Safety Data Sheet

1-Methyl-3-nitro-1-nitrosoguanidine

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, AND MUTAGENIC. IT MAY EXPLODE IN SEALED CONTAINERS. ALKALINE HYDROLYSIS PRODUCES DIAZOALKANES, WHICH ARE HIGHLY TOXIC, IRRITATING, CARCINOGENIC, AND EXPLOSIVE GASES.

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, DRINK MILK. REFER FOR GASTRIC LAVAGE. 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 WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

1-Methyl-3-nitro-1-nitrosoguanidine (MNNG) is toxic, carcinogenic, and mutagenic in experimental test systems. Its primary use is for tumor induction and related research in experimental animals and as a research mutagen. MNNG can explode on heating or high impact.

B. Chemical and Physical Data

1. Chemical Abstract No.: 70-25-7

issued 3/82

Synonyms:

MNG MNNG NG

N-Methyl-N-nitroso-N'-nitroguanidine

N-Methyl-N'-nitro-N-nitrosoguanidine (9CI)

Methylnitrosoguanidine (inaccurate nomenclature)

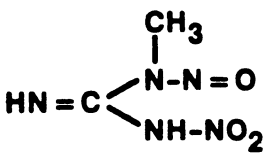
N'-Nitro-N-nitroso-N-methylguanidine

1-Nitro-N-nitroso-N-methylguanidine

Nitrosoguanidine (inaccurate nomenclature)

Molecular formula: $C_2H_5N_5O_3$

structure:



weight: 147.09

Density: No data.

Absorption spectroscopy: Reported by Ioki et al. (1975).
UV (MeOH): λ (log ε) = 275 (4.26), 306 (3.18), and 402 (2.30)

Volatility: No data.

Solubility: Less than 5% in water. Soluble in polar organic solvents (frequently with decomposition).

Description, appearance: Pale yellow to pink crystals.

Boiling point: No data.

Melting point: 118-123°C; has exploded during melting point determination in a sealed capillary.

Stability: Hydrolyzes in water and more rapidly in strong acid. Yields diazomethane, a highly toxic gas, in alkaline solution. Decomposed by sunlight in the solid state or in solution.

Chemical reactivity: MNNG is an alkylating agent. It reacts with primary amines to yield N-alkyl-N'-nitroguanidines. MNNG reacts with cysteine with evolution of nitrous oxide; it react with thiosulfate and with nucleic acids, yielding 7-methylgua-nine.

12. Flash point: Does not apply.

13. Autoignition temperature: No data.

14. Flammable limits: Does not apply.

Fire, Explosion, and Reactivity Hazard Data

1. Dry chemical or carbon dioxide extinguishers may be used. Fire fighters should wear air-supplied respirators with full-face masks.

2. Decomposition products may be explosive. Sealed bottles at room temperature may explode due to gas pressure. MNNG can explode on heating or high impact (Eisendrath, 1953; Bretherick, 1975).

3. Sensitive to light and moisture.

4. Incompatible with water.

5. Alkaline hydrolysis produces diazomethane, which is a highly toxic, irritating, flammable, and explosive gas.

6. Avoid contact with alkaline solutions. Nonspark tools and other equipment are recommended.

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 MNNG.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by MNNG or the materials used for cleanup. If more than 1 g 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. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with a polar organic solvent, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing MNNG shall be disposed of in sinks or general refuse. Surplus MNNG or chemical waste

streams contaminated with MNNG 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 MNNG 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 MNNG shall be packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with MNNG 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 MNNG shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store working quantities of MNNG and its solutions in a safety refrigerator in the work area. Store stocks of MNNG below -10°C in amber bottles with caps and Teflon cap liners. Do not store in ampoules since these could explode. Avoid exposure to light and moisture.

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

1. Sampling: MNNG could be found in aerosols formed in the laboratory, but no reliable sampling method for this potential hazard has been reported.

2. Separation and analysis: MNNG can be determined with a thermal energy analyzer using the direct inlet (Fine et al., 1975). MNNG can also be determined as nitrite after acidic hydrolysis (Preussmann and Schaper-Druckrey, 1972).

Biological Effects (Animal and Human)

1. Absorption: Although limited data are available, MNNG seems to be well absorbed after oral administration. No human data available.

2. Distribution: Studies with radiolabeled MNNG indicate that the guanidine carbon is retained primarily by the stomach and intestine, whereas the methyl carbon is also found in the heart, lungs, liver, kidney, and adrenals.

3. Metabolism and excretion: MNNG is reactive without metabolic activation and methylates nucleic acids both in vivo and in vitro. The main product is 7-methylguanine. Thiols enhance the rate markedly at neutral pH. After oral administration, denitrosation of MNNG occurs in the stomach, liver, and kidney;

90% of the dose is excreted in urine within 9 hours as metabolic products, with the main urinary metabolite being N-methyl-N'-nitroguanidine (IARC, 1974).

4. Toxic effects: Acute LD50s are 400 mg/kg (rat, oral), 420 mg/kg (rat, subcutaneous), and 1,070 mg/kg (hamster, oral). Target organs for toxicity have not been identified.

5. Carcinogenic effects: MNNG is carcinogenic in rodents and dogs. It is primarily a locally acting carcinogen, producing cancers of the stomach and duodenum on oral administration, squamous cell carcinomas and fibrosarcomas when painted on the skin, and tumors at or near the injection site, usually in the connective tissue, when injected.

6. Mutagenic and teratogenic effects: MNNG is mutagenic in microorganisms, plants, animals, and cultured human cells. Teratogenic effects have not 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: Vomiting might reexpose the mouth and esophagus. Drink milk; it may react with nitrosamides. Refer for gastric lavage.

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

4. Refer to physician.

References

Bretherick, L. 1975. Handbook of Reactive Chemical Hazards. CRC Press, Cleveland, OH.

Ehrenberg, L., and C.A. Wachtmeister. 1977. Safety precautions in work with mutagenic and carcinogenic chemicals. In B.J. Kilbey, M. Legator, W. Nichols, and C. Ramel, eds. Handbook of Mutagenicity Procedures. Elsevier, Amsterdam, Netherlands.

Eisendrath, J.N. 1953. Letter to the editor. Chem Eng News 31:3016.

Fine, D.H., F. Rufeh, D. Lieb, and D.P. Rounbehler. 1975. Description of volatile and nonvolatile N-nitroso compounds. Anal Chem 47:1188-1190.

IARC. 1974. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man. Some Aromatic Amines, Hydrazine and Related Substances, N-Nitroso Compounds and Miscellaneous Alkylating Agents, Vol. 4. World Health Organization, Geneva, Switzerland.

Ioki, Y., A. Imamura, C. Nagata, and M. Nakadate. 1975. Photochemical formation of nitroxide radicals from carcinogenic N-methyl-N'-nitro-N-nitrosoguanidine and related compounds. Photochem Photobiol 21:387-391.

Preussmann, R., and E. Schaper-Druckrey. 1972. Investigation of colorimetric procedure for determination of nitrosamides and comparison with other methods. Page 81 in P. Bogovski, R. Preussmann, and E. A. Walker, eds. N-Nitroso Compounds Analysis and Formation: Proceedings of a Working Conference Held at the Deutsches Krebforschungszentrum, Heidelberg, Federal Republic of Germany, 13-15 October, 1971. IARC Scientific Publications No. 3. World Health Organization, Geneva, Switzerland.