STANDARD OPERATING PROCEDURE

Procedure Title	**Passivation of n-Butyl Lithium.** *This SOP is also valid for passivation of other alkyl lithium solutions, of Grignard reagents, and of lithium alkyl amides.*
Procedure Author	Patrick Frank/Cynthia Patty
Date of Creation/Revision	14 November 2016
Name of Responsible Person *(The PI, Lab Supervisor, or Autonomous Researcher)*	Cynthia Patty/Patrick Frank
Location to be Performed (building/lab #, beam lines)	SSRL B131, Rm 209.
Proposal #s:	

#1	**Process or Experiment Description:** *Briefly summarize the process or experiment, including an estimate of how long the process takes and how frequently it will be conducted. Include total quantities (volume, mass) of the materials you to expect to use.*

Commercial n-butyl lithium, 1.6 M in hexane, will be passivated in a two-step process, using anaerobic Schlenk-line methods.

The full passivation will require two reactions:

$$C_4H_9Li + (CH_3)_2CHOH \rightarrow C_4H_{10} + (CH_3)_2CHOLi \quad \textbf{1}$$

$$(CH_3)_2CHOLi + CH_3COOH \rightarrow (CH_3)_2CHOH + CH_3COOLi \quad \textbf{2}$$

Reaction 1 is a quench by dropwise addition of n-butyl lithium to very cold (-60 to -70 C) 2-propanol, producing lithium 2-propoxide.

Reaction 2 is acetic acid neutralization of lithium 2-propoxide, producing lithium acetate/acetic acid buffer in 2-propanol/hexane solution.

Table of Properties

Compound	FW (gm)	Quantity	moles	Properties	pK_a
n-butyl lithium; 1.6 M (in hexanes)[a]	64.055	50 mL	0.080	pyrophoric	50[b]
2-propanol[c]	60.096	100 mL	1.31	d^{20} = 0.786 gm/mL	16.5[b]
Acetic acid	60.053	10 mL	0.175	d^{20} = 1.049 gm/mL	4.756[d]

a. A 1.6 M solution includes 102.5 mg of n-butyl lithium per mL = 1.6 mmols. b. reference [1], Table 8.1; pK_a of the parent acid. c. anhydrous reagent. d. reference [2].

[1] Smith, M.B. and J. March, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*. 6 ed. 2007, New York: McGraw-Hill, Table 8.1, pp. 359-364.

[2] ACS, *Dissociation Constants of Organic Acids and Bases*, in *CRC Handbook of Chemistry and Physics*, W.W. Haynes, Editor. 2016-2017 (internet Version 2017), CRC Press/Taylor & Francis: Boca Raton, FL.

In the event this SOP is adapted to passivate a lithium alkylamide, the two-fold excess of acetic acid will be sufficient to also neutralize the alkyl amine product of a revised reaction 1.

#2	**Risk Assessment:**. *Identify potential safety hazards. For chemical hazards, be specific (e.g. flammability, corrosivity, reactivity/explosion, acute toxicity, or carcinogenicity). List OSHA Hazards, NPFA ratings, and occupational exposure limits.*

n-butyl lithium: pyrophoric, flammable liquid, toxic, corrosive, skin and eye damage, inhalation hazard
NFPA Rating: Health hazard: 3; Fire Hazard: 3; Reactivity Hazard: 3.
2-propanol: flammable liquid, eye irritation
NFPA Rating: Health hazard: 2; Fire Hazard: 3; Reactivity Hazard: 1
Acetic acid: flammable liquid, corrosive, eye damage
NFPA Rating; Health hazard: 3; Fire Hazard: 2; Reactivity Hazard: 0
Dry ice (solid CO_2): frost bite hazard
NFPA Rating: Health hazard: 3; Fire Hazard: 0; Reactivity hazard: 0

#3	**Safety Equipment:** *Specify all equipment needed to safely perform research or experiment.*

#3a Engineering/Ventilation Controls: *(e.g. fume hood use, explosion shielding, equipment interlocks, absorbent bench paper)*

n-butyl lithium is provided in a crimp-capped nitrogen-filled serum bottle. This procedure must be carried out in a fume hood equipped with a Schlenk line having both nitrogen and vacuum manifolds.

#3b Personal Protective Equipment and Other Safety Equipment: *(e..g safety glasses, nitrile gloves, cryo gloves)*
Safety glasses or face shield; nitrile gloves; lab coat.

#3c Location of Nearest Emergency Safety Equipment:

Item:	Location:
Eyewash/Safety Shower	**Eyewash drench hoses are located, next to the sinks (B120, Rm 257, 258; B131, Rm 113, 209). An eyewash/facewash is located next to the water system, near the lab entrance (B120, Rm 257). Safety showers are located in front of the sink (B131, Rm 113),near the water system and cold room entrance (B131, Rm 209), and near the lab entrance (B120, Rm 257).**
First Aid Kit	**First aid kits are located at 4 Safety Stations around the experimental floor, near BL2-2, 9-3, 6-2, and 4-2. Contact SLAC Medical (x2281) or Security (x5555) for non-life threatening injuries. Call 911 for life threatening situations.**
Chemical Spill Kit	**Spill kits are located near the sinks (B120, Rm 257, 258), underneath the bench tops (B131, Rm 113), or next to the entrance to the lab (B131, Rm 209).**

Fire Extinguisher	**Fire extinguishers are located near the lab entrance (B120, Rm 257, 258; B131, Rm 209) or just outside the laboratory door (B120, Rm 260; B131, Rm 113).**
Telephone	**Telephones are located near the entrance to the labs.**
Fire Alarm Manual Pull Station	**A fire alarm pull station is located outside the laboratory, on the outside stairway door frame between rooms 252A& 254 (B120) or near the building exit door, between beam lines 11-2 and 4-3 (B131).**
Safety Stations	**Safety Stations around the experimental floor, near BL2-1, 9-3, 6-2, and 4-2. Contact SLAC Medical (x2281) or Security (x5555) for non-life threatening injuries. Call 911 for life threatening situations.**

#4	**Shipping and Receiving Requirements:** *Describe shipping or receiving requirements, especially for highly toxic, highly reactive/ unstable materials, highly flammables, and corrosives. .*

Follow standard SSRL shipping and receiving protocols. N/A

#5	**Designated Area:** *Where highly toxic materials,, highly flammable/pyrophoric, highly corrosive, reactive/unstable, or nanomaterials are used, identify the designated work area(s), and the necessary personnel decontamination after completion of work.*

Work-area: Schlenk-line equipped fume hood.

#6	**Step-By-Step Operating Procedure:** *Provide a sequential description of work, including details such as chemical concentrations and when special safety equipment is to be utilized. Include temperature, pressure, and other experimental conditions. Schematics, or pictures are suggested for complex set ups.*

Equipment:
Schlenk line (vacuum and nitrogen purge manifold)
Schlenk flask, 250 mL; equipped with a serum stopper
Magnetic stirrer and ptfe-coated stir bar
Double-pointed stainless steel cannula
Schlenk-line port needles
Ice bath vessel (Dewar bowl is ideal)
Dry ice
Two three-prong clamps (ring-stand optional)

Procedure:

Step 1: *Preparation of the 2-propanol quenchant.*

1.1 In the Schlenk hood, clamp a 250 mL Schlenk flask to the rack. Support the flask on a magnetic stirrer equipped with a cold-bath Dewar. Make a vacuum tubing hose connection between the Schlenk flask side-arm and the Schlenk line. Seal the Schlenk hose and side-arm connection using a hose clamp (see Figure below).

1.2 Fill the 250 mL Schlenk flask with 100 mL of 2-propanol. Add a ptfe magnetic stir bar. Close with a white sleeve-type serum stopper. Secure the serum stopper sleeve using a hose-clamp. Add dry ice to the Dewar and cool the 2-propanol with stirring.

1.3 Subject the cold 2-propanol to three evacuation-nitrogen equilibration purges on the Schlenk line. Follow the SSRL SOP for degassing water. Leave the anaerobic 2-propanol in the cold bath for heat-removal during the quench.

1.4 After completion of the degassing sequence, leave the cold anaerobic 2-propanol stirring under static Schlenk line nitrogen pressure. Leave the Schlenk flask stem valve open.

Step 2: *Set-up*

2.1 The nitrogen side of the Schlenk line has been prepared for use by way of the evacuation cycles of the 2-propanol. Prepare a Schlenk hose with an 18-gauge needle tip.

2.2 Remove the septum-sealed bottle of n-buyl lithium from the glove box, and carry it to the hood containing the Schlenk line. Clamp the sealed bottle to a ring-stand or the hood-rack, six to eight inches (within ready cannula distance) from the cold stirring 2-propanol Schlenk flask.

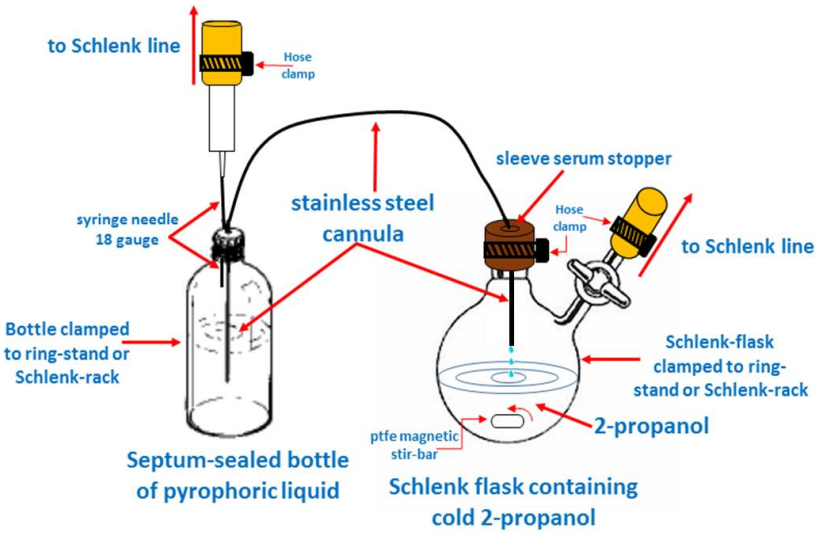

Figure: Schlenk line set-up to quench n-butyl lithium by dropwise addition into cold stirred 2-propanol. Ring-stand or rack clamps are not shown. The dry ice cold bath is not shown; nor the magnetic stir-plate.

2.3 Flow nitrogen through the needle-tipped hose for about 30 seconds, to replace all the air in the hose with Schlenk nitrogen. Following this, pierce the needle through the bottle serum cap. The needle tip should be well above the surface level of the n-butyl

lithium solution. The solutions of n-butyl lithium and 2-propanol are now under the identical nitrogen pressure-head. The Figure above shows the Schlenk line arrangement for the quenching step.

Step 3: *Final connections*

3.1 One end of the cannula is inserted through the middle of the septum on the Schlenk flask containing 2-propanol. The tip of the cannula should be well-above the level of the solvent.

3.2 Nitrogen flow out through the open end of the cannula is verified with the wetted tip of a finger. Flow is to continue for about 30 seconds, to allow displacement of all the air inside the cannula.

3.3 After this time, the free tip of the cannula is inserted through the serum cap septum of the bottle of n-butyl lithium.

3.4 Push the cannula further, until the tip goes right down to the bottom of the n-butyl lithium solution.

Both the bottle and the Schlenk flask are at identical pressures. Therefore, no flow will occur between the vessels.

Step 4: *The Quench*

4.1 At the 2-propanol Schlenk flask, close the Schlenk line nitrogen manifold inlet valve.

4.2 Carefully, slowly, and cautiously, on the 2-propanol Schlenk flask side, open the Schlenk line vacuum manifold valve. Monitor the sound of the pump. Cease opening the Schlenk line vacuum manifold valve as soon as the pump tone changes.

4.3 Monitor the tip of the cannula above the 2-propanol solution. Watch for the appearance of a flow of n-butyl lithium solution. The flow should be slow dropwise.

4.4 If the flow of n-butyl lithium is a stream, close the vacuum manifold valve, and open the nitrogen manifold valve to again equal pressure. The flow of n-butyl lithium solution will stop.

4.4.1 Repeat steps 4.2 and 4.3, but with a more gradual opening of the valve on the Schlenk line vacuum manifold. Watch for a drop-wise flow of n-butyl lithium solution.

4.4.2 When the dropwise flow is successfully achieved, allow to proceed. The vacuum valve can be adjusted from time-to-time to maintain flow.

4.5 Watch the quench. If it proceeds in a quiet fashion (the 2-propanol is relatively quiescent), the rate of flow of n-butyl lithium can be increased.

4.6 Continue addition, until all of the n-butyl lithium solution has migrated over into the cold 2-propanol solution.

4.7 Close the vacuum manifold valve to the 2-propanol quench, and open the nitrogen manifold valve. The empty reagent bottle and the Schlenk flask are now again at equal internal pressure.

Step 5: *Final rinse*

5.1 After all the n-butyl lithium solution has migrated through the cannula into the cold 2-propanol, the original reagent bottle will be rinsed.

5.2 At the n-butyl lithium reagent bottle, pull the cannula tip up to about half-way between top and bottom
5.3 At the 2-propanol Schlenk flask, push the cannula tip about half-way into the cold solution.
5.4 At the n-butyl lithium side, close the nitrogen manifold valve, and slowly open the vacuum manifold valve. Cold 2-propanol solution will traverse the cannula and flow into the empty reagent bottle.
5.5 Continue flow until about 1 cm (0.5 inch) of cold 2-propanol collects in the previously empty n-butyl lithium reagent bottle.
5.6 When 5.5 is achieved, and at the reagent bottle, close the vacuum manifold valve and open the nitrogen manifold valve, equalizing pressure with the Schlenk flask.
5.7 Unclamp the reagent bottle. Carefully raise and tip the bottle, then swirl the contents to wash down the internal surface. Tip far enough to swirl the 2-propanol up onto the serum cap.
5.8 Continue until the entire internal surface of the reagent bottle has been rinsed.
5.9 Reclamp the rinsed n-butyl lithium reagent bottle. At the Schlenk side, raise the cannula tip above the level of the 2-propanol. At the reagent bottle side, lower the cannula tip to the bottom of the bottle.
5.10 Repeat steps 4.1-4.9, to transfer all the 2-propanol rinsate back into the 2-propanol Schlenk flask.
5.11 After 5.10, all the 2-propanol rinsate solution should be in the Schlenk flask, which now contains a solution of 2-propanol, lithium 2-propoxide, and hexanes. Pyrophoricity is no more.

Step 6: *Acetic acid neutralization*
6.1 Remove the cannula from both the empty reagent bottle and the Schlenk flask. Close the Schlenk flask stem valve. Remove the Schlenk nitrogen inlet lines from both vessels.
6.2 Remove the cold bath from beneath the Schlenk flask.
6.3 Remove the sleeve serum cap from the Schlenk flask. The contents are not pyrophoric, but is very alkaline (lithium 2-propoxide).
6.4 Slowly add, with rapid stirring, 10 mL of acetic acid.
6.5 The neutralized solution is now about 150 mL of 33% hexane in 2-propanol, containing 0.53 M lithium acetate and 0.63 M acetic acid.
6.6 The neutralized solution is allowed to warm to ambient temperature and is disposed as flammable hazardous waste.
6.7 The empty reagent bottle is also disposed as hazardous waste. If permitted, the cap can be removed in a fume hood. There is no danger of reaction. The bottle can be left in a fume hood, as permitted, to allow the residues of hexane and 2-propanol to safely evaporate away. These residues should amount to far less than 1 mL. If this procedure is permitted, the clean dry bottle and cap can be disposed as trash.

#7	**Special Handling Procedures, Transport & Storage Requirements:** *Describe special handling and storage requirements for hazardous chemicals in your laboratory, especially for highly reactive/ unstable materials, highly*

	flammables, and corrosives. Describe transport and secondary containment requirements, between the laboratory and beam lines or between facilities.
The n-butyl lithium in its crimp-closed bottle will be carried from the glove box to the Schlenk hood.	
#8	**Beam Line Handling and Storage Requirements:** *Describe sample handling procedures and sampling set up at the beam lines. Are samples sealed or open? Is ventilation required? Are heating, cooling, or gas distribution systems present?*
N/A no beam line experiment	
#9	**Emergency Procedures:** *Indicate how spills, personnel exposure/ injury, and other accidents should be handled and by whom. List emergency contact numbers.*
Safety Shower/Eye Shower: Any serious chemical self-contamination. Evacuate the Lab, and call 911 if: 1. Serious chemical self-contamination 2. Large hazardous material release. 3. Smoke, chemical fire, explosion. Call x5555 if: 1. Non-life threatening injury 2. Non-life threatening chemical or radiation incident. Additional Emergency Procedures:	
#10	**Waste Disposal:** *Identify amounts of waste anticipated and appropriate disposal procedures.*
Waste will be segregated by hazard class (e.g. flammable, corrosive) and state (e.g. solid, liquid), appropriately labeled, and placed in the laboratory's hazardous waste cabinet. Additional Waste Guidelines:	

#11	**Training Requirements:** *List the general and lab-specific trainings required*

SSRL Laboratory Training.

Additional Training Requirements:
Schlenk line training
Glove box training.

#12	**Approval Required:** *Identify any tasks that require prior approval by the PI/ Laboratory Supervisor (e.g., use of Restricted Chemicals and other higher hazard chemicals, and running of higher hazard operations). List Subject Matter Experts (SMEs) consulted for approval.*

Procedures must be approved by Laboratory Manager and SSRL Safety Coordinators.

Additional Approvers:

Approved by: _____ Approval date: _____

Approved by: _____ Approval date: _____

Approved by: _____ Approval date: _____

Approved by: _____ Approval date: _____