UMassAmherst | Environmental Health & Safety

Sodium Azide and Azide Compounds SOP

What are azides, and what are they used for?

Azides (N_3^-) are compounds that contain a linear arrangement of three nitrogen atoms that can behave as an anion or functional group depending on specfic bonding partners in particular compounds. Azide compounds have a wide variety of applications, including but not limited to:

- sodium azide as a preservative and the propellant in automotive airbags
- organic azides for synthesis, including azide-alkyne click reactions, Staudinger reactions, and amine and isocyanate precursors. The antiretroviral drug AZT is an organic azide compound.
- heavy metal azides as detonators and rocket propellants

All work with azide compounds at the University must adhere to the guidelines present in this SOP. Any work with compounds that are known or suspected to be explosive or highly toxic must be submitted to the ICSC for review. Any work that deviates from these guidelines should be submitted to the ICSC for review.

What are the hazards?

Many azide compounds present both health and physical hazards. As an anion, azide is similar in biological effect to cyanide (CN^-) and functions by inhibiting the uptake of oxygen. As such, metal salts, and other azide compounds used in conditions capable of liberating azide anion, should be treated with great care. Also like cyanide, reaction of azide with acid produces a toxic gas, hydrazoic acid. Hydrazoic acid is also potentially shock sensitive and explosive. Sodium azide readily penetrates skin and can lead to brain damage with chronic or acute high dose exposure.

Most metal azide salts are unstable and exhibit explosive properties. Sodium azide, and other alkali metal azides, are generally stable unless heated to above their melting points (275°C for sodium azide) where they rapidly decompose to release nitrogen gas. Lead, iron, copper, mercury, zinc, silver, cadmium, and other heavy metal salts of azides are shock sensitive and may spontaneously detonate. Note that these explosive salts can be formed if solutions containing sodium, or other alkali metal, azide are disposed of in drains made of piping or solder containing any of these metals. Contact of alkali azide salts with all metals should be avoided.

Azide anions are also excellent nucleophiles and readily undergo S_N2 additions with halogenated hydrocarbons to yield organic azides. In the case of dichloromethane and chloroform, this reaction can produce the highly toxic and explosive diazomethane and triazidomethane, respectively. As such all contact of azide salts with dichloromethane, chloroform, and other halogenated aliphatic or benzylic solvents, must be avoided. Other materials that are, or may be, incompatible with azide anions include, but are not limited to:

- carbon disulfide
- dimethyl sulfate
- bromine
- heavy metals and their salts
- halogenated compounds
- acids

Many organic azides can also be shock sensitive, particularly when heated, and should therefore be treated with care. The lower the ratio of carbon to nitrogen in a compound, the more likely it is to exhibit explosive properties. It has been observed that violent decomposition reactions occur for compounds having a ratio of atoms: $(C+O)/N < 3$. Always do a thorough review of the literature and SDS before beginning work with, or attempting the synthesis of, azide compounds. Scaling up reactions and concentrating products (e.g., rotovapping, distilling, recrystallizing) can lead to increased risk of explosion. Some organic azides have also exhibited explosive reactions with sulfuric acid, lewis acids (such as aluminum chloride), and other compounds. Always handle organic azides as potentially explosive compounds unless there is clear empirical evidence to the contrary.

Occupational Exposure Limits and Symptoms of Exposure

Sodium Azide:

OSHA and NIOSH Ceiling, dermal = 0.3 mg/m3

NIOSH Ceiling, inhalation = 0.1 ppm

ACGIH Ceiling, inhalation = 0.11 ppm

Sodium azide exposure results in health effects that can be dependent on the route, length, and dose of exposure. Sodium azide is toxic by ingestion, inhalation, and dermal absorption (and it can readily penetrate intact skin). For all doses and routes of exposure, eventual onset of hypotension (low blood pressure) and headaches are common symptoms of exposure. Low dose exposure through all routes typically results in: irritation (eyes, respiratory, and mucosal membranes for inhalation and airborne exposure, skin burns or irritation from dermal contact), dizziness, nausea and vomiting, rapid breathing and heart rate, restlessness, and weakness. High dose exposures can result in: immediate drop in blood pressure, convulsions, loss of consciousness, lung injury and respiratory failure leading to death (if inhaled), and slow heart rate. Chronic exposure to can lead to heart and brain damage. Though this information is specific to sodium azide, other metal azides are expected to have similar health effects.

Organic azides can exhibit a vast array of health effects depending on the specific compound, and many of these materials are not well studied. Always do a thorough review of the SDS and literature to determine what health effects are likely.

What Activities Could Pose a Risk?

Azide compounds present both health and physical hazards. Health effects result from exposures occurring through inhalation, dermal absorption, and ingestion. Inhalation is a likely route of exposure for powdered materials that become airborne, for liquids with high vapor pressure, or for materials undergoing a chemical reaction to produce gaseous hydrazoic acid. Absorption is likely for dermal or mucosal contact with powders, solutions, liquids, or gaseous materials. Ingestion can occur from inadvertent contaminated hand-to-mouth contact or by swallowing cleared solid materials from the respiratory tract. The types of processes that could result in exposure to azides include, but are not limited to:

- Handling fine powders or volatile liquids azides outside of appropriate enclosures, such as a chemical fume hood
- Handling solids, liquids, and solutions of azides without gloves or with incorrect gloves for the material and process
- Generating aerosols of azide containing materials outside of appropriate enclosures (e.g., sonicating or vortex mixing concentrated solutions, etc.)
- Cleaning up spills or equipment (e.g., dry sweeping powders from a balance or the bench)

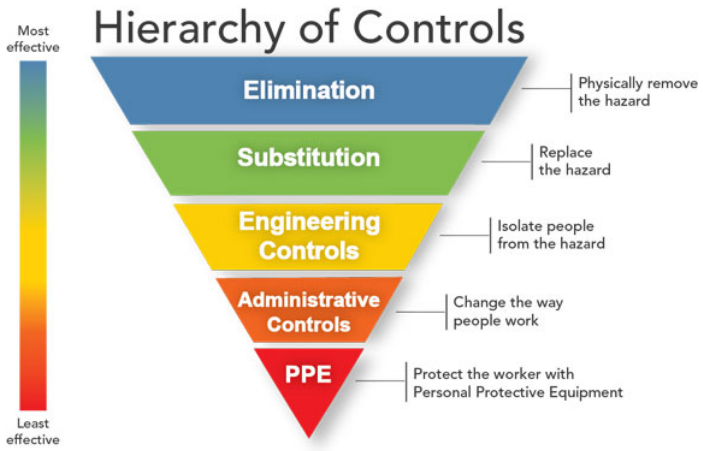
Physical hazards result from uncontrolled or unintended reactions. The types of processes that could pose a risk with azides include, but are not limited to:

- Using heat to carry out reactions or during reaction work ups (e.g., recrystallizing, distilling, rotovapping, subliming, etc.)
- Purifying and concentrating azides
- Grinding, scratching, strong agitation or otherwise causing friction with azides, particularly with pure materials

- Allowing azides to come in to contact with metals such as in plumbing, spatulas, containers, surfaces, etc., or other incompatible materials (e.g., halogenated solvents, acids)
- Using or producing large quantities of azides (e.g., scaling up reactions)

How Can Exposures and Physical Hazards Be Minimized?

When working with any hazardous material or process, always conduct a thorough risk assessment and employ the hierarchy of controls to minimize risk. Some specific applications of the hierarchy of controls to the unique hazards of azide compounds are listed below. Always apply the controls in the order of most effective to least effective (see graphic), and apply as many controls as possible to reduce the risk to the lowest achievable level.



Elimination/Substitution

- Use and produce the smallest quantity of azide material possible for a given experiment.
- Solvents that increase skin and glove permeability should be avoided in so far as possible for work with azides.
- Avoid synthesizing or working with azide compounds that are known or suspected to exhibit instability whenever possible.

Engineering Controls

- Work must be conducted in fume hoods, glove boxes, or other appropriate enclosures when using open containers of volatile liquid azides and for any other activity that generates airborne powders or aerosols.
- Blast shields and a fume hood should be used for all materials that are known to be or are suspected of being potentially explosive. Treat all azide compounds as potentially explosive unless there is data to suggest otherwise for the particular conditions of use.

Administrative Controls

- Avoid activities that might generate airborne dusts or aerosols in so far as possible.
- Keep containers closed while mixing, or performing other activities which could generate aerosols, in so far as possible. Allow aerosols to settle before opening containers.

- Clean areas where azides are used regularly to prevent build up and inadvertent exposure to materials. Use bench paper, or other disposable coverings or enclosures, when possible to facilitate clean up.
- Minimize handling and transport of containers of azide compounds to prevent spills. Use appropriate, sealed secondary containment to transport azide containing materials.
- Ensure laboratory personnel are thoroughly trained on the hazards of azide compounds, routes of exposure, symptoms of exposure, hazard mitigation techniques, and emergency procedures. Conduct thorough reviews of SDSs and the literature for hazards of particular azide compounds. Consider conducting tests to assess the stability of new azide compounds such as impact sensitivity, friction sensitivity, electrostatic discharge, differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). It is particularly necessary to adequately characterize the stability of compounds before scaling up use.
- Never use metal spatula or metal containers for handling or storing azide compounds. Never allow azide materials, even small quantities, to come in contact with metal surfaces, plumbing, or apparatus.
- Avoid grinding, scratching, strong agitation or otherwise causing friction with azides, particularly with pure materials when possible. Avoid heat when possible.
- Avoid purifying azides when possible. Keep in solution when possible. Large crystals are more likely to detonate than smaller crystals. Thus, if recrystallization is necessary as a work up for purification for a potentially unstable compound, lower the temperature rapidly with agitation to avoid formation of large crystals.
- Store and use azides away from acids and other incompatible materials.
- Use remote handling devices for azides that are known or suspected of exhibiting instability.
- Use plastic coated glassware to reduce fragmentation in the event of an explosion.

Personal Protective Equipment

- Always wear appropriate eye protection. Chemical splash goggles and safety glasses rated for impact (ANSI Z87+) should be worn. Face shields with neck protection should be worn whenever work with materials that are known or are suspected of exhibiting instability occurs.
- A lab coat must be worn for all work with azide compounds. Launder lab coats on a regular basis. Garments made of leather or Kevlar can be worn under lab coats to protect against shrapnel from explosions.
- Appropriate gloves must be worn while working with azide compounds. For liquid suspensions, ensure glove selection is based on the solvents and other materials that are used. For highly toxic azides, which may be of high concern for skin permeability, Silver Shield gloves (https://industrialsafety.honeywell.com/en-us/products/by-category/hand-protection/gloves/silvershield--ssg) under exam grade nitrile gloves are

recommended. Remove and dispose of contaminated gloves promptly. Gloves made of Kevlar or leather should be used for any items which are known or suspected of being unstable. These can be coupled with chemically resistant gloves to afford protection from both the physical and chemical hazard. Contact EH&S for any questions on glove selection.

Requirements for Small Scale Use of Sodium Azide As a Preservative

If your work only involves using small amounts of dilute aqueous solutions (no more than 100 mL of a 10% by mass solution) of sodium azide, or preparation of these solutions, you must adhere to the following procedures.

- Always wear gloves (exam grade nitrile), a lab coat, and safety glasses or chemical splash goggles while handling sodium azide or solutions that contain it.
- Clean up all spills promptly. Liquid spills can be absorbed with a paper towel and discarded as hazardous waste. Small spills of solid material (e.g., around balances) can be scooped up with a paper towel and discarded as hazardous waste.
- Never use a metal spatula to weigh out sodium azide. Use plastic or other materials.
- When preparing solutions, use a fume hood to dissolve solid sodium azide. Small amounts of the toxic and volatile hydrazoic acid can be produced during the dissolution process.
- Never dispose of solutions containing sodium azide, even very small quantities, down the drain.
- Ensure solutions are discarded as hazardous waste. Do not use metal containers for disposal. Ensure the container has only compatible contents (e.g., no acids or halogenated solvents).
- Clean areas where sodium azide solutions and solid are used regularly. Use of bench covers can facilitate easy cleanup.
- Store sodium azide solutions and solid away from incompatible materials, particularly acids, halogenated solvents, and metals. Store away from heat.

Waste Handling

All lab waste containing azide compounds should be handled as hazardous waste. Sodium azide is listed by the EPA as an acutely hazardous waste; ensure that empty containers of virgin material are triple rinsed, and that each of these rinses is discarded as hazardous waste. Ensure that an appropriate waste container is used (i.e., not metal and no metal in the cap), and that all contents are compatible. Do not add azide containing waste to acidic or halogenated waste. Do not store containers of waste azide in the same secondary containment as acidic or halogenated waste. When in doubt about waste stream compatibility, start a new waste container for the azide waste stream, or consult with EH&S for guidance. To have the waste picked up by EH&S staff, complete a Hazardous Materials Pickup Request Form in CEMS.

Exposure and Spill Procedure

In the event of a spill involving an azide compound that does not involve the contamination of a person, the material may be cleaned up if it is safe to do so following the general procedure for small spills detailed in the University's Chemical Hygiene Plan.

- Ensure that cleaning up the material will not generate airborne dust or aerosols.
    - Spills of highly volatile azides outside of enclosures (fume hoods or other enclosure devices) should be immediately referred to EH&S (413-54-2682) and the area should be evacuated. Do not permit entry to the area until EH&S arrives.
- Place all items used for cleanup in a labeled hazardous waste container and request a pickup through CEMS.
- If at any point you are uncomfortable cleaning up the spill or require assistance, stop and call EH&S (413-545-2682).

Exposures to azide compounds should follow the general procedures for exposures to hazardous materials outlined in the University's Chemical Hygiene Plan.

For a major exposure requiring the use of a drench shower or eyewash:

- Have someone call 911 (report the building name, room number, and street address) or 413-545-3111 (or simply 5-3111 from a campus line) to report the incident and request medical help. Have someone obtain the SDS for the material (if there is one) and provide it to the first responders when they arrive, if possible.
- Help the affected individual to position their head over the eyewash and activate it, or position them under the drench shower and activate it as appropriate.
    - Always ensure your own safety before helping others. Only help if it is safe for you to do so.
    - Wear gloves, safety glasses, and a lab coat.
- If using an eyewash: Instruct the affected individual to open their eyes and roll them around while the water is flowing. Help them to hold their eyes open if necessary and safe to do so.
- If using a drench shower: Remove all clothing from the affected area while under the shower.
- Flush the affected area for 15 minutes with water.

For minor exposures such as a spill to readily accessible extremities (e.g., hand):

- Flush the affected area in a sink equipped with potable water for at least 15 minutes.
- Go to University Health Services (UHS) for medical evaluation, and tell them you have had a lab exposure.
- Provide the SDS for the material if possible.

- Notify EH&S (413-545-2682) as soon as possible and complete the lab incident form (https://ehs.umass.edu/lab-incidents-and-lab-incident-report-form).

References and Additional Resources

- Organic Azides: Synthesis and Applications: https://www.researchgate.net/profile/Abdelkader_Bouaziz/post/How_can_we_convert_a_linear_azide_into_an_amine/attachment/59d625aec49f478072e9a733/AS%3A272166501715968%401441900958045/download/Organic+Azides+-+Syntheses+and+Applications.pdf
- CDC Facts About Sodium Azide: https://emergency.cdc.gov/agent/sodiumazide/basics/facts.asp
- Chemistry LibreTexts Sodium Azide: https://chem.libretexts.org/Ancillary_Materials/Demos%2C_Techniques%2C_and_Experiments/Chemical_Safety/Reagent_Specific_Hazards/Sodium_Azide
- Strategies for Safely Handling Industrial Azide Reactions: https://pubs.acs.org/doi/pdfplus/10.1021/bk-2014-1181.ch003