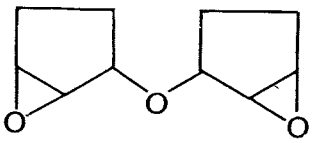
BIS(2,3-EPOXYCYCLOPENTYL)ETHER

1. Chemical and Physical Data

1.1 Synonyms

Chem. Abstr. Services Reg. No.: 2386-90-5
Chem. Abstr. Name: 2,2′-Oxybis(6-oxabicyclo[3.1.0]hexane)

1.2 Structural and molecular formulae and molecular weight



$C_{10}H_{14}O_3$

Mol. wt: 182.22

1.3 Chemical and physical properties of the pure substance

From Union Carbide Corp. (1985) unless otherwise noted

(*a*) *Description*: Homogeneous liquid at 43 °C and above; mixture of liquids and solids at lower temperatures

(*b*) *Boiling-point*: 203°C at 100 mm Hg

(*c*) *Freezing-point*: 29.7°C

(*d*) *Solubility*: Miscible with acetone (Holland *et al.*, 1979); < 0.3% by weight at 30 °C in water

(*e*) *Volatility*: Vapour pressure, 0.01 mg Hg at 20 °C; evaporation rate, 0.0017 (*n*-butyl acetate = 1.0)

(*f*) *Flash-point*: 138°C (open-cup)

(*g*) *Reactivity*: Reacts with amines, bases, acids and alcohols

(*h*) *Conversion factor*: mg/m³ = 7.45 × ppm[1]

1.4 Technical products and impurities

Trade names: ERL® 4205; W95

2. Production, Use, Occurrence and Analysis

2.1 Production and use

(*a*) *Production*

This compound was produced in the USA from the mid-1960s until 1985 but is not believed to have been produced commercially elsewhere. No data on production levels were available.

(*b*) *Uses*

Bis(2,3-epoxycyclopentyl)ether was developed as a high-performance component and modifier of epoxy resins (Hine *et al.*, 1981).

(*c*) *Regulatory status and guidelines*

No data were available to the Working Group.

2.2 Occurrence

Bis(2,3-epoxycyclopentyl)ether is not known to occur as a natural product. No data on its presence in the environment or on occupational exposure to this compound were available to the Working Group.

2.3 Analysis

The identity and purity of bis(2,3-epoxycyclopentyl)ether have been determined by infrared spectroscopy and nuclear magnetic resonance analysis (Holland *et al.*, 1979).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals

(*a*) *Skin application*

Mouse: A group of 30–40 C3H mice [number and sex unspecified], 13 weeks old, received applications of a 30% solution of bis(2,3-epoxycyclopentyl)ether [purity and dose un-

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[1]Calculated from: mg/m³ = (molecular weight/24.45) × ppm, assuming standard temperature (25°C) and pressure (760 mm Hg)

specified] in acetone three times a week for up to 21 months. Ten mice survived to month 17. No skin tumour occurred (Weil *et al.*, 1963). [The Working Group noted the incomplete reporting of the results and that no untreated control was included.]

Groups of 40 male and 40 female C3H and 20 male and 20 female C57Bl/6 mice, ten to 12 weeks of age, received applications of 50 µl (0, 15 or 75 mg per week for C3H mice and 0, 7.5 or 37.5 mg per week for C57Bl/6 mice) commercial-grade bis(2,3-epoxycyclopentyl)ether (no impurity detected by nuclear magnetic resonance analysis) on the shaved dorsal skin three times a week for 24 months. Survival of C3H mice at 24 months was 22, 25 and 22 for males and 23, 18 and 15 for females in the control, low- and high-dose groups. In the high-dose males, one skin papilloma and one skin carcinoma and in high-dose females, one skin papilloma and two skin carcinomas, were observed. No skin tumour occurred in the low-dose group of either sex, whereas a skin papilloma was found in a single control female. The incidences of lung tumours [type unspecified] were 2/22, 4/25 and 5/22 in males and 1/23, 3/18 and 9/15 in females of the control, low-dose and high-dose groups [$p = 0.02$ for positive trend in females]. Only grossly observed lung tumours were examined microscopically. Survival of C57Bl/6 mice at 24 months was 20, 16 and 13 in males and 15, 17 and 16 in females of the control, low- and high-dose groups. One papilloma and three carcinomas of the skin were seen in high-dose males, and one carcinoma was observed in a high-dose female. No skin tumour was seen in the control or low-dose groups (Holland *et al.*, 1979).

(*b*) *Combined exposure*

Mouse: Groups of 40 male and 40 female C3H mice and 20 male and 20 female C57Bl/6 mice, ten to 12 weeks of age, received 0, 15 or 75 mg per week of a mixture of equal parts of bis(2,3-epoxycyclopentyl)ether and bisphenol A diglycidyl ether (see monograph, p. 237) in acetone on the shaved back skin for 24 months. Survival of C3H mice at 24 months was 22, 20 and 23 for males and 23, 23 and 19 for females in the control, low- and high-dose groups. Skin tumours occurred in 14 low-dose males (four papillomas and ten carcinomas) and in 32 high-dose males (13 papillomas and 19 carcinomas), in five low-dose females (three papillomas and two carcinomas) and in 19 high-dose females (12 papillomas and seven carcinomas). One skin papilloma occurred among control females and no skin tumour was observed in control males. In C57Bl/6 mice, survival at 24 months was 20, 15 and four for males and 15, 14 and four for females in the respective dose groups. The difference between control and high-dose groups was statistically significant ($p < 0.05$). Skin tumours (mostly carcinomas) were observed in one low-dose (carcinoma) and 17 high-dose (carcinomas) males and in two low-dose (one papilloma, one carcinoma) and 15 high-dose (two papillomas, 13 carcinomas) females, but not in controls of either sex. When tested alone at the same dose levels, each substance revealed a much lower tumour response (see above and the monograph on bisphenol A diglycidyl ether, p. 245), indicating a synergistic effect of the compounds when tested as a mixture (Holland *et al.*, 1979).

3.2 Other relevant data

(*a*) *Experimental systems*

(i) *Absorption, distribution, excretion and metabolism*

No data were available to the Working Group.

(ii) *Toxic effects*

The single oral LD_{50} of bis(2,3-epoxycyclopentyl)ether in rats has been reported to be 2.14 ml/kg bw and the single dermal penetration LD_{50} for rabbits, >5.0 ml/kg bw. Bis(2,3-epoxycyclopentyl)ether has been reported to be only mildly irritant to rabbit skin and to produce moderate corneal injury in rabbits; it was reported not to induce sensitization reactions three weeks after eight intracutaneous injections of 0.1 ml diluted compound in guinea-pigs (Weil *et al.*, 1963).

Male and female C3H and C57Bl/6 mice received daily skin applications of 50 µl of a 50% solution of bis(2,3-epoxycyclopentyl)ether in acetone on shaved back skin on five days per week for two weeks. No mortality or sign of toxicity was observed in C3H mice; 5/9 C57Bl/6 mice died after four applications. Gross necropsy revealed pale, swollen liver and kidney (Holland *et al.*, 1979).

(iii) *Effects on reproduction and prenatal toxicity*

No data were available to the Working Group.

(iv) *Genetic and related effects*

Bis(2,3-epoxycyclopentyl)ether was mutagenic to *Salmonella typhimurium* TA98 [details not given] and TA100 in the presence and absence of an exogenous metabolic system. It also increased the frequency of sister chromatid exchange in human lymphocytes *in vitro* and induced micronuclei in mice *in vivo* (Xie & Dong, 1984).

(*b*) *Humans*

No data were available to the Working Group.

3.3 Epidemiological studies of carcinogenicity to humans

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Exposures

Bis(2,3-epoxycyclopentyl)ether is a synthetic organic liquid which has been used as a component and modifier of epoxy resins. Measurements of occupational exposure levels have not been reported.

4.2 Experimental carcinogenicity data

Bis(2,3-epoxycyclopentyl)ether was tested for carcinogenicity by skin application in one experiment in two strains of mice, producing a small number of skin tumours in both strains; an increased incidence of lung tumours was observed in females of one strain. Another experiment by skin application in mice was inadequate for evaluation.

4.3 Human carcinogenicity data

No data were available to the Working Group.

4.4 Other relevant data

Bis(2,3-epoxycyclopentyl)ether induced sister chromatid exchange in cultured human cells and micronuclei in mice. It was mutagenic to bacteria. (See Appendix 1.)

4.5 Evaluation[1]

There is *limited evidence* for the carcinogenicity of bis(2,3-epoxycyclopentyl)ether in experimental animals.

No data were available from studies in humans on the carcinogenicity of bis(2,3-epoxycyclopentyl)ether.

Overall evaluation

Bis(2,3-epoxycyclopentyl)ether *is not classifiable as to its carcinogenicity to humans (Group 3).*

5. References

Hine, C., Rowe, V.K., White, E.R., Darmer, K.I., Jr & Youngblood, G.T. (1981) Epoxy compounds. In: Clayton, G.D. & Clayton, F.E., eds, *Patty's Industrial Hygiene and Toxicology*, 3rd rev. ed., Vol. 2A, New York, John Wiley & Sons, pp. 240–241

Holland, J.M., Gosslee, D.G. & Williams, N.J. (1979) Epidermal carcinogenicity of bis(2,3-epoxycyclopentyl)ether, 2,2-bis(*p*-glycidyloxyphenyl)propane and *m*-phenylenediamine in male and female C3H and C57BL/6 mice. *Cancer Res., 39*, 1718–1725

Union Carbide Corp. (1985) *Material Safety Data Sheet: Bis(2,3-epoxycyclopentyl)ether*, Hahnville, LA

Weil, C.S., Condra, N., Haun, C. & Striegel, J.A. (1963) Experimental carcinogenicity and acute toxicity of representative epoxides. *Am. ind. Hyg. Assoc. J., 24*, 305–325

[1]For definitions of the italicized terms, see Preamble, pp. 27–30.

Xie, D. & Dong, S. (1984) Mutagenicity of bis(2,3–epoxycyclopentyl)ether (Chin.). *Acta acad. med. sin.*, *6*, 210–212