

Safety Data Sheet

N-Nitroso-N-methylurethane

Division of Safety
National Institutes
of Health



WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, AND MUTAGENIC. ALKALINE HYDROLYSIS PRODUCES DIAZOMETHANE, WHICH IS A HIGHLY TOXIC, IRRITATING, CARCINOGENIC, HIGHLY FLAMMABLE, AND EXPLOSIVE GAS.

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

N-Nitroso-N-methylurethane (MNUT) 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.

B. Chemical and Physical Data

1. Chemical Abstract No: 615-53-2

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Synonyms:

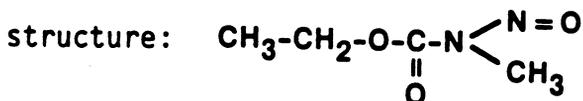
MNUN	N-Methyl-N-nitrosourethane
MNUT	Methyl-N-nitrosourethane
NMU	N-Nitroso-N-methylurethane
NMUT	Nitrosomethylurethane
N-Methyl-N-nitroso-ethylcarbamate	N-Methyl-N-nitroso carbonic acid, ethyl ester
Methylnitrosourethane	Ethyl N-methyl-N-nitrosocarbamate
Methylnitroso-carbamic acid, ethyl ester (9CI)	

Molecular

formula:



structure:



weight:

132.14

Density: 1.113 g/cm³.

Absorption spectroscopy: IR, UV, NMR spectra have been reported by Heyns and Roper (1974). UV (CH₂Cl₂): λ (log ε) = 236 (3.83), 385 (2.59), 398 (2.08), and 417 (2.07) (Mirvish, 1971).

Volatility: Concentration of saturated vapor, < 1,000 ppm (estimated). The boiling point is low and the air:water distribution coefficient is very high (10⁵ · K = 100 at 37°C) (Mirvish et al., 1976). Hence MNUT is probably very volatile at room temperature.

Solubility: 3.7% in water at 23-25°C; soluble in most organic solvents.

Description, appearance, odor: Yellow to pink sweet-smelling oil of low viscosity.

Boiling point: 65°C at 13 mm Hg; explodes if distilled at atmospheric pressure.

Melting point: No data.

Stability: Sensitive to light and humidity. Should be stored in tightly sealed containers in the dark at less than -10°C and protected from moisture. Stability of aqueous solutions is pH dependent (Druckrey et al., 1967; McCalla et al., 1968).

11. Chemical reactivity: MNUT is an alkylating agent. It is hydrolyzed by strong alkali (liberating diazomethane, a highly toxic gas) and by strong acid. Reacts with thiol compounds.
12. Flash point: No data.
13. Autoignition temperature: No data.
14. Flammable limits: No data.

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.
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.

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 MNUT.

1. Chemical inactivation: No validated method reported.
2. Decontamination: Turn off equipment that could be affected by MNUT 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. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with an organic solvent, followed by soap and water. Animal cages should be washed with water.
3. Disposal: No waste streams containing MNUT shall be disposed of in sinks or general refuse. Surplus MNUT or chemical waste streams contaminated with MNUT 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 MNUT 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 MNUT shall be packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with MNUT 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 MNUT shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store working quantities of MNUT and its solutions in a safety refrigerator in the work area. Store stocks of MNUT 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: No data.
2. Separation and analysis: MNUT can be separated from mixtures by high-speed/high-pressure liquid chromatography (Heyns and Roper, 1974). It can be determined with a thermal energy analyzer (Fine et al., 1975). MNUT is also readily determined colorimetrically as nitrite after acid hydrolysis (Preussmann and Schaper-Druckrey, 1972), and, while the yield of nitrite is only 50% of theoretical, it appears to be quite consistent.

Biological Effects (Animal and Human)

1. Absorption: Very few data available. MNUT is absorbed by rodents after ingestion and parenteral injection. It is a strong skin irritant, but there is no indication whether it produces systemic effects by this route or by inhalation.
2. Distribution: The tritium label of ^3H -MNUT, fed by stomach tube to pregnant guinea pigs, is found in maternal liver, brain, kidney, pancreas, and spleen, as well as in fetal brain and liver; part of it is incorporated into the DNA of these organs.
3. Metabolism and excretion: The high chemical reactivity of MNUT in vitro with proteins, nucleic acids, and low-molecular-weight thiol compounds makes it unlikely that an enzymatic metabolism is involved in its action. Its breakdown leads to formation of methylcarbonium ion that alkylates proteins and nucleic acids in vivo (IARC, 1974). Excretion products have not been identified.

4. Toxic effects: Acute LD50s are 4 and 180 mg/kg in rats (intravenous and oral routes, respectively) and 37 mg/kg in mice (intraperitoneal). The great discrepancy between intravenous and oral toxicity is noteworthy and is not found with other nitrosamides; it indicates large-scale destruction of MNUT in the stomach. No target organs for toxicity have been identified. There are no human data available.
5. Carcinogenic effects: MNUT is carcinogenic in all species tested. The effects are, in part, local and vary with route of administration (gastrointestinal tract, particularly the stomach and pancreas, on oral administration; local fibrosarcomas on subcutaneous injection); there are also systemic effects, particularly pulmonary tumors with single doses given intravenously and intraperitoneally. Prenatal exposure to MNUT produces mainly tumors of the central nervous system in mice and rats.
6. Mutagenic and teratogenic effects: MNUT is highly mutagenic in plants, but no such effect has been demonstrated in experimental animals. No evidence for 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: 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

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