Benzene

Safety Data Sheet

Division of Occupational Health and Safety
National Institutes of Health

WARNING:

This compound is acutely toxic, carcinogenic, embryotoxic, and mutagenic. It is readily absorbed by various body tissues through the skin and respiratory and intestinal tracts and transplacentally. It may irritate the eyes, mucous membranes, and lungs. 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 exposes, wash with soap and water. Avoid washing with solvents. Avoid rubbing of skin or increasing its temperature.

Benzene is flammable and explosive. Keep away from sparks and open flames. In case of fire, use carbon dioxide or dry chemical extinguisher.

For eye exposure, irrigate immediately with large amounts of water. For ingestion, do not induce vomiting. Drink milk or water. 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 or vapors. Use absorbent paper to mop up spill. After the residue has evaporated, wash down area with water. Dispose of waste solutions and materials appropriately. Monitor laboratory air and check for benzene residues after cleanup.

A. Background

Benzene is a clear, colorness, volatile, highly flammable liquid. It is moderately toxic in animals and man and is carcinogenic, embryotoxic, and mutagenic. Benzene is used in the manufacture of many organic compounds, artificial leather, varnishes, lacquer, and other products. However, because of stringent governmental restrictions on occupational exposure to benzene, its industrial use is being curtailed; where possible, substitute solvents are sought.

The permissible exposure limit is 1 ppm as an 8-hour time-weighted average; the short-term exposure limit is 5 ppm average over any 15 minute period (Federal Register, 1987). The current threshold limit value for benzene is 10 ppm (ACGIH, 1988). IARC (1982), p. 97 lists official exposure limits imposed by various countries.

Recent reviews of the chemical and biological properties of benzene include IARC (1982), Mehlman (1983), and Aksoy (1988a).

B. Chemical and Physical Data

1. Chemical Abstract No.: 71-43-2
2. Synonyms:[A] Phene, Pyrobenzole, Benzol, Phenylhydride, Benzole, Cyclohexatriene, Pyrobenzol, Bicarburet of hydrogen.
3. Molecular formula, weight and structure:

   C_6H_6 78.11 

4. Density: Liquid, 0.8787 g/cm^3 at 15°C relative to water at 4°C; vapor, 2.7 (air = 1.0).
5. Absorption spectroscopy: UV (C_2H_5OH): λ (log ε) = 243 (2.2), 249 (2.3), 256 (2.4), and 261 (2.2). Infrared (Robinson, 1974) and mass (Monahan and Stanton, 1962) spectra have been reported.
6. Volatility: Vapor pressure, 74.6 mm Hg at 20°C. (For vapor pressures below and above 1 atmosphere, see pages D-201 and D-212, respectively, in Weast, 1988.)
7. Solubility: Water, 0.8 parts per 1,000 by weight at 20°C; miscible with ethanol, ether, acetone, chloroform, carbon disulfide, glacial acetic acid, and oils.
8. Description: Clear, colorless, volatile liquid.
9. Boiling point: 80.1°C.

   Melting point: 5.5°C.
10. Stability: Stable at normal temperatures; highly flammable.
11. Chemical reactivity: Benzene has relatively low reactivity; it is reduced (to cyclohexane) and oxidized (ring cleavage) only under very stringent conditions. It is however, subject to substitution reactions such as nitration, sulfonation, halogenation, alkylation, and acrylation in the presence of suitable catalysts. For a general review, see standard textbooks (*e.g.*, p. 337 ff, Morrison and Boyd, 1973).
12. Flash point: -11.1°C (closed cup).
13. Autoignition temperature: 538°C.
14. Explosive limits in air: 1.4 – 7.1%.

C. Fire, Explosion, and Reactivity Hazard Data

1. Use dry chemical fire extinguisher. Fire-fighting personnel should wear air-supplied respirators will full-face masks.
2. Benzene is flammable and its vapors in air can form explosive mixtures (see above).
3. No other conditions contributing to instability are known.
4. No hazardous decomposition products have been identified.

[A] "Benzin," "benzine," and "petroleum benzin" are terms used for a mixture of low-boiling aliphatic hydrocarbons and should not be confused with benzene.

5. Do not expose to sparks or open flames. Use nonspark tools and equipment.

D. 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 NIH 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 benzene.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable to other institutions. Administer and/or researchers at other institutions should modify the following items as needed to reflect their individual management system and current occupational and environmental regulations.

Benzene penetrates various glove materials (Sansone and Tewari, 1978). This factor should be taken into account when handling materials or equipment containing benzene.

Chemical inactivation: No validated method reported.

1. Decontamination: Turn off equipment that could be affected by benzene or thematerials used for cleanup. If there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 911) for assistance. Use absorbent paper to mop up spill. After the residue has evaporated, wash 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.
2. Disposal: No waste streams containing benzene shall be disposed of in sinks or general refuse. Surplus benzene or chemical waste streams contaminated with benzene 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 benzene 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 benzene shall be packaged for incineration, as above. Burnable waste (*e.g.*, absorbent bench top liners) minimally contaminated with benzene 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 benzene shall be handled in accordance with the NIH radioactive waste disposal system.
3. Storage: Store is 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 or explosion-safe refrigerator. Store working quantities of benzene and its solutions in an explosion-safe refrigerator in the work area.

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

1. Sampling: The procedure for air sampling recommended by the Intersociety Committee on Methods for Air Sampling and Analysis (Sawicki *et al.*, 1975) and NIOSH (1977) is absorption on charcoal and desorption with carbon disulfide. Because of the toxicity and flammability of CS2, as well as its unsuitability when electron capture or photoionization detectors are used in conjunction with gas chromatography, silica gel or commercial polymers with elution by methanol or ethanol have been proposed as substitutes (van Tassel *et al.*, 1981). Methods for the extraction of blood (Snyder *et al.*,

1975) and tissue (Snyder *et al*., 1977) for subsequent gas chromatographic analysis have been published.

2. Analysis: Methods of analysis have been reviewed (Snyder, 1977; Ikeda and Okuno, 1988); IARC (1982, p. 107) provides an overview of methods through 1980. The method of choice is gas chromatography with a variety of detectors. Special high-pressure liquid chromatographic methods have been developed for the separation and quantitation of benzene metabolites for pharmacokinetic studies (Greenlee *et al*., 1981; Sabourin *et al*., 1988a).

F. Biological Effects (Animal and Human)

1. Absorption: Benzene is absorbed readily by inhalation, ingestion, and parenteral injection. Percutaneous absorption used to be considered as slight but has recently been shown (in hairless mice) to contribute a significant portion of the total absorbed dose (Susten *et al*., 1985).

2. Distribution and pharmacokinetics: On inhalation of benzene by animals, the 40-50% amount retained (the rest being exhaled unchanged) is transported by the blood (preferentially, the red cells) to the liver, bone marrow, and tissues with high lipid content where it is subsequently metabolized (Schrenk *et al*., 1941). Excretion in the lungs follows a biphasic pattern, suggesting a two-compartment model for distribution, in the rat (Rickert *et al*., 1979). Similar results were found in humans where, however, a three-compartment model is indicated (Srbova et al., 1950; Berlin *et al*., 1979).

3. Metabolism and excretion: Schemes of the metabolic pathways of benzene have been depicted (Pellack-Walker *et al*., 1985; Kalf *et al*., 1987; and Copper and Snyder, 1988 among others). Essentially they consist of oxidation to phenol (probably via benzene epoxide) and further by two pathways either to hydroquinone and benzoquinone, or to catechol and 1,2,4benzene tricl. These are excreted in the urine as glucuronides and sulfates. In addition, benzene is also excreted in the urine unchanged, the relative amounts of benzene and metabolites depending on the amount administered since the capacity of mammalin liver to oxidize benzene is limited (Sabourin *et al*., 1987, 1988b). A further excretion product, transmuconic acid, is the result of oxidative opening of the catechol ring. This oxidation has been demonstrated in liver and bone marrow and is mediated by cytochrome P-450 or reactive oxygen species. Further details are discussed in IARC (1982) and the above-named references.

4. Toxic effects: The acute oral LD50 of benzene in the mouse and rat has been reported as 3-5 g/kg. The inhalation LC50 in these species in 10,000 ppm for a 7-hour exposure. The target organ for acute poisoning is mainly the central and peripheral nervous system, and this poisoning results in muscle tremors, convulsions, salivation, nystagmus, and asphyxiation due to paralysis of the respiratory center. Chronic poisoning effects in man have been summarized as follows: "The net effect in the human is a disease characterized by gradual decreases in white cell levels, among which the granulocytes are most severly affected, but decreases in lymphocytes, the form more sensitive in rodents, are also affected. Red Cell and platelet levels may also fall … Reason for pancytopenia is severe bone marrow damage and the disease is called aplastic anemia" (Snyder, 1984).

   These toxic effects have been reviewed in detail by van Raalte and Grasso (1982) and Aksoy (1988b). The biochemical basis for these toxic actions appears to be covalent binding of benzene metabolites to nucleic acids and protein in liver, and inhibition of thymidine uptake in bone marrow DNA (Cooper and Snyder, 1988).

5. Carcinogenic effects: IARC (1982) summarizes its extensive review of the literature as follows: "There is limited evidence that benzene is carcinogenic in experimental animals… There is sufficient evidence that benzene is carcinogenic to man." The evidence has been further reviewed and updated by Aksoy (1988c). Oral administration or inhalation of benzene in BD Wistar rats and Swiss mice

results in carcinomas of the Zymbal glands, oral and nasal cavity, skin, forestomach and mammary glands, hepatomas and pulmonary tumors (Maltoni *et al*., 1985).

6. Mutagenic and teratogenic effects: Benzene is not mutagenic in the Ames test or in the E. coli DNA repair test (DeFlora *et al*., 1984; Rexroat and Probst, 1985). Evidence to date indicates that benzene is not teratogenic in doses which are fetotoxic and embryolethal. In vitro studies on human lymphocytes have demonstrated sister chromatid exchanges on exposure to benzene, but potency in this respect is far lower than that of benzene metabolites (Erexson *et al*., 1985).

G. Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Skin should not be rinsed with organic solvents. Since benzene is readily absorbed through the skin, avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.
2. Ingestion: Drink plenty of water or milk. Do not induce vomiting. (Vomiting might re-expose the mouth and esophagus.) Refer for gastric lavage.
3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.
4. Refer to physician at once. Consider treatment for pulmonary irritation.

H. References

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