

# Safety Data Sheet

# Benzidine

Division of Safety  
National Institutes  
of Health



## WARNING!

THIS COMPOUND IS ABSORBED THROUGH THE SKIN AND THE RESPIRATORY AND INTESTINAL TRACTS. IT IS TOXIC, CARCINOGENIC, AND MUTAGENIC. AVOID FORMATION AND BREATHING OF AEROSOLS.

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

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND WATER.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK WATER, INDUCE VOMITING, OR 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. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS. USE ETHANOL TO DISSOLVE COMPOUND. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

### A. Background

Benzidine (BEN) is very toxic to animals and man, affecting chiefly the blood, urinary system, liver, and skin. It is carcinogenic to animals and produces bladder cancer in occupational exposures. It is mutagenic in the Ames test. BEN is used commercially as a starting material in the production of azo dyes and in the analytical laboratory for the detection or determination of a variety of compounds.

issued 8/82

## Chemical and Physical Data

1. Chemical Abstract No.: 92-87-5

2. Synonyms:

BEN

Fast Corinth Base B

4,4'-Bianiline

4,4'-Diaminodiphenyl

4,4'-Biphenyldiamine

4,4'-Diphenylene diamine

4,4'-Diaminobiphenyl

C.I. Azoic Diazo Component 112

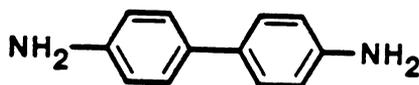
(1,1'-Biphenyl)-4,4'-diamine (9CI)

3. Molecular

formula:

$C_{12}H_{12}N_2$

structure:



weight:

184.23

4. Density: 1.250 g/cm<sup>3</sup>.

5. Absorption spectroscopy: UV:  $\lambda$  (log  $\epsilon$ ) = 287 (4.4) (Weast, 1979, p. C-211). Fluorescence excitation and emission spectra have been listed (Bowman et al., 1976).

6. Volatility: No data.

7. Solubility: 0.4 g/liter at 12°C, 9.4 g/liter at 100°C in water; soluble in hot alcohol and methyl ether.

8. Description, appearance: White to slightly reddish crystalline powder that darkens on exposure to air and light.

9. Boiling point: 400-401°C at 740 mm Hg.

Melting point: Of the three isotropic forms of BEN that coexist at room temperature, the stable form melts at 128°C and the two unstable forms melt at 125°C and 122°C.

10. Stability: Darkens in air and light.

11. Chemical reactivity: BEN exhibits the usual reactivity of primary aromatic amines (salt formation, acylation, alkylation, isocyanide formation, tetrazotization, oxidation by neutral and basic permanganate) and of aromatic compounds in general (ring substitution). Most oxidizing agents give a blue product. BEN forms a nearly insoluble sulfate with sulfuric acid or alkali

12. Flash point: No data.
13. Autoignition temperature: No data.
14. Explosive limits in air: No data.

#### Fire, Explosion, and Reactivity Hazard Data

1. Fire-fighting personnel should wear air-supplied respirators with full-face masks.
2. No conditions contributing to instability, other than oxidation in presence of air and light, are known to exist. Aromatic amines in general are slightly flammable.
3. No incompatibilities are known.
4. Aromatic amines may form toxic fumes when heated to decomposition.
5. BEN does not require nonspark equipment. When handled in flammable solvents, the precautions required for such solvents apply.

#### 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 BEN.

1. Chemical inactivation: No validated method reported.
2. Decontamination: Turn off equipment that could be affected by BEN or the materials used for cleanup. Call the NIH Fire Department (dial 116) for assistance. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with ethanol, followed by soap and water. Animal cages should be washed with water.
3. Disposal: No waste streams containing BEN shall be disposed of in sinks or general refuse. Surplus BEN or chemical waste streams contaminated with BEN 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 BEN 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 BEN shall be disinfected by heat using a standard autoclave treatment and

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

4. Storage: Store in glass ampoules or in amber screw-capped bottles with Teflon cap liners, preferably under refrigeration. Avoid unnecessary exposure to light.

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

1. Sampling: For airborne particles smaller than  $0.3 \mu\text{m}$ , impingers or bubblers filled with dilute hydrochloric acid are used; for large particles, a high-volume air sampler with a fiberglass filter trap may be used. For surface sampling, a cotton applicator moistened with an aqueous buffer is employed, and identification is made with spectrophotofluorimetry. Techniques for sampling metal, painted, and concrete surfaces have been reported (Weeks et al., 1976).
2. Separation and analysis: The most commonly used procedure is spectrophotofluorimetry in methanol, preceded by solvent extraction and cleanup on an alumina column (Holder et al., 1976; Bowman et al., 1976). This procedure has been applied to waste water and biological materials. GC (Masuda and Hoffman, 1969) reportedly has a detection limit of 0.2 ppb. Colorimetric procedures (sensitive but not specific for BEN) have been applied to measurement of BEN in air and clothing (Butt and Strafford, 1956) and in urine (Glassman and Meigs, 1951).

#### Biological Effects (Animal and Human)

1. Absorption: BEN may be absorbed by animals and humans by inhalation, by ingestion, and through the skin. The most common route of entry in occupational exposures is through the intact skin (Meigs et al., 1951).
2. Distribution:  $^{14}\text{C}$  derived from intravenous injection of labeled BEN in rats and dogs is widely distributed; major amounts are found in the bladder, intestine, lung (rat), and bile (dog) (Kellner et al., 1973).
3. Metabolism and excretion: BEN is metabolized by hydroxylation at various positions and conjugation of the phenolic products with sulfuric and glucuronic acid and by acylation of one or both amino groups. All these metabolic products are found in the urine and feces of numerous species. Pertinent data have been reviewed and summarized (Haley, 1975).

- BE  
7
4. Toxic effects: BEN is carcinogenic in humans (Althouse et al., 1980). The acute oral LD50s of BEN are 309 and 214 mg/kg in the rat and mouse, respectively. In the dog, oral doses of 200 mg/kg and subcutaneous injections of 400 mg/kg are lethal. Target organs in humans and several animal species are generally the blood, urinary system, liver, and skin. These results have been reviewed (Haley, 1975).
  5. Carcinogenic effects: BEN has produced bladder carcinomas in humans and dogs and carcinomas of the liver, biliary system, and sebaceous glands in mice, rats, and hamsters. These effects were produced by ingestion or subcutaneous injection. In humans, occupational exposure to BEN, either by inhalation or skin exposure, results in bladder tumors (Zavon et al., 1973).
  6. Mutagenic and teratogenic effects: BEN is an active mutagen in the Ames test. There are no data concerning its teratogenicity.

#### Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes. Consider ophthalmological consultation.
2. Ingestion: Drink plenty of water. Induce vomiting or refer for gastric lavage.
3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.
4. Refer to physician. Oxygen may be necessary during transport. Observe for methemoglobinemia.

#### References

- Althouse, R., J. Huff, L. Tomatis, and J. Wilbourn. 1980. An evaluation of chemicals and industrial processes associated with cancer in humans based on human and animal data: IARC Monographs Volumes 1 to 20: Report of an IARC Working Group. *Cancer Res* 40:1-12.
- Bowman, M.C., J.R. King, and C.L. Holder. 1976. Benzidine and congeners: Analytical chemical properties and trace analysis in five substrates. *Int J Environ Anal Chem* 4:205-223.
- Butt, L.T., and N. Strafford. 1956. Papilloma of the bladder in the chemical industry: Analytical methods for the determination of benzidine and  $\beta$ -naphthylamine, recommended by ABCM Sub-Committee. *J Appl Chem* 6:525-539.
- Glassman, J.M., and J.W. Meigs. 1951. Benzidine (4,4'-diaminobiphenyl) and substituted benzidines. *Arch Ind Hyg Occup Med* 4:519-532.
- Haley, T.J. 1975. Benzidine revisited: A review of the literature and problems associated with the use of benzidine and its congeners. *Clin Toxicol* 8:12-42.

- Holder, C.L., J.R. King, and M.C. Bowman. 1976. 4-Aminobiphenyl, 2-naphthylamine and analogues: Analytical properties and trace analysis in five substrates. *J Toxicol Environ Health* 2:111-129.
- Kellner, H.M., O.E. Christ, and K. Lotsch. 1973. Animal studies on the kinetics of benzidine and 3,3'-dichlorobenzidine. *Arch Toxicol* 31:61-79.
- Masuda, Y., and D. Hoffman. 1969. A method for the determination of primary amines of polynuclear aromatic hydrocarbons. *J Chromatogr Sci* 7:694-697.
- Meigs, J.W., R.M. Bowman, and L.J. Sciarini. 1951. A study of the exposure to benzidine and substituted benzidines in a chemical plant. *Arch Ind Hyg Occup Med* 4:533-540.
- Scott, T.S. 1962. *Carcinogenic and Chronic Toxic Hazards of Aromatic Amines*. Elsevier Publishing Company, New York.
- Weast, R.C., ed. 1979. *Handbook of Chemistry and Physics*, 60th ed. CRC Press, Cleveland, OH.
- Weeks, R.W., B.J. Dean, and S.K. Yasuda. 1976. Detection limits of chemical spot tests towards certain carcinogens on metal, painted and concrete surfaces. *Anal Chem* 48:2227-2233.
- Zavon, M.R., U. Hoegg, and E. Bingham. 1973. Benzidine exposure as a cause of bladder tumors. *Arch Environ Health* 27:1-7.