NDM Research Building
GUIDELINES FOR THE SAFE HANDLING OF AZIDES

1.0 Introduction

This document provides guidance on how to manage risks during the storage, handling and use of azides. The use of the term azides througout this document refers to any compound (e.g. trimethylsilylazide) or salt (e.g. sodium azide) containing the functional group N_3. (NB, for this document, sodium azide is used as the prototypical azide salt and TMS-Azide is used as the prototypical organic azide). Azides are important buliding blocks in many chemical syntheses. There are a number of risks associated with the use of azides which should be consideres before use.

2.0 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.

2.1 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, (unless specified by individual supplier MSDS) and in the absence of light (preferably in plastic amber containers). Concentrations should not exceed 1 M.

2.2 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.* Less than six carbons per functional group can result in the material being explosive.

3. 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.

4. 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.

5. PREPARATION AND HANDLING

- 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.
- Azides should never be mixed with metals as these mixtures can result in the creation of metal azides, which are highly unstable and explosive.
- Azides should not be manipulated using metal utensils (e.g. metal spatulas), as this can result in the formation of metal azides.
- 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.
- A blast shield should be set up when working with Azides as a matter of cause to protect end users and their colleagues from potential explosions.

6. 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 or glass amber containers, and away from light.

7. DISPOSAL

- All azide-containing materials should be disposed via the University's chemical waste program.
- Azide-containing waste streams must be collected separately, and must be clearly labelled detailing the specific azide and any additional compatible chemical constituents. Speak to the lab manager to arrange collection with the safety office.
- DO NOT co-mingle azide and acidic wastes, as this can produce highly toxic and explosive hydrazoic acid.

8.0 References

- Safety documentation from the suppliers/manufacturers website regarding specific azide in use
- 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 Löbbecke

- **University of Pittsburgh Safety Manual, EH&S Guideline Number: 04-028**

9.0 Review

This document should be reviewed by the relevant person every three years