

Safety Data Sheet

N-Nitroso- diethylamine

Division of Safety
National Institutes
of Health



WARNING!

THIS COMPOUND IS TOXIC, CARCINOGENIC, AND MUTAGENIC. IT IS READILY ABSORBED BY VARIOUS BODY TISSUES. 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

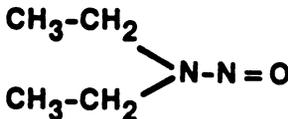
N-Nitrosodiethylamine (DEN) is toxic, carcinogenic, and mutagenic in experimental test systems. Its primary use is for tumor induction in experimental animals and for related research. Use of this compound for other purposes, such as organic synthesis, should be avoided. The volatility of this compound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

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Chemical and Physical Data

1. Chemical Abstract No.: 55-18-5
2. Synonyms:

DEN	Diethylnitrosamine
DANA	Diethylnitrosoamine
DENA	Nitrosodiethylamine
NDEA	N,N-Diethylnitrosamine

Ethanamine, N-ethyl-N-nitroso- (9CI)
3. Molecular formula: $C_4H_{10}N_2O$
weight: 102.16
structure: 

CH_3-CH_2
 CH_3-CH_2
N-N=O
4. Density: 0.9422 g/cm³.
5. Absorption spectroscopy: UV (CCl₄): λ (log ϵ) = 364 (1.017). IR (CCl₄): 1,459 cm⁻¹ (N=O); 1,061 cm⁻¹ (N=N) (Magee et al., 1976). For MS data, see Pensabene et al. (1972) and Rainey et al. (1978).
6. Volatility: 1.7 mm Hg at 20°C (extrapolated). The concentration of DEN in the saturated vapor is approximately 2,000 ppm or 0.2 percent (v/v). Air:water distribution coefficient: $10^5 \cdot K = 30$ at 37°C (Mirvish et al., 1976).
7. Solubility: 10% in water; soluble in alcohol, ether, other organic solvents, and lipids.
8. Description, appearance: Yellow, volatile liquid.
9. Boiling point: 177°C.
10. Stability: Stable in neutral or alkaline aqueous solution in the absence of light. Less stable in acid. Sensitive to visible and UV light. Nonexplosive.
11. Chemical reactivity: Relatively resistant to hydrolysis, but cleaved in strong acid to nitrous acid and diethylamine. Oxidized and reduced by appropriate reagents.
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 or CO₂ fire extinguisher. 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. Absorbed by many elastomers. 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 DEN.

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

1. Chemical inactivation: Validated methods have been reported (Castegnaro et al., 1982).
2. Decontamination: Turn off equipment that could be affected by DEN 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 DEN before disposal. For details, see Castegnaro et al. (1982). No waste streams containing DEN shall be disposed of in sinks or general refuse. Surplus DEN or chemical waste streams contaminated with DEN 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 DEN 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 DEN shall be packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with DEN 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 DEN 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: DEN is rapidly absorbed by ingestion, inhalation, and parenteral injection. No human data.
2. Distribution: DEN is rapidly distributed throughout the body water after administration by all routes. Principal target organs for distribution are the liver, respiratory tract, nasal cavity, kidney, and gall bladder.
3. Metabolism and excretion: DEN requires metabolic activation to exert its toxic and carcinogenic effects. Activation involves oxidative de-ethylation to a presumed monoethylnitrosamine intermediate that rapidly decomposes to an ethyl carbonium ion that ethylates proteins and nucleic acids. Other metabolic pathways may be operative, but these have not been worked out. Some DEN is excreted unchanged in urine and expired air, but most of the

administered compound is probably oxidized to carbon dioxide and nitrogen (Heath, 1962).

4. Toxic effects: The acute LD50 of DEN is in the range of 180-280 mg/kg in rodents (mouse, rat, hamster) by the oral and parenteral routes. The chief target organs are the liver, respiratory tract, and kidneys. In these organs, DEN alkylates nucleic acids.
5. Carcinogenic effects: The most frequently observed target organ is the liver; hepatomas and hepatocellular carcinomas are produced by small repeated doses in rats, mice, hamsters, rabbits, monkeys, and dogs by ingestion or inhalation. In addition, lung and esophagus adenomas and tumors of the nasal cavity and ovaries have been found frequently. Transplacental effects have been noted though not as consistently as with N-nitrosodimethylamine.
6. Mutagenic and teratogenic effects: DEN is mutagenic in rats on oral administration and in Drosophila. Teratogenicity has been reported in rats, mice, and hamsters after relatively high doses during the later stages of gestation.

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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