Standard Operating Procedure (SOP)

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PI/Advisor: Process Name:	David A. Shultz **Lithium-Halogen Exchange**		
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This SOP details the procedure for lithium-halogen exchange using *tert*-butyl lithium. **This reaction should only be conducted after (1) observing an experienced graduate student or postdoc perform the procedure at least once, and (2) under direct supervision of an experienced graduate student or postdoctoral researcher**.

I. Purpose

This SOP details the step-by-step procedure to perform lithium-halogen exchange.

It is the responsibility of the user to read and acknowledge their understanding of this SOP.

Prior to using the equipment, the users must:

1- Read this SOP.
2- Be a registered worker or formally allowed to enter the lab with the corresponding safety trainings.

II. Outline of Method

1. Use of correct PPE (disposable gloves, protective eyewear, and lab coat)
2. Oven dry a single-neck round-bottom flask (or Schlenk flask) containing a stir bar
3. Assemble apparatus while still hot using appropriate gloves by securing a septum, and then via needle, connect to inert gas (N_2) line
4. Purge flask by inserting a second needle through the septum and turn stopcock on gas line to push dry N_2 through the flask out the second needle and into the hood; 30 seconds should be sufficient
5. Simultaneously remove the exit needle and turn the stopcock on the gas line to allow gas to flow to both the flask and the gas line bubbler
6. Via cannula or syringe, add a solution of organic halide (typically bromides or iodides) into the flask; flask should never be more than half full
7. Cool flask and contents to -78°C with a dry ice/acetone bath
8. Add 2 equivalents of *tert*-butyllithium dropwise via syringe making sure not to add so fast as to increase the temperature of the reaction mixture

9. Following addition of the *tert*-butyllithium solution, let the reaction stir for 1 hour at -78°C
10. Slowly add electrophile of choice as a solution in THF or ether via syringe or cannula
11. Remove cold bath and allow reaction to warm slowly to room temperature
12. Stir for ~1 hour at room temperature
13. Cool the reaction to -10°C and quench the reaction with excess water
14. Perform aqueous workup/organic solvent extractions according to published procedure

III. Hazards

- Fume hazard
- Fire Hazard (*tert*-butyllithium is pyrophoric)

IV. Laboratory Equipment, Materials & Personal Protective Equipment (PPE)

- **Materials:** *tert*-butyllithium solution (commercial), anhydrous/N_2 saturated tetrahydrofuran or diethyl ether, anhydrous electrophile of choice
- **PPE:** safety goggles, lab coat, and gloves.

V. Emergency Procedures

In case of emergency, dial 911 or 919-515-3000. In case of mercury spill, contact 919-515-7915 (EHSA).

Contact Emergency: David A. Shultz (919) 656-9774

VI. Relevant Photos of Glassware Setups

- Below is a photo of a Schlenk flask in which the integrated stopcock is attached to an inert gas line via flexible tubing (preferably Tygon). A cannula (needle with pointed and flat ends) is inserted for transfer of a liquid or solution from a second Schlenk flask on the right. For lithium halogen exchange, a cold bath would be under the Schlenk flask. To transfer liquids from the flask on the right to the flask on the left, positive gas pressure would be applied via the stopcock with the stopcock on the left opened to the bubbler on the gas line. When properly assembled and with the canula above the level of liquid in the right flask, gas will flow from the right flask to the left flask and out the gas line to a bubbler. When the canula is pushed below the level of the liquid on the right flask, gas pressure will push the liquid through the canula into the flask on the left.

- For addition of larger volumes of solutions to a reaction flask, a self-equilibrating addition funnel should be used.

- The top of the funnel uses a “duck head” adapter to connect to the gas line using flexible tubing (preferably Tygon). For aerobically stable reagents and
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VII. Authorized Personnel

Record acknowledgements that the SOP has been read and understood.
Authorized Users:
I have read this Standard Operating Procedure, understand the contents, have been trained on implementing the contents, and will utilize this procedure without exception.

NAME (print)	Signature	Date	PI Initial
