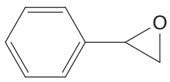
Styrene-7,8-oxide

CAS No. 96-09-3

Reasonably anticipated to be a human carcinogen

First listed in the *Tenth Report on Carcinogens* (2002)

Also known as 1,2-epoxyethylbenzene



Carcinogenicity

Styrene-7,8-oxide is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Oral exposure to styrene-7,8-oxide caused tumors in two rodent species and at two different tissue sites. Styrene-7,8-oxide (styrene oxide) administered by stomach tube caused cancer of the forestomach (squamous-cell carcinoma) in both sexes of mice (one strain) and rats (three strains) (IARC 1994). It also caused liver tumors (hepatocellular tumors) in male mice (Lijinsky 1986).

Cancer Studies in Humans

No epidemiological studies were identified that evaluated the relationship between human cancer and exposure specifically to styrene-7,8-oxide.

Studies on Mechanisms of Carcinogenesis

Styrene oxide given orally to rabbits, rats, and mice is absorbed and broken down rapidly in the acid environment of the stomach and excreted almost completely in the urine. Styrene oxide can be metabolized by epoxide hydrolase to form the glycol or by glutathione S-transferase to glutathione conjugates. Styrene glycol is further metabolized to mandelic, phenylglyoxylic, and hippuric acids, which are excreted in urine (IARC 1976, 1994). Workers exposed to styrene oxide vapors excreted large amounts of mandelic acid and phenylglyoxylic acid in their urine. (Fustinoni *et al.* 1998).

Styrene oxide caused mutations in bacteria, yeast, insects, and cultured mammalian cells, including mutations at the *hprt* locus in Chinese hamster V79 cells and human T lymphocytes. It caused chromosomal aberrations or sister chromatid exchange in Chinese hamster V79 cells, Chinese hamster ovary cells, mouse bone marrow cells *in vivo*, and cultured human lymphocytes. It also caused DNA strand breaks in cultured primary animal hepatocytes, human embryonal cells, human lymphocytes, mouse lymphocytes, and mouse liver and kidney cells (IARC 1994).

Styrene oxide–DNA adducts were observed at low levels in the forestomachs of male rats given styrene oxide orally (Lutz *et al.* 1993). DNA adducts that formed at very low levels in the livers of mice administered styrene orally were attributed to styrene oxide, as styrene was presumed to have been almost completely metabolized to styrene oxide (Cantoreggi and Lutz 1993). A study of workers in a boat-making facility where styrene concentrations ranged from 1 to 235 mg/m^3 (mean = 65.6 mg/m^3, or 13.3 ppm) found elevated levels of styrene oxide–DNA adducts in mononuclear cells (Huff 1984, McConnell and Swenberg 1993). Styrene oxide–DNA and styrene oxide–albumin adducts were found in the blood of plastics workers exposed to styrene oxide (Fustinoni *et al.* 1998). Styrene oxide–DNA adducts in rodents and humans appear to be similar. There is no evidence to suggest that mechanisms by which styrene oxide causes genotoxic effects and tumors in experimental animals would not also operate in humans.

Properties

Styrene-7,8-oxide is an epoxide of styrene that exists at room temperature as a colorless to pale yellow liquid with a pleasant sweet odor. It is soluble in alcohol, ether, benzene, acetone, methanol, carbon tetrachloride, and heptane, and miscible with most other organic solvents. It is only slightly soluble in water. Styrene-7,8-oxide polymerizes exothermally and reacts vigorously in the presence of catalysts with compounds with available hydrogen ions (IARC 1994). Physical and chemical properties of styrene-7,8-oxide are listed in the following table.

Property	Information
Molecular weight	120.2[a]
Specific gravity	1.0523 at 16°C/4°C[a]
Melting point	–35.6°C[a]
Boiling point	194.1°C[a]
Log K_{ow}	1.61[a]
Water solubility	3.000 g/L at 20°C[b]
Vapor pressure	0.3 mm Hg at 20°C[a]
Vapor density relative to air	4.3[a]

Sources: [a]HSDB 2009, [b]ChemIDplus 2009.

Use

Styrene oxide is used as a chemical intermediate in the production of styrene glycol and its derivatives, cosmetics, surface coatings, and agricultural and biological chemicals. It also is used as a reactive diluent for epoxy resins and in cross-linked polyesters and polyurethanes. Styrene oxide has been used as a raw material for the production of 2-phenylethanol (oil of roses) used in perfumes and in the treatment of fibers and textiles. Small quantities are used to improve the stability of hydraulic fluids, chlorinated cleaning compositions, petroleum distillates, dielectric fluids, and acid-sensitive polymers and copolymers (IARC 1994, HSDB 2009).

Production

Styrene oxide was listed by the U.S. Environmental Protection Agency as a high-production-volume chemical in 1990, indicating that annual production exceeded 1 million pounds (EPA 2006). In 2009, one U.S. manufacturer of styrene oxide was identified (HSDB 2009). Reports filed under EPA's Toxic Substances Control Act Inventory Update Rule indicated that U.S. production plus imports of styrene oxide totaled over 1 million to 10 million pounds in 1990 and 10,000 to 500,000 pounds in 1986, 1994, 1998, and 2002 (EPA 2004).

Exposure

The general population may be exposed to styrene oxide by contact with contaminated air or water; however, according to EPA's Toxics Release Inventory, annual environmental releases of styrene oxide from industrial facilities were less than 100 lb until 2006. In 2006 and 2007, larger quantities (246 lb and 380 lb, respectively) were sent to off-site hazardous-waste landfills (TRI 2009). No quantitative exposure data were found.

In a study in the United Kingdom, various plastics and resins were analyzed to determine whether styrene oxide could migrate to food. Styrene oxide was found in items that came into contact with food, including 9 base resins and 16 samples of polystyrene articles. Concentrations of styrene oxide in typical polystyrene materials were low, ranging from undetectable (< 0.5 mg/kg) to 3 mg/kg. Assuming that styrene oxide migrates in the same pattern as the styrene monomer, estimated concentrations in food resulting from migration ranged from 0.002 to 0.15 μg/kg (Philo *et al*. 1997).

Occupational exposure to styrene oxide occurs most often in the fabricated rubber products, paints, and allied products industry (HSDB 2009). Occupational exposure to styrene oxide is primarily indirect via exposure to styrene. Styrene oxide can form in air at low levels (< 1 mg/m^3, or < 203 ppb) when styrene reacts with oxygen or hydroperoxides (used to initiate the curing of reinforced plastics) (Yeowell-O'Connell *et al.* 1997). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 333,212 workers, including 86,902 women, potentially were exposed to styrene, and that 458 workers potentially were exposed to styrene oxide (NIOSH 1990).

In personal exposure air samples for 19 workers at a U.S. boat manufacturing company who were heavily exposed to styrene by inhalation (at a mean concentration of 64 mg/m^3), the average concentration of styrene oxide was 0.14 mg/m^3 (28.5 ppb) (IARC 1994). Nylander-French *et al*. (1999) studied levels of styrene oxide exposure and factors contributing to exposure in workers who manufactured reinforced plastics. From laboratory experiments, they hypothesized that styrene oxide formed by (1) breakdown of polymeric styrene peroxide radicals resulting from the copolymerization of styrene and oxygen, (2) epoxidation of the styrene monomer, or (3) reaction of styrene with volatile organic peroxides used in curing reinforced plastics. However, no measurements in manufacturing plants have confirmed these hypotheses. Among workers, styrene oxide exposure increased with increasing styrene exposure, but this correlation was statistically significant only among hand laminators, who were exposed to the highest levels of styrene and styrene oxide. Resin use also was an important factor in predicting styrene oxide exposure, regardless of the quantity of resin used. It was concluded that styrene oxide exposure was affected by factors other than styrene exposure.

Regulations

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Listed as a hazardous air pollutant.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ) = 100 lb.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Listed substance subject to reporting requirements.

References

Cantoreggi S, Lutz WK. 1993. Covalent binding of styrene to DNA in rat and mouse. *Carcinogenesis* 14(3): 355-360.

ChemIDplus. 2009. *ChemIDplus Advanced*. National Library of Medicine. http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp and select Registry Number and search on CAS number. Last accessed: 10/22/09.

EPA. 2004. *Non-confidential IUR Production Volume Information.* U.S. Environmental Protection Agency. http://www.epa.gov/oppt/iur/tools/data/2002-vol.html and search on CAS number.

EPA. 2006. *1990 HPV Challenge Program Chemical List.* U.S. Environmental Protection Agency. Revised 1/20/06. http://www.epa.gov/chemrtk/pubs/update/hpv_1990.pdf.

Fustinoni S, Colosio C, Colombi A, Lastrucci L, Yeowell-O'Connell K, Rappaport SM. 1998. Albumin and hemoglobin adducts as biomarkers of exposure to styrene in fiberglass-reinforced-plastics workers. *Int Arch Occup Environ Health* 71(1): 35-41.

HSDB. 2009. *Hazardous Substances Data Bank*. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB and search on CAS number. Last accessed: 10/22/09.

Huff JE. 1984. Styrene, styrene oxide, polystyrene, and beta-nitrostyrene/styrene carcinogenicity in rodents. *Prog Clin Biol Res* 141: 227-238.

IARC. 1976. Styrene oxide. In *Cadmium, Nickel, Some Epoxides, Miscellaneous Industrial Chemicals and General Considerations on Volatile Anaesthetics*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 11. Lyon, France: International Agency for Research on Cancer. pp. 201-208.

IARC. 1994. Styrene-7,8-oxide. In *Some Industrial Chemicals*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 60. Lyon, France: International Agency for Research on Cancer. pp. 321-346.

Lijinsky W. 1986. Rat and mouse forestomach tumors induced by chronic oral administration of styrene oxide. *J Natl Cancer Inst* 77(2): 471-476.

Lutz WK, Cantoreggi S, Velic I. 1993. DNA binding and stimulation of cell division in the carcinogenicity of styrene 7,8-oxide. In *Butadiene and Styrene: Assessment of Health Hazards,* IARC Scientific Publication No. 127. Sorsa M, Peltonen K, Vainio H, Hemminki K, eds. Lyon, France: International Agency for Research on Cancer. pp. 245-252.

McConnell EE, Swenberg JA. 1993. Styrene and styrene oxide: results of studies on carcinogenicity in experimental animals. *IARC Sci Publ* (127): 323-333.

NIOSH. 1990. *National Occupational Exposure Survey (1981-83).* National Institute for Occupational Safety and Health. Last updated 7/1/90. http://www.cdc.gov/noes/noes1/84819sic.html.

Nylander-French LA, Kupper LL, Rappaport SM. 1999. An investigation of factors contributing to styrene and styrene-7,8-oxide exposures in the reinforced-plastics industry. *Ann Occup Hyg* 43(2): 99-105.

Philo MR, Fordham PJ, Damant AP, Castle L. 1997. Measurement of styrene oxide in polystyrenes, estimation of migration to foods, and reaction kinetics and products in food simulants. *Food Chem Toxicol* 35(8): 821-826.

TRI. 2009. *TRI Explorer Chemical Report.* U.S. Environmental Protection Agency. http://www.epa.gov/triexplorer and select Styrene Oxide.

Yeowell-O'Connell K, Pauwels W, Severi M, Jin Z, Walker MR, Rappaport SM, Veulemans H. 1997. Comparison of styrene-7,8-oxide adducts formed via reaction with cysteine, N-terminal valine and carboxylic acid residues in human, mouse and rat hemoglobin. *Chem Biol Interact* 106(1): 67-85.