Overview of Firefighter

"Occupational Brain Cancer"

Treating Physicians Packet

This packet is designed to guide a treating physician in making an educated diagnosis of a Firefighters Cancer. The following studies and documents support the claim that the cancer can be tied to the occupation of firefighting.

Included are multiple studies and conclusions, along with NIOSH, International Agency on the Research of Cancer (IARC) and Chapter 607 of the Texas Government Code, which states the requirements of attaining a cancer presumption.

1. IARC 100F, pages 258-262 documents "FORMALDEHYDE" as an apparent cause of BRAIN cancer (Page 262).
2. IARC 100F page 332- Rubber manufacturing (burning tires)
3. Supplement 7, page 211 documents "Formaldehyde" as a known cause of Brain Cancer
4. IARC 98, PAGE 185, 455, 456, 457, 499, 498, 500, 501, 502, 512, 513, 521, states "BRAIN cancer as a significant ECCESS"
5. IARC 98, Composition of Fire smoke lists "Formaldehyde" as a known composition of smoke from fire, during overhaul as well as being present in vehicle exhaust. Firefighters spend much time standing and working near exhaust of running apparatus.

GOVERNMENT CODE

TITLE 6. PUBLIC OFFICERS AND EMPLOYEES

SUBTITLE A. PROVISIONS GENERALLY APPLICABLE TO PUBLIC OFFICERS AND EMPLOYEES

CHAPTER 607. BENEFITS RELATING TO CERTAIN DISEASES AND ILLNESSES

SUBCHAPTER A. CONTAGIOUS DISEASES

Sec. 607.001. DEFINITION. In this chapter, "public safety employee" means a peace officer, fire fighter, detention officer, county jailer, or emergency medical services employee of this state or a political subdivision of this state.

Added by Acts 1993, 73rd Leg., ch. 268, Sec. 1, eff. Sept. 1, 1993.
Amended by:

Acts 2005, 79th Leg., Ch. 986 (H.B. 1928), Sec. 1, eff. September 1, 2005.

Sec. 607.002. REIMBURSEMENT. A public safety employee who is exposed to a contagious disease is entitled to reimbursement from the employing governmental entity for reasonable medical expenses incurred in treatment for the prevention of the disease if:

(1) the disease is not an "ordinary disease of life" as that term is used in the context of a workers' compensation claim;

(2) the exposure to the disease occurs during the course of the employment; and

(3) the employee requires preventative medical treatment because of exposure to the disease.

Added by Acts 1993, 73rd Leg., ch. 268, Sec. 1, eff. Sept. 1, 1993.

Sec. 607.003. PHYSICIAN OF CHOICE. A public safety employee who is exposed to a disease described by Section 607.002 is entitled to be treated for the prevention of that disease by the physician of the employee's choice.

Added by Acts 1993, 73rd Leg., ch. 268, Sec. 1, eff. Sept. 1, 1993.

Sec. 607.004. PREVENTATIVE IMMUNIZATIONS AND VACCINATIONS. (a) A certified fire fighter or other governmental employee who operates an ambulance or who responds to emergency medical calls is entitled to preventative immunization for any disease to which the fire fighter or other governmental employee may be exposed in performing official duties and for which immunization is possible.

(b) The employee and any member of the employee's immediate family are entitled to vaccination for a contagious disease to which the employee is exposed during the course of employment.

(c) The employing governmental entity may satisfy the requirements of this section by:

(1) providing the immunization or vaccination without charge; or

(2) reimbursing the employee for any necessary and reasonable expenses incurred by the employee for the immunization or vaccination.

Added by Acts 1993, 73rd Leg., ch. 268, Sec. 1, eff. Sept. 1, 1993.

SUBCHAPTER B. DISEASES OR ILLNESSES SUFFERED BY FIREFIGHTERS AND EMERGENCY MEDICAL TECHNICIANS

Sec. 607.051. DEFINITIONS. In this subchapter:

(1) "Disability" means partial or total disability.

(2) "Emergency medical technician" means an individual who is certified as an emergency medical technician by the Department of State Health Services as provided by Chapter 773, Health and Safety Code, and who is employed by a political subdivision.

(3) "Firefighter" means:

(A) an individual who is defined as fire protection personnel under Section 419.021; or

(B) an individual who is a volunteer firefighter certified by the Texas Commission on Fire Protection or the State Firemen's and Fire Marshals' Association of Texas.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.052. APPLICABILITY. (a) Notwithstanding any other law, this subchapter applies only to a firefighter or emergency medical technician who:

(1) on becoming employed or during employment as a firefighter or emergency medical technician, received a physical examination that failed to reveal evidence of the illness or disease for which benefits or compensation are sought using a presumption established by this subchapter;

(2) is employed for five or more years as a firefighter or emergency medical technician; and

(3) seeks benefits or compensation for a disease or illness covered by this subchapter that is discovered during employment as a firefighter or emergency medical technician.

(b) A presumption under this subchapter does not apply:

(1) to a determination of a survivor's eligibility for benefits under Chapter 615;

(2) in a cause of action brought in a state or federal court except for judicial review of a proceeding in which there has been a grant or denial of employment-related benefits or compensation;

(3) to a determination regarding benefits or compensation under a life or disability insurance policy purchased by or on behalf of the firefighter or emergency medical technician that provides coverage in addition to any benefits or compensation required by law; or

(4) if the disease or illness for which benefits or compensation is sought is known to be caused by the use of tobacco and:

(A) the firefighter or emergency medical technician is or has been a user of tobacco; or

(B) the firefighter's or emergency medical technician's spouse has, during the marriage, been a user of tobacco that is consumed through smoking.

(c) This subchapter does not create a cause of action.

(d) This subchapter does not enlarge or establish a right to any benefit or compensation or eligibility for any benefit or compensation.

(e) A firefighter or emergency medical technician who uses a presumption established under this subchapter is entitled only to the benefits or compensation to which the firefighter or emergency medical technician would otherwise be entitled to receive at the time the claim for benefits or compensation is filed.

(f) For purposes of this subchapter, an individual described by Section 607.051(3)(B) is considered to have been employed or compensated while the individual actively served as a volunteer firefighter. An individual who actively serves as a volunteer firefighter is one who participates in a minimum of 40 percent of the drills conducted by the individual's department and 25 percent of the fire or other emergency calls received by the department during the time that the volunteer firefighter is on call.

(g) This subchapter applies to a firefighter or emergency medical technician who provides services as an employee of an entity created by an interlocal agreement.

(h) Subsection (b)(4) only prevents the application of the presumption authorized by this subchapter and does not affect the right of a firefighter or emergency medical technician to provide proof, without the use of that presumption, that an injury or illness occurred during the course and scope of employment.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.053. IMMUNIZATION; SMALLPOX. (a) A firefighter or emergency medical technician is presumed to have suffered a disability or death during the course and scope of employment if the firefighter or emergency medical technician:

(1) received preventative immunization against smallpox, or another disease to which the firefighter or emergency medical technician may be exposed during the course and scope of employment and for which immunization is possible; and

(2) suffered death or total or partial disability as a result of the immunization.

(b) An immunization described by this section is considered preventative whether the immunization occurs before or after exposure to the disease for which the immunization is prescribed.

(c) A presumption established under Subsection (a) may not be rebutted by evidence that the immunization was:

(1) not required by the employer;

(2) not required by law; or

(3) received voluntarily or with the consent of the firefighter or emergency medical technician.

(d) A firefighter or emergency medical technician who suffers from smallpox that results in death or total or partial disability is presumed to have contracted the disease during the course and scope of employment as a firefighter or emergency medical technician.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.054. TUBERCULOSIS OR OTHER RESPIRATORY ILLNESS. A firefighter or emergency medical technician who suffers from tuberculosis, or any other disease or illness of the lungs or respiratory tract that has a statistically positive correlation with service as a firefighter or emergency medical technician, that results in death or total or partial disability is presumed to have contracted the disease or illness during the course and scope of employment as a firefighter or emergency medical technician.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.055. CANCER. (a) A firefighter or emergency medical technician who suffers from cancer resulting in death or total or partial disability is presumed to have developed the cancer during the course and scope of employment as a firefighter or emergency medical technician if:

(1) the firefighter or emergency medical technician:

(A) regularly responded on the scene to calls involving fires or fire fighting; or

(B) regularly responded to an event involving the documented release of radiation or a known or suspected carcinogen while the person was employed as a firefighter or emergency medical technician; and

(2) the cancer is known to be associated with fire fighting or exposure to heat, smoke, radiation, or a known or suspected carcinogen, as described by Subsection (b).

(b) This section applies only to a type of cancer that may be caused by exposure to heat, smoke, radiation, or a known or suspected carcinogen as determined by the International Agency for Research on Cancer.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.056. ACUTE MYOCARDIAL INFARCTION OR STROKE. (a) A firefighter or emergency medical technician who suffers an acute myocardial infarction or stroke resulting in disability or death is presumed to have suffered the disability or death during the course and scope of employment as a firefighter or emergency medical technician if:

(1) while on duty, the firefighter or emergency medical technician:

(A) was engaged in a situation that involved nonroutine stressful or strenuous physical activity involving fire suppression, rescue, hazardous material response, emergency medical services, or other emergency response activity; or

(B) participated in a training exercise that involved nonroutine stressful or strenuous physical activity; and

(2) the acute myocardial infarction or stroke occurred while the firefighter or emergency medical technician was engaging in the activity described under Subdivision (1).

(b) For purposes of this section, "nonroutine stressful or strenuous physical activity" does not include clerical, administrative, or nonmanual activities.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.057. EFFECT OF PRESUMPTION. Except as provided by Section 607.052(b), a presumption established under this subchapter applies to a determination of whether a firefighter's or emergency medical technician's disability or death resulted from a disease or

illness contracted in the course and scope of employment for purposes of benefits or compensation provided under another employee benefit, law, or plan, including a pension plan.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

Sec. 607.058. PRESUMPTION REBUTTABLE. (a) A presumption under Section 607.053, 607.054, 607.055, or 607.056 may be rebutted through a showing by a preponderance of the evidence that a risk factor, accident, hazard, or other cause not associated with the individual's service as a firefighter or emergency medical technician caused the individual's disease or illness.

(b) A rebuttal offered under this section must include a statement by the person offering the rebuttal that describes, in detail, the evidence that the person reviewed before making the determination that a cause not associated with the individual's service as a firefighter or emergency medical technician caused the individual's disease or illness.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.
Amended by:

Acts 2015, 84th Leg., R.S., Ch. 224 (H.B. 1388), Sec. 1, eff. May 29, 2015.

Sec. 607.059. PROHIBITED PAYMENT. No payment shall be made to the subsequent injury fund under Section 403.007, Labor Code, for any death resulting from a disease or illness presumed to have been contracted in the course and scope of employment under this subchapter.

Added by Acts 2005, 79th Leg., Ch. 695 (S.B. 310), Sec. 3, eff. September 1, 2005.

SUBCHAPTER C. OTHER DISEASES OR ILLNESSES SUFFERED BY FIREFIGHTERS AND EMERGENCY MEDICAL TECHNICIANS

Sec. 607.101. DEFINITIONS. In this subchapter:

(1) "Emergency medical technician" means an individual who is certified as an emergency medical technician by the Department of State Health Services as provided by Chapter 773, Health and Safety Code, and who is a full-time employee of a political subdivision.

(2) "Firefighter" means an individual who is defined as fire protection personnel under Section 419.021 and is a full-time employee of a political subdivision.

Added by Acts 2009, 81st Leg., R.S., Ch. 1049 (H.B. 4560), Sec. 1, eff. September 1, 2009.

Sec. 607.102. NOTIFICATION. An emergency response employee or volunteer, as defined by Section 81.003, Health and Safety Code, who is exposed to methicillin-resistant Staphylococcus aureus or a disease caused by a select agent or toxin identified or listed under 42 C.F.R. Section 73.3 is entitled to receive notification of the exposure in the manner prescribed by Section 81.048, Health and Safety Code.

Added by Acts 2009, 81st Leg., R.S., Ch. 1049 (H.B. 4560), Sec. 1, eff. September 1, 2009.
Amended by:

Acts 2015, 84th Leg., R.S., Ch. 1278 (S.B. 1574), Sec. 2, eff. September 1, 2015.

H.B. No. 1388

AN ACT

relating to certain diseases or illnesses suffered by firefighters and emergency medical technicians.

BE IT ENACTED BY THE LEGISLATURE OF THE STATE OF TEXAS:

SECTION 1. Section 607.058, Government Code, is amended to read as follows:

Sec. 607.058. PRESUMPTION REBUTTABLE. (a) A presumption under Section 607.053, 607.054, 607.055, or 607.056 may be rebutted through a showing by a preponderance of the evidence that a risk factor, accident, hazard, or other cause not associated with the individual's service as a firefighter or emergency medical technician caused the individual's disease or illness.

(b) A rebuttal offered under this section must include a statement by the person offering the rebuttal that describes, in detail, the evidence that the person reviewed before making the determination that a cause not associated with the individual's service as a firefighter or emergency medical technician caused the individual's disease or illness.

SECTION 2. Section 409.022, Labor Code, is amended by adding Subsection (d) to read as follows:

(d) In this subsection, the terms "emergency medical technician" and "firefighter" have the meanings assigned by Section 607.051, Government Code. In addition to the other requirements of this section, if an insurance carrier's notice of refusal to pay benefits under Section 409.021 is sent in response to a claim for compensation resulting from an emergency medical technician's or a firefighter's disability or death for which a presumption is claimed to be applicable under Subchapter B, Chapter 607, Government Code, the notice must include a statement by the carrier that:

(1) explains why the carrier determined a presumption under that subchapter does not apply to the claim for compensation; and

(2) describes the evidence that the carrier reviewed in making the determination described by Subdivision (1).

SECTION 3. The changes in law made by this Act apply to a claim for benefits or compensation brought on or after the effective date of this Act. A claim for benefits or compensation brought before that date is covered by the law in effect on the date the claim was made, and that law is continued in effect for that purpose.

SECTION 4. This Act takes effect immediately if it receives a vote of two-thirds of all the members elected to each house, as provided by Section 39, Article III, Texas Constitution. If this Act does not receive the vote necessary for immediate effect, this Act takes effect September 1, 2015.

President of the Senate

Speaker of the House

I certify that H.B. No. 1388 was passed by the House on April 28, 2015, by the following vote: Yeas 143, Nays 3, 1 present, not voting.

BRAIN CANCER/TUMOURS

IARC MONOGRAPH'S

IARC SUPPLEMENT 7

PAGE 79, 206, 211, 213, 230, 332, 346 AND 373 WITH WIKIPEDIA ATTACHED

IARC 45

PAGE 83, 92, 96, 98 AND 108

IARC 98

PAGE 185, 399, 400, 455, 456, 457, 498, 499, 500, 501, 502, 512, 513 AND 521

IARC 100F

PAGES 401, 409, 411, 503 AND 509

IARC CHEMICAL LISTS OF SMOKE, SOOT AND EXHAUST

IARC

SUPPLEMENT 7

urinary bladder and the adrenal glands; however, because of the lack of matched controls, it could not be concluded whether tumour induction was due to a combined effect of the three chemicals or of any one of them[4].

C. Other relevant data

Neither chromosomal aberrations (in two patients) nor sister chromatid exchanges (in three patients) were induced following administration of 5-fluorouracil[5].

5-Fluorouracil induced micronuclei but not specific locus mutations in mice treated *in vivo*. It induced aneuploidy, chromosomal aberrations and sister chromatid exchanges in cultured Chinese hamster cells. It did not induce sex-linked recessive lethal mutations in *Drosophila*, but caused genetic crossing-over in fungi. Studies on mutation in bacteria were inconclusive[5].

References

[1]*IARC Monographs, 26*, 217-235, 1981

[2]Boice, J.D., Greene, M.H., Keehn, R.J., Higgins, G.A. & Fraumeni, J.F., Jr (1980) Late effects of low-dose adjuvant chemotherapy in colorectal cancer. *J. natl Cancer Inst., 64*, 501-511

[3]Ferguson, T. (1980) Prevention and delay of spontaneous mammary and pituitary tumors by long- and short-term ingestion of 5-fluorouracil in Wistar-Furth rats. *Oncology, 37*, 353-356

[4]Habs, M., Schmähl, D. & Lin, P.Z. (1981) Carcinogenic activity in rats of combined treatment with cyclophosphamide, methotrexate and 5-fluorouracil. *Int. J. Cancer, 28*, 91-96

[5]*IARC Monographs, Suppl. 6*, 316-318, 1987

FORMALDEHYDE (Group 2A)

A. Evidence for carcinogenicity to humans (*limited*)

A number of epidemiological studies using different designs have been completed on persons in a variety of occupations with potential exposure to formaldehyde[1-24]. Cancers that occurred in excess in more than one study are: Hodgkin's disease, leukaemia, and cancers of the buccal cavity and pharynx (particularly nasopharynx), lung, nose, prostate, bladder, brain, colon, skin and kidney[1]. The studies reported are not entirely independent; the plant studied by Liebling *et al.*[2] and Marsh[1,3] is also included in the study by Blair *et al.*[4]; the case-control study of Fayerweather *et al.*[5] includes some subjects who were later studied by Blair *et al.*[4]. Detailed estimates of formaldehyde exposure levels were made in the studies of British chemical workers[6], US formaldehyde producers and users[4], Finnish wood workers[7] and US chemical workers[5], and for the case-control studies of Vaughan *et al.*[8,9] and Hayes *et al.*[10].

In the study of US producers and users of formaldehyde, 11% of the subjects were not exposed, 12% had an estimated time-weighted average (TWA) exposure of <0.1 ppm (<0.12 mg/m^3), 34% a TWA of 0.1-<0.5 ppm (0.12-<0.6 mg/m^3), 40% a TWA of 0.5-<2 ppm

Slight excesses in the occurrence of lung cancer have been noted in several studies[2,4,7,12,18,19]. These excesses have shown no consistent pattern with increasing level or duration of exposure to formaldehyde. A statistically significant excess (SMR, 132) was reported among wage workers 20 or more years after first exposure. The risk of lung cancer did not increase among this, or any other group, with either level or duration of exposure[4]. In the UK, the risk of lung cancer rose with level of exposure in one factory from an SMR of 58 among those with low exposure to an SMR of 118 among those with high exposure[6]. No such pattern was seen, however, for the other factories[6], nor was risk associated with cumulative exposure[20]. In a case-control study of respiratory cancer among Finnish plywood and particle-board workers, an odds ratio of 1.6 (adjusted for smoking) was found after ten years of latency. RRs, however, decreased with level and duration of exposure to formaldehyde[7]. In a cohort mortality study of 1332 workers in a formaldehyde-resin plant in Italy, there was an overall excess of lung cancer (SMR, 186). The excess occurred among those not exposed to formaldehyde (SMR, 148) as well as among those exposed (SMR, 136), with the greatest excess among those with uncertain exposure (SMR, 358). Lung cancer mortality was not clearly associated with duration of exposure[19].

Studies of professional groups have shown rather consistent deficits of lung cancer. None of these studies, however, included information on smoking, and the lower prevalence of tobacco use in these groups would probably lead to such deficits. No excess occurrence of lung cancer was noted among Danish physicians[21] or among persons exposed to formaldehyde at a US chemical production facility[22].

Mortality from leukaemia and/or cancer of the brain has been found consistently to be elevated in studies of professional groups[1,12,13,16,23,24]. Except for a very slight excess of leukaemia reported in one study[5] (which was not statistically significant), excesses of these tumours have not been found among industrial workers exposed to formaldehyde. Among professionals, gliomas were the predominant cell type of brain cancer, and the leukaemias were predominantly of the myeloid type. The absence of excesses for these cancers among industrial workers, however, argues against a role of formaldehyde.

Mortality from prostatic cancer has been found to be elevated among professionals[13] and among industrial workers[4,5], but the excess was statistically significant only among embalmers[13]. This tumour has shown a dose-response gradient in both studies of industrial workers, although the test for trend in the study of Blair[4] was not statistically significant.

Slight excesses of mortality from bladder cancer have been reported among professionals[13,23] and among industrial workers[5]. No such excess occurred, however, in the other large industrial cohorts, and none of the excesses was statistically significant. Significant excesses of colon cancer were noted among professionals[12,13] and among industrial workers[2]; nonsignificant elevations have also been reported[11,16]. A significant excess mortality from cancer of the skin was reported among New York embalmers (proportionate mortality ratio, 221)[12], and a slight excess was noted among industrial workers (based on two deaths)[11]. Excesses of Hodgkin's disease were seen among white industrial workers in

LEAD AND LEAD COMPOUNDS:
LEAD AND INORGANIC LEAD COMPOUNDS (Group 2B)
ORGANOLEAD COMPOUNDS (Group 3)

A. Evidence for carcinogenicity to humans (*inadequate*)

Three epidemiological studies of workers exposed to lead and lead compounds were reviewed previously[1]: one on smelters and battery workers in the USA, one on workers exposed to tetraethyllead in the USA, and one on copper smelters in the USA; data on the first of these populations have been updated[2]. A study on battery workers in the UK[3] is now available, and studies of a US lead smelter[4] and of a Swedish copper smelter[5] have also been reported. A statistically significant excess of cancers of the digestive system (21 observed, 12.6 expected) was found in the study of battery workers in the UK, spanning 1925-1976, although the excess was confined to the years 1963-1966[3]. Significant excesses of stomach cancer (34 observed, 20.2 expected) and of respiratory cancers (116 observed, 93.5 expected) were seen in the study of US battery plant workers[2], although there was a downward trend in standardized mortality ratio by number of years of employment; in the lead production facilities, the excesses noted for stomach and respiratory cancers were not significant[2]. A nonsignificant excess of respiratory cancer (41 observed, 36.9 expected) was reported in one of the studies of smelters[4], with 28 observed and 25.7 expected in the group with high exposure to lead. Excesses were also noted in this study for kidney cancer (6 observed, 2.9 expected) and bladder cancer (6 observed, 4.2 expected)[4]. A small study of workers at a Swedish smelter[5] with long-term exposure to lead demonstrated a nonsignificant excess of lung cancers (8 observed, 5 expected). Two cases of kidney cancer in lead smelter workers have also been reported[6,7].

The excesses of respiratory cancer in these studies were relatively small, showed no clear-cut trend with length or degree of exposure, and could have been confounded by factors such as smoking or exposure to arsenic (see p. 100).

[A study of workers manufacturing tetraethyllead revealed excesses of respiratory cancer (15 observed, 11.2 expected) and brain cancer (3 observed, 1.6 expected)[8].]

B. Evidence for carcinogenicity to animals (*sufficient* for inorganic lead compounds; *inadequate* for organolead compounds)

Lead acetate and lead subacetate were tested for carcinogenicity by oral, subcutaneous and intraperitoneal administration in rats, lead phosphate was tested by subcutaneous and intraperitoneal administration in rats, and lead subacetate was tested by oral administration in mice. Renal tumours were produced in animals of each species by each route of administration. Rats given lead acetate or lead subacetate orally developed gliomas. Lead subacetate also produced an increased incidence of lung adenomas in mice after its intraperitoneal administration[1]. Oral administration of lead dimethyldithiocarbamate (ledate) increased the incidence of reticulum-cell sarcomas in male mice of one strain[9] but was not carcinogenic to mice or rats in another experiment[10].

[8]Ross, R.K., Paganini-Hill, A., Krailo, M.D., Gerkins, V.R., Henderson, B.E. & Pike, M.C. (1984) Effects of reserpine on prolactin levels and incidence of breast cancer in postmenopausal women. *Cancer Res., 44*, 3106-3108

[9]Muradyan, R.Y. (1986) A study of possible carcinogenicity of reserpine (Russ.). *Vopr. Onkol., 32*, 76-81

[10]Gerard, S.S., Gardner, B., Patti, J., Husain, V., Shouten, J. & Alfonso, A.E. (1980) Effects of triiodothyronine and reserpine on induction and growth of mammary tumors in rats by 3-methylcholanthrene. *J. surg. Oncol., 14*, 213-218

[11]Verdeal, K., Ertürk, E. & Rose, D.P. (1983) Effects of reserpine administration on rat mammary tumors and uterine disease induced by *N*-nitrosomethylurea. *Eur. J. Cancer clin. Oncol., 19*, 825-834

[12]Lupulescu, A. (1983) Reserpine and carcinogenesis: inhibition of carcinoma formation in mice. *J. natl Cancer Inst., 71*, 1077-1083

[13]*IARC Monographs, Suppl. 6*, 485-487, 1987

THE RUBBER INDUSTRY (Group 1)

A. Evidence for carcinogenicity to humans (*sufficient*)

A large number of studies have been conducted on rubber industries in Canada, China, Finland, Norway, Sweden, Switzerland, the UK and the USA[1-19]. Workers employed in the industry before 1950 have a high risk of bladder cancer, probably associated with exposure to aromatic amines. Leukaemias have been associated with exposure to solvents and with employment in back processing, tyre curing, synthetic rubber production and vulcanization. Excess occurrence of lymphomas has been noted among workers exposed to solvents in such departments as footwear and in tyre plants[20]. Other cancers, including those of the lung, renal tract, stomach, pancreas, oesophagus, liver, skin, colon, larynx and brain, have been reported as occurring in excess in workers in various product areas and departments, but no consistent excess of any of these cancers is seen across the various studies.

B. Evidence for carcinogenicity to animals (*inadequate*)

In one inadequately reported experiment, three groups of rats were kept either in the compounding room or in the mixing or mastication area of a Banbury mill at a tyre factory. Increased incidences of respiratory and digestive carcinomas were found in rats maintained for two years at the latter two locations when compared with control rats maintained in the institute laboratory[17].

C. Other relevant data

No increase in the incidence of chromosomal aberrations was observed among 55 rubber workers as compared to 35 control subjects, with the exception of a small group of

Smoking habits were not controlled for, but a low mortality from respiratory and cardiovascular diseases suggests that smoking rates were not excessively high[4].

Two cohort studies showed no excess of lymphoma or leukaemia, or of any other cancer. Both studies had low statistical power because the cohorts had a young age structure and there had been short follow-up since the commencement of exposure; they will provide useful information only when updated[5,6].

Two other studies are uninformative because of diluting errors in design and analysis[7,8]. There is an anecdotal report of three deaths from leukaemia and two from lymphoma among a group of workers exposed to styrene, benzene and butadiene, but the study population was ill-defined[9].

In a case-referent study, designed to investigate a possible connection between background radiation and acute myeloid leukaemia, three cases out of 59 (rate ratio, 18.9; 95% confidence interval, 1.9-357) and one referent out of 354 reported past exposure to styrene[10].

B. Evidence for carcinogenicity to animals (*limited*)

Styrene has been tested for carcinogenicity by oral administration to dams and to offspring of two strains of mice and of one strain of rats. In mice, it increased the incidence of lung tumours in male and female offspring of one strain after administration of a high dose. In rats, no statistically significant increase in tumour incidence was observed[9]. In experiments by oral administration to mice and rats, an increased incidence of lung tumours was observed only in male mice[11]. In an inadequately reported study in rats, exposure to styrene by inhalation or ingestion was associated with a small, nonstatistically significant increase in the incidence of brain tumours[12]. A further study in rats by oral administration using a small number of animals gave equivocal results[13].

There is *sufficient evidence* for the carcinogenicity in experimental animals of styrene oxide, a metabolite of styrene *in vivo*[14].

C. Other relevant data

Styrene is metabolized in humans and mammals to styrene oxide. In humans exposed to styrene, chromosomal aberrations and micronuclei were induced in peripheral lymphocytes; a slight increase in the incidence of sister chromatid exchanges was noted in one study, while no increase was reported in several others[15].

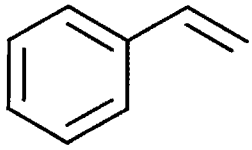
In animals treated *in vivo*, styrene induced micronuclei, sister chromatid exchanges and DNA strand breaks; however, conflicting results were obtained for chromosomal aberrations. Styrene bound covalently to DNA in mice *in vivo*. In human lymphocytes *in vitro*, styrene induced chromosomal aberrations, micronuclei and sister chromatid exchanges. In Chinese hamster cells *in vitro*, it induced chromosomal aberrations, sister chromatid exchanges (the latter only when epoxide hydratase was inhibited) and mutation, and, in rat hepatocytes, DNA strand breaks. It induced sex-linked recessive lethal mutations but not sex-chromosome loss or nondisjunction in *Drosophila*. Styrene induced mutation and mitotic recombination in yeast and chromosomal aberrations in plants. It was mutagenic to

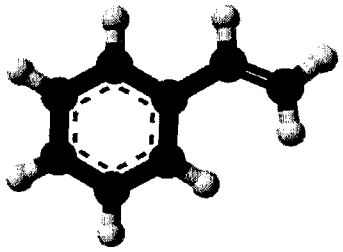
Styrene

From Wikipedia, the free encyclopedia

Styrene, also known as **ethenylbenzene, vinylbenzene**, and **phenylethene**, is an organic compound with the chemical formula $C_6H_5CH{=}CH_2$. This derivative of benzene is a colorless oily liquid that evaporates easily and has a sweet smell, although high concentrations have a less pleasant odor. Styrene is the precursor to polystyrene and several copolymers. Approximately 25 million tonnes (55 billion pounds) of styrene were produced in 2010.[4]

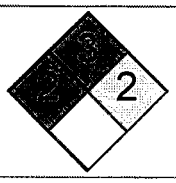
Styrene





Names	
Preferred IUPAC name	
Ethenylbenzene[1]	
Other names	
Styrene[1] Vinylbenzene Phenylethene Phenylethylene Cinnamene Styrol Diarex HF 77 Styrolene Styropol	
Identifiers	
CAS Number	100-42-5 (http://www.commonchemistry.org/ChemicalDetail.aspx?ref=100-42-5) ✓
ChEBI	CHEBI:27452 (https://www.ebi.ac.uk/chebi/searchId.do?chebiId=27452) ✓
ChEMBL	ChEMBL285235 (https://www.ebi.ac.uk/chembldb/index.php/compound/inspect/ChEMBL285235) ✓
ChemSpider	7220 (http://www.chemspider.com/Chemical-Structure.7220.html) ✓
ECHA InfoCard	100.002.592 (https://echa.europa.eu/substance-information/-/substanceinfo/100.002.592)
Jmol 3D model	Interactive image (http://chemapps.stolaf.edu/jmol/jmol.php?model=c1ccccc1C%3DC)
KEGG	C07083 (http://www.kegg.jp/entry/C07083) ✗
PubChem	7501 (https://pubchem.ncbi.nlm.nih.gov/compound/7501)
RTECS number	WL3675000
UNII	44LJ2U959V (http://fdasis.nlm.nih.gov/srs/srsdirect.jsp?regno=44LJ2U959V) ✓
InChI	
SMILES	
Properties	

Contents

Chemical formula	C_8H_8
Molar mass	104.15 g/mol
Appearance	colorless oily liquid
Odor	sweet, floral[2]
Density	0.909 g/cm^3
Melting point	−30 °C (−22 °F; 243 K)
Boiling point	145 °C (293 °F; 418 K)
Solubility in water	0.03% (20°C)[2]
Vapor pressure	5 mmHg (20°C)[2]
Refractive index (n_D)	1.5469
Viscosity	0.762 cP at 20 °C
Structure	
Dipole moment	0.13 D
Hazards	
Main hazards	flammable, toxic
Safety data sheet	MSDS (http://www.sciencelab.com/msds.php?msdsId=9925112)
R-phrases	R10 R36
S-phrases	S38 S20 S23
NFPA 704	
Flash point	31 °C (88 °F; 304 K)
Explosive limits	0.9%-6.8%[2]
Lethal dose or concentration (*LD*, *LC*):	
LC_{50} (median concentration)	2194 ppm (mouse, 4 hr) 5543 ppm (rat, 4 hr)[3]
LC_{Lo} (lowest published)	10,000 ppm (human, 30 min) 2771 ppm (rat, 4 hr)[3]
US health exposure limits (NIOSH):	
PEL (Permissible)	TWA 100 ppm C 200 ppm 600 ppm (5-minute maximum peak in any 3 hours)[2]
REL (Recommended)	TWA 50 ppm (215 mg/m^3) ST 100 ppm (425 mg/m^3)[2]
IDLH (Immediate danger)	700 ppm[2]
Related compounds	
Related styrenes; related aromatic compounds	Polystyrene, Stilbene; Ethylbenzene
Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa).	
✘ verify (what is ✓✘ ?)	
Infobox references	

Occurrence, history, and use

Natural occurrence

Styrene is named for styrax balsam, the resin of Liquidambar trees of the Altingiaceae plant family. Styrene occurs naturally in small quantities in some plants and foods (cinnamon, coffee beans, and peanuts), and is also found in coal tar.

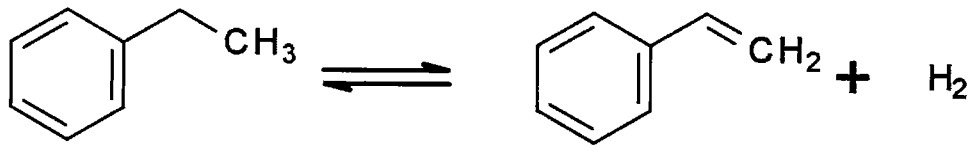
History

In 1839, the German apothecary Eduard Simon isolated a volatile oil from the resin (called "storax" or *styrax* (Latin)) of the American sweetgum tree (*Liquidambar styraciflua*). He called the oil "Styrol" (now: "styrene").[5][6] He also noticed that when Styrol was exposed to air, light, or heat, it gradually transformed into a hard, rubber-like substance, which he called "Styroloxyd" (styrol oxide, now: "polystyrene").[7] By 1845, the German chemist August Hofmann and his student John Blyth (1814–1871) had determined Styrol's empirical formula: C_8H_8.[8] They had also determined that Simon's "Styroloxyd" — which they renamed "Metastyrol" — had the same empirical formula as Styrol.[9] Furthermore, they could obtain Styrol by dry distilling Metastyrol.[10] In 1865, the German chemist Emil Erlenmeyer found that Styrol could form a dimer,[11] and in 1866 the French chemist Marcelin Berthelot stated that Metastyrol was a polymer of Styrol.[12] Meanwhile, other chemists had been investigating another component of storax, namely, cinnamic acid. They had found that cinnamic acid could be decarboxylated to form *cinnamène* (or *cinnamol*), which appeared to be Styrol. In 1845, French chemist Emil Kopp suggested that the two compounds were identical,[13] and in 1866, Erlenmeyer suggested that both cinnamol and Styrol might be vinyl benzene.[14] However, the Styrol that was

obtained from cinnamic acid seemed different from the Styrol that was obtained by distilling storax resin: the latter was optically active.[15] Eventually, in 1876, the Dutch chemist van 't Hoff resolved the ambiguity: the optical activity of the Styrol that was obtained by distilling storax resin was due to a contaminant.[16]

Industrial production from ethylbenzene

The modern method for production of styrene by dehydrogenation of ethylbenzene was first achieved in the 1930s.[17] The production of styrene increased dramatically during the 1940s, when it was popularized as a feedstock for synthetic rubber. Because it is produced on such a large scale, ethylbenzene in turn prepared on a prodigious scale (by alkylation of benzene with ethylene).[17] Ethylbenzene is mixed in the gas phase with 10–15 times its volume in high-temperature steam, and passed over a solid catalyst bed. Most ethylbenzene dehydrogenation catalysts are based on iron(III) oxide, promoted by several percent potassium oxide or potassium carbonate.



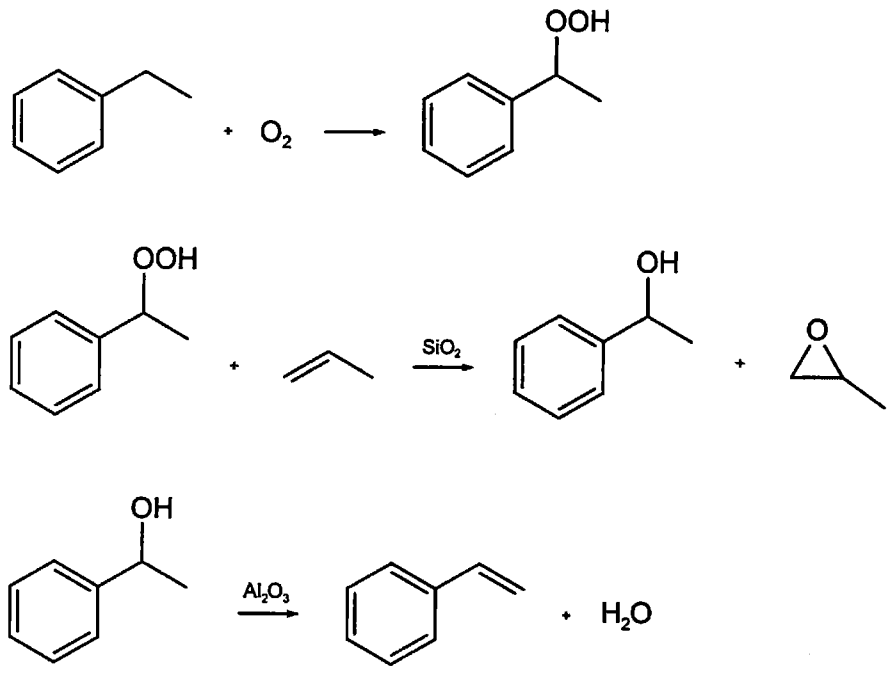
Steam serves several roles in this reaction. It is the source of heat for powering the endothermic reaction, and it removes coke that tends to form on the iron oxide catalyst through the water gas shift reaction. The potassium promoter enhances this decoking reaction. The steam also dilutes the reactant and products, shifting the position of chemical equilibrium towards products. A typical styrene plant consists of two or three reactors in series, which operate under vacuum to enhance the conversion and selectivity. Typical per-pass conversions are ca. 65% for two reactors and 70-75% for three reactors. Selectivity to styrene is 93-97%. The main byproducts are benzene and toluene. Because styrene and ethylbenzene have similar boiling points (145 and 136 °C, respectively), their separation requires tall distillation towers and high return/reflux ratios. At its distillation temperatures, styrene tends to polymerize. To minimize this problem, early styrene plants added elemental sulfur to inhibit the polymerization. During the 1970s, new free radical inhibitors consisting of nitrated phenol-based retarders were developed. More recently, a number of additives have been developed that exhibit superior inhibition against polymerization. However, the nitrated phenols are still widely used because of their relatively low cost. These reagents are added prior to the distillation.

Improving conversion and so reducing the amount of ethylbenzene that must be separated is the chief impetus for researching alternative routes to styrene. Other than the POSM process, none of these routes like obtaining styrene from butadiene have been commercially demonstrated.

Other industrial routes

From ethylbenzene hydroperoxide

Styrene is also co-produced commercially in a process known as POSM (Lyondell Chemical Company) or SM/PO (Shell) for styrene monomer / propylene oxide. In this process ethylbenzene is treated with oxygen to form the ethylbenzene hydroperoxide. This hydroperoxide is then used to oxidize propylene to propylene oxide. The resulting 1-phenylethanol is dehydrated to give styrene:



From toluene and methanol

Styrene can be produced from toluene and methanol, which are cheaper raw materials than those in the conventional process. This process has suffered from low selectivity associated with the competing decomposition of methanol.[18] Exelus Inc. claims to have developed this process with commercially viable selectivities, at 400-425 °C and atmospheric pressure, by forcing these components through a proprietary zeolitic catalyst. It is reported[19] that an approximately 9:1 mixture of styrene and ethylbenzene is obtained, with a total styrene yield of over 60%.[20]

From benzene and ethane

Another route to styrene involves the reaction of benzene and ethane. This process is being developed by Snamprogetti S.p.A. and Dow. Ethane, along with ethylbenzene, is fed to a dehydrogenation reactor with a catalyst capable of simultaneously producing styrene and ethylene. The dehydrogenation effluent is cooled and separated and the ethylene stream is recycled to the alkylation unit. The process attempts to overcome previous shortcomings in earlier attempts to develop production of styrene from ethane and benzene, such as inefficient recovery of aromatics, production of high levels of heavies and tars, and inefficient separation of hydrogen and ethane. Development of the process is ongoing.[21]

Laboratory synthesis

A laboratory synthesis of styrene entails the decarboxylation of cinnamic acid:[22]

$$C_6H_5CH{=}CHCO_2H \rightarrow :C_6H_5CH{=}CH_2 + CO_2$$

Styrene was first prepared by this method.[23]

Polymerization

The presence of the vinyl group allows styrene to polymerize. Commercially significant products include polystyrene, ABS, styrene-butadiene (SBR) rubber, styrene-butadiene latex, SIS (styrene-isoprene-styrene), S-EB-S (styrene-ethylene/butylene-styrene), styrene-divinylbenzene (S-DVB), styrene-acrylonitrile resin (SAN), and unsaturated polyesters used in resins and thermosetting compounds. These materials are used in rubber, plastic, insulation, fiberglass, pipes, automobile and boat parts, food containers, and carpet backing.

Health effects

Styrene is regarded as a "hazardous chemical", especially in case of eye contact, but also in case of skin contact, of ingestion and of inhalation, according to several sources.[17][24][25][26] Styrene is largely metabolized into styrene oxide in humans, resulting from oxidation by cytochrome P450. Styrene oxide is considered toxic, mutagenic, and possibly carcinogenic. Styrene oxide is subsequently hydrolyzed *in vivo* to styrene glycol by the enzyme epoxide hydrolase.[27] The U.S. Environmental Protection Agency (EPA) has described styrene to be "a suspected toxin to the gastrointestinal tract, kidney, and respiratory system, among others".[28][29] On 10 June 2011, the U.S. National Toxicology Program has described styrene as "reasonably anticipated to be a human carcinogen".[30][31] However, a STATS author describes[32] a review that was done on scientific literature and concluded that "The available epidemiologic evidence does not support a causal relationship between styrene exposure and any type of human cancer".[33] Despite this claim, work has been done by Danish researchers to investigate the relationship between occupational exposure to styrene and cancer. They concluded, "The findings have to be interpreted with caution, due to the company based exposure assessment, but the possible association between exposures in the reinforced plastics industry, mainly styrene, and degenerative disorders of the nervous system and pancreatic cancer, deserves attention".[34] The Danish EPA recently concluded that the styrene data do not support a cancer concern for styrene.[35]

Various regulatory bodies refer to styrene, in various contexts, as a possible or potential human carcinogen. The International Agency for Research on Cancer considers styrene to be "possibly carcinogenic to humans".[36] Chronic exposure to styrene leads to tiredness/lethargy, memory deficits, headaches and vertigo.[37]

The U.S. EPA does not have a cancer classification for styrene,[38] but is has been the subject of their Integrated Risk Information System (IRIS) program.[39] The U.S. National Toxicology Program of the U.S. Department of Health and Human Services has determined that styrene is "reasonably anticipated to be a human carcinogen". [40]

References

1. *Nomenclature of Organic Chemistry : IUPAC Recommendations and Preferred Names 2013 (Blue Book)*. Cambridge: The Royal Society of Chemistry. 2014. pp. 4, 55, 379. doi:10.1039/9781849733069-FP001. ISBN 978-0-85404-182-4.
2. "NIOSH Pocket Guide to Chemical Hazards #0571". National Institute for Occupational Safety and Health (NIOSH).
3. "Styrene". *Immediately Dangerous to Life and Health*. National Institute for Occupational Safety and Health (NIOSH).
4. New Process for Producing Styrene Cuts Costs, Saves Energy, and Reduces Greenhouse Gas Emissions (http://www1.eere.energy.gov/office_eere/pdfs/exelus_case_study.pdf), U.S. Department of Energy.
5. Simon, E. (1839) "Ueber den flüssigen Storax (Styrax liquidus)" (https://babel.hathitrust.org/cgi/pt?id=uva.x002457910;view=1up;seq=277) (On liquid storax (Styrax liquidus), *Annalen der Chemie*, **31** : 265–277. From p. 268: *"Das flüchtige Oel, für welches ich den Namen* Styrol *vorschlage, ... "* (The volatile oil, for which I suggest the name "styrol", ...)
6. For further details of the history of styrene, see: F. W. Semmler, *Die ätherischen Öle nach ihren chemischen Bestandteilen unter Berücksichtigung der geschichtlichen Entwicklung* [The volitile oils according to their chemical components with regard to historical development], vol. 4 (Leipzig, Germany, Veit & Co., 1907), § 327. Styrol, pp. 24-28. (https://books.google.com/books?id=nA9aAAAAYAAJ&pg=PA24#v=onepage&q&f=false)
7. (Simon, 1839), p. 268. From p. 268: *"Für den festen Rückstand würde der Name Styroloxyd passen."* (For the solid residue, the name "styrol oxide" would fit.)
8. Blyth, John and Hofmann, Aug. Wilh. (1845) "Ueber das Styrol und einige seiner Zersetzungsproducte" (https://books.google.com/books?id=A8MwAAAAYAAJ&pg=PA289#v=onepage&q&f=false) (On styrol and some of its decomposition products), *Annalen der Chemie und Pharmacie*, **53** (3) : 289-329 ; see p. 297. Note that Blyth and Hofmann state the empirical formula of Styrol as $C_{16}H_8$ because at that time, chemists used the wrong atomic mass for carbon (6 instead of 12).
9. (Blyth and Hofmann, 1845), p. 312. From p. 312: *"Analyse sowohl als Synthese haben in gleicher Weise dargethan, dass Styrol und die feste glasartige Materie, für welche wir den Namen* Metastyrol *vorschlagen, dieselbe procentische Zusammensetzung besitzen."* (Analysis as well as synthesis have equally demonstrated, that styrol and the solid, glassy material, for which we suggest the name "metastyrol", possess the same percentage composition.)
10. (Blyth & Hofmann, 1845), p. 315.
11. Erlenmeyer, Emil (1865) "Ueber Distyrol, ein neues Polymere des Styrols" (https://babel.hathitrust.org/cgi/pt?id=uva.x002457969;view=1up;seq=134) (On distyrol, a new polymer of styrol), *Annalen der Chemie*, **135** : 122–123.
12. Berthelot, M. (1866) "Sur les caractères de la benzine et du styrolène, comparés avec ceux des autres carbures d'hydrogène" (https://archive.org/stream/bulletin27frangoog#page/n295/mode/2up) (On the characters of benzene and styrene, compared with those of other hydrocarbons), *Bulletin de la Société Chimique de Paris*, 2nd series, **6** : 289–298. From p. 294: *"On sait que le styrolène chauffé en vase scellé à 200°, pendant quelques heures, se change en un polymère résineux (métastyrol), et que ce polymère, distillé brusquement, reproduit le styrolène."* (One knows that styrene [when] heated in a sealed vessel at 200°C, for several hours, is changed into a resinous polymer (polystyrene), and that this polymer, [when] distilled abruptly, reproduces styrene.)
13. Kopp, E. (1845), "Recherches sur l'acide cinnamique et sur le cinnamène" (http://gallica.bnf.fr/ark:/12148/bpt6k6449135m/f38.item.zoom) (Investigations of cinnamic acid and cinnamen), *Comptes rendus*, **21** : 1376-1380. From p. 1380: *"Je pense qu'il faudra désormais remplacer le mot de styrol par celui de cinnamène, et le métastyrol par le métacinnamène."* (I think that henceforth one will have to replace the word "styrol" with that of "cinnamène", and "metastyrol" with "metacinnamène".)
14. Erlenmeyer, Emil (1866) "Studien über die s.g. aromatischen Säuren" (https://babel.hathitrust.org/cgi/pt?id=uva.x002457970;view=1up;seq=339) (Studies of the so-called aromatic acids), *Annalen der Chemie*, **137** : 327–359 ; see p. 353. (https://babel.hathitrust.org/cgi/pt?id=uva.x002457970;view=1up;seq=365)

15. Berthelot, Marcellin (1867) "Sur les états isomériques du styrolène" (On the isomeric states of styrene), *Annales de Chimie et de Physique*, 4th series, **12** : 159–161. From p. 160: *"1° Le carbure des cinnamates est privé de pouvoir rotatoire, tandis que le carbure du styrax dévie de 3 degrés la teinte de passage (l = 100 mm)."* (1. The carbon [atom] of cinnamates is bereft of rotary power [i.e., the ability to rotate polarized light], whereas the carbon of styrax deflects by 3 degrees the neutral tint [i.e., the relative orientation of the polarized quartz plates at which the light through the polarimeter appears colorless] (length = 100 mm). [For further details about 19th century polarimeters, see: William Spottiswode, *Polarisation of Light*, 4th ed. (London, England: Macmillan and Co., 1883), pp. 51-52. (https://archive.org/stream/polarisationofli00spotrich#page/52/mode/2up/))
16. van 't Hoff, J. H. (1876) "Die Identität von Styrol und Cinnamol, ein neuer Körper aus Styrax" (https://babel.hathitrust.org/cgi/pt?id=uiug.30112025695146;view=1up;seq=13) (The identity of styrol and cinnamol, a new substance from styrax), *Berichte der deutschen chemischen Gesellschaft*, **9** : 5-6.
17. Denis H. James; William M. Castor (2007), "Styrene", *Ullmann's Encyclopedia of Industrial Chemistry* (7th ed.), Wiley, p. 1, doi:10.1002/14356007.a25_329.pub2
18. Yashima, Tatsuaki; Sato, Keiichi; Hayasaka, Tomoki; Hara, Nobuyoshi (1972). "Alkylation on synthetic zeolites: III. Alkylation of toluene with methanol and formaldehyde on alkali cation exchanged zeolites". *Journal of Catalysis*. **26**: 303–312. doi:10.1016/0021-9517(72)90088-7.
19. Peter Taffe, ICIS.com, 21 Jan 2008 (based on an paper given at The 6th European.Aromatics & Derivatives Conference – Antwerp, Belgium - 14-15 November, 2007.) (http://www.icis.com/Articles/2008/01/21/9093889/new-process-may-rescue-styrenics-industry.html)
20. Stephen K. Ritter, Chemical & Engineering News, 19 March 2007, p.46.
21. Styrene/Ethylbenzene 07/08-4 Report, ChemSystems, March 2009, p.64-73. (http://www.chemsystems.com/reports/search/docs/toc/0708_4_toc.pdf)
22. Abbott, T. W.; Johnson, J. R. (1941). "Phenylethylene (Styrene)". *Org. Synth.* ; *Coll. Vol.*, **1**, p. 440
23. R. Fittig und F. Binder "Ueber die Additionsproducte der Zimmtssaure" in "Untersuchungen über die ungesättigten Säuren. I. Weitere Beiträge zur Kenntnifs der Fumarsäure und Maleïnsäure" Rudolph Fittig, Camille Petri, Justus Liebigs *Annalen der Chemie* 1879, volume 195, p 56-179. doi:10.1002/jlac.18791950103 (https://dx.doi.org/10.1002%2Fjlac.18791950103)
24. MSDS (1 November 2010). "Material Safety Data Sheet Styrene (monomer) MSDS". MSDS. Retrieved 2011-06-11.
25. US EPA (December 1994). "OPPT Chemical Fact Sheets (Styrene) Fact Sheet: Support Document (CAS No. 100-42-5)" (PDF). US EPA. Retrieved 2011-06-11.
26. http://www.atsdr.cdc.gov/tfacts53.pdf
27. Kenneth C. Liebman (1975). "Metabolism and toxicity of styrene" (PDF). *Environmental Health Perspectives*. **11**: 115–119. doi:10.2307/3428333. JSTOR 3428333.
28. "EPA settles case against Phoenix company for toxic chemical reporting violations". U.S. Environmental Protection Agency. Retrieved 2008-02-11.
29. "EPA Fines California Hot Tub Manufacturer for Toxic Chemical Release Reporting Violations". U.S. Environmental Protection Agency. Retrieved 2008-02-11.
30. Harris, Gardiner (10 June 2011). "Government Says 2 Common Materials Pose Risk of Cancer". New York Times. Retrieved 2011-06-11.
31. National Toxicology Program (10 June 2011). "12th Report on Carcinogens". National Toxicology Program. Retrieved 2011-06-11.
32. http://stats.org/stories/2011/styrene_crosshairs_sept14_11.html
33. Boffetta, P., et al., Epidemiologic Studies of Styrene and Cancer: A Review of the Literature (http://journals.lww.com/joem/Abstract/2009/11000/Epidemiologic_Studies_of_Styrene_and_Cancer__A.5.aspx), *J. Occupational and Environmental Medicine*, Nov.2009, V.51, N.11.
34. Kolstad, HA; Juel K; Olsen J; Lynge E. (May 1995). "Exposure to styrene and chronic health effects: mortality and incidence of solid cancers in the Danish reinforced plastics industry.". *Occupational and Environmental Medicine*. **52** (5): 5. doi:10.1136/oem.52.5.320. PMC 1128224. PMID 7795754.
35. Danish EPA 2011 review http://www.compositesworld.com/cdn/cms/uploadedFiles/danish_epa_styrene_review(2).pdf
36. Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 82 (2002), Some Traditional Herbal Medicines, Some Mycotoxins, Naphthalene and Styrene, pp. 436 - 550. (http://apps.who.int/bookorders/anglais/detart1.jsp?sesslan=1&codlan=1&codcol=72&codcch=82)
37. http://www.epa.gov/ttnatw01/hlthef/styrene.html
38. [1] (http://www.epa.gov/iris/subst/0104.htm) US environmental protection agency. Section I.B.4 relates to neurotoxicology.
39. EPA IRIS track styrene page (http://cfpub.epa.gov/ncea/iristrac/index.cfm?fuseaction=viewChemical.showChemical&sw_id=1051)
40. Styrene entry in National Toxicology Program's Thirteenth Report on Carcinogens (http://ntp.niehs.nih.gov/ntp/roc/content/profiles/styrene.pdf)

External links

- CDC - Styrene - NIOSH Workplace Safety and Health Topic (http://www.cdc.gov/niosh/topics/styrene/)
- Safety and Health Topics | Styrene (OSHA) (http://www.osha.gov/SLTC/styrene/index.html)

expected number was 0.52. There was also a statistically significant excess of deaths from stomach cancer (5 observed, 0.6 expected; in addition, a sixth incident case was reported). These excesses were confined to the workers exposed all day[1,2]. It should be noted that these workers had been exposed to a mixture of chemical compounds, including dichloromethane (see p. 194), ethylene chlorohydrin and small amounts of bis(2-chloroethyl)ether[1].

A third Swedish cohort consisted of 355 workers exposed at a plant producing ethylene oxide through oxygenation of ethylene. Of these, 128 workers had had almost pure exposure to ethylene oxide. Eight deaths occurred compared with 11.6 expected. There was one case of myelogenous leukaemia (0.16 expected) and one of lung cancer among men with mixed exposure[2].

The total number of leukaemias observed in the three Swedish studies was thus eight, with 0.83 expected. Stomach cancer occurred in excess in one plant only (six cases in a group of 89 workers)[2].

In a cohort study of 767 ethylene oxide production workers in the USA, no case of leukaemia was found. However, there was only low potential exposure to ethylene oxide among the workforce and an unusually large deficit in total deaths compared to the number expected, indicating diluting errors in the design of the study[1].

A cohort study of 602 factory workers in the Federal Republic of Germany exposed to ethylene oxide, propylene oxide (see p. 328), benzene (see p. 120) and ethylene chlorohydrin showed a deficit of all deaths compared with four different expected figures. There were 14 deaths due to cancer (16.6 expected from national statistics), one of which was a myeloid leukaemia (0.15 expected) and four of which were stomach cancers (2.7 expected). The expected numbers used were not calendar period-specific over the whole observation period, however, and it is not clear whether they were computed on the basis of the 92% of identified workers or the full cohort[1].

In the light of these data, a causal relationship between exposure to ethylene oxide and leukaemia is possible, but the five small epidemiological studies so far available suffer from various disadvantages, especially confounding exposures, which make their interpretation difficult.

B. Evidence for carcinogenicity to animals (*sufficient*)

Ethylene oxide was tested by intragastric intubation in rats and produced local tumours, mainly squamous-cell carcinomas, of the forestomach. When rats were fed diets fumigated with ethylene oxide, no increased incidence of tumours was observed[1]. In two experiments in which rats of one strain were exposed by inhalation, ethylene oxide increased the incidences of mononuclear-cell leukaemia, brain tumours and proliferative lesions of the adrenal cortex in animals of each sex and of peritoneal mesotheliomas in males[1,3,4]. In mice, inhalation of ethylene oxide resulted in increased incidences of alveolar/bronchiolar lung tumours and tumours of the Harderian gland in animals of each sex and of uterine adenocarcinomas, mammary carcinomas and malignant lymphomas in females[5]. Ethylene oxide was also tested by subcutaneous injection in mice, producing local tumours, which were mainly fibrosarcomas[1].

Ethylene oxide

From Wikipedia, the free encyclopedia

Ethylene oxide, properly called **oxirane** by IUPAC, is the organic compound with the formula C_2H_4O. It is a cyclic ether. (A cyclic ether consists of an alkane with an oxygen atom bonded to two carbon atoms of the alkane, forming a ring.) Ethylene oxide is a colorless flammable gas at room temperature, with a faintly sweet odor; it is the simplest epoxide: a three-membered ring consisting of one oxygen atom and two carbon atoms. Because of its special molecular structure, ethylene oxide easily participates in addition reactions; e.g., opening its ring and thus easily polymerizing. Ethylene oxide is isomeric with acetaldehyde and with vinyl alcohol.

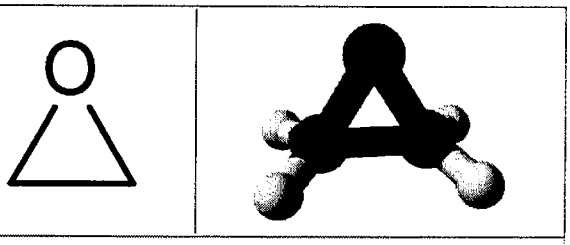
Although it is a vital raw material with diverse applications, including the manufacture of products like polysorbate 20 and polyethylene glycol (PEG) that are often more effective and less toxic than alternative materials, ethylene oxide itself is a very hazardous substance. At room temperature it is a flammable, carcinogenic, mutagenic, irritating, and anaesthetic gas, with a misleadingly pleasant aroma.

The chemical reactivity that is responsible for many of ethylene oxide's hazards has also made it a key industrial chemical. Although too dangerous for direct household use and generally unfamiliar to consumers, ethylene oxide is used industrially for making many consumer products as well as non-consumer chemicals and intermediates. Ethylene oxide is important or critical to the production of detergents, thickeners, solvents, plastics, and various organic chemicals such as ethylene glycol, ethanolamines, simple and complex glycols, polyglycol ethers and other compounds. As a poison gas that leaves no residue on items it contacts, pure ethylene oxide is a disinfectant that is widely used in hospitals and the medical equipment industry to replace steam in the sterilization of heat-sensitive tools and equipment, such as disposable plastic syringes.[4]

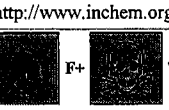
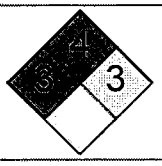
Ethylene oxide is industrially produced by direct oxidation of ethylene in the presence of silver catalyst. It is extremely flammable and explosive and is used as a main component of thermobaric weapons;[5][6] therefore, it is commonly handled and shipped as a refrigerated liquid.[7]

Contents

Ethylene oxide



Names	
IUPAC name	oxirane [1]
Other names	epoxyethane, ethylene oxide, dimethylene oxide, oxacyclopropane, 1,2-Epoxy ethane
Identifiers	
CAS Number	75-21-8 (http://www.commonchemistry.org/ChemicalDetail.aspx?ref=75-21-8) ✓
Abbreviations	EO, EtO
ChEBI	CHEBI:27561 (https://www.ebi.ac.uk/chebi/searchId.do?chebiId=27561) ✓
ChemSpider	6114 (http://www.chemspider.com/Chemical-Structure.6114.html) ✓
ECHA InfoCard	100.000.773 (https://echa.europa.eu/substance-information/-/substanceinfo/100.000.773)
EC Number	200-849-9
Jmol 3D model	Interactive image (http://chemapps.stolaf.edu/jmol/jmol.php?model=C1CO1)
KEGG	D03474 (http://www.kegg.jp/entry/D03474) ✓
MeSH	Ethylene+Oxide (https://www.nlm.nih.gov/cgi/mesh/2014/MB_cgi?mode=&term=Ethylene+Oxide)
PubChem	6354 (https://pubchem.ncbi.nlm.nih.gov/compound/6354)
RTECS number	KX2450000
UNII	JJH7GNN18P (http://fdasis.nlm.nih.gov/srs/srsdirect.jsp?regno=JJH7GNN18P) ✓
InChI	
SMILES	
Properties	
Chemical formula	C_2H_4O
Molar mass	44.05 g mol^{-1}
Appearance	colorless gas
Odor	ether-like
Density	0.882 g/mL, 7.360 lbs/gallon
Melting point	−111.3 °C (−168.3 °F; 161.8 K)
Boiling point	10.7 °C (51.3 °F; 283.8 K)
Solubility in water	miscible
Vapor pressure	1.46 atm (20°C)[2]
Thermochemistry	
	243 J mol^{-1} K^{-1}

Std molar entropy (S°_{298})	
Std enthalpy of formation ($\Delta_f H^\circ_{298}$)	−52.6 kJ mol^{-1}
Hazards	
Main hazards	carcinogen extremely flammable
Safety data sheet	ICSC 0155 (http://www.inchem.org/documents/icsc/icsc/eics0155.htm)
EU classification (DSD)	 F+ T Carc. Cat. 1
R-phrases	R45, R46, R12, R23, R36/37/38
S-phrases	S53, S45
NFPA 704	
Flash point	−20 °C (−4 °F; 253 K)
Autoignition temperature	429 °C (804 °F; 702 K)
Explosive limits	3 to 100%
Lethal dose or concentration (*LD*, *LC*):	
LC_{50} (median concentration)	836 ppm (mouse, 4 hr) 4000 ppm (rat, 4 hr) 800 ppm (rat, 4 hr) 819 ppm (guinea pig, 4 hr) 1460 ppm (rat, 4 hr) 835 ppm (mouse, 4 hr) 960 ppm (dog, 4 hr)[3]
US health exposure limits (NIOSH):	
PEL (Permissible)	TWA 1 ppm 5 ppm [15-minute Excursion][2]
REL (Recommended)	Ca TWA <0.1 ppm (0.18 mg/m^3) C 5 ppm (9 mg/m^3) [10-min/day][2]
IDLH (Immediate danger)	Ca [800 ppm][2]
Related compounds	
Related heterocycles	Aziridine, Thiirane, Borirane
Except where otherwise noted, data are given for materials in their standard state (at 25 °C [77 °F], 100 kPa).	
✓ verify (what is ✓✗ ?)	
Infobox references	

History

Ethylene oxide was first reported in 1859 by the French chemist Charles-Adolphe Wurtz,[8] who prepared it by treating 2-chloroethanol with potassium hydroxide:

$$Cl–CH_2CH_2–OH + KOH \rightarrow (CH_2CH_2)O + KCl + H_2O$$

Wurtz measured the boiling point of ethylene oxide as 13.5 °C, slightly higher than the present value, and discovered the ability of ethylene oxide to react with acids and salts of metals.[9] Wurtz mistakenly assumed that ethylene oxide has the properties of an organic base. This misconception persisted until 1896 when Georg Bredig found that ethylene oxide is not an electrolyte.[9][10] That it differed from other ethers — particularly by its propensity to engage in addition reactions, which are typical of unsaturated compounds — had long been a matter of debate. The heterocyclic triangular structure of ethylene oxide was proposed by 1868 or earlier.[11]

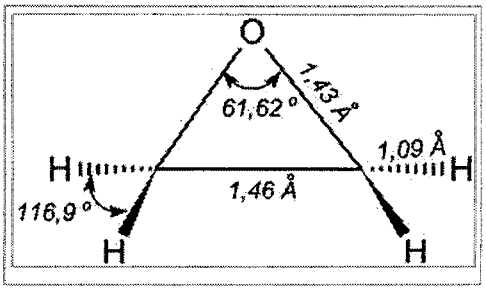
Wurtz's 1859 synthesis long remained the only method of preparing ethylene oxide, despite numerous attempts, including by Wurtz himself, to produce ethylene oxide directly from ethylene.[12] Only in 1931 did French chemist Theodore Lefort develop a method of direct oxidation of ethylene in the presence of silver catalyst.[13] Since 1940, almost all industrial production of ethylene oxide has relied on this process.[14] Sterilization by ethylene oxide for the preservation of spices was patented in 1938 by the American chemist Lloyd Hall. Ethylene oxide achieved industrial importance during World War I as a precursor to both the coolant ethylene glycol and the chemical weapon mustard gas.

Molecular structure and properties

The epoxy cycle of ethylene oxide is an almost regular triangle with bond angles of about 60° and a significant angular strain corresponding to the energy of 105 kJ/mol.[15][16] For comparison, in alcohols the C–O–H angle is about 110°; in ethers, the C–O–C angle is 120°. The moment of inertia about the principal axes are $I_A = 32.921\times10^{-40}$ g·cm², $I_B = 37.926\times10^{-40}$ g·cm² and $I_C = 59.510\times10^{-40}$ g·cm².[17] The dipole moment at a temperature in the range 17 −176 °C is 6.26×10^{-30} C·m.[18]

The relative instability of the carbon-oxygen bonds in the molecule is revealed by the comparison in the table of the energy required to break two C–O bonds in the ethylene oxide or one C–O bond in ethanol and dimethyl ether:[19]

Reaction	$\Delta H°_{298}$, kJ/mol	Method
$(C_2H_4)O \rightarrow C_2H_4 + O$ (cleavage of two bonds)	354.38	Calculated, from atomic enthalpies
$C_2H_5OH \rightarrow C_2H_5 + OH$ (breaking one bond)	405.85	Electron impact
$CH_3OCH_3 \rightarrow CH_3O + CH_3$ (breaking one bond)	334.72	Calculated using enthalpies of radicals formation



This instability determines the chemical activity of ethylene oxide and explains the ease of opening its cycle in addition reactions (see Chemical properties).

Physical properties

Ethylene oxide is a colorless gas at 25 °C and is a mobile liquid at 0 °C – viscosity of liquid ethylene oxide at 0 °C is about 5.5 times lower than that of water. The gas has a characteristic sweet odor of ether, noticeable when its concentration in air exceeds 500 ppm.[20] Ethylene oxide is readily soluble in water, ethanol, diethyl ether and many organic solvents.[21]

Main thermodynamical constants are:[22]

- Standard molar heat capacity, $C_p° = 48.19$ J/(mol·K);
- Standard enthalpy of formation, $\Delta H°_{298} = -51.037$ kJ/mol;
- Standard entropy, $S°_{298} = 243.4$ J/(mol·K);
- Gibbs free energy, $\Delta G°_{298} = -11.68$ kJ/mol;
- Heat of combustion, $\Delta H_c° = -1306$ kJ/mol.[23]

The surface tension of liquid ethylene oxide, at the interface with its own vapor, is 35.8 mJ/m^2 at −50.1 °C and 27.6 mJ/m^2 at −0.1 °C.[24]

The boiling point increases with the vapor pressure as follows:[25] 57.7 (2 atm), 83.6 (5 atm) and 114.0 (10 atm).

Viscosity decreases with temperature with the values of 0.577 kPa·s at −49.8 °C, 0.488 kPa·s at −38.2 °C, 0.394 kPa·s at −21.0 °C and 0.320 kPa·s at 0 °C.[26]

Between −91 °C and 10.5 °C, vapor pressure p (in mmHg) varies with temperature (T in °C) as $\lg p = 6.251 - 1115.1/(244.14 + T)$.[27]

Properties of liquid ethylene oxide[12]

Temperature, °C	Steam pressure, kPa	Enthalpy of the liquid, J/g	Enthalpy of vaporization, J/g	Density, kg/L	Heat capacity, J/(kg·K)	Thermal conductivity, W/(m·K)
−40 °C	8.35	0	628.6	0.9488	1878	0.20
−20 °C	25.73	38.8	605.4	0.9232	1912	0.18
0 °C	65.82	77.3	581.7	0.8969	1954	0.16
20 °C	145.8	115.3	557.3	0.8697	2008	0.15
40 °C	288.4	153.2	532.1	0.8413	2092	0.14
60 °C	521.2	191.8	505.7	0.8108	2247	0.14
80 °C	875.4	232.6	477.4	0.7794	2426	0.14
100 °C	1385.4	277.8	445.5	0.7443	2782	0.13
120 °C	2088	330.4	407.5	0.7052	3293	N/A*
140 °C	3020	393.5	359.4	0.6609	4225	N/A
160 °C	4224	469.2	297.1	0.608	N/A	N/A
180 °C	5741	551.2	222.5	0.533	N/A	N/A
195.8 °C	7191	N/A	N/A	N/A	N/A	N/A

*N/A – data not available.