Standard Operating Procedure

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Task: Working with pyrophoric chemicals
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Background:

- This guide was written in consultation with numerous resources, particularly a guide authored by Kevin McGhee and Jack Norton of Columbia University and the Aldrich Technical Guide.
- Pyrophoric chemicals are extremely reactive with air and/or moisture, resulting in spontaneous combustion when exposed to air. Pyrophoric materials include alkyl lithium, Grignard, alkylaluminium, and alkylzinc reagents; boranes, alanes and phosphines; alkali metals (sodium, potassium).
- Prepare thoroughly ahead of time. Obtain all required training. Wear appropriate PPE. Clean your hood of any extraneous materials, especially solvents. Know the precise location of eyewash and safety shower stations and be prepared to operate in case of emergency. Keep a container of sand within arm's reach in case a small fire occurs. Know the precise location of an appropriate fire extinguisher: Class ABC dry chemical extinguishers are usually appropriate for situations where organic solvents are involved, including metals or organometallics that are dissolved in organic solvents, such as n-butyllithium in hexanes. In many cases, fires involving pyrophoric reagents are mainly due to the organic solvent or nearby paper goods, so Class ABC extinguishers are well-suited for these purposes. If the fire is a neat pyrophoric reagent (such as potassium metal or an alkylaluminum) and does not involve other propellants such as organic solvents or paper, smothering with a sand bucket is recommended. **NEVER use a CO_2 extinguisher** on a fire with pyrophoric reagents, because the reagents can react with CO_2 exothermically.

Training Requirements:

- Lab safety training
- Mentored training specific to pyrophoric chemicals, including introductory discussions with PI and observation and training with an experienced mentor
- Schlenk line and/or glovebox training

Potential Hazards:

- Spontaneous combustion in the presence of air and/or moisture.
- Serious fire and explosive hazards.
- Possible exothermic reaction with CO_2 fire extinguisher.

Special PPE Requirements:

- Clothing with natural fibers (no fleece or polyester due to high flammability)

- A 100% cotton or approved flame-retardant lab coat made of fire resistant material, such as Nomex
- Leather or Kevlar gloves to wear beneath nitrile gloves for fire protection purposes are recommended

Materials Needed:

- Dry ice
- Suitable air- and moisture-free working environment (Schlenk line or glove box)
- Syringe and needle equipped with a locking mechanism (e.g. Luer lock) or a flexible double-tipped needle (cannula). A sixteen-gauge needle of appropriate length to reach the liquid in the bottles
- Secondary oil bubbler to provide an outlet for the receiving flask (for cannula transfers)
- Container of sand in case of fire
- Erlenmeyer flask
- Toluene
- Isopropanol

Procedure:

TECHNIQUES FOR REAGENT TRANSFER IN A FUME HOOD

Syringe transfer - For 10 mL or less.

The following procedures are appropriate for flasks with rubber seals, including Schlenk flasks and PTFE-sealed glass bottles from commercial vendors.

1. Confirm that all required glassware and equipment are clean and dried either by heating in an oven or by flame / heated blower before cooling under vacuum or under an inert atmosphere.

2. Prepare the vessel that will receive the pyrophoric (reaction flask, addition funnel, secondary flask that will be added subsequently to a reaction, etc.). Place the vessel under an inert atmosphere, either by flushing with nitrogen or argon or by evacuation cycles. The use of a manifold delivering anhydrous, high purity nitrogen or argon and equipped with a mineral oil bubbler (to release excess pressure) is highly recommended. Typically, reactions are carried out in a Schlenk flask under positive pressure from the inert gas manifold, connected via a stopcock valve to the rubber tubing. A Schlenk vessel is highly recommended, as it provides better control of the atmosphere.

3. Use a clamp to hold your reagent container firmly in place. Insert an inert gas line to provide a low positive pressure (1-2 psi; a needle at the end of the thick rubber tubing can be used to insert the line through the septum of the reagent container). Ensure that excess pressure is released through the mineral oil bubbler that is attached to the gas

manifold. *Never stick a syringe needle through a septum without a positive pressure of inert gas in place, and never use a balloon to provide/relieve pressure!*

4. Test the syringe for leaks: insert the needle into a rubber stopper and compress the syringe; the plunger should depress to half its original volume if there are no leaks. The needle can be left in the rubber stopper when not in use to prevent the entry of air; but the syringe should be flushed just prior to transferring the reagent as well. *Be sure to use a long (ca. 10") syringe needle to facilitate removal of bubbles during the transfer.*

5. Do a final safety check: the area should be clear and uncluttered, with no unnecessary solvent containers; you should have a sand bath at the ready and a plan in place for if a spill or fire occurs.

6. Flush your syringe-needle assembly, with dry, high-quality inert gas such as nitrogen or argon before starting. Pierce the septum with the syringe, without inserting the needle into the liquid. Slowly fill the syringe with the inert gas, being careful to watch the bubbler and maintain a positive pressure. Remove the syringe and purge out the gas. Repeat this procedure twice more to flush all air from the syringe.

7. Draw the reagent. Pierce the septum again, this time moving the needle into the liquid to be transferred. Slowly fill the syringe with the liquid, drawing 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. *Never fill a syringe more than half-way, to avoid accidental failure of the plunger and never transfer more than 10 mL of liquid by syringe, instead use a cannula and an addition funnel* . Always keep a good grip on BOTH the needle and the plunger to ensure that neither comes off. Do not use an overpressure of inert gas to fill the syringe. If the pressure is too high, the plunger could be ejected with its contents resulting in a dangerous fire!

8. Once the syringe is filled with slightly more than the required reagent, invert the syringe while keeping the needle pierced through the septum and above the liquid level. A long needle is required for this procedure, which allows the inert gas bubbles to rise to the top of the syringe. Once bubbles are collected at the tip of the syringe, push the plunger to eject the inert gas and excess reagent back into the reagent vessel and obtain the desired volume of reagent (free of bubbles). Then, draw a small amount of inert gas into the syringe as a buffer in the needle. The inert gas buffer prevents spills and provides an inert atmosphere blanket to protect the reagent from exposure to air during transfer.

9. Transfer the reagent. Remove the needle from the bottle, keeping the inert gas layer at the syringe tip. Do not panic if you observe a small flame at the tip of the needle. It will either quickly self-extinguish or you can douse the needle in a beaker of sand to extinguish it. Insert the syringe into the septum of the reaction vessel (previously prepared under inert atmosphere and open to a positive pressure), keeping the inert gas layer between the syringe and needle. Holding the plunger down and stabilizing the syringe-needle connection, carefully inject the inert gas and your pyrophoric reagent

into the flask. Pyrophoric reagents are often added dropwise or slowly, so as to maintain a constant temperature and avoid violent exothermic reactions.

Cannula/Double-Tipped Needle Transfer - Recommended for 10 mL or more. Do not use multiple syringe transfers to bypass the limit.

1. Prepare the vessel that will receive the pyrophoric (reaction flask, addition funnel, secondary flask that will be added subsequently to a reaction, etc.). To accurately measure the volume added while using a cannula, an addition funnel is best. Place the vessel under an inert atmosphere, either by flushing with nitrogen or argon or by evacuation cycles. The use of a manifold delivering anhydrous, high purity nitrogen or argon and equipped with a mineral oil bubbler (to release excess pressure) is highly recommended. Typically, reactions are carried out in a Schlenk flask under positive pressure from the inert gas manifold, connected via a stopcock valve to the rubber tubing. A Schlenk vessel is highly recommended, as it provides better control of the atmosphere.

2. Use a clamp to hold your reagent container firmly in place. Connect the reagent bottle to an inert gas line to provide positive pressure. Ensure that the line is equipped with a mineral oil bubbler to relieve excess pressure. *Never use a syringe needle through the septum to relieve pressure!*

3. Insert one end of the cannula into the reagent container, but do not allow the tip to reach the reagent itself. Flush the cannula with inert gas using the positive pressure being supplied by the inert gas manifold. Insert the other end of the cannula through the septum of the receiving vessel. It is recommended to position the sending and receiving flasks at the same height, at a distance that puts minimal strain on the natural shape of the cannula. *If using a Schlenk line, remember that the receiving flask must be affixed with its own bubbler (independent of the main inert gas manifold) to create a pressure differential.*

4. Transfer the reagent. Carefully push the end of the cannula that is in the reagent container down into the liquid. The pressure from the inert gas line will begin forcing the liquid through the cannula.

5. After the desired amount of reagent has been transferred, pull the end of the cannula that is in the reagent container up into the headspace, flushing it with inert gas. Remove the end of the cannula from the receiving vessel first, and then remove the other end of the cannula from the reagent container. If a flame forms at either tip, extinguish it in a beaker of sand.

TECHNIQUES FOR USING PYROPHORIC REAGENTS IN A GLOVE BOX

Pyrophoric reagents can be conveniently and safely handled in a glove box. Even in the inert atmosphere of the glove box, special precautions must be made, including considerations of scale and difficulties with controlling exothermic reactions.

Running reactions in a fume hood after preparing reagents in the glove box

1. Prepare the vessel that will receive the pyrophoric (reaction flask, addition funnel, secondary flask that will be added subsequently to a reaction, etc.). Place the vessel under an inert atmosphere in a fume hood, either by flushing with nitrogen or argon or by evacuation cycles. The use of a manifold delivering anhydrous, high purity nitrogen or argon and equipped with a mineral oil bubbler (to release excess pressure) is highly recommended. Typically, reactions are carried out in a Schlenk flask under positive pressure from the inert gas manifold, connected via a stopcock valve to the rubber tubing. A Schlenk vessel is highly recommended, as it provides better control of the atmosphere.

2. Bring the reagent into the glovebox. This can be accomplished by transferring into a Teflon-sealed pressure vessel on a Schlenk line, followed by pumping through the antechamber. Alternatively, the cap of a previously unused commercial container can be tightly taped and carefully pumped through the antechamber, followed by opening the lead and purging the glove box atmosphere to remove any air that was present between the cap and the septum seal.

3. Bring in a syringe (no larger than 10 mL) and a small septum in a secondary containment tray. Load the syringe under the inert atmosphere of the glove box, carefully removing any bubbles before. Long (ca. 10”) needles are ideal for subsequent handling outside the box, as this allows for drawing a blanket of inert atmosphere into the syringe after the desired quantity is measured. Carefully insert the needle into the septum to protect the contents from exposure to air upon removal from the glove box.

4. Place the loaded syringe in the metal secondary container, and remove from the glove box (wearing all of the PPE required above and with a bucket of sand at hand). Carefully and promptly bring the syringe to the hood, where you have already prepared a septum-fitted reaction flask. Pierce the syringe through the septum, and proceed as described above.

Running reactions inside the glove box

The glove box is only recommended for small-scale reactions, or reactions that can be safely carried out at room temperature. Most reactions are carried out at low temperature; in this case, the glovebox must be equipped with a cold well, which will be used to cool the reaction flask. Maintaining a consistent low temperature over the course of a large-scale addition is difficult, and should not be attempted. The safest way to add pyrophoric reagents at a constant temperature is using Schlenk techniques (see above). A small amount of pyrophoric reagent can be safely added to a thawing or warming reaction mixture.

CLEANUP AND DISPOSAL

Equipment Cleanup

A. Needles and syringes used in the transfer may contain a small amount of pyrophoric material. Always clean needles and syringes quickly to avoid clogging the bore (which could potentially trap reactive chemicals inside). Draw an aliquot of degassed, anhydrous high boiling point aprotic solvent in which the reagent is soluble into the syringe (toluene usually works well), then inject the contents into a Schlenk flask that has been placed under an inert gas (N_2 or Ar) and equipped with a stir bar. Repeat for a total of three rinses, at which time the syringe can be disposed of in a sharps container (if disposable) or further cleaned using standard procedures (e.g. isopropanol/water/acetone) and returned to storage. Cool the Schlenk flask in an ice bath and slowly add isopropanol while stirring. The reaction may bubble or exotherm; adjust the rate of isopropanol addition accordingly and ensure uniform mixing. Once bubbling/exotherm has stopped, add a large excess of water and continue stirring for at least an hour. Once quenched, the mixture can be added to the appropriate waste container or labeled as its own waste.

B. Rinse cannulas by passing degassed, anhydrous high boiling point aprotic solvent in which the reagent is soluble (toluene usually works well) through the cannula into a Schlenk flask that has been placed under an inert gas (N_2 or Ar) and equipped with a stir bar. Then cool the flask in an ice bath and while stirring rinse the cannula by passage of isopropanol followed by water. Watch carefully for bubbling and adjust the rate of addition as necessary to control any possible exotherm. Then the cannula can be cleaned using standard procedures as needed and returned to storage. The solvent mixture, once quenched, can be added to the appropriate waste container or labeled as its own waste stream.

C. Spatulas used to transfer solid pyrophoric reagents (e.g. Na, K, NaK) can be contaminated with trace metals stuck to the surface. These can be cleaned using toluene/isopropanol mixtures under an N2 stream.

Disposal

A. Contact EHS for assistance with disposal of large quantities of pyrophoric chemicals. If only trace amounts of the reagent remain, use a relatively unreactive hydrocarbon solvent such as toluene to triple rinse the bottle, collecting the rinse in a Schlenk flask that has been placed under an inert gas (N_2 or Ar) and is equipped with a stir bar. Cool the Schlenk flask in an ice bath and slowly add isopropanol while stirring. The reaction will likely bubble and exotherm, so adjust the rate of isopropanol addition accordingly. Once bubbling/exotherm has stopped, add a large excess of water and continue stirring for at least an hour. Once quenched, the mixture can be added to the appropriate waste container or labeled as its own waste. Small amounts of pyrophoric solids (e.g. Na, K, NaK) can be quenched in analogous fashion: the solid is placed under N2 in a flask, toluene is added, and then small amounts of isopropanol are add by syringe under N2 flow. Use caution, as solids can sometimes have oxide layers that lead to delayed reactions. Stir vigorously and confirm that bubbles are forming as expected before adding water.

References and Related SOPs

- Quenching SOP
- Waste SOP
- Degassing SOP
- Columbia University EHS: http://ehs.columbia.edu/pyrophorics.pdf
- Aldrich Technical Bulletin AL-164: http://www.sigmaaldrich.com/etc/medialib/docs/Aldrich/Bulletin/al_techbull_al164.Par.0001.File.tmp/al_techbull_al164.pdf