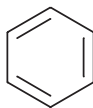


B47 benzene



C_6H_6

Mol. Wt. 78.11

CAS Registry No. 71-43-2

Synonyms benzol; benzole; coal naphtha; mineral naphtha; phenylhydride; pyrobenzol; pyrobenzole

EINECS No. 200-753-7

RTECS No. CY 1400000

Uses Solvent for fats, inks, oils, paints, plastics and rubber. Starting material in chemical manufacture of resins, plastics, nylon-66, polyamides and styrene. Used in the manufacture of detergents, explosives and pharmaceuticals (1).

Physical properties

M.Pt. 5.5°C B.Pt. 80.1°C Flash point -11°C Specific gravity 0.8786 at 20°C with respect to water at 4°C

Partition coefficient $\log P_{ow}$ 2.15 Volatility v.p. 76 mmHg at 20°C; v.den. 2.77

Solubility Water: 1780 mg l⁻¹ at 20°C. Organic solvents: miscible acetone, ethanol, diethyl ether

Occupational exposure

FR-VME 5 ppm (16 mg m⁻³)

JP-OEL 10 ppm (32 mg m⁻³)

SE-LEVL 0.5 ppm (1.5 mg m⁻³)

SE-STEL 3 ppm (9 mg m⁻³)

UK-LTEL MEL 5 ppm (16 mg m⁻³)

US-TWA 0.5 ppm (1.6 mg m⁻³)

US-STEL 2.5 ppm (8 mg m⁻³)

UN No. 1114 HAZCHEM Code 3WE Conveyance classification flammable liquid

Supply classification highly flammable, toxic

Risk phrases May cause cancer – Highly flammable – Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed (R45, R11, R48/23/24/25)

Safety phrases Restricted to professional users – Avoid exposure – obtain special instruction before use – In case of accident or if you feel unwell, seek medical advice immediately (show label where possible) (S53, S45)

Ecotoxicity

Fish toxicity

LC₅₀ (24-96 hr) fathead minnow, bluegill sunfish, goldfish 36-22 mg l⁻¹ (1).

LC₅₀ (96 hr) bass 6-11 ppm (1).

Invertebrate toxicity

LC₅₀ (96 hr) grass shrimp 20-27 ppm (1,2).

Cell multiplication inhibition test, *Pseudomonas putida* 92 mg l⁻¹, *Microcystis aeruginosa* >1400 mg l⁻¹, *Entosiphon sulcatum* >700 mg l⁻¹ (1).

LC₅₀ *Brachionus calyciflorus* and *Brachionus plicatilis* >1000 mg l⁻¹ (3).

EC₅₀ (8 day) *Selenastrum capricornutum* 41 mg l⁻¹ (4).

Bioaccumulation

Bioconcentration factor in pacific herring larvae, eel 3.5-3.9 (1).

Environmental fate

Nitrification inhibition

Not inhibited at 500 mg l⁻¹ (5).

Benzene inhibited ammonia oxidation, by ammonia monooxygenase, in *Nitrosomonas europaea* (concentration unspecified) (6).

Degradation studies

ThOD 3.07 g g⁻¹, COD 0.92 7 g⁻¹ (7).

BOD₁₀ 67% reduction of dissolved oxygen in acclimatised sludge (1).

Benzene is subject to rapid volatilisation in water and from soil surfaces, and is very mobile in soil.

Biodegradation may occur in shallow aerobic ground water, but not under anaerobic conditions (8).

Confirmed biodegradable (9).

Mammalian and avian toxicity

Acute data

LD₅₀ oral rat, mouse 3400, 4700 mg kg⁻¹ respectively (10,11).

Short-term acute exposure in humans may cause initial exhilaration, followed by dizziness, headache, nausea, drowsiness and pulmonary irritation. 7500 ppm and above for approximately 30 min may produce narcosis and death (12).

Sub-acute and sub-chronic data

Exposure of rats to 50 ppm benzene vapour for several wk, led to a reduction in red and white blood cells and platelets; exposure to concentrations <100 ppm produced leucopenia and aplasia (12).

♂ mice were fed 0-790 mg l⁻¹ in drinking water for 28 days. Stimulation of the hypothalamic-pituitary-adrenocortical axis and increased circulatory levels of corticosterone were observed at high dose levels (13).

Oral mouse (3 day) 660 mg kg⁻¹ once day⁻¹ in feed. Increase in the number of mature activated macrophages in the bone marrow, and enhanced production of hydrogen peroxide by bone marrow granulocytes and mononuclear phagocytes (14).

Carcinogenicity and chronic effects

Sufficient evidence for carcinogenicity to humans and animals, IARC classification group 1 (15). Chronic exposure to benzene, in humans, at concentrations that produce changes in the blood may result in leukaemia, especially acute myelogenous leukaemia (12).

There is clear evidence of carcinogenicity in mice and rats treated by gavage (103 wk) 100 and 200 mg l⁻¹.

Tumours have been reported in various tissues including adrenals, lung, liver, ovary, oral cavity, stomach and skin (16).

Benzene administered by gavage produced ovarian atrophy, cysts, hyperplasia and neoplasia in mice (17).

National Toxicology Program tested ♂ and ♀ rats and mice via gavage. Clear evidence of carcinogenicity in ♂ and ♀ rats and mice (18).

Rat Zymbal glands, nasal and oral cavities, mammary gland and bone marrow all have higher peroxidase activity than non-target tissue for benzene carcinogenicity. This ability to oxidise benzene to phenolic metabolites could explain the greater susceptibility of these tissues to benzene induced tumourigenesis (19).

Target organs of carcinogenicity: mouse and rat Zymbal's gland, mouse Harderian gland, mouse lung, mouse mammary gland, rat oral cavity, rat skin, rat stomach, and rat vascular system (20).

Teratogenicity and reproductive effects

Teratogenicity has been reported at high concentrations in rats, but there is no evidence of foetal malformations at concentrations which produce no maternal toxicity. Women are considered hypersusceptible to benzene, particularly during pregnancy and breast feeding, however there are no reports of teratogenic effects or any increase in spontaneous abortion in women occupationally exposed to benzene (17,21).

Benzene shows concentration-dependent embryotoxicity in rats. Lowest embryotoxic concentration is 1.5 μ mol ml⁻¹ (22).

Metabolism and toxicokinetics

Benzene is partly eliminated unchanged in the breath and urine of humans. Oxidation occurs producing benzene epoxide, phenols and diphenols, including catechol, hydroquinone, benzoquinone and 1,2,4-benzenetriol, which are in turn conjugated in the liver and excreted in the urine (12,23).

Toxic amounts of benzene can readily be absorbed through the skin (12).

Cytochrome P450 (CYP) 2E1 activity in human liver microsomes metabolizes benzene to hydroquinone and catechol (24).

EC₅₀ mitochondrial respiration 525 ppm (species unspecified) (25).

Cynomolgus monkeys were given 5, 50 or 500 mg of radiolabelled benzene intraperitoneally. Urine was collected for up to 24 h. The proportion of excreted radiolabel decreased from 50 to 15% with increasing dose. The proportion of hydroquinone derivatives and muconic acid in the urine also decreased with increasing dose. Catechol conjugates were not detected (26).

The *in vitro* penetration of ¹⁴C-benzene was studied using freshly prepared human skin. The permeability coefficient under standard conditions (26°C) was 0.14 cm hr⁻¹. This increased to 0.26 cm hr⁻¹ at 50°C. Application of baby oil, moisturizer or insect repellent had no effect, however pretreatment with sunscreen caused an increase to 0.24 cm hr⁻¹ (27).

Benzene oxide has been shown to be a product of hepatic benzene metabolism in man, rats, and mice *in vitro*. After 18 minutes of incubation of mouse liver microsomes with 1 mM benzene, 7% of the total benzene metabolites were benzene oxide (28).

Irritancy

Dermal rabbit (24 hr) 15 mg caused mild irritation, and 2 mg instilled into rabbit eye caused severe irritation (29,30).

Genotoxicity

Salmonella typhimurium TA97, TA98, TA100, TA1535, TA1537 with and without metabolic activation negative (16,31).

Salmonella typhimurium TA102 with metabolic activation negative (32).

Escherichia coli K-12 *uvrB/recA* DNA repair host-mediated assay with and without metabolic activation negative (33).

In vitro human lymphoblastoid MCL-5 cells induced micronucleus formation (34).

In vitro rat bone marrow cells, induced micronucleated polychromatic erythrocytes and sister-chromatid exchange (35).

In vitro rat spleen lymphocytes, induced micronucleated polychromatic erythrocytes and sister-chromatid exchange (35).

In vivo rodent bone marrow autogenetic test positive induction of micronuclei and chromosomal aberrations (31). Chromosomal aberrations in white blood cells and bone marrow in humans which could initiate leukaemia have been reported, but there is no evidence of aberrations at exposure levels of 25 ppm or less (12).

Inhalation ♂ mice 1 ppm induced chromosomal aberrations in spermatocytes and sister chromatid exchange in spermatogonia (36,37).

Other effects

Other adverse effects (human)

Thirteen published population-based and hospital-based case-control studies of multiple myeloma up to 1995 were examined for any relationship between this cancer and exposure to benzene or to surrogates for benzene exposure. No increased association was found between multiple myeloma and benzene or groups of chemicals that included benzene. Exposure to petroleum products, employment in petroleum-related occupations and cigarette smoking were not risk factors for multiple myeloma. However, there was a significant association with exposure to combustion products in engine exhaust (38).

Haematological and immunochemical investigation of 270 workers with chronic exposure to benzene evidenced changes to lymphocyte nuclei and disorders of the humoral immune response (39).

A cohort of 74,828 benzene-exposed and 35,805 non-exposed workers employed during 1972-1987 in 12 cities in China was studied to determine mortality from all causes. Demographic and occupational data were examined. Mortality was slightly increased in workers with greater cumulative exposure to benzene, the excess being largely due to cancer deaths. Mortality from lymphatic and haematopoietic malignancies, lung cancer and occupational injuries increased in direct relation to cumulative benzene exposure. Suggestive associations were also noted for nasopharyngeal and oesophageal cancer (40).

Other comments

Originally produced by coal carbonisation, but now largely derived from petroleum or by cyclisation and aromatisation of paraffinic hydrocarbons. LC₅₀ (48 hr) Mexican axolotl (3-4 wk after hatching) 370 mg l⁻¹ (41). Benzene exposure, experimental toxicology, epidemiology studies, human health and environmental effects have been extensively reviewed (42-67).

Epidemiological evidence on benzene and lymphatic and haematopoietic cancers reviewed (68).

World Health Organisation guidelines on drinking water, provisional limit 10 µg l⁻¹.

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