

Safe Use of Azides

1. Introduction

Azides are a versatile class of compounds commonly used in synthetic chemistry. Common reactions of alkyl azides include reduction to the amine or reaction with an alkyne to form triazoles (click chemistry). It is important to recognise that azides are potentially hazardous materials that need to be handled with care. Safety topics associated with the use of azides are highlighted below.

2. Toxicity

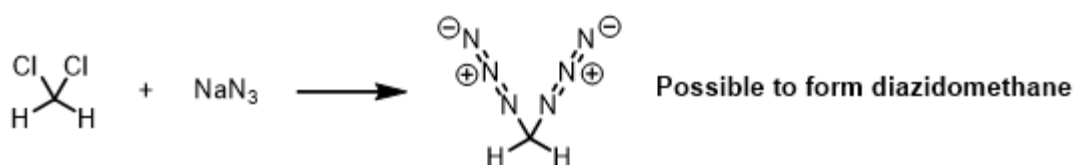
Inorganic azides and hydrazoic acid (see below) are acutely toxic. The toxicity levels are comparable to inorganic cyanides so it is important to take precautions to ensure the material is not inhaled, absorbed through the skin or ingested. Simply following laboratory practice including using fume cupboards, wearing protective nitrile gloves and good hygiene practices all help accidental exposure.

3. Incompatibility with Acids

Inorganic azides (e.g. sodium azide) are commonly used for the formation of alkyl azides. **Inorganic azides must not be mixed with strong acids** as this will result in the formation of hydrazoic acid (HN_3), which is both highly toxic and potentially explosive.

4. Incompatibility with Halogenated Solvents

Inorganic azides must not be used with halogenated solvents. The reaction of sodium azide with dichloromethane or chloroform has the potential to generate di- or tri-azidomethane. These species have been implicated in several reported explosions.



5. Azide Stability

5.1 Blast Shield

Reactions involving azides should be performed behind a blast shield to protect lab users in the event of an unexpected decomposition.

5.2 Isolation of Azides

Many azides are known to be unstable, especially if isolated. Give careful consideration as to whether the azide needs to be isolated and, wherever possible, generate and react the azide *in-situ*. If the stability of the azide is unknown, determine its carbon / nitrogen ratio. If the C/N ratio is <1 , the azide should not be isolated.

If it is deemed necessary to isolate an organic azide, it should not be concentrated by distillation as several incidents have been reported. Once isolated, azides should only be manipulated with plastic spatulas as metal spatulas increase the risk of forming metal azides and/or inducing decomposition.

Most azides are sensitive to heat, shock and friction so care must be taken to avoid direct heating or grinding as they can induce decomposition.

6. Reaction Scale

Wherever possible, perform reactions with azides on as small a scale as possible. If a large-scale is ultimately required, it is good practice to initially perform the reaction on a reduced scale to gauge the reactivity / stability of the azide.

7. Azide Containing Waste

Aqueous solutions of sodium azide should not be washed down the sink as they can form explosive azides with copper or lead used in pipework. Solutions of inorganic azides can be decomposed using nitrous acid or ceric ammonium nitrate, however, please speak to the safety coordinator for advice before proceeding.

Organic azides can be reduced to the corresponding amine with triphenylphosphine or a tin / hydrochloric acid.

If azide containing waste is disposed of via an external waste contractor, it should be placed in a plastic container rather than those made of metal.

It is worth noting that aqueous solutions containing azide may generate hydrazoic acid that can concentrate in the condensate, which poses an explosion risk. In such cases, low-boiling solvents such as ether or pentane can be added to help dilute the condensate by their own evaporation. Further information can be found at the link below:

“How Dangerous Is Too Dangerous? A Perspective on Azide Chemistry”

<https://pubs.acs.org/doi/10.1021/acs.joc.2c01402>