Safety Data Sheet

N-Nitroso-piperidine

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, AND MUTAGENIC. AVOID FORMATION AND BREATHING OF AEROSOLS OR VAPORS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, INDUCE VOMITING. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. WASH DOWN AREA. SEE CASTEGNARO ET AL. (1982) FOR DETAILS. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY. MONITOR LABORATORY AIR AND CHECK FOR NITROSAMINE RESIDUES AFTER CLEANUP.

A. Background

N-Nitrosopiperidine (NPIP) is toxic, carcinogenic, and mutagenic in experimental test systems. Its primary use is for tumor induction in experimental animals and for related research. Use of this compound for other purposes, such as organic synthesis, should be avoided. The volatility of this compound requires use of special precautions and containment procedures to prevent its release into the laboratory and general environment.

B. Chemical and Physical Data

1. Chemical Abstract No.: 100-75-4

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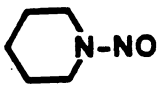
This data sheet is provided by the Division of Safety, NIH, to accompany the *NIH Guidelines for the Laboratory Use of Chemical Carcinogens.* The information included in this document is believed to be current and accurate, but no warranty is expressed or implied.

2. Synonyms:

NPIP

Piperidine, 1-nitroso- (9CI)

3. Molecular formula: $C_5H_{10}N_2O$

structure: 

weight: 114.17

4. Density: 1.063 g/cm^3 at 18.5°C.

5. Absorption spectroscopy: UV: λ (log ε) = 235 (3.98) and 337 (1.92) (Druckrey et al., 1967). General UV and IR characteristics of N-nitrosamines are discussed by Magee et al. (1976). For MS data, see Pensabene et al. (1972) and Rainey et al. (1978)

6. Volatility: 0.15 mm Hg at 20°C (extrapolated). The concentration of NPIP in saturated vapor is approximately 200 ppm or 0.02 percent (v/v). Air:water distribution coefficient: $10^5 \cdot K$ = 4.4 at 37°C (Mirvish et al., 1976).

7. Solubility: 7.7% in water. Soluble in hydrochloric acid, methylene chloride, ethylene chloride, and lipids.

8. Description, appearance: Pale yellow, oily liquid.

9. Boiling point: 215°C at 721 mm Hg.

10. Stability: Stable; nonexplosive.

11. Chemical reactivity: Relatively resistant to hydrolysis, but cleaved in strong acid to nitrous acid and piperidine.

12. Flash point: No data.

13. Autoignition temperature: No data.

14. Flammable limits: No data.

Fire, Explosion, and Reactivity Hazard Data

1. Use dry chemical fire extinguisher, water, or soda-acid. Fire-fighting personnel should wear air-supplied respirators with full-face masks.

2. The explosive range of the vapors is unknown.

3. Decomposed by strong acids, liberating nitrous acid.

4. May be absorbed by elastomers and may cause deterioration of these materials.

5. Volatilization during combustion produces hazardous vapors. Combustion products contain nitrogen oxides.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving NPIP.

Solutions of NPIP penetrate various glove materials (Walker et al., 1978). This factor should be taken into account when handling NPIP.

1. Chemical inactivation: Validated methods have been reported (Castegnaro et al., 1982).

2. Decontamination: Turn off equipment that could be affected by NPIP or the materials used for cleanup. If more than 10 ml has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Consult Castegnaro et al. (1982) for details concerning decontamination of surfaces, glassware, and animal cages.

3. Disposal: It may be possible to decontaminate waste streams containing NPIP before disposal. For details, see Castegnaro et al. (1982). No waste streams containing NPIP shall be disposed of in sinks or general refuse. Surplus NPIP or chemical waste streams contaminated with NPIP shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing NPIP shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing NPIP shall be packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with NPIP shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing NPIP shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store in sealed ampoules or in bottles with caps with polyethylene cone liners inside a sealed secondary container. This should be kept in a solvent storage cabinet, deep freeze, or explosion-safe refrigerator. Avoid exposure to light and moisture.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: Air samples may be collected using cold traps, impingers (Fine et al., 1977), or solid adsorbents (Issenberg and Sornson, 1976; Pellizzari et al., 1976).

2. Separation and analysis: After extraction and concentration, volatile nitrosamines may be determined by GC using a thermal energy analyzer (TEA) detector or a nitrogen specific detector, such as the thermionic nitrogen detector or Hall electrolytic conductivity detector, or by GC-MS. Electron capture detection of nitramine derivatives (Telling, 1972) or of heptafluorobutyrate derivatives of amines formed by cleavage of nitrosamines with hydrogen bromide in glacial acetic acid (Eisenbrand, 1972) may be appropriate for laboratories not equipped with more selective detectors. GC-TEA and GC-MS are the preferred methods. No acceptable direct field measurement methods are available.

Biological Effects (Animal and Human)

1. Absorption: NPIP is absorbed in animals through the gastrointestinal tract after ingestion and by parenteral injection. No human data.

2. Distribution: The tritium label of ^{3}H-NPIP is found in relatively high amounts in liver, kidney, and stomach.

3. Metabolism and excretion: Few in vivo data. It has been suggested that metabolism proceeds via ring hydroxylation and ring opening, which would lead through further oxidation to an alkyl carbonium ion, which would be the active carcinogen, in analogy with N-nitrosodialkylamines. Oral and intraperitoneal NPIP causes alkylation and breaks in liver nucleic acids. In in vitro systems, oxidation at the 4-position of NPIP occurs (Rayman et al., 1975). No urinary metabolites have been identified.

4. Toxic effects: Acute LD50s are 60, 100, and 200 mg/kg in the rat (intravenous, subcutaneous, and oral routes, respectively) and 324 mg/kg in the hamster (subcutaneous). Target organs for toxicity have not been identified.

5. Carcinogenic effects: NPIP produces tumors of the nasal cavities, trachea, esophagus, and lungs in mice, rats, and hamsters. It is noteworthy that, in contrast to N-nitrosodialkylamines, no liver, kidney, or bladder carcinomas have been reported.

6. Mutagenic and teratogenic effects: NPIP is mutagenic in the Ames test following activation. No mammalian mutagenicity or teratogenicity has been reported.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.

2. Ingestion: Drink plenty of water. Induce vomiting.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician.

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