Readings

This guide was prepared based on:

- Columbia University Environmental health and Safety *"The Safe Use of Pyrophoric Reagents"*. April 2009.
- University of California, Irvine, EH&S *"Procedures for Safe Use of Pyrophoric Reagents"* rev. 05/10/09.

The documents below contain useful information.

- Aldrich Chemical Company, Inc.; *Handling Pyrophoric Reagents – Technical Bulletin AL-164*; May 1995.
- Aldrich Chemical Company, Inc.; *Handling Air-Sensitive Reagents – Technical Bulletin AL-134*; March 1997.