1,2-EPOXYBUTANE

Data were last evaluated in IARC (1989).

1. Exposure Data

1.1 Chemical and physical properties

1.1.1 *Nomenclature*

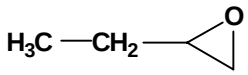
Chem. Abstr. Services Reg. No.: 106-88-7

Chem. Abstr. Name: Ethyloxirane

IUPAC Systematic Name: 1,2-Butylene oxide

Synonyms: 1-Butene oxide; 1,2-butene oxide; 1,2-butylene epoxide; α-butylene oxide; 1-butylene oxide; epoxybutane; ethyl ethylene oxide; 2-ethyloxirane

1.1.2 *Structural and molecular formula and relative molecular mass*



C_4H_8O Relative molecular mass: 72.12

1.1.3 *Chemical and physical properties of the pure substance*

(*a*) *Description*: Clear, colourless liquid with pungent odour (Dow Chemical Co., 1988)

(*b*) *Boiling-point*: 63.3°C (Lide, 1997)

(*c*) *Melting-point*: –60°C (Verschueren, 1996)

(*d*) *Solubility*: Soluble in water (82.4 mg/L at 25°C); miscible with diethyl ether; very soluble in acetone, ethanol and most organic solvents (Verschueren, 1996; Lide, 1997)

(*e*) *Density*: d_{20}^{20} 0.83

(*f*) *Vapour pressure*: 18.6 kPa at 20°C (Dow Chemical Co., 1988); relative vapour density (air = 1), 2.49 (Verschueren, 1996)

(*g*) *Flash-point*: –22°C (closed-cup) (Dow Chemical Co., 1988)

(*h*) *Reactivity*: Extremely inflammable; reacts with water and other sources of labile hydrogen, especially in the presence of acids, bases or other oxidizing substances. Reactive monomer which can polymerize exothermically. Undergoes atmospheric hydrolysis; atmospheric half-life for oxidation estimated to be

six days (Hine *et al*., 1981; Dow Chemical Co., 1988; United States National Toxicology Program, 1988)

(*i*) *Conversion factor*: $mg/m^3 = 2.95 \times ppm$

1.2 Production and use

It has been reported that 3600 tonnes of 1,2-epoxybutane were produced in the United States in 1978 (United States National Toxicology Program, 1988). Data on production elsewhere in the world were not available. Information available in 1995 indicated that it was produced in Germany, Japan and the United States (Chemical Information Services, 1995).

1,2-Epoxybutane is widely used as a stabilizer for chlorinated hydrocarbon solvents. It is also used as a chemical intermediate for the production of butylene glycols and their derivatives (polybutylene glycols, mixed poly glycols and glycol ethers and esters), butanolamines, surface-active agents and other products, such as gasoline additives (Hine *et al*., 1981; Parmeggiani, 1983; Lewis, 1993).

1.3 Occurrence

1.3.1 *Occupational exposure*

According to the 1981–83 National Occupational Exposure Survey (NOES, 1997), approximately 47 900 workers in the United States were potentially exposed to 1,2-epoxybutane (see General Remarks). Occupational exposures to 1,2-epoxybutane may occur in its production and use as a monomer and chemical intermediate and as a stabilizer in chlorinated solvents.

1.3.2 *Environmental occurrence*

No information on environmental occurrence of 1,2-epoxybutane was available to the Working Group.

1.4 Regulations and guidelines

The American Conference of Governmental Industrial Hygienists (ACGIH) (1997) has not proposed any occupational exposure limit for 1,2-epoxybutane in workplace air. However, manufacturers in the United States have recommended a voluntary standard of 40 ppm [118 mg/m^3] for an 8-h time-weighted average exposure limit (United States National Toxicology Program, 1988).

No international guideline for 1,2-epoxybutane in drinking-water has been established (WHO, 1993).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

1,2-Epoxybutane was tested for carcinogenicity by inhalation exposure in one study in mice and in one study in rats, producing nasal papillary adenomas in rats of both sexes and pulmonary alveolar/bronchiolar tumours in male rats. It did not induce skin tumours when tested by skin application in one study in mice. Oral administration of trichloroethylene containing 1,2-epoxybutane to mice induced squamous-cell carcinomas of the forestomach, whereas administration of trichloroethylene alone did not (IARC, 1989).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

No data were available to the Working Group.

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

1,2-Epoxybutane caused inflammatory and degenerative changes in the nasal mucosa and myeloid hyperplasia in the bone marrow in rats and mice (IARC, 1989).

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

1,2-Epoxybutane did not cause prenatal toxicity in rats or rabbits (IARC, 1989).

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems* (see Table 1 for references)

The genetic activity of 1,2-epoxybutane has been reviewed (Ehrenberg & Hussain, 1981). It is a direct-acting alkylating agent.

1,2-Epoxybutane has been shown to induce SOS repair activity in *Salmonella typhimurium* TA1525/pSK1002 and to produce differential killing zones in various *pol*- and *rec*-proficient and -deficient strains of *Escherichia coli*. It induced streptomycin-resistant

Table 1. Genetic and related effects of 1,2-epoxybutane

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
PRB, Prophage, induction/SOS response/strand-breaks/or cross-links, *Salmonella typhimurium* TA1525/pSK1002	+	NT	780	Nakamura *et al*. (1987)
ECL, *Escherichia coli pol A*, differential toxicity	+	NT	50	Rosenkranz & Poirier (1979)
ECL, *Escherichia coli pol A*, differential toxicity	+	NT	20000	McCarroll *et al*. (1981)
ERD, *Escherichia coli rec*, differential toxicity	+	NT	4300	McCarroll *et al*. (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	NT	2100	McCann *et al*. (1975)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	7	Speck & Rosenkranz (1976)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	2100	Henschler *et al*. (1977)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	2.5	De Flora (1979)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	NG	McMahon *et al*. (1979)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	250	Simmon (1979a)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	2000	De Flora (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	NG	De Flora *et al*. (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	–	167	Dunkel *et al*. (1984)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	1100	Gervasi *et al*. (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	500	Canter *et al*. (1986)
SA0, *Salmonella typhimurium* TA100, reverse mutation	–	NT	360	Rosman *et al*. (1987)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	500	US National Toxicology Program (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	NT	500	McGregor *et al*. (1989)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	+	NT	17000	Chen *et al*. (1975)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	NT	2100	McCann *et al*. (1975)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	42	Rosenkranz & Poirier (1979)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	250	Simmon (1979a)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	2000	De Flora (1981)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	1250	Weinstein *et al*. (1981)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	NG	De Flora *et al*. (1984)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	–	–	167	Dunkel *et al*. (1984)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	500	Canter *et al*. (1986)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	NT	90	Rosman *et al*. (1987)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	+	500	US National Toxicology Program (1988)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	NT	50	McGregor *et al*. (1989)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	250	Simmon (1979a)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	20000	De Flora (1981)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	167	Dunkel *et al*. (1984)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	5000	Canter *et al*. (1986)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	–	–	5000	US National Toxicology Program (1988)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	250	Simmon (1979b)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	167	Dunkel *et al*. (1984)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	5000	US National Toxicology Program (1988)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	–	–	20000	De Flora (1981)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	250	Simmon (1979a)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	20000	De Flora (1981)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	NT	2200	Gervasi *et al*. (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	–	–	5000	Canter *et al*. (1986)
SAS, *Salmonella typhimurium* TA100-FR1, reverse mutation	+	NT	3.5	Rosenkranz & Speck (1975)
SAS, *Salmonella typhimurium* TA1536, reverse mutation	–	–	250	Simmon (1979a)
ECW, *Escherichia coli* WP2 *uvrA*, reverse mutation	+	NT	NG	McMahon *et al*. (1979)
ECW, *Escherichia coli* WP2 *uvrA*, reverse mutation	–	–	167	Dunkel *et al*. (1984)
KPF, *Klebsiella pneumoniae*, forward mutation	(+)	+	72	Voogd *et al*. (1981)
KPF, *Klebsiella pneumoniae*, forward mutation	+	NT	72	Knaap *et al*. (1982)
SCH, *Saccharomyces cerevisiae* D3, homozygosis	+	+	5000	Simmon (1979b)
SZF, *Schizosaccharomyces pombe* P1, forward mutation	+	+	29	Migliore *et al*. (1982)
NCR, *Neurospora crassa*, reverse mutation	(+)	NT	14	Kolmark & Giles (1955)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	+		8400 inj × 1	Knaap *et al*. (1982)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	+		50000 ppm feed	US National Toxicology Program (1988)
DMH, *Drosophila melanogaster*, heritable translocations	+		50000 ppm feed	US National Toxicology Program (1988)
URP, Unscheduled DNA synthesis, rat primary hepatocytes *in vitro*	–	NT	1000	Williams *et al*. (1982)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	NT	63	Amacher *et al*. (1980)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	+	400	McGregor *et al*. (1987)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	+	55	Mitchell *et al*. (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	+	50	Myhr & Caspary (1988)
G5T, Gene mutation, mouse lymphoma L5178Y cells, *tk* locus *in vitro*	+	+	50	US National Toxicology Program (1988)
G51, Gene mutation, mouse lymphoma L5178Y cells, *hprt* locus *in vitro*	+	NT	360	Knaap *et al*. (1982)

Table 1 (contd)

Test system	Result[a]		Dose[b] (LED or HID)	Reference
	Without exogenous metabolic activation	With exogenous metabolic activation		
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	+	16	US National Toxicology Program (1988)
SIC, Sister chromatid exchange, Chinese hamster ovary CHO cells *in vitro*	+	+	16	Anderson *et al*. (1990)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	(+)	(+)	500	US National Toxicology Program (1988)
CIC, Chromosomal aberrations, Chinese hamster ovary CHO cells *in vitro*	(+)	(+)	500	Anderson *et al*. (1990)
TBM, Cell transformation, BALB/c 3T3 mouse cells	–	NT	50	Dunkel *et al*. (1981)
TCS, Cell transformation, Syrian hamster embryo cells, clonal assay	+	NT	NG	Pienta *et al*. (1981)
TFS, Cell transformation, Syrian hamster embryo cells, focus assay	(+)	NT	50	Dunkel *et al*. (1981)
TRR, Cell transformation, RLV/Fischer 344 rat embryo cells	+	NT	10	Price & Mishra (1980)
TRR, Cell transformation, RLV/Fischer 344 rat embryo cells	+	NT	700	Dunkel *et al*. (1981)

[a] +, positive; (+), weakly positive; –, negative; NT, not tested
[b] LED, lowest effective dose; HID, highest ineffective dose; in-vitro tests, μg/mL; in-vivo tests, mg/kg bw/day; NG, not given; inj, injection

mutants in *Klebsiella pneumoniae.* It was shown to be mutagenic to *E. coli* WP2 *uvr*A$^-$ in one of two studies. In *S. typhimurium*, it induced base–pair substitutions (strains TA100 and TA1535) but not frameshift mutations in the presence or absence of exogenous metabolic activation. 1,2-Epoxybutane induced forward mutation in *Schizosaccharomyces pombe* P1 and mitotic recombination in *Saccharomyces cerevisiae* D3. It was weakly mutagenic at the adenine locus in *Neurospora crassa*. It induced sex-linked recessive lethal mutations and translocations in *Drosophila melanogaster* after either feeding or injection.

It did not induce unscheduled DNA synthesis in rat primary hepatocytes but did induce mutation in L5178Y TK$^{+/-}$ mouse lymphoma cells in the absence or presence of an exogenous metabolic system. In one study, 1,2-epoxybutane gave marginally positive results for induction of 6-thioguanine-resistant mutations in L5178Y cells. It increased the frequency of sister chromatid exchanges and chromosomal aberrations in Chinese hamster ovary CHO cells with or without exogenous metabolic activation. It induced morphological transformation in Syrian hamster embryo cells and virally enhanced Fischer 344 rat embryo cells but not in BALB/c 3T3 cells.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Exposure to 1,2-epoxybutane may occur in its production and use as a monomer, chemical intermediate and stabilizer.

5.2 Human carcinogenicity data

No data were available to the Working Group.

5.3 Animal carcinogenicity data

1,2-Epoxybutane was tested for carcinogenicity by inhalation exposure in one study in mice and in one study in rats, producing nasal papillary adenomas in rats of both sexes and pulmonary alveolar/bronchiolar tumours in male rats. It did not induce skin tumours when tested by skin application in one study in mice.

5.4 Other relevant data

1,2-Epoxybutane induced morphological transformation, sister chromatid exchanges, chromosomal aberrations and mutation in cultured animal cells; however, in a single study, it did not induce unscheduled DNA synthesis in rat primary hepatocytes. It induced sex-linked recessive lethal mutations and translocations in *Drosophila melanogaster*, mitotic recombination in yeast, and mutations in yeast and fungi. 1,2-Epoxybutane induced DNA damage and mutations in bacteria.

5.5 Evaluation

No epidemiological data relevant to the carcinogenicity of 1,2-epoxybutane were available.

There is *limited evidence* in experimental animals for the carcinogenicity of 1,2-epoxybutane.

Overall evaluation

1,2-Epoxybutane is *possibly carcinogenic to humans (Group 2B)*.

In making the overall evaluation, the Working Group took into consideration that 1,2-epoxybutane is a direct-acting alkylating agent which is mutagenic in a range of test systems.

6. References

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