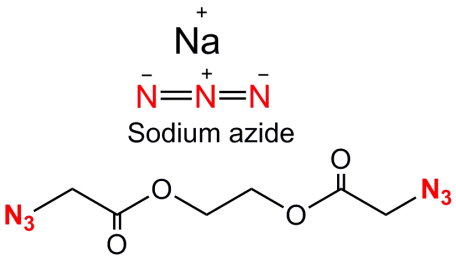
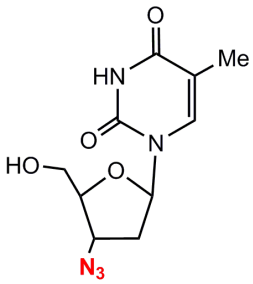
Safe Handling of Sodium Azide (SAZ)

Sodium azide (SAZ, **CAS# 26628-22-8**)[1,2] is a white crystalline solid [molecular formula of (NaN_3)] used in organic synthesis and also as a well-known preservative at low concentrations in molecular biology reagents. Azide chemistry[3,4] offers an effective means to synthesize a range of nitrogen-containing compounds with a wide variety of functional groups. But SAZ poses some significant risks. It is highly toxic and can react to form potentially explosive compounds. Azide reagents and intermediates react with some metals[5], strong acids, and certain chlorinated solvents[6] and this needs to be considered when using SAZ or when developing routes that involve azide-containing intermediates.





Health Hazards & Physical Hazards of SAZ

Hazard Statements
Fatal if swallowed or in contact with skin. Very toxic to aquatic life with long lasting effects.

Health Hazards: SAZ is highly toxic when ingested orally or absorbed through the skin. Azides form strong complexes with hemoglobin, and consequently block oxygen transport in the blood. They are more harmful to the heart and the brain than to other organs, because the heart and the brain use a lot of oxygen. Symptoms of exposure include headache, dizziness, nausea and vomiting, rapid breathing and heart rate, and skin burns and blisters (direct skin contact) and in the case of serious overexposure, convulsions and death.

It will also react with acids to form hydrazoic acid (HN_3). Unlike sodium azide, which is a crystalline solid, hydrazoic acid is a low-boiling, volatile, liquid. Hydrazoic acid is also highly toxic and its volatility makes it more readily inhaled causing lung irritation and potentially bronchitis and lung edema. Hydrazodic acid has a sharp, pungent odor.

Physical Hazards: SAZ itself is fairly stable and can be handled under routine conditions without a significant risk of an explosion. There is no risk of explosion in aqueous solutions of SAZ. The solid is, however, thermally unstable and if heated above 275 °C undergoes violent decomposition. In fact, sodium azide is used

in airbags for this very reason. A vehicle, upon sensing an impact, will send an electrical charge that heats the SAZ to high temperatures – causing the rapid formation of nitrogen gas.

The danger associated with SAZ is its ability to form explosive azides when reacted with compounds of heavy metals such as **lead, copper, zinc, cadmium,** or **nickel**. These compounds, as well as some organic azides, are notoriously heat and shock sensitive and can explosively decompose with little input of external energy.[7,8] [Note that lead (II) azide is commonly used as a detonator.] Sodium azide reacts with **carbon disulfide, bromine, nitric acid,** and **dimethyl sulfate** to produce violently decomposable compounds. SAZ can react with **dichlormethane** and **chloroform** to create highly unstable diazidomethane and triazidomethane, respectively.

Best Practices for Safe Handling

The inherent health hazards associated with SAZ apply regardless of its usage. On the other hand, the explosive hazards vary greatly depending on how SAZ is manipulated. Using SAZ as part of a synthetic chemistry method greatly increases the risk due to the potential for forming azides of greater instability than the original SAZ. Below are some recommended and required practices for safe use of SAZ.

- Sodium azide should not be allowed to come into contact with the following as they can form sensitive, unstable compounds:
    - Heavy metals or their salts (including barium, lead, and copper)
    - nitric acid and other acids (acids can also form the highly toxic and volatile hydrazoic acid)
    - Chlorinated solvents such as dichloromethane and chloroform
    - bromine
    - dimethyl sulfate
- Do not pour SAZ solutions into a copper or lead drain. These may form heavy metal azides which are much less soluble and may precipitate out and accumulate.
- Bottles containing pure powders or solutions of SAZ at 5% or greater must be opened and handled only in a chemical hood. During use, the sash must be lowered to operating height or below. Containers of SAZ must always be closed when not in use.
- Never expose organic azides to ground **glass joints** as the glass-on-glass friction may cause the azide to decompose explosively.
- Never use elevated temperature distillation or sublimation as purification techniques. Purification should be limited to extraction, precipitation and other suitable methods.
- C**oncentrating azide-containing reaction mixtures and products** through rotary evaporation have caused documented explosions.[9-12] This should be avoided or the possibility of explosion taken into account through the proper engineering controls. In some instances it is thought that the azide penetrating the ground glass joints was responsible, though other mechanisms for the explosions are also possible.
- Never use **metal spatulas** for weighing and transferring azides. Never scratch solid azides.

Personal Protective Equipment and Engineering Controls

- A lab coat, safety glasses, and gloves (nitrile preferred) with adequate chemical resistance must be worn during any SAZ manipulations.

- When performing chemical reactions involving SAZ, conduct the experiment behind a blast shield in a fume hood with the sash positioned as low as possible. If use of a blast shield is not feasible, use a face shield. Keep the hood clear of any unnecessary chemicals and equipment. Clearly label your containers, and post a sign on the fume hood as notification that there is an azide experiment in progress. [Note: This is not necessary for most molecular biology uses of SAZ].
- Above precautions should be used for the whole period of the experiment, including set up, work up, and clean up.

Exposures to SAZ

- **Skin Exposure:** Immediately wash all the affected areas of skin. Using the sink may be appropriate for exposures to the hands and forearms, but contamination of the head, legs or torso should be handled with a safety shower. When using a safety shower remove all affected clothing.
- **Eye Exposure:** Flush eyes with tepid water keeping eyelids apart. Seek medical advice.
- **Inhalation:** Move person into fresh air if SAZ breathed in. Consult a physician.
- **Ingestion (Swallowing):** Rinse mouth with water. Never give anything by mouth to an unconscious person. Seek immediate medical aid.

SAZ Spill Clean-up and Decontamination

Students or staff using SAZ should be prepared to handle spills. Spill materials must be readily available to handle the volume of your largest container. Individuals cleaning spills must wear appropriate PPE as described in the Personal Protective Equipment section of this document in order to prevent exposure to SAZ. Double-gloving for all spill clean-ups is highly recommended. Solids must be cleaned up in a manner that prevents dust generation. *DO NOT clean up a spill if you have not received proper training or if you do not feel you can handle the spill. Contact your supervisor or Environment, Health & Safety (EH&S) immediately.*

Small spills of SAZ solutions (less than 250 ml) or crystalline solid (less than 250 g): Small spills of SAZ can generally be handled with routine spill control measures; however, great care should be taken to prevent spread of the solution or solid. Absorbent spill materials from your spill kit should effectively handle all aqueous spills. Crystalline SAZ can be carefully swept up. Minimize dust generation by slow, careful sweeping with a bench duster or whisk into the receiving pan. Collect SAZ and spill materials and otherwise unrinse-able cleaning material into an appropriate container (glass jar or plastic, but *not* metal). Contact the Chemical Safety Office to request a pick-up (see below). Surfaces should be cleaned with tap water to remove residual amounts of SAZ. Anything used for spill clean-up to that comes in contact with the SAZ should be rinsed into the sink with tap water (enough to clear the drain trap) in order to remove the residual amounts of SAZ. Contact the Chemical Safety Office to request a pick-up (see below).

Larger spills or spills that have mixed with other materials: Cordon off the area to prevent the spread of the material (e.g. close doors to affected area, post warning signs, alert others in immediate vicinity to avoid the spill area). Notify others in the area of the spill. Contact EH&S (**265-5000**) during working hours and **911** after hours.

Training

Experienced researchers in SAZ manipulations should train new users of sodium azide in labs. Develop a Standard Operating Procedure (SOP) for any experiment involving SAZ and review it with your PI, lab manager or senior student. The task of developing an SOP provides an opportunity to fully evaluate the hazards associated with the experiment and the materials you will be working with. First time users of SAZ must use a minimum quantity of SAZ for manipulations.

Storing SAZ

Store synthesized azides below room temperature and away from sources of heat, light, pressure, and shock. Store SAZ (*solid as well as solutions*) away from bromine, carbon disulfide, dimethyl sulfate, nitric acid, heavy metals and their salts. Avoid water and strong acids which can lead to the formation of potentially explosive hydrazoic acid and its toxic vapors.

Disposal

Unwanted SAZ powders and solutions of SAZ from chemical manufacturers should be picked up by the Chemical Safety Office staff. Check the EH&S website for details on requesting a pick-up. Buffers solutions which have been treated SAZ as a preservative generally contain low concentrations of SAZ can often be disposed of down the drain. However, you should contact Chemical Safety Office staff to ensure that this can be done in your particular situation. You should understand that most water streams contain some heavy metals such as copper, lead, mercury, iron nickel, etc. Consequently, disposing of solutions containing sodium azide into water streams such as sewer water can result in the precipitation of insoluble azides such as lead azide. Since these insoluble azides are explosive, great care needs to be exercised to prevent there precipitation and accumulation in sewer lines and sewer holes.

References and Important Links

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12. http://cenblog.org/the-safety-zone/2014/06/explosion-injures-university-of-minnesota-graduate-student/

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