

Procedures¹ for Safe Use of Pyrophoric Organolithium Reagents

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Scope

Storage, transfer and use of organolithium reagents including (but not necessarily limited to):

Alkyls –

- Methyl-d3-lithium, as complex with lithium iodide solution 0.5 M in diethyl ether
- Methyllithium lithium bromide complex solution
- Methyllithium solution purum, ~5% in diethyl ether (~1.6M)
- Methyllithium solution purum, ~1 M in cumene/THF
- Methyllithium solution 3.0 M in diethoxymethane
- Methyllithium solution 1.6 M in diethyl ether
- Ethyllithium solution 0.5 M in benzene/cyclohexane (9:1)
- Isopropyllithium solution 0.7 M in pentane
- Butyllithium solution 2.0 M in cyclohexane
- Butyllithium solution purum, ~2.7 M in heptane
- Butyllithium solution 10.0 M in hexanes
- Butyllithium solution 2.5 M in hexanes
- Butyllithium solution 1.6 M in hexanes
- Butyllithium solution 2.0 M in pentane
- Butyllithium solution ~1.6 M in hexanes
- Butyllithium solution technical, ~2.5 M in toluene
- Isobutyllithium solution technical, ~16% in heptane (~1.7 M)
- sec-Butyllithium solution 1.4 M in cyclohexane
- tert-Butyllithium solution purum, 1.6-3.2 M in heptane
- tert-Butyllithium solution 1.7 M in pentane
- (Trimethylsilyl)methyllithium solution 1.0 M in pentane
- (Trimethylsilyl)methyllithium solution technical, ~1 M in pentane
- Hexyllithium solution 2.3 M in hexane
- 2-(Ethylhexyl)lithium solution 30-35 wt. % in heptane

Alkynyls –

- Lithium acetylide, ethylenediamine complex 90%
- Lithium acetylide, ethylenediamine complex 25 wt. % slurry in toluene
- Lithium (trimethylsilyl)acetylide solution 0.5 M in tetrahydrofuran
- Lithium phenylacetylide solution 1.0 M in tetrahydrofuran

Aryls –

- Phenyllithium solution 1.8 M in di-n-butyl ether

Others –

- 2-Thienyllithium solution 1.0 M in tetrahydrofuran
- Lithium tetramethylcyclopentadienide
- Lithium pentamethylcyclopentadienide

Hazards

In general these materials are pyrophoric; they ignite spontaneously when exposed to air. This is the primary hazard and reagents must be handled so as to rigorously exclude air/moisture. They all tend to be toxic and come dissolved in a flammable solvent.. Other common hazards include corrosivity, teratogenicity, water reactivity, peroxide formation, along with damage to the liver, kidneys, and central nervous system.

Controlling the Hazards

BEFORE working with pyrophoric reagents, read the relevant Material Safety Data Sheets (MSDS) and understand the hazards. The MSDS must be reviewed before using an unfamiliar chemical and periodically as a reminder. Pyrophorics users must be thoroughly-trained in proper lab technique and working alone with pyrophorics is strongly discouraged.

Set up your work in a laboratory fume hood or glove box and ALWAYS wear the appropriate personal protective equipment.

Minimize the quantity of pyrophoric reagents used and stored.

The use of smaller syringes is encouraged. If handling more than 20 ml of sample - one should use a cannula for transfer or use a 20 ml syringe repeatedly.

Personal Protective Equipment (PPE)

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 glasses will NOT provide adequate protection unless they also meet this standard. When there is the potential for splashes, goggles must be worn, and when appropriate, a face shield added.
- A face shield is required any time there is a risk of explosion, large splash hazard or a highly exothermic reaction. All manipulations of pyrophoric chemicals which pose this risk should occur in a fume hood with the sash in the lowest feasible position. Portable shields, which provide protection to all laboratory occupants, are acceptable.

Skin Protection

- Gloves must be worn when handling pyrophoric chemicals. Nitrile gloves should be adequate for handling most of these in general laboratory settings but they are combustible. Be sure to use adequate protection to prevent skin exposures. Sigma-Aldrich recommends the use of nitrile gloves underneath neoprene gloves².
- A lab coat or apron (not made from easily ignited material like nylon or polyester) *must be worn*. Special fire-resistant lab coats made from Nomex are more expensive, but recommended for labs using these reagents routinely.

- No open toe shoes are allowed.

Equipments and Notification

- Have the proper equipment and the phone number for the Police (9-1-1) readily available for any emergencies.

Designated Area

Eyewash

- Suitable facilities for quick drenching or flushing of the eyes should be within 10 seconds travel time for immediate emergency use. Bottle type eyewash stations are not acceptable.

Safety Shower

- A safety or drench shower should be available within 10 seconds travel time where pyrophoric chemicals are used.

Fume Hood

- Many pyrophoric chemicals release noxious or flammable gases and should be handled in a laboratory hood. In addition, some pyrophoric materials are stored under kerosene (or other flammable solvent), therefore the use of a fume hood (or glove box) is required to prevent the release of flammable vapors into the laboratory.

Glove (dry) box

- Glove boxes are an excellent device to control pyrophoric chemicals when inert or dry atmospheres are required.

Important Steps to Follow

Handling pyrophoric Reagents –

- By using proper syringe techniques, these reagents can be handled easily in the laboratory.

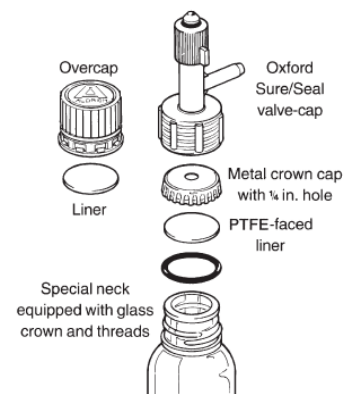


Fig. 1A Sure/Seal components

The Aldrich³ Sure/Seal™ Packaging System

The Sure/Seal packaging system (**Fig. 1A**) provides a convenient method for storing and dispensing air-sensitive reagents. The reagent can be dispensed using a syringe or double-tipped needle (16, 18 or 20 gauge) inserted through the hole in the metal cap. When inserting a needle through a septum, a layer of silicone or hydrocarbon grease on the septum will help. Upon withdrawal of the needle, the small hole that remains in the PTFE liner will not cause the reagent to deteriorate under normal circumstances. However, it is recommended that the plastic cap be replaced after each use and in particular for long-term storage.

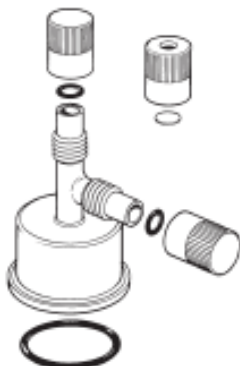


Fig. 1B Sure/Seal septum-inlet transfer adapter

For extended storage of unused reagents, use the solid plastic cap, or equip the bottle with an Oxford Sure/Seal valve cap, or transfer the reagent to a suitable storage vessel.

The Sure/Seal septum-inlet transfer adapter (**Fig. 1B**) can be used when repeated dispensing is necessary. The adapter protects the contents of the bottles from air and moisture.

Transferring Pyrophoric Reagents with Syringe

- In a fume hood or glove box, clamp the reagent bottle to prevent it from moving
- Clamp/secure the receiving vessel too.
- After flushing the syringe with inert gas, depress the plunger and insert the syringe into the Sure/Seal bottle with the tip of the needle below the level of the liquid
- Secure the syringe so if the plunger blows out of the body it, and the contents will not impact anyone (aim it toward the back of the containment)
- Insert a needle from an inert gas source carefully keeping the tip of the needle above the level of the liquid
- Gently open the inert gas flow control valve to slowly add nitrogen gas into the Sure/Seal bottle.
- This will allow the liquid to slowly fill the syringe (up to 100mL) as shown in **Fig. 2A**. Pulling the plunger causes gas bubbles.
- Let nitrogen pressure push the plunger to reduce bubbles. Excess reagent and entrained bubbles are then forced back into the reagent bottle as shown in **Fig. 2B**.
- The desired volume of reagent in the syringe is quickly transferred to the reaction apparatus by puncturing a rubber septum as illustrated in **Fig. 2C**.

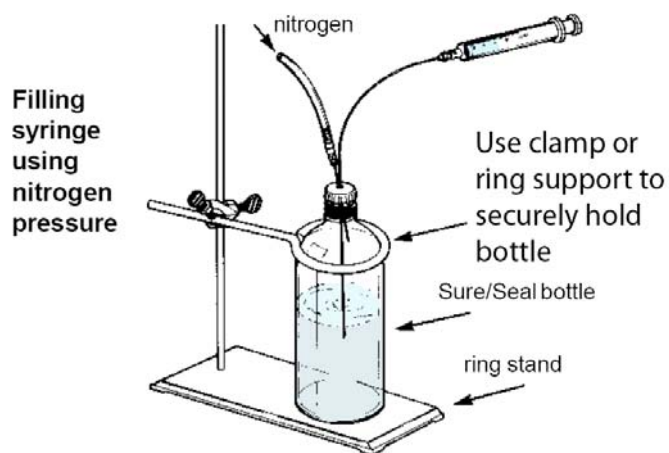


Fig. 2A Filling syringe using nitrogen pressure

Removing gas bubbles and returning excess reagent to the Sure/Seal bottle

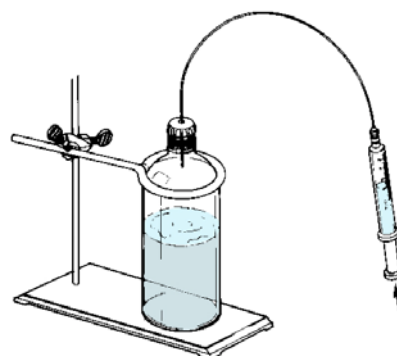


Fig. 2B Removing gas bubbles and returning excess reagent to the Sure/Seal bottle

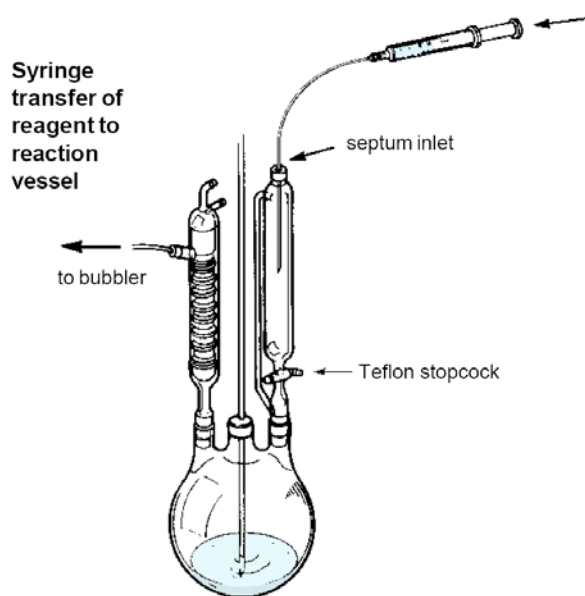


Fig. 2C Syringe transfer of reagent to reaction vessel

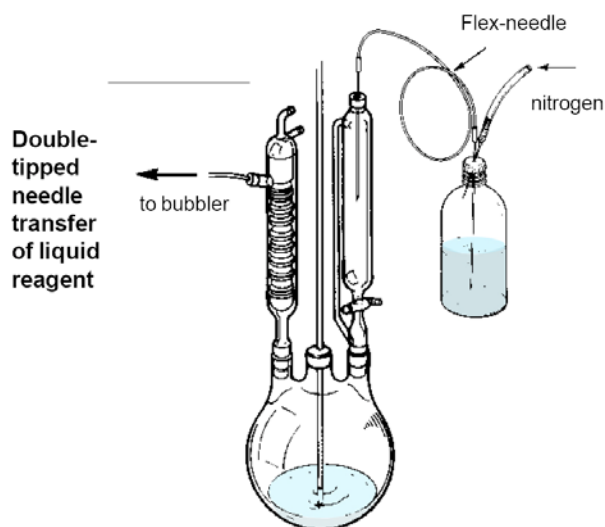


Fig. 3A Double-tipped needle transfer of liquid reagent

Transferring Pyrophoric Reagents with a Double-Tipped Needle

- The double-tipped needle technique is recommended when transferring 50 mL or more.
- Pressurize the Sure/Seal bottle with nitrogen and then insert the double-tipped needle through the septum into the headspace above the reagent. Nitrogen will pass through the needle. Insert the other end through the septum at the calibrated addition funnel on the reaction apparatus. Push the needle into the liquid in the Sure/Seal reagent bottle and transfer the desired volume. Then withdraw the needle to above the liquid level. Allow nitrogen to flush the needle. Remove the needle first from the reaction apparatus and then from the reagent bottle. (**Fig. 3A**)
- For an exact measured transfer, convey from the Sure/Seal bottle to a dry nitrogen flushed graduated cylinder fitted with a double-inlet adapter (**Fig. 3B**). Transfer the desired quantity and then remove the needle from the Sure/Seal bottle and insert it through the septum on the reaction apparatus. Apply nitrogen pressure as before and the measured quantity of reagent is added to the reaction flask.

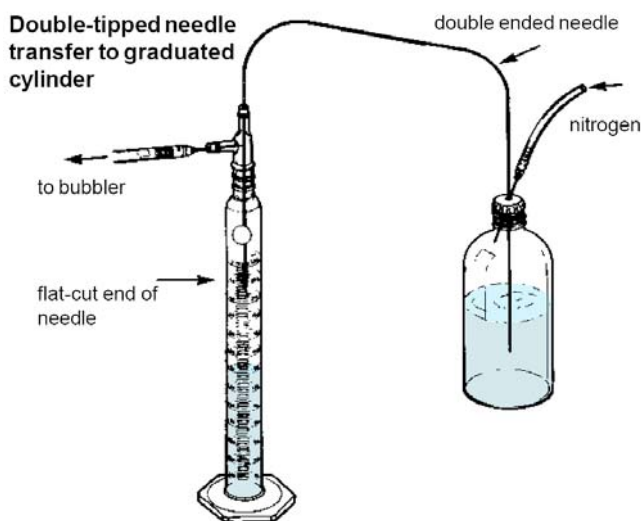


Fig. 3B Double-tipped needle transfer to graduated cylinder

- To control flow rate, fit a Luer lock syringe valve between two long needles as shown in (Fig. 3C).

Storage

- Pyrophoric chemicals should be stored under an atmosphere of inert gas or under kerosene as appropriate.
- Avoid areas with heat/flames, oxidizers, and water sources.
- Containers carrying pyrophoric materials must be clearly labeled with the correct chemical name and hazard warning.
- For storage prepare a storage vessel with a septum filled with an inert gas
 - Select a septum that fits snugly into the neck of the vessel
 - Dry any new empty containers thoroughly
 - Insert septum into neck in a way that prevents atmosphere from entering the clean dry (or reagent filled) flask.
 - Insert a needle to vent the flask and quickly inject inert gas through a second needle to maintain a blanket of dry inert gas above the reactive reagent.
 - Once the vessel is fully purged with inert gas, remove the vent needle then the gas line.
- For long-term storage, the septum should be secured with a copper wire (figure 4A).

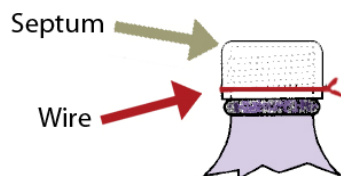


Fig. 4A Septa wired to vessel

- For extra protection a second same-sized septa (sans holes) can be placed over the first (figure 4b).
- Use parafilm around the outer septa and (obviously) remove the parafilm and outer septa before accessing the reagent through the primary septa

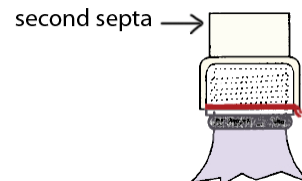


Fig. 4B For long-term storage, use a second septa

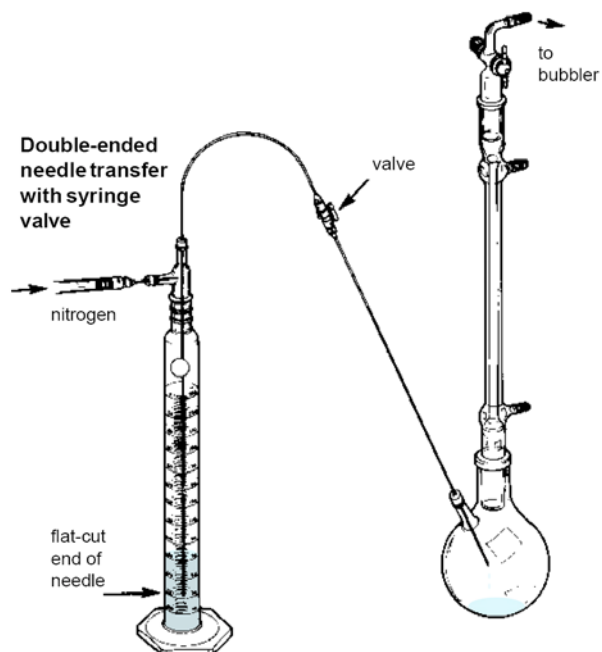


Fig. 3C Double-ended needle transfer with syringe valve

Disposal of Pyrophoric Reagents

- A container with any residue of pyrophoric materials should never be left open to the atmosphere.
- Any unused or unwanted pyrophoric materials must be destroyed by transferring the materials to an appropriate reaction flask for hydrolysis and/or neutralization with adequate cooling.
- The essentially empty container should be rinsed three times with an inert dry solvent; this rinse solvent must also be neutralized or hydrolyzed.
- After the container is triple-rinsed, it should be left open in back of a hood or atmosphere at a safe location for at least a week. After the week, the container should then be rinsed 3 times again.

Disposal of Pyrophoric Contaminated Materials

- All materials that are contaminated with pyrophoric chemicals should be disposed of as hazardous waste.
- Alert EH&S for any wastes contaminated by pyrophoric chemicals.
- The contaminated waste should not be left overnight in the open laboratory but must be properly contained to prevent fires.

Emergency Procedures

Spill

- Powdered lime should be used to completely smother and cover any spill that occurs.
- A container of powdered lime should be kept within arm's length when working with a pyrophoric material.
- If anyone is exposed, or on fire, wash with copious amounts of water.
- The recommended fire extinguisher is a standard dry powder (ABC) type. Class D extinguishers are recommended for combustible solid metal fires (e.g, sodium, LAH), but not for organolithium reagents.
- Call 9-1-1 for emergency assistance

¹ Created from a variety of resources, principally the Sigma-Aldrich Technical Bulletins and these websites: www.safety.rochester.edu/ih/standops8.html & www.brandeis.edu/ehs/labs/pyrophoric.html another good resource is Advanced Practical Organic Chemistry by J. Leonard, B. Lygo, and G. Procter esp. pages 76-98

² Private communication to Rebecca Lally (rrlally@uci.edu) at UC Irvine in January 2009

³ Images and advice from Sigma-Aldrich Technical Bulletins AL-134 and AL-164 at: <http://www.sigmaaldrich.com/chemistry/aldrich-chemistry/tech-bulletins/tech-bulletin-numbers.html>