Standard Operating Procedure (SOP):

Ligand for nanorod (1-Br)

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| Date last updated: | 9/9/2020 |
| Principal Investigator: | Smith |
| SOP Prepared By: | Michelle |
| Lab Phone: | 617-282-XXXX |
| Location(s) covered by this SOP: | *HVD-1892* |
| (Building/Room Number) |

**References:**

**Chemical SOP Hazards:**

* [Safety Data Sheets](https://www.ehs.harvard.edu/news/material-safety-data-sheets-msds)
* [Lab Safety Guidelines](https://www.ehs.harvard.edu/programs/safe-chemical-work-practices)
* [LabPoint](https://ehs.labpoint.sph.harvard.edu/inventories) Chemical Inventory Summary (ask your LSO) – Boston Only

**PPE guides:**

* Safety Data Sheets
* General Lab Safety PPE
  + By [Type of PPE](https://www.ehs.harvard.edu/sites/ehs.harvard.edu/files/ppe_selection_guide_by_type_0.pdf)
  + By [Task or Activity (chemical, biological, radiation)](https://www.ehs.harvard.edu/sites/ehs.harvard.edu/files/ppe_selection_guide_by_task_or_activity.pdf)

**COMS requirements**

* [BL1 Practices](https://hms.harvard.edu/departments/committee-microbiological-safety/registering-coms/coms-policies/minimum-biosafety-level-1-laboratory-requirements-coms-approved-projects)
* [BL2 Practices](https://hms.harvard.edu/departments/committee-microbiological-safety/registering-coms/coms-policies/minimum-biosafety-level-2-laboratory-requirements-coms-approved-projects)
* [BL2+ Practices](https://hms.harvard.edu/departments/committee-microbiological-safety/registering-coms/coms-policies/minimum-biosafety-level-2-laboratory-requirements-coms-approved-projects-0)

**Required** [**Training**](https://trainingportal.harvard.edu/Saba/Web_spf/NA1PRD0068/app/dashboard)**:**

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| --- | --- |
| Training | Yes |
| General Laboratory Safety | X |
| Laboratory Biosafety |  |
| Laser Safety |  |
| Radioactive Materials Safety |  |
| Machine Shop and Makerspace Safety |  |
| Respiratory Protection |  |
| Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ |  |

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| Hazardous Chemicals Used | Acutely Toxic | Corrosive | Flammable | Oxidizer | Irritant | Explosive | Health Hazard | Compressed Gas | Environmental Hazard |
| * 2-hydroxyethyl 2-nitrobenzyl thioether ([3878-41-9](https://www.sigmaaldrich.com/catalog/search?term=3878-41-9&interface=CAS%20No.&N=0&mode=partialmax&lang=en&region=US&focus=product)) |  |  |  |  |  |  |  |  |  |
| * Tetrabromomethane (CBr4) ([558-13-4](https://www.sigmaaldrich.com/catalog/search?term=558-13-4&interface=CAS%20No.&N=0&mode=partialmax&lang=en&region=US&focus=product)) |  |  |  |  |  |  |  |  |  |
| Dichloromethane (DCM) |  |  |  |  |  |  |  |  |  |
| Triphenylphosphine (PPh3) (603-35-0) |  |  |  |  |  |  |  |  |  |
| 20% ethyl acetate ( 141-78-6) in hexanes ( 110-54-3) |  |  |  |  |  |  |  |  |  |
| * 5-ethynyl-1-methyl1H-imidazole ([71759-92-7](https://www.sigmaaldrich.com/catalog/search?term=71759-92-7&interface=CAS%20No.&N=0&mode=partialmax&lang=en&region=US&focus=product)) |  |  |  |  |  |  |  |  |  |
| * Toluene ([108-88-3](https://www.sigmaaldrich.com/catalog/search?term=108-88-3&interface=CAS%20No.&N=0&mode=partialmax&lang=en&region=US&focus=product)) |  |  |  |  |  |  |  |  |  |
| silica gel |  |  |  |  |  |  |  |  |  |

**Storage considerations/segregation:** (Segregate Acids and bases, oxidizers from flammables and combustibles).

**Step #1: 2-bromoethyl 2-nitrobenzyl sulfide**

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| --- | --- |
| PPE |  |
| Gloves | Nitrile  Latex  Neoprene  Insulated ☐ Other: \_\_\_\_ |
| Eye Protection | Goggles  Face shield  Safety Glasses  Other: \_\_\_\_\_ |
| Body Protection | Lab coat  Apron  Flammable Lab coat  None  Other: \_\_\_\_ |
| Respiratory Protection | N95  Other: \_\_\_\_\_ |
| Other |  |

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| Administrative and Engineering Controls | |
| Air quality | Fume Hood  BSC  Snorkel  Filter (isoflurane) |
| Work area | Fume Hood  BSC  Bench  Core/facility \_\_\_\_\_  Other: \_\_\_\_\_ |
| System controls | Pressure relief  Emergency stop button  Other \_\_\_\_\_ |
| Signage | Yes, specify: ‘RXN in progress’ |
| Clean/Decontaminate  work area | water & soap  70% Ethanol  \_\_% Bleach  None  Specify \_\_\_\_\_\_\_\_\_ |

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| Waste |  |
| Generated | Yes  No |
| Disposal of waste | Hazardous liquid  Hazardous solid  Biological liquid ☐ Biological solid  Sink  Trash  Regulated  Other \_\_\_\_\_\_\_ |
| Hazardous  Waste Label | Liquid:19% ethyl acetate, 79% hexanes, 2% dichloromethane, Trace: 2-hydroxyethyl 2-nitrobenzyl thioether, triphenylphosphine oxide, carbon tetrabromide, acetone  Solid: Spatulas contaminated with triphenylphosphine oxide, carbon tetrabromide, silica gel |
| Decontamination | Procedure: Redissolve product in ethyl acetate, rinse 3 times. Rinse the glass round bottom with acetone. Collect all rinsate as hazardous waste. Allow round bottom to dry then clean with soap and water. Wipe down hood bench area with soap and water. |

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| Spills |  |
| Spill containment procedure | Reaction, column and rotavaping should occur in fume hood. If a spill occurs, close fume hood and turn on emergency purge. Absorb with spill pillows and clean surface with soap and water. Dispose of contaminated spill materials in hazardous solid waste. |
| Spill Supplies | Spill pillows, tweezers (for broken glass), paper towel |

**Procedure:**

To a solution of 945 mg of 2-hydroxyethyl 2-nitrobenzyl thioether (2.0 mmol, 1.0 eq.) and 796 mg of CBr4 (2.4 mmol, 1.2 eq.) in 12.7 mL DCM, 630 mg of PPh3 (2.4 mmol, 1.2 eq.) is added. The reaction mixture is stirred for 5 h in a sealed vial. It is then concentrated under vacuum and purified by column chromatography (silica gel, 20% ethyl acetate in hexanes). Product: 2-bromoethyl 2-nitrobenzyl sulfide (2).

Same procedure but more detailed for training:

To a 20 mL vial containing a stir bar, weigh 945 mg of 2-hydroxyethyl 2-nitrobenzyl thioether (2.0 mmol, 1.0 eq.) and 796 mg of CBr4 (2.4 mmol, 1.2 eq.). The weighing can be done on the open benchtop surface, but needs to be moved to the fume hood before adding the 12.7 mL DCM. Swirl solution to dissolve the reagents and add 630 mg of PPh3 (2.4 mmol, 1.2 eq.). The vial is capped, and the reaction mixture is stirred for 5 h in the fume hood. The stir bar is removed, and an adaptor is added to allow concentration within the vial. The mixture is concentrated under vacuum on a rotavap and purified by column chromatography (silica gel, 20% ethyl acetate in hexanes) and fractions are concentrated on the rotavap, these steps occur in a fume hood. Product: 2-bromoethyl 2-nitrobenzyl sulfide (2).

**Step # 2: 1-Br-Alkyne**

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| PPE |  |
| Gloves | Nitrile  Latex  Neoprene  Insulated ☐ Other: \_\_\_\_ |
| Eye Protection | Goggles  Face shield  Safety Glasses  Other: \_\_\_\_\_ |
| Body Protection | Lab coat  Apron  Flammable Lab coat  None  Other: \_\_\_\_ |
| Respiratory Protection | N95  Other: \_\_\_\_\_ |
| Other |  |

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| --- | --- |
| Administrative and Engineering Controls | |
| Air quality | Fume Hood  BSC  Snorkel  Filter (isoflurane) |
| Work area | Fume Hood  BSC  Bench  Core/facility \_\_\_\_\_  Other: \_\_\_\_\_ |
| System controls | Pressure relief  Emergency stop button  Other: Shield in case pressure vessel cracks in addition to fume hood sash |
| Signage | Yes, specify: ‘Pressure RXN’ |
| Clean/Decontaminate  work area | water & soap  70% Ethanol  \_\_% Bleach  None  Specify \_\_\_\_\_\_\_\_\_ |

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| --- | --- |
| Waste |  |
| Generated | Yes  No |
| Disposal of waste | Hazardous liquid  Hazardous solid  Biological liquid ☐ Biological solid  Sink  Trash  Regulated  Other \_\_\_\_\_\_\_ |
| Hazardous  Waste Label | Liquid: 95% toluene, 4% acetone trace: 5-ethynyl-1-methyl1H-imidazole, 2-bromoethyl 2-nitrobenzyl sulfide  Solid: filter paper and pressure vessel cap contaminated with 5-ethynyl-1-methyl1H-imidazole, 2-bromoethyl 2-nitrobenzyl sulfide |
| Decontamination | Procedure: Once product is removed from vessel: spatula, reaction flask and filter apparatus should be rinsed with acetone and rinsate must be disposed of as hazardous waste. Clean equipment, and hood area with soap and water. |

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| Spills |  |
| Spill containment procedure | Reaction and filtration should be performed in a fume hood. If a spill occurs, close fume hood and turn on emergency purge. Absorb with spill pillows and clean surface with soap and water. Dispose of contaminated spill materials in hazardous solid waste. |
| Spill Supplies | Spill pillows, tweezers (for broken glass), paper towel |

**Procedure:**

1370 mg of 2 (4.95 mmol, 1.05 eq.) and 500 mg (4.71 mmol, 1.00 eq.)) of 5-ethynyl-1-methyl1H-imidazole (1) were added to a pressure vessel. The reaction mixture was sealed and heated overnight at 60 °C. The white solid that formed was filtered and washed with toluene. Product: 1-Br-Alkyne

Same procedure but more detailed for training:

To a 20 mL microwave pressure vessel containing a stir bar weigh500 mg (4.71 mmol, 1.00 eq.)) of 5-ethynyl-1-methyl1H-imidazole (1). 1370 mg of 2-bromoethyl 2-nitrobenzyl sulfide (4.95 mmol, 1.05 eq.) is also added using a pipette as it is a viscous oil. The weighing is done on the open benchtop surface and is quickly sealed. The vessel is placed in an oil bath at 60 °C, the bath is located in the fume hood. A shield is placed in front of the hot plate in case the vessel is not stable. The reaction was removed from the bath, allowed to cool to RT, uncapped, the stir bar is removed, and white solid that formed was filtered and washed with toluene. The product is removed from the filter paper and transferred to a vial and dried on a vacuum line to remove trace solvents. These steps occur in a fume hood. Product: 2-bromoethyl 2-nitrobenzyl sulfide (2).

**Appendix A**

[*Lab Safety Guidelines*](https://www.ehs.harvard.edu/programs/lab-safety-guidelines-sops)

**Personal Protective Equipment (PPE)**

* Use appropriate personal protective equipment (PPE)

[Respirator](https://www.ehs.harvard.edu/programs/lab-personal-protective-equipment-ppe) – Respirator selection, personnel training, medical evaluations and fit-test are prerequisites and must be successfully completed before any required respirator can be used. Contact EHS for assistance.

**Special Handling and Storage Requirements***.*

* Return all original chemical containers to storage area following Harvard University [Laboratory Chemical Storage Guide](https://www.ehs.harvard.edu/node/7968)
  + Store in original containers or other appropriate containers;
  + Store primary container in designated and compatible secondary containers;

Store away from incompatibles;

**Decontamination/Waste Disposal Procedure**

* Dispose of waste following Harvard University [Hazardous Waste Procedures](https://www.ehs.harvard.edu/programs/chemical-waste)
* Wash hands and forearms thoroughly with soap and water before leaving the lab.

**Spill and Accident Procedure**

**Before beginning work**

* Review manufacturer’s Safety Data Sheet and additional chemical information at [ehs.harvard.edu/safety-data-sheets-sds](http://www.ehs.harvard.edu/safety-data-sheets-sds);
* Ensure that a written experimental protocol including safety information is available;
* Be familiar with general University emergency procedures in the [EHS Lab Emergency Response Guide](https://ehs.harvard.edu/sites/ehs.harvard.edu/files/lab_emergency_response_guide_.pdf);
* Order the most dilute solutions available that will meet experimental needs. Order only the quantity that you need;
* Identify the location of the nearest eyewash and shower and verify that they are accessible;
* Locate and verify that appropriate spill cleanup materials are available, including the following:
  + Spill pillows, tweezers located in drawer across from fume hood
  + Do not remove contaminated spill materials from fume hood until dry to prevent inhalation.

**First Aid**

For serious medical emergencies, go to the closest emergency room or call 911.

SKIN CONTACT

* Wash with plenty of tepid water for at least 15 minutes using the closest available sink, safety shower or drench hose. Remove any exposed clothing as well as any jewelry.
* Seek medical attention;

EYE CONTACT

* Using eyewash, flush eyes while holding eyelids open;
* Seek medical attention;

INHALATION

* Remove person immediately to fresh air;
* Seek medical attention;

INGESTION

* Never give anything by mouth to an unconscious person as it can block their airway;
* Seek medical attention;

**Spill Response**

* Alert others and evacuate to a safe distance and prevent entry.
* Assess spill hazard (location, volume, volatility, health risk, etc..) and follow guidance in [Emergency Response Guide](https://www.ehs.harvard.edu/system/files/lab_emergency_response_guide.pdf).
* Spills that cannot be handled by the lab include: spills involving elemental mercury, anything requiring respiratory protection to clean, spills where appropriate spill supplies are not available, spills that individuals are not comfortable cleaning, and/or spills has been released into the environment (down a drain, spilled outside, etc.). Call operations immediately.
* Contact the University Operations Center at (617) 49**5-5560** [HMS/HSDM (617) 43**2-1901**]
* Remain in a safe location until EH&S or other response personnel arrive.
* Otherwise, if trained and confident, you may assist in the clean-up effort of small amounts, wearing PPE described above and using appropriate spill supplies.
  + Since the reaction is carried out in the fume hood, the only out of fume hood spills would be of stock reagents. For solids, alert others in the area and minimize dispersion on the floor and air. Wipe up and wash area with soap and water several times. For solvents, evacuate the area, turn on the emergency exhaust on the fume hood with sash open and contain spill with spill pillows.
  + Collect debris in appropriate container and move to your Satellite Accumulation Area. Label with appropriately completed hazardous waste tag and request a waste pickup.

INSIDE FUME HOOD OR VENTILATED ENCLOSURE (< 500 ml)

* If trained and confident, you may assist in the clean-up effort of small amounts, wearing PPE described above and using appropriate spill supplies.
  + Outside of weighing solids, all work was performed in a fume hood. The emergency exhaust should be utilized in the event of a spill. If solids are spilled during weighing. They should be wiped up with a dry cloth into solid hazardous waste using slow motions to limit dispersing the chemical and then the area cleaned with soap and water. The contaminated paper towel should also go into hazardous waste.
  + Collect debris in appropriate container and move to your Satellite Accumulation Area. Label with appropriately completed hazardous waste tag and request a waste pickup.
* Otherwise close the fume hood sash and await support.

Information for example from: Johnson, Jeremiah A. et al. (2018). Robust gold nanorods stabilized by bidentate N-heterocyclic-carbene–thiolate ligands. *Nature Chemistry,* *11*(1), 57-63.

To append:

* + SOP for dichloromethane (should be modified to fit lab specifics)

You can use outside resources to create your SOPS. For example University of Washington has an SOP template for dichloromethane: https://www.ehs.washington.edu/resource/dichloromethane-methylene-chloride-964