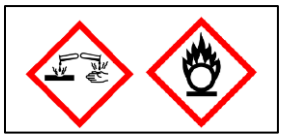
JOINT SAFETY TEAM

Safety Module

Safety Topic: Aqua Regia and Nitric Acid

Author: *Suzanne Szewczyk*



- **Purpose –** Nitric acid (HNO_3) is used as a strong acid and oxidant. Aqua regia, a 3:1 (v:v)mixture of concentrated HCl and HNO_3, is used for cleaning glassware of organic materials and is specifically good for dissolving metals.
- **Equipment –** Glass Erlenmeyer, glass graduated cylinder, empty glass waste bottle, concentrated acid(s), thick butyl gloves
- **Process –** Generate and use concentrated acids exclusively in a fume hood. Prepare behind the hood sash/panel. Slowly add 1 portion of HNO_3 to 3 portions of concentrated HCl. Use the solution immediately by carefully pouring or pipetting into pre-rinsed and dried glassware to be cleaned. Let react overnight in the back of a fume hood with proper ventilation away from other things such as solvent, organic materials, bases, metals, etc.
- **Specific considerations –** Do not cap, store, or re-use aqua regia. Aqua regia decomposes rapidly generating gasses and can over-pressurize a closed container. A spill >100 mL outside of the hood requires lab evacuation and EHS response. Strong acids can be neutralized and cleaned up with solid $NaHCO_3$.
    - Concentrated HNO_3 decomposes over time from exposure to O_2 and light becoming discolored. Store in a cool dark place such as a corrosives cabinet.
    - Oxidizing acids can react with cyanides, carbides, organic materials, and metallic powders violently, generating a multitude of gasses.
    - Strong acids can damage the skin, eyes, and respiratory tract. Only thick butyl rubber gloves can protect from corrosive acids.
    - Standard first-aid treatment for spills on the skin or in the eyes is irrigation with large quantities of water for 15 min.
- **Waste handling –** Once the aqua regia is fully reacted (no more gasses are being generated, ~12 hours) it can be carefully poured into a waste container. Use a glass waste container such as an empty HCl reagent bottle as to avoid any unintended reactions or the bottle being mistaken for something else. Other waste bottles should be emptied, rinsed, and blown dry. Do not fully tighten the cap immediately upon addition or when in doubt and keep container in the hood until it can be safely tightened. Label the waste bottle immediately and place in a satellite waste area in a secondary container preferably in a waste cabinet for pickup.
- **For more information see –**
    - Aqua regia SOP https://ehs.yale.edu/sites/default/files/files/aqua-regia-sop.pdf
    - Corrosives SOP https://ehs.yale.edu/sites/default/files/files/corrosives-sop.pdf

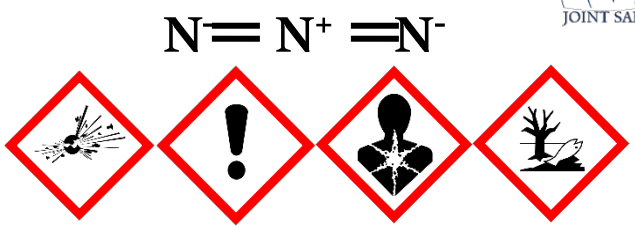
JOINT SAFETY TEAM

Safety Module

Safety Topic: Azide Compounds

Author: *Victor Beaumont*

Compound **CAS#** *14343-69-2 (azide anion)*



- **Purpose –** Azides are highly toxic compounds that contain the N_3^- anion. Inorganic azides, such as sodium azide, are typically used as a preservative, biocide, or mutagen. Organics azides are useful in many different reactions, namely azide-alkyne click reactions.

- **Equipment –** Lab glasses, lab coat, nitrile gloves, plastic secondary container, and plastic spatulas or glass pipette

- **Process –**Azides are extremely toxic and symptoms of acute exposure include rapid breathing, restlessness, dizziness, weakness, headaches, nausea, vomiting, elevated heart rate, red eyes, coughing, burns, and blisters. Neither organic nor inorganic azides are very stable and even a small amount of energy applied to azides can be dangerous. Heating or impinging either organic or inorganic azides causes rapid decomposition and results in an explosion. Azides can be stored indefinitely in plastic amber containers, refrigerated (if necessary), and away from reactive materials, such as heavy metals, acids, bases, and halogenated solvents. Use plastic spatulas when handling azides to reduce impact.

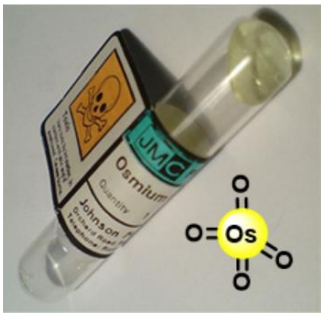
- **Specific considerations –** When synthesizing an azide, make sure that your azide obeys the following equation: $\frac{(N_C+N_O)}{N_N} \geq 3$. N denotes the number of the designated atoms in the azide molecule. If the target azide contradicts this equation, take extra precaution in its purification and handling. Use extraction or precipitation methods for purifying azides; never use distillation or sublimation.

- **Waste handling –** Waste containing azides should be placed in a separate waste bottle and never added with acids and bases. Acids form toxic and volatile HN_3 when mixed with azides. Sodium azide can form explosive, insoluble compounds with heavier metals and should therefore never be poured in the drain. Azide can be quenched by diluting the azide in water to ≤ 5% with stirring, 20% sodium nitrite solution, and slowly adding 20% sulfuric acid until gas evolution has ceased.

- **For more information see –**
  - Stanford EHS: ehs.stanford.edu/reference/information-azide-compounds
  - More information on quenching here.
  - UCSB EHS: www.ehs.ucsb.edu/files/docs/ls/factsheets/Azides_FS26.pdf
  - Pittsburgh EHS: www.ehs.pitt.edu/assets/docs/SafeHandlingofAzides.pdf

JOINT SAFETY TEAM

Safety Module



Safety Topic: Osmium tetroxide

Author: Aneta Turlik

OsO_4 (CAS 20816-12-0)

- **Purpose –** Osmium tetroxide (OsO_4) is a highly toxic compound used most prevalently for the dihydroxylation of alkenes to *syn*-diols. It is commonly supplied as a pale yellow solid in a glass ampule, as a 4 wt % solution in water, or as a 2.5 wt % in *t*-BuOH. The compound has an acrid, "chlorine-like" odor.
- **Toxicity –** OsO_4 is a severe irritant to the eyes, respiratory tract, skin, kidneys, and liver. Exposure to OsO_4 can lead to damage and staining of the cornea and subsequent blindness as OsO_4 can react with the multiple double bonds in retinal. Exposure of volatile OsO_4 to the eyes results in tears, "a gritty feeling in the eyes", and the appearance of rings around lights. In addition, high levels of exposure can lead to pulmonary edema (fluid accumulation in the lungs), and consequently death. Contact with the skin can cause skin burns, and the appearance of black staining arising from the conversion of OsO_4 to osmium dioxide (OsO_2). The LD_{50} of OsO_4 is 14mg/kg in rats, and 162 mg/kg in mice.
- **Handling –** Due to its high toxicity and volatility, OsO_4 should be handled in a fume hood, with full PPE including a buttoned labcoat with the sleeves rolled down, safety goggles, and double Nitrile gloves. If solid OsO_4 is used, it must be weighed in a fume hood.
- **Storage –** OsO_4 is commonly supplied as a solution, and should be stored in glass under refrigeration, as it can penetrate plastic.
- **Waste handling –** All glassware that has contacted OsO_4 should be decontaminated by rinsing with corn oil (whose double bonds will react with the excess OsO_4) or sodium sulfite (which will reduce OsO_4 to less toxic forms).
- **For more information see –**
  - E-eros page for OsO_4 https://onlinelibrary.wiley.com/doi/pdf/10.1002/047084289X.ro007.pub3
  - UCLA SOP https://www.chemistry.ucla.edu/sites/default/files/safety/sop/SOP_Osmium_Tetroxide.pdf

JOINT SAFETY TEAM

Safety Module

Safety Topic: Peroxide Forming Chemicals (PFCs)

Author: Maria-Elena Liosi

- **Purpose –** Certain types of chemicals react with atmospheric oxygen over time to form peroxides and may explode upon impact, heat, or friction.

Classification of PFCs

Class A *Severe Peroxide Hazard*	can form peroxides and decompose without concentration (e.g. isopropyl ether, sodium amide)
Class B *Concentration Hazard*	can form explosive peroxides when concentrated (e.g. diethyl ether, dioxane)
Class C *Shock and Heat Sensitive*	can violently auto-polymerize after internal peroxide accumulation (e.g. acrylonitrile, styrene)
Class D *Potential Peroxide Forming Chemicals*	normally stable compounds - may form peroxides under the right conditions (e.g. furan, benzyl ether)

- **Equipment –** Lab glasses, lab coat, nitrile gloves, peroxide test strips
- **Safety Practices for PFCs-**
  - Purchase PFCs which contain a peroxide formation inhibitor or stabilizer like butylated hydroxytoluene (BHT) if possible
  - Date containers of PFCs upon arrival & opening
  - Store in cool dark place, in the original container and inspect frequently
  - Test with peroxide test strips periodically (every 6 months for classes B, C and once a year for class D)
- **Specific considerations –**
  - Signs of crystallization, discoloration, and stratification may indicate that the compound has become shock sensitive– do not move or open the container; contact EHS for disposal
  - Confirm that PFCs have been tested for peroxide formation before distillation or evaporation, do not distill to dryness
- **Disposal:**
  - Class A PFCs after 3 months (after opening) or 12 months (unopened)
  - Containers of PFCs as hazardous waste if suspected (e.g., from visual evidence) or known to contain peroxides and alert EHS
  - Containers of unknown age especially of Class A and B peroxides.
- **For more information see –**
  - http://ccc.chem.pitt.edu/wipf/SOPs/Peroxide%20Forming%20Chemicals.pdf
  - https://www.vumc.org/safety/chem/peroxide-forming-chemicals (Full List of PFCs)
  - https://ehs.yale.edu/sites/default/files/files/organic-peroxides-sop.pdf (SOPs)

JOINT SAFETY TEAM

Safety Module

Safety Topic: Titration of Butyl Lithium Solutions

Author: *Suzanne Szewczyk*

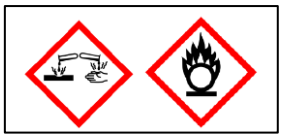
- **Purpose –** To determine the exact concentration of active base in a bottle of commercial butyl lithium (BuLi) reagent. The concentration of active base often decreases over time as the reagents is quenched by water, oxygen, or otherwise decomposes.
- **Equipment –** Bottle of BuLi, medium cork ring, *N*-benzyl benzamide, anhydrous THF, small round bottom with stir bar and septa, nitrogen balloon, 1 mL syringe, cold bath, aq ammonium chloride, 50:1 hexanes:methanol solution.
- **Process –** To a flame dried 10 mL round bottom with a stir bar was added ~100 mg of *N*-benzylbenzamide (record the exact mass). The flask was evacuated and back filled with nitrogen and ~5 mL of THF was added. The *N*-benzylbenzamide was stirred to fully dissolve. The flask was cooled to -40 °C for *n*-BuLi and -78 °C for *t*-BuLi or *s*-BuLi. The bottle of BuLi is place into a cork ring to avoid being knocked over. A nitrogen balloon was placed into the bottle. The BuLi is added to the flask by syringe drop-wise until a blue color just persists. The concentration of butyl lithium was back calculated from the exact mmols of *N*-benzylbenzamide used and the volume of butyl lithium solution added. This is typically repeated 3x and averaged for an accurate result.
- **Specific considerations –** Be sure to hold the syringe and needle to prevent disconnection at the joint especially as you empty the syringe. Only use a nitrogen balloon on bottles of pyrophoric reagents not "spaghetti lines" or nitrogen lines connected directly to a manifold. (This can result in over pressurization of the bottle, disconnection of the needle from the syringe, and/or a stream of pyrophoric reagent from the bottle.)
- **Waste handling –** The resultant amide solutions in the flask are quenched with sat. aq. ammonium chloride and transferred to an organic waste container. Quench remaining BuLi in the syringe by adding it slowly to a 50:1 solution of hexanes:methanol. Empty or "bad" organometallic reagents in sealed "Sure-Seal" bottles can be removed by EHS without further treatment. Only an individual waste label sticker on the bottle with the contents spelled out is necessary.
- **For more information see –**
  - Handling pyrophorics https://www.sigmaaldrich.com/content/dam/sigma-aldrich/docs/Aldrich/Bulletin/al_techbull_al164.pdf
  - Titration of organometallic reagents www.chemistry.mcmaster.ca/emslie/Assets/Titrating%20RLi.pdf
  - Pyrophoric and water-reactive substrates https://ehs.yale.edu/restricted-particularly-hazardous-substances

JOINT SAFETY TEAM

Safety Module

Safety Topic: Piranha Cleaning Solution

Author: *Suzanne Szewczyk*



- **Purpose –** Piranha (piranha etch) is an acidic and oxidizing solution used to remove organic material from glassware. Piranha is particularly useful when cleaning fritted glassware. The traditional piranha solution is a 3:1 (v:v) mixture of sulfuric acid and 30% aqueous hydrogen peroxide. Piranha may result in an explosion if not handled with extreme caution.
- **Equipment –** Sulfuric acid, 30% aqueous hydrogen peroxide, glass Erlenmeyer flask, glass waste container, glass graduated cylinder, thick butyl gloves
- **Process –** Piranha must be made and used exclusively in a fume hood. Remove all other compounds from the immediate area. Work behind the hood sash/panel. Slowly add 1 portion of hydrogen peroxide to the 3 portions of sulfuric acid with stirring to keep the concentration of peroxide low. The solution may become hot. Carefully add the solution to pre-washed and dried glassware to be cleaned. Let sit overnight in the back of a hood away from other materials.
- **Specific considerations –**
  - Do not use plastic containers as they will react with the solution.
  - Piranha generates $O_2(g)$ which can lead to a fire or explosion.
  - Prepare the solution immediately prior to using. Never store piranha and do not put piranha in a closed container or it will explode.
  - Mixing hot piranha with organic compounds such as acetone, isopropanol, nylon or photoresist and may cause an explosion.
  - Neutralize small spills with sodium bicarbonate. A larger spill or a spill outside a fume hood requires EHS assistance for cleanup.
  - Skin or eye exposure to piranha can cause severe burns. The vapor is highly corrosive to mucosal membranes and lungs.
- **Waste handling –** Allow the solution to cool to room temperature and stop generating gasses (~12 hours) before transferring into a clean and dry waste container for disposal. Label the waste as hydrogen peroxide and sulfuric acid.
- **For more information see –**
  - NOCHROMIX® is a safer and more stable cleaning solution alternative (inorganic persulfate solid to be mixed with sulfuric acid) - detailed information on handling and SDS: http://godax.com/msds-directions-for-use
  - Piranha SOP https://ehs.yale.edu/sites/default/files/files/piranha-sop.pdf
  - Acid Piranha guidelines https://www.safety.admin.cam.ac.uk/files/hsd176c.pdf