

**STANDARD OPERATING PROCEDURE TEMPLATE**

***tert*-Butyllithium**

|  |  |
| --- | --- |
| #1 | **CONTACT INFORMATION**  |

|  |  |
| --- | --- |
| **Procedure Title** | **[Specify** – Note: All guidance text in brackets may be deleted**]** |
| **Procedure Author** | **[Specify]** |
| **Creation/Revision Date** | **[Specify]** |
| **Responsible Person**  | [Name of PI, Lab Supervisor, or Autonomous Researcher, as appropriate] |
| **Location of Procedure** | [Building and room number] |
| **Approval Signature** | [Obtain prior approval, as appropriate. See section #10 of this template.] |
| #2 | **THIS STANDARD OPERATING PROCEDURE (SOP) IS FOR A:**  |
| [ ]  **Specific laboratory procedure or experiment** **[Examples: synthesis of chemiluminescent esters, folate functionalization of polymeric micelles, etc.]**[ ]  **Generic laboratory procedure that covers several chemicals [Examples: distillation, chromatography, etc.]**[ ]  **Generic use of specific chemical or class of chemicals with similar hazards [Examples: organic azides, mineral acids, etc.]** |
| #3 | **PROCESS OR EXPERIMENT DESCRIPTION** |
| [Provide a brief description of your process or experiment, including its purpose. Do not provide a detailed sequential description as this will be covered by section #6 of this template. Indicate the frequency and duration below.]

|  |  |
| --- | --- |
| **Frequency:** |  [ ]  one time [ ]  daily [ ]  weekly [ ]  monthly [ ]  other: \_\_\_\_\_\_\_ |
| **Duration per Expt:** | \_\_\_\_\_\_\_ minutes; or \_\_\_\_\_\_\_hours |

 |
| #4 | **SAFETY LITERATURE REVIEW & HAZARD SUMMARY** |
| 1. Hazardous Substances

**tert-butyllithium**t-BuLi is pyrophoric and will catch fire spontaneously in contact with air.Water reactive – in contact with water, including water vapor in the air or on glassware, will release flammable gases, which may ignite spontaneously.Causes severe skin burns and eye damage.Typically used as a solution in other flammable solvents.1. Other Hazards

[List nonchemical hazards, e.g., biological hazards, electrical hazards, mechanical hazards, nonionizing radiation, or ionizing radiation.]1. References

Information on Pyrophoric Compounds <https://ehs.stanford.edu/reference/information-on-pyrophoric-compounds> Aldrich Technical Bulletin, “Handling Pyrophoric Reagents” <https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/marketing/global/documents/255/911/al_techbull_al164.pdf> Aldrich Technical Bulletin, “Handling Air Sensitive Reagents” AL-134 <https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/marketing/global/documents/685/583/al_techbull_al134.pdf> Rathman, T. and Schwindeman, J.A. “Preparation, Properties, and Safe Handling of Commercial Organolithiums: Alkyllithiums, Lithium sec-Organoamides, and Lithium Alkoxides”. *Org. Process Res. Dev.* 2014, 18, 10, 1192–1210. <https://doi.org/10.1021/op500161b> <https://www.youtube.com/watch?v=21iC4YEgOAs&ab_channel=UCLA> [List all references you are using for the safe and effective design of your process or experiment, including safety literature and peer-reviewed journal articles. Safety resources are available at <http://web.stanford.edu/dept/EHS/cgi-bin/lcst/creating-standard-operating-procedures/>.]  |
| #5 | **STORAGE REQUIREMENTS** |
| t-BuLi should be stored in the original manufacturer’s container and the outside of the lid sealed with parafilm tape after use. If the seal under the cap or cap is damaged, request EH&S pickup. Store in an appropriate flammables refrigerator with other group B chemicals. Note: Sigma-Aldrich warns that the [SureSeal](https://www.sigmaaldrich.com/US/en/technical-documents/technical-article/chemistry-and-synthesis/organic-reaction-toolbox/sureseal) cap (and similar caps from other suppliers) may lose integrity over multiple uses. If the bottle will be used multiple times and stored, they recommend transferring the contents to Schlenkware or using an [Oxford Valve Cap](https://www.sigmaaldrich.com/US/en/product/aldrich/z406260) or [similar](https://www.sigmaaldrich.com/US/en/product/aldrich/z407186) covering the SureSeal. See [AL-134](https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/marketing/global/documents/685/583/al_techbull_al134.pdf) and [AL-195](https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/product/documents/409/105/al_techbull__al195.pdf).The degradation products for nBuLi are 1-butene, which is very soluble in the hydrocarbon solvent and produces very little increase in pressure, and LiH, which is insoluble and forms as a finely divided grayish powder. The LiH is usually the primary hazard of alkyllithium solution degradation as it is a flammable corrosive solid. (OPRD, 2014) If you observe signs of degradation, dispose of the container. |
| #6 | **STEP-BY-STEP OPERATING PROCEDURE** |
| [For each step’s description, include any step-specific hazard, personal protective equipment, engineering controls, and designated work areas in the left-hand column.1. **Guidance on Engineering and Ventilation Controls – Review safety literature and peer-reviewed journal articles to determine appropriate engineering and ventilation controls for your process or experiment. Guidance is available from health and safety specialists at Stanford EH&S and online in the General Use SOPs and Laboratory Safety Sheets in the Laboratory Chemical Safety Toolkit (**<http://chemtoolkit.stanford.edu/>**)**
2. **Guidance on Personal Protective Equipment - To assist with your PPE selection, refer to** <http://chemtoolkit.stanford.edu/LabPPE>**. Respiratory protection is generally not required for lab research, provided the appropriate engineering controls are employed. For additional guidance on respiratory protection, consult with EH&S, 723-0448.**
3. **D*e*signated work area(s)** - Required whenever carcinogens, highly acutely toxic materials, or reproductive toxins are used. The intent of a designated work area is to limit and minimize possible sources of exposure to these materials. The entire laboratory, a portion of the laboratory, or a laboratory fume hood or bench may be considered a designated area. See the Chemical Safety Toolkit for more information*.*

Describe the possible risks involved with failure to follow a step in the SOP in the right-hand column.]

|  |  |
| --- | --- |
| **Step-by-Step Description of YourProcess or Experiment** | **Potential Risks if Step is Not Done or Done Incorrectly (if any)** |
| 1. Don personal protective equipment. [x]  appropriate street clothing (long pants, closed-toed shoes)[x]  gloves; indicate type: \_\_\_\_\_\_\_[x]  safety goggles [x]  safety glasses [x]  face shield [ ]  lab coat [x]  flame-resistant lab coat[x]  other: Tie back hair and remove or constrain loose sleeves (e.g., in a cuffed FR lab coat).\_\_\_ |  |
| 2. Check the location/accessibility/certification of the safety equipment that serves your lab:

|  |  |
| --- | --- |
| **Item** | **Status** |
| **Laboratory Fume Hood/Glove Box or other Ventilation Control** | Location: \_\_\_\_\_\_\_*Check sticker to ensure that hood was certified within last 12 months.* |
| **Eyewash/Safety Shower** | Location: \_\_\_\_\_\_\_*Ensure that it is accessible, not blocked.**Check tag that it has been tested within last month.* |
| **First Aid Kit**  | Location: \_\_\_\_\_\_\_ |
| **Chemical Spill Kit**  | Location: \_\_\_\_\_\_\_ |
| **Fire Extinguisher- CO2****Fire Extinguisher–Class ABC** | Location: \_\_\_\_\_\_\_Location: \_\_\_\_\_\_\_ |
| **Telephone** | Location: \_\_\_\_\_\_\_ |
| **Fire Alarm Manual Pull Station** | Location: \_\_\_\_\_\_\_ |

 |  |
| 3. Find a buddy in lab who has been trained on *t*-BuLi safety and notify them of your upcoming work with *t*-BuLi. Ask the buddy to stay in the lab until you’ve completed your work. Provide *t*-BuLi‑appropriate PPE, the [Pyrophorics fact sheet](https://ehs.stanford.edu/reference/information-on-pyrophoric-compounds), and your SOP to the buddy. Notify other nearby lab members that you will be using *t‑*BuLi before beginning work. | *t*-BuLi work should not be done alone. Having a buddy in lab reduces response time in an incident/exposure. |
| 1. Gather safety equipment, including CO2 and Class ABC fire extinguishers, so that they are easily accessible but not obstructing your work area.
 | Safety equipment is necessary for appropriate emergency response.  |
| 1. Remove any unnecessary combustible or flammable materials from the fume hood that will be used. Also clear the floor of unnecessary furniture and clutter to allow access to the eyewash/safety shower and quick egress from the lab.
 | Combustible/flammable materials may allow a fire to spread if there is an incident. |
| 1. Dry all glassware, Luer-lock syringes (plastic or glass with a Teflon plunger tip), needles (if storing *t*-BuLi for further use, use a non-coring needle/cannula no larger than 16 gauge), etc. Ensure Schlenk line is properly set up and gas line (typically nitrogen or argon) is pre-dried through DriRite. The use of balloons to provide an inert atmosphere technique is not recommended for work with pyrophoric reagents.

Glassware and metal syringes can be dried by flaming under vacuum or in an oven overnight. Allow the flask to cool in a dry atmosphere, such as a Schlenk line or in a desiccator.Compatible plastic syringes can be dried by storing in a desiccator with the plunger removed. If you are not certain the syringe is compatible, test it with the same solvent used in your *t*-BuLi solution before attempting to use it for *t*-BuLi.Solvents can be dried using a solvent system or by adding dried molecular sieves to a fresh bottle. Please note that solvent stills are discouraged due to excessive quantities of flammable solvents and water reactive drying agents (e.g., sodium metal) in combination with heat and a nearby water-cooled condenser. | *t*-BuLi is water and air reactive and can ignite spontaneously. Dry/air-free equipment reduces risk of adverse reaction and fire. |
| 1. [Describe the next step in the procedure. Insert additional rows in table, as needed.]
 |  |
| 1. [Describe the next step in the procedure. Insert additional rows in table, as needed.]
 |  |
| 1. [Describe the next step in the procedure. Insert additional rows in table, as needed.]
 |  |
| 1. Transfer *t*-BuLi to a pressure-equalizing addition funnel or receiving flask. There are two methods for transferring *t*-BuLi. In both cases use a clamp or ring stand to support the bottle of *t*­*­*-BuLi, the reaction vessel, the addition funnel, and any other glassware used. Add a layer of silicone or hydrocarbon grease to the *t*-BuLi bottle SureSeal cap (or similar) before inserting a line of dry, inert gas into the headspace above the liquid, using a new puncture hole each time. Ensure the reaction vessel/addition funnel setup has a flow of dry, inert gas and that any glassware joints or seals are airtight using silicone or hydrocarbon grease or a [Teflon sleeve](https://us.vwr.com/store/product/4638090/vwr-ptfe-thin-sleeves) and ring clamps. **Diagrams and images for both transfer options are shown in** [**AL-134**](https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/marketing/global/documents/685/583/al_techbull_al134.pdf)**.**
* Syringe transfer
	+ Use a syringe of at least twice the volume of reagent to be dispensed.
	+ Flush the syringe with inert gas from the headspace of the reaction vessel.
	+ To avoid creating a vacuum in the reagent bottle, slightly and slowly pressurize the bottle of *t*-BuLi with dry, inert gas that is routed to an oil bubbler. Observe slow gas bubbling in the reagent-side oil bubbler.
	+ Insert the syringe tip below the level of *t*-BuLi liquid.
	+ Gently pull back on the syringe to slowly fill it, observing that inert gas is still flowing through the bubbler. Do not tip the bottle upside down.
	+ Once filled to a desired level, direct the syringe vertical to allow gas to rise to the top and slowly eject gas and excess reagent to the bottle until the desired amount is achieved.
	+ Pull the syringe up above the liquid level and gently draw in a small amount of inert gas. (This step may be skipped if very precise quantities are needed).
	+ Quickly and carefully withdraw the needle tip from the bottle and insert it into the septum of the reaction vessel or addition funnel (stopcock closed). (Note: a brief, small flash of flame at the tip of the needle may occur, be prepared).
	+ Addition of *t*-BuLi may be done by addition funnel or slow dropwise addition from the syringe. Use of an addition funnel is more controlled.
	+ Only use the syringe once. Get a new dry syringe/needle for subsequent transfers or use the cannula method.
	+ Rinse the syringe with dry heptane or similar by withdrawing the solvent from a flask (can be open to atmosphere). Release the withdrawn solvent back into the flask. Retain the *t*-BuLi/heptane (or similar) rinse solution for later quenching.
* Cannula transfer
	+ NOTE – If you haven’t done a cannula transfer before, practice with low hazard solutions (e.g., water).
	+ For large volumes (>20 mL) transfer *t*-BuLi via cannula directly into a calibrated addition funnel. (Addition funnel may be calibrated prior to drying by adding a known quantity of water and marking the outside with a marker).
		- An exact measurement of the transfer quantity can be determined by weighing the reagent bottle before and after transfer.
	+ To begin creating the pressure differential between the two sides of the cannula, add a vent needle to the reaction flask that is routed to an oil bubbler and turn off inert gas flow to the receiving side. This will allow excess gas to flow out as liquid is transferred into this flask, while preventing backfill of air into the flask.To finish creating the pressure differential, slightly and slowly pressurize the bottle of *t*-BuLi by inserting a needle that has been flushed with dry, inert gas and is routed to an oil bubbler through the manifold. Observe slow gas bubbling in the reagent-side oil bubbler.
	+ Insert the cannula into the headspace of the *t*-BuLi bottle and allow inert gas to flow through it.
	+ Insert the other end of the cannula into the septum of the addition funnel or receiving flask. You will observe slow gas bubbling in the receiving-side oil bubbler.
		- Selecting a smaller gauge vent needle than the cannula can help control the rate at which gas flows out of the system.
	+ Push the cannula below the liquid level and transfer the desired quantity of reagent. Due to the pressure differential, the *t*-BuLi will begin transferring from the bottle of *t*-BuLi to the addition funnel upon insertion.
		- Adjust the rate of addition by increasing or decreasing the inert gas flow to the bottle of *t*-BuLi.
	+ Raise the tip of the cannula above the *t*-BuLi liquid level in the reagent bottle to stop the flow. Allow inert gas to flush the cannula.
	+ Remove the vent needle from the receiving side. Turn on the inert gas flow through the manifold to the flask/addition funnel.
	+ Remove the cannula first from the reagent bottle, then from the addition funnel/receiving flask. Turn off the inert gas flow to the reagent after removing the cannula. Remove the needle from the reagent bottle.
	+ Rinse the cannula with dry n-heptane or similar (can be open to atmosphere). Retain the *t*-BuLi/heptane (or similar) rinse solution for quenching.

Cap the *t*-BuLi reagent bottle upon completion of the transfer and seal the outside with parafilm or use a valve cap. It is at this point that it may be removed from the clamp or ring stand and stored (Section #5 Storage Requirements).  | Not clamping the *t*-BuLi bottle can cause a spill and fire.* Not flushing with gas can introduce ambient air/water, causing fire.
* Tipping bottle can cause spill/fire. Withdrawing reagent too quickly can cause a vacuum and pull in air.
* Not drawing in inert gas to syringe can allow direct contact between t-BuLi and air > fire.
* A flash of flame is surprising and can cause user to drop syringe then spill and larger fire.
* Quick addition of *t*-BuLi can cause rapid temperature increase, leading to a runaway reaction.
* Multiple uses of the same syringe can clog the needle, causing user to push/pull too hard > spill > fire.
* Not rinsing needle/syringe can leave residual *t*-BuLi exposed to air > fire.
* Larger volumes are inherently more hazardous. Larger syringes require more pressure to push/pull plunger, can lead to catastrophic spill/fire.
* Not flowing inert gas through cannula can allow contact between *t*-BuLi and air > fire.
* Not rinsing needle/syringe can leave residual *t*-BuLi exposed to air > fire.
* Poor sealing / capping of the *t*-BuLi reagent bottle can lead to degradation of the reagent or under-cap seal.
 |
| 1. [Describe the next step in the procedure. Insert additional rows in table, as needed.]
 |  |
| 1. [Describe the next step in the procedure. Insert additional rows in table, as needed.]
 |  |
| 1. Dispose of hazardous solvents, solutions, mixtures, and reaction residues as hazardous waste.

*Quench rinse solutions (Transfer step)*The small quantity of *t*-BuLi in the rinse solutions (from the syringe, cannula, or other glassware) can be quenched with cold 2M isopropanol in heptane. Calculate a gross excess of isopropanol compared to *t*-BuLi.* Make a 2M solution of isopropanol in n-heptane or similar.
* Cool the above mixture to 0C with a water ice bath
* Transfer the rinse solution via syringe or cannula to an addition funnel (follow steps from t-BuLi transfer)
* Slowly add the rinse solution to the 2M isopropanol solution with stirring.
* Allow to warm to room temperature.
* Add an equal volume (to quantity of isopropanol) of methanol, followed by water.
* Dispose as hazardous waste.
 |  |
| Clean up work area and lab equipment.1. [Describe specific cleanup procedures for work areas and lab equipment that must be performed after completion of your process or experiment. For carcinogens and reproductive toxins, designated areas must be immediately wiped down following each use.]
 |  |
| 1. Remove PPE and wash hands.
 |  |

 |
| #7 | **EMERGENCY PROCEDURES**  |
| **General procedures**1. Call 911.
2. Alert people in the vicinity and activate the local alarm systems.
3. Evacuate the area and go to your Emergency Assembly Point (EAP): [Indicate EAP location]
4. Remain nearby to advise emergency responders.
5. Once personal safety is established, call EH&S at 650-725-9999.
6. Provide local notifications (local notifications are listed at the end of this section)

**Exposures and Injuries*** If a hazardous material has come into contact with your body, remove contaminated clothing and use either the eyewash or safety shower for 15 minutes before seeking further medical attention.
	+ Call for help if needed.
	+ If only one eye is affected, be careful not to flush contaminated water into the other eye by keeping the affected eye lower.
	+ **Use the eyewash or safety shower even if materials are water reactive**, as the high flow rate will deprive the fire of oxygen and rapidly cool flammable materials.
* If an incident occurs, bring along a copy of the SDS(s) when seeking medical attention.
* For all serious injuries that require medical attention, call 911 or go to the Stanford Hospital Emergency Department (1199 Welch Road, Palo Alto).
* After the injured person and the scene is secure, report the serious injury to EH&S by calling 650-725-9999 (answered 24 hours a day, 7 days a week).
* For non-emergency injuries and illnesses, go to the Stanford Occupational Health Center (484 Oak Road, Stanford). Contact 650-725-5308 for consultation (open Monday through Friday, 8 am – 4 pm).
* After hours, the Stanford Hospital Emergency Department is available for prompt medical attention.
* After any incident (spills, near-miss, fire, or injury), complete the [Incident Report (SU-17) form](http://su17.stanford.edu/).

**Spills*** Exert extreme caution due to potential spontaneous combustion and potential ignition of flammable solvents or other materials in the area.
* Only clean up a spill of a pyrophoric material if it is not on fire, smoking, or otherwise showing signs of instability.
* If a spill is on fire, smoking, or otherwise showing signs of instability, pull the fire alarm and call 911.
* To report a hazardous material spill or any other incidents which may affect health, safety, or the environment, call 650-725-9999 (answered 24 hours a day, 7 days a week), even if you have also called 911. Spills <30 mL can be reported via Incident Report form (SU-17) rather than a phone call, unless assistance is needed to clean up.
* After any incident (spills, near-miss, fire, or injury), complete the [Incident Report (SU-17) form](http://su17.stanford.edu/).

**Fires*** If the fire is small (less than knee height) and has not spread from the point of origin, you may use the appropriate fire extinguisher, if you have been trained and are comfortable doing so.
* Pull the fire alarm and call 911 for any fire that is larger than knee height or has spread.
* NEVER use more than one fire extinguisher. If it’s not out after one, you cannot fight it.
* Use an ABC fire extinguisher for a *t*-BuLi fire
* To report the incident, call 650-725-9999 (answered 24 hours a day, 7 days a week), even if you have also called 911.
* After any incident (spills, near-miss, fire, or injury), complete the [Incident Report (SU-17) form](http://su17.stanford.edu/).
1. **Lab-Specific Procedures**

[This section is for any emergency procedures different from standard responses, or for additional emergency information due to the nature of materials or task. Include information on gas leaks, chemical spills, and personal exposure/medical emergency as appropriate.]1. **Building Maintenance Emergencies**

Call Facilities Operations at 650-723-2281 (or 650-721-2146 in the School of Medicine) for building maintenance emergencies (e.g., power outages, plumbing leaks).1. **Local Notifications**

[Identify the area management staff that must be contacted and include their work and after-hours numbers. This must include the principal investigator and may include the lab safety coordinator, facilities manager, and/or business manager.] |
| #8 | **WASTE DISPOSAL**  |
| * Reactions should be quenched before disposal. Ensure proper training before quenching procedures are attempted.
* Bulk materials, like excess reagent in the original manufacturer’s container, should not be quenched prior to disposal; they can be tagged with a waste tag at [wastetag.stanford.edu](https://ehsapps.stanford.edu/waste-tag/).

[Describe the quantities of waste you anticipate generating and appropriate waste disposal procedures. Include any special handling or storage requirements for your waste. Contact EH&S at 650-723-0448 for questions and additional guidance.]  |
| #9 | **TRAINING REQUIREMENTS** |
| **General Training** ***(check all that apply):***[x]  General Safety & Emergency Preparedness (EHS-4200)[x]  Chemical Safety for Laboratories (EHS-1900)[x]  Compressed Gas Safety (EHS-2200)[ ]  Biosafety (EHS-1500)[ ]  Life Sciences Research Laboratory Safety Training (EHS-4875)**[**In the School of Medicine, EHS-4875 is required for laboratory personnel in lieu of EHS-1900, 2200, and 1500.] [x]  Other: \_\_[EHS-3700 Fire Extinguisher Use in Labs](https://ehs.stanford.edu/training/ehs-3700-fire-extinguisher-training)\_\_\_\_\_Depending on the hazardous materials and processes you will be working with in this SOP, additional safety training may be required.

|  |  |
| --- | --- |
| **Location Where Records Maintained:** |  |

**Laboratory-specific training** ***(check all that apply):***[x]  Review of SDS for chemicals involved in process/experiment[x]  Review of this SOP[x]  Other: Review of [SU Information on Pyrophoric Compounds](https://ehs.stanford.edu/reference/information-on-pyrophoric-compounds)

|  |  |
| --- | --- |
| **Location Where Records Maintained:** |  |

 |
| #10 | **PRIOR APPROVALS**  |
| *t*-BuLi is a Restricted Chemical under the [SU Chemical Hygiene Plan](https://ehs.stanford.edu/manual/chemical-hygiene-plan) (section 5.1) and users must receive PI approval prior to work with this chemical. **Prior Approval *(check if applicable):***[x]  Prior approval from the PI or lab supervisor is required for this procedure  |