

University of Pittsburgh Safety Manual	EH&S Guideline Number: 04-028	
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GUIDELINES FOR THE SAFE HANDLING OF AZIDES

Azides are a highly reactive and versatile class of chemicals that are commonly used in both chemical synthesis and biomedical research applications. Organic azides are especially useful in various types of synthetic conversions. Azides (inorganic and organic) possess toxic properties and can be potentially explosive and shock sensitive under certain conditions. Therefore, azides require precaution during preparation, storage, handling and disposal.

All University employees who work with azides must complete Chemical Hygiene Training before handling these materials. Safety Data Sheets (SDS) should be reviewed to identify the specific hazards and necessary precautions when working with particular azide compounds.¹

1. STABILITY OF ORGANIC AZIDES

Organic azides are especially sensitive to violent decomposition from external energy sources such as light, heat, friction, and pressure. The stability of an organic azide is dependent upon its chemical structure, and the guidelines below should be reviewed prior to working with an organic azide. Always consider the *total* number of energetic functionalities (“explosophores”) in a compound while making a stability assessment. Azides, nitro groups, peroxides, diazophenols and numerous nitrogen-rich compounds derived from guanidine and its derivatives, will have a *cumulative* effect.

1.1 Carbon to Nitrogen Ratio (C/N)

With a few exceptions, the number of nitrogen atoms should not exceed the number of carbon atoms in an organic azide. Although some azides that have a C/N ratio between 1 and 3 can be synthesized in small quantities, the azides should be used or quenched as soon as possible. The azides should be stored at -18 °C, and in the absence of light (preferably in plastic amber containers). Concentrations should not exceed 1 M.

1.2 Rule of Six

Another method of assessing the stability of an organic azide is the “Rule of Six,” which states that there should be no less than six carbons per energetic functional group. *Six carbons (or other atoms of about the same size) per energetic functional group (azide, diazo, nitro, etc.) provides sufficient dilution to render the compound relatively safe.*² Less than six carbons per functional group can result in the material being explosive.

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2. STABILITY of INORGANIC AZIDES

Most inorganic azides are explosive under certain conditions, and should be handled carefully and protected from light, shock, and heat. Azides and metal parts (copper/brass) can form reactive mixtures. Substitute less reactive materials such as PVC for metal parts and/or metal instruments. Mixtures of inorganic azides and chlorinated solvents should be avoided. Dried mixtures of inorganic azides and organic materials should be considered highly hazardous. Mixing inorganic azides and acids must be avoided.

3. HEALTH HAZARDS

The health hazards of azides are dependent upon the type of azide, concentration, and type of exposure. Azide exposure can occur through inhalation, ingestion, or absorption. Symptoms of exposure may include irritation to the eyes and skin, dizziness, blurred vision, weakness/exhaustion, low blood pressure, heart arrhythmia, kidney effects, convulsions, and respiratory failure.

4. PREPARATION AND HANDLING

- 4.1 Azides should never be mixed with acidic and aqueous materials. This mixture can result in the formation of hydrazoic acid, which is highly toxic and explosive.
- 4.2 Azides should never be mixed with metals as these mixtures can result in the creation of metal azides, which are highly unstable and explosive.
- 4.3 Azides should not be manipulated using metal utensils (e.g. metal spatulas), as this can result in the formation of metal azides.
- 4.4 Halogenated solvents (such as dichloromethane and chloroform) should never be used as reaction media with azides. Using these materials can result in the formation of di- and tri- azidomethane, which are extremely unstable.

5. STORAGE

Azides should be stored separately from bromine, carbon disulfide, chromyl chloride, dimethyl sulfate, acids, and heavy metals and their salts. Azides should be stored plastic amber containers, and away from light.

6. DISPOSAL

- 6.1 Organic azides should be converted to a stable derivative (such as an amine) prior to being disposed as chemical waste.
- 6.2 All azide-containing materials should be disposed via the University's chemical waste program.

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6.3 Azide-containing waste streams must be collected separately, and must be clearly labeled with a completed orange WASTE CHEMICALS label detailing the specific azide and any additional compatible chemical constituents.

6.4 DO NOT co-mingle azide and acidic wastes, as this can produce highly toxic and explosive hydrazoic acid.

If you have any questions about the handling, storage, or disposal of azides, please call EH&S at 412-624-9505.

References

¹ Azides, add a ref to Bräse, S.; Banert, K., *Organic azides: Synthesis and applications*. Wiley: Chichester, 2010. Especially relevant is Chapter 1, Lab-Scale Synthesis of Azido Compounds: Safety Measures and Analysis by Thomas Keicher and Stefan Löbbbecke

² Kolb, H.C., Finn, M.G., Sharpless, K.B., "Click Chemistry: Diverse Chemical Function from a Few Good Reactions," *Angew. Chem. Int. Ed.* 2001, 40, 2004-2021.